



SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 12-022024- -00000-0000

Fecha: 2012-02-08 15:51:36
Tra. 11 PATENTEIYII
Act. 411 PRESENTACION

Dep. 2020 DIR.NUEVASCR
Eve: 378 FASENACIONALI
Folios: 245

Delegatura de Propiedad Industrial
División de Nuevas Creaciones

SOLICITUD DE

**PATENTE DE INVENCION
PCT ENTRADA EN FASE NACIONAL**

21. EXPEDIENTE No. _____

54. TITULO: HETEROCICLOS MICROBICIDAS

52. CLASIFICACION INTERNACIONAL: C07D 413/04, C07D 413/14, C07D
417/04, C07D 417/14, A01P 3/00,
A01N 43/78, A01N 43/76, A01N
43/836

71. SOLICITANTE: SYNGENTA PARTICIPATIONS AG

DOMICILIO: Schwarzwaldallee 215, CH-4058 Basilea –
SUIZA

74. APODERADO: Dra. MARGARITA CASTELLANOS A.

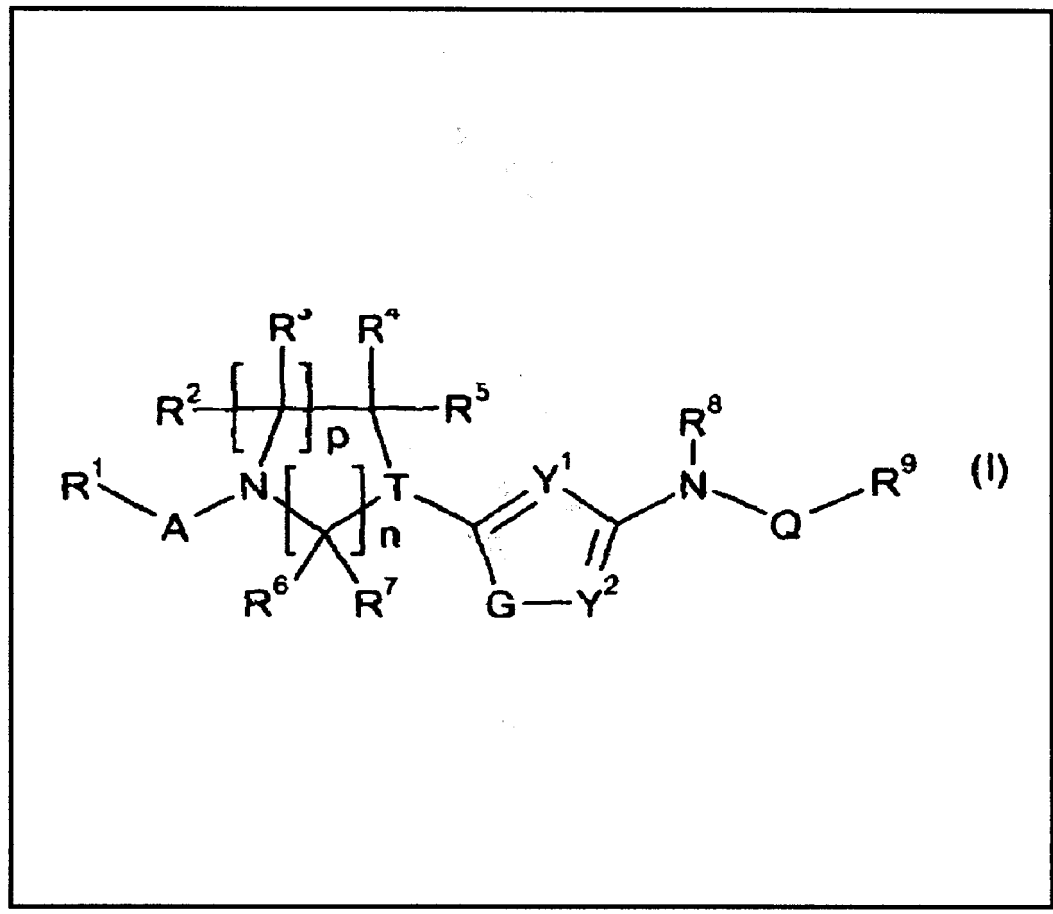
22. BOGOTA, D.C., _____

 Industria y Comercio SUPERINTENDENCIA		PETITORIO		SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO	
				No. 12-022024- -00000-0000	
		Fecha: 2012-02-08 15:51:36		Dep. 2020 DIR.NUEVASCR	
		Tra. 11 PATENTEIYII		Eve: 378 FASENACIONALI	
		Act. 411 PRESENTACION		Folios: 245	
FORMULARIO UNICO DE SOLICITUD DE PATENTES PCT ENTRADA EN FASE NACIONAL					
SOLICITUD DE:					
☒ Patente de Invención. ☐ Patente de Modelo de Utilidad.					
☒ Capítulo I ☐ Capítulo II					
② SOLICITANTE (71)		Nombre: SYNGENTA PARTICIPATIONS AG Dirección: Schwarzwaldallee 215, CH-4058 Basilea - SUIZA Nacionalidad o Domicilio: Basilea - SUIZA Lugar de Constitución: SUIZA Teléfono: Fax: E-mail:		IDENTIFICACIÓN C.C. ☐ NIT ☐ C.E. ☐ Otro ☐ Cual _____ Número _____	
③ REPRESENTANTE O APODERADO		Nombre: MARGARITA CASTELLANOS A. Dirección: CALLE 94A No. 7A-09 Teléfono: 756 0770 Fax: 755 0158 E-mail: info@castellanosyco.com		IDENTIFICACIÓN C.C. ☒ NIT ☐ C.E. ☐ Otro ☐ Cual _____ Número 39'779.654 TPA 70.819	
④ INVENTOR (ES) (72)		SARAH SULZER-MOSSE Syngenta Crop. Protection Münchwilen AG Schaffhauserstrasse CH-4332 Stein SUIZA MATHIAS STEPHAN RESPONDEK Syngenta Crop. Protection Münchwilen AG Schaffhauserstrasse CH-4332 Stein SUIZA		CLEMENS LAMBERTH Syngenta Crop. Protection Münchwilen AG Schaffhauserstrasse CH-4332 Stein SUIZA LAURA QUARANTA Syngenta Crop. Protection Münchwilen AG Schaffhauserstrasse CH-4332 Stein SUIZA	
⑤ PCT (86) Solicitud Internacional No. PCT/EP2010/061381 Fecha 05/08/2010 Publicación Internacional No. WO 2011/018401 A1 Fecha 17/02/2011					
⑥ Título (54) HETEROCICLOS MICROBICIDAS					
⑦ Clasificación Internacional (51) C07D 413/04, C07D 413/14, C07D 417/04, C07D 417/14, A01P 3/00, A01N 43/78, A01N 43/76, A01N 43/836					
⑧ Prioridad SI ☒ NO ☐		(33) País de Origen EP	(32) Fecha 12/08/2009	(31) Número de Solicitud 09167736,9	
⑨ Comprobante de pago No. 12-006299 y 12-006303 Fecha Enero 23 de 2012					
Instrucciones para el diligenciamiento del presente formulario, ver reverso de esta página.					

10 Anexos

- ☒ Comprobante de pago de la tasa de presentación de la solicitud.
- ☒ Documento que acredita la existencia y representación legal cuando el solicitante sea persona jurídica.
- ☒ Poderes, si fuere el caso, junto con la sustitución del mismo a mi favor
- ☒ Documento de cesión del inventor al solicitante o a su causante.
- ☐ Declaraciones.
- ☒ Copia de la solicitud internacional (Resumen, descripción, reivindicaciones, dibujos).
- ☒ Traducción de la solicitud internacional al castellano (Resumen, descripción, reivindicaciones, dibujos).
- ☐ Copia del examen preliminar internacional efectuado por la Autoridad Internacional de Examen Preliminar (IPEA).
- ☐ Traducción del examen preliminar internacional efectuado por la IPEA.
- ☐ De ser el caso, copia del contrato de acceso.
- ☐ De ser el caso, documento que acredite la licencia o autorización de uso de conocimientos tradicionales de las comunidades indígenas.
- ☐ De ser el caso, certificado de depósito del material biológico.
- ☒ Arte final 12x12
- ☐ De ser el caso, información sobre otras solicitudes de patente o títulos obtenidos en el extranjero por el mismo titular o su causante, relacionadas parcial o totalmente con la invención de esta solicitud.
- ☐ De ser el caso, modificaciones efectuadas a la solicitud internacional.
- ☒ Otros: Tarjeta Propietario, Extracto para la publicación

11 FIGURA CARACTERISTICA:



12 Solicito la concesión de la patente,

NOMBRE: MARGARITA CASTELLANOS ABONDANO
FIRMA: *Margarita Castellanos*
C.C. No. 89'779.654 Usaquén - TPA 70.819 C.S.J.

08 FEB. 2012

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO NIT : 800.176.089-2 - / -					
 Industria y Comercio SUPERINTENDENCIA	RECIBO DE CAJA			No. 12 - 006299	
				Bogotá D.C., Enero 23 de 2012 - 14:20:58	
RECIBIDO DE : CASTELLANOS Y Y CO				NI 800.174.641	
*** Soporte del Pago ***					
TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PAGO	VR. PAGO
CONSIGNACION	BANCO DE BOGOTA	062754387	457586791	20/01/2012	7.210.000.00
*** Conceptos Pagados ***					
CANT.	RENTISTICO	CONCEPTO	Vr. UNIDITARIO	Vr. CONCEPTO	
1	50005-01-01 SOLICITUDES	1 TRAMITES DE SOL. DE PATENTE DE INVENCIÓN	590.000.00	590.000.00	
				\$590.000.00	
=====					
SON: **QUINIENTOS NOVENTA MIL PESOS MONEDA CORRIENTE**					
Responsable: _____ *****			SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO		
Recibo de Caja Aplicado al Expediente No. _____					
			No. 12-022024- -00000-0000		
			Fecha: 2012-02-08 15:51:36 Dep. 2020 DIR.NUEVASCR		
			Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI		
			Act. 411 PRESENTACION Folios: 245		
Sede Centro: Carrera 13 No. 27 - 00 Pisos 3,4,5 y 10 Bogotá, D.C.- Colombia					
Web: www.sic.gov.co e-mai: info@sic.gov.co Conmutador: (571) 5870000 Fax: (571) 5870284 Linea: 018000-910165 Call Center: (571) 6513240					
Enero 23 de 2012 - 14:21:00					

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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
NIT : 800.176.089-2
- / -

 Industria y Comercio SUPERINTENDENCIA	RECIBO DE CAJA	No. 12 - 006303
		Bogotá D.C., Enero 23 de 2012 - 14:20:58

RECIBIDO DE : CASTELLANOS Y Y CO	NI 800.174.641
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*** Soporte del Pago ***					
TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PAGO	VR. PAGO
CONSIGNACION	BANCO DE BOGOTA	062754387	457586791	20/01/2012	7.210.000.00

*** Conceptos Pagados ***			
CANT. RENTISTICO	CONCEPTO	Vr. UNDITARIO	Vr. CONCEPTO
5 50005-01-01 SOLICITUDES	1607 REIVINDICACION UNITARIA ADICIONAL A LAS 10 INICIALES	30.000.00	150.000.00
			\$150.000.00
=====			

SON: **CIENTO CINCUENTA MIL PESOS MONEDA CORRIENTE***

Responsable: _____
Recibo de Caja Aplicado al Expediente No. _____

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 12-022024- -00000-0000

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COLOMBIA

PODER

El (los) Gregory W. Warren
 → SYNGENTA PARTICIPATIONS AG

Nombran por el presente a **XIMENA CASTELLANOS A. y/o MARGARITA CASTELLANOS A.** abogadas con oficinas en la Carrera 9 No. 93-09, Bogotá-Colombia para

y para obtener la protección de mi (nuestra) propiedad Industrial y con este fin autorizamos a dichos apoderados para que nos representen ante cualesquiera autoridades o personas de los órdenes administrativo, contencioso -administrativo y judicial en todo lo relacionado con los siguientes actos y gestiones:

a) Obtención de patentes de invención, modelos y dibujos industriales; registro de marcas de fabrica, de servicio, colectivas o defensivas y de denominaciones de origen, depósito de nombres y enseñas comerciales; su renovación, prórroga, inscripción de traspaso y cambio de nombre o domicilio, cancelación voluntaria y el registro de licencias de uso de esos derechos; b) Para la obtención de registros sanitarios; c) Acciones de oposición, observación, cancelación, nulidad, medidas cautelares y en general los juicios civiles, penales, administrativos o contencioso - administrativos que promovamos o se nos promuevan, pudiendo en todos los actos y gestiones arriba mencionados sustituir éste mandato, transigir, desistir, recibir, cancelar, renunciar, aceptar notificaciones y nombrar apoderados judiciales y extrajudiciales.

Dado y firmado hoy 24 de Marzo de 2004

en Research Triangle Park, Carolina
 del Norte 27709
 por Gregory W. Warren

(El notario debe suscribir el documento en la pagina siguiente)

(Se requiere legalización consular)

POWER OF ATTORNEY

I (we) the undersigned Gregory W. Warren
 Syngenta Participations AG

hereby grant(s) Power of Attorney to **XIMENA CASTELLANOS A. and for MARGARITA CASTELLANOS A.** attorneys residing at Carrera 9 No. 93-09, Bogota- Colombia, to prosecute

and to obtain the protection of my (our Industrial Property, for which purpose we authorize the said attorneys to represent us before any authorities, or persons, specially those, administrative, contentious and judicial, in all matters concerning the following:

a) Obtention of patents, models and designs, registration of trademarks, service, collective and defensive marks, and of designations of origin; the deposit of trade names and ensings; its renewal, extension, recordal of assignments, change of name or domicile, voluntary cancellation, and the registration of licenses of use of the above rights; b) For the obtention of Sanitary registrations; c) Actions of opposition, cancellation, nullity, infringement, granting of licenses; and in general the civil, criminal and administrative suits related to those rights; actions and suits instituted by us or against us; and that in all the above matters they may substitute this power of attorney, compromise, desist, cancel, receive, renounce, accept notifications and appoint attorneys in fact, in or out of court.

Given and signed this 24th March 2004

in Research Triangle Park, North Carolina 27709

by Gregory W. Warren

Gregory W. Warren

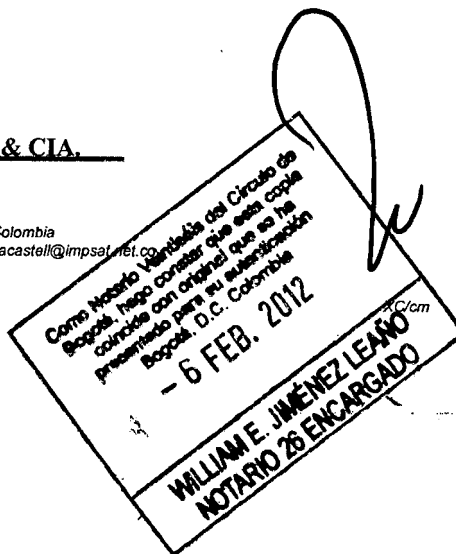
(Notary shall execute on the other side)

(Consular legalization required)

ALVARO CASTELLANOS M. & CIA.

ABOGADOS COLOMBIA

Carrera 9 No. 93-09- P.O.Box 6349 - Bogotá, Colombia
 Tels.: (571) 610 74 20 / 60 / 80 - Fax (571) 610 07 06 - e-mail acastell@impsat.net.co



COLOMBIA

CERTIFICADO NOTARIAL (Sociedad)

Hoy 24 de Marzo del año 2004
compareció(eron) personalmente Gregory W. Warren
a quienes conozco como la(s) personas que firma(n) en
representación de la Sociedad (Compañía denominada
Certifico: Syngenta Participations AG
a) Que es una sociedad/Compañía legalmente
constituida y existente de acuerdo con las leyes de
b) Que el domicilio de dicha Sociedad/Compañía es Basel, Suiza
c) Que el objeto u objetos para los cuales se otorga el
presente poder están comprendidos dentro del objeto
social de la mencionada Sociedad /Compañía.
d) Que el Sr. Gregory W. Warren
esta autorizado para otorgar el presente poder. Lo anterior
esta probado por medio de los siguientes documentos, que
certifico he visto*

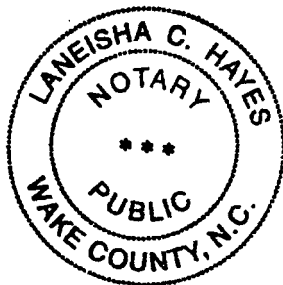
(Ciudad) REsearch Triangle Park

(Estado) Carolina del Norte 27709

Hoy del 24 de Marzo de 2004

(Notario Público) LANEISHA C. HAYES

*Los documentos debe identificarse con fecha y origen.



ALVARO CASTELLANOS M. & CIA.

ABOGADOS COLOMBIA

Carrera 9 No. 93-09 - P.O.Box 6349 - Bogotá, Colombia
Tels.: (571) 610 74 20 / 60 / 80 - Fax (571) 610 07 06 - e-mail acastell@impsat.net.co

NOTARIAL (Corporation)

On this 24th day of March of 2004 personally appeared
Gregory W. Warren whom I know to be the
person(s) who signed this document as representative(s)
of the Corporation /Company named Syngenta
Participations AG

I certify:

- a) That Syngenta Participations AG is a corporation
(Company legally constituted and in existence in
accordance with the laws of Basel, Switzerland
- b) That the domicile of said Corporation/Company is
Basel, Switzerland
- c) That the purpose or purposes for which the present
Power of Attorney is granted are comprised within the
object set forth in the charter of the mentioned
Corporation/Company.
- d) That Mr. Gregory W. Warren
is (are) authorized to grant the present Power of Attorney.
The aforementioned was duly proven through the following
documents and I duly certify having seen them*: on the
24th day of March, 2004 in Research Triangle Park, North
Carolina 27709.

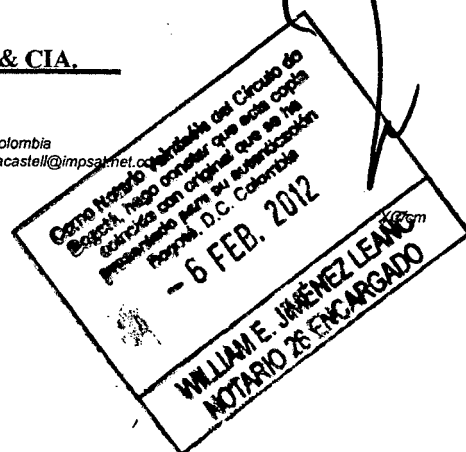
(City) Research Triangle Park

(State) North Carolina, 27709

this 24th day of March of the year 2004

(Notary Public)

Laneisha C. Hayes
*Documents must be identified with date and origin
3/24/04 - Research Triangle
Park, North Carolina
27709 -
Syngenta Biotech, Inc.



000007



Wake County Register of Deeds
Post Office Box 1897
Raleigh, North Carolina 27602-1897

Laura M. Riddick
Register Of Deeds

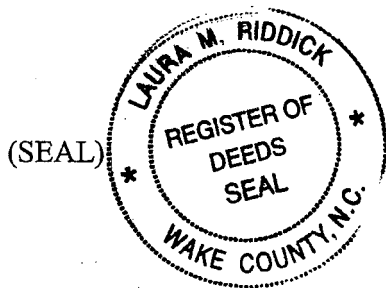
STATE OF NORTH CAROLINA

WAKE COUNTY

**CERTIFICATE OF REGISTER OF DEEDS THAT
NOTARY PUBLIC WAS ACTING NOTARY
AT TIME OF SIGNATURE**

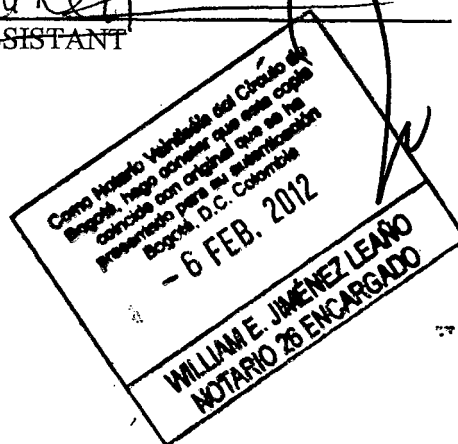
I, LAURA M. RIDDICK, REGISTER OF DEEDS OF THE AFORESAID COUNTY AND STATE, DO HEREBY CERTIFY THAT Laneisha C. Hayes WAS, AT THE TIME OF SIGNING THE FOREGOING (OR ANNEXED) CERTIFICATE, A DULY COMMISSIONED AND QUALIFIED NOTARY PUBLIC IN AND FOR THE COUNTY OF WAKE, STATE OF NORTH CAROLINA, AND AS SUCH FULL FAITH AND CREDIT IS DUE TO HIS OFFICIAL ACTS; AND, FURTHER, THAT HIS SIGNATURE THERETO IS IN HIS OWN PROPER HANDWRITING.

IN TESTIMONY WHEREOF, I HAVE HEREUNTO SET MY HAND AND SEAL OF OFFICE THIS, THE 30TH DAY OF MARCH, 2004.



Laura M. Riddick
REGISTER OF DEEDS

Carol
DEPUTY / ASSISTANT



APOSTILLE

(Convention de La Haye 5 octobre 1961)

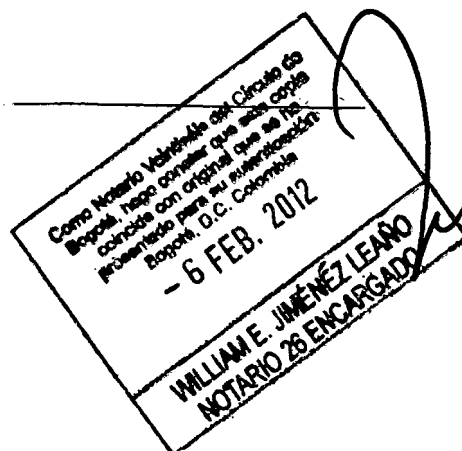
1. COUNTRY: **UNITED STATES OF AMERICA**
2. This Public Document
has been signed by CARLA N. BROWN
3. acting in the capacity of DEPUTY REGISTER OF DEEDS
LAURA M. RIDDICK, REGISTER OF DEEDS
4. bears the seal/stamp of COUNTY OF WAKE, NORTH CAROLINA

CERTIFIED

5. at Raleigh, North Carolina
6. the 1ST DAY OF APRIL, 2004
7. by Deputy Secretary of State, State of North Carolina
8. No. 8117
9. Seal/Stamp:
10. Signature



Robyns. Mosch...



-----TRADUCCION OFICIAL No. -040417-----

de un documento escrito en INGLES, el cual para su identificación
lleva el sello de la Traductora e Intérprete oficial, Res. 2755/68 y
01144/97 de Minjusticia, al igual que la presente.-----

------(Anexos a un poder otorgado por Syngenta
Participations AG)

(fdo) ilegible

3/24/04 Research Triangle Park, NC 27709

ESTADO DE CAROLINA DEL NORTE

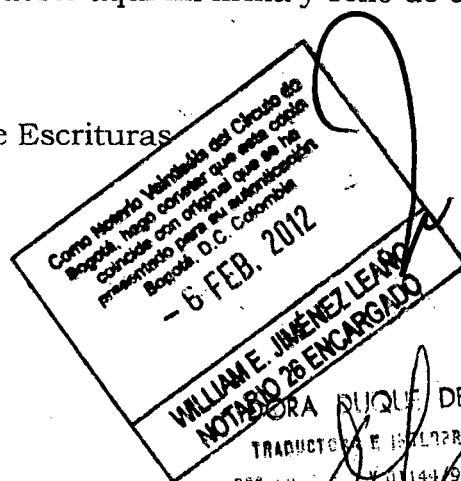
CONDADO DE WAKE

Yo, Laura M. Riddick, Registrador de Escrituras del condado y estado
antes mencionados, certifico por medio del presente que Laneisha C.
Hayes, al momento de firmar este documento era un Notario Público
debidamente comisionado y habilitado en y para el Condado de Wake,
Estado de Carolina del Norte, y como tal debe dars plena fe y crédito a
sus actos oficiales, y además, que su firma en el mismo es de su propia
letra.

En testimonio de lo cual, he impuesto aquí mi firma y sello de oficio,
hoy día 30 de Marzo de 2004.

Laura M. Riddick, Registrador de Escrituras

Por (fdo) ilegible



ORA BLIQUE DE BERNAL
TRADUCTORA E INTÉRPRETE OFICIAL
RES. 2755/68 Y 01144/97 - MINJUSTICIA
REP. DE COLOMBIA

Delegado

APOSTILLA

(Convención de La Haya de octubre 5, 1961)

1. País: Estados Unidos de América
 2. Este documento público ha sido firmado por CARLA N. BROWN
 3. actuando en su carácter de Delegado del Registrador de Escrituras
 4. lleva el sello de Laura M. Riddick, Registrador de Escrituras
- Condado de Wake, Carolina del Norte

CERTIFICADO

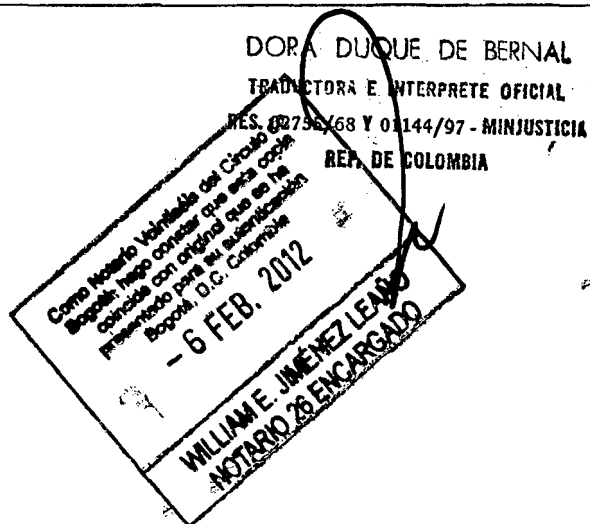
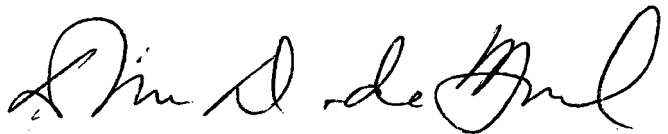
5. En Raleigh. Carolina del Norte
6. el día 1 de Abril de 2004
7. por el Secretario de Estado Delegado, Estado de Carolina del Norte
8. No. 8117
9. Sello: (sello en oblea ocre)

10. Firma

(fdo) Rodney S. Maddox

ES TRADUCCION FIEL Y COMPLETA, a la cual me remito,

Bogotá, Abril 15, 2004



MINISTERIO DE
RELACIONES EXTERIORES

210992

Dora Duque
CUBA
DOCUMENTOS DESLAMPERA
LAS FUNCIONES INDICADAS

Como Anexo Verificado del Grupo de
Bogotá, hago constar que este copia
coincide con original que se ha
presentado para su autenticación
Bogotá, D.C. Colombia

- 6 FEB. 2012

WILLIAM E. JIMÉNEZ LEANO
NOTARIO 28 ENCARGADO

TELEXIO

2:42

13

CO 72584

000011

**DOCUMENTO DE CESIÓN
ASSIGNMENT DOCUMENT**

El (los) suscrito (s), en su calidad de inventor (es) de

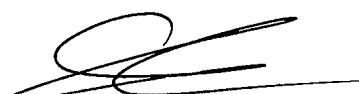
HETEROCICLOS MICROBIOCIDAS

declara (an) que cede (n) y traspasa (n) todos los derechos que les correspondan en y sobre el invento atrás mencionado a **SYNGENTA PARTICIPATIONS AG, Schwarzwaldallee 215, 4058 Basel, Switzerland**, en cuanto se refiere a la República de Colombia.

The undersigned, as inventor (s) of

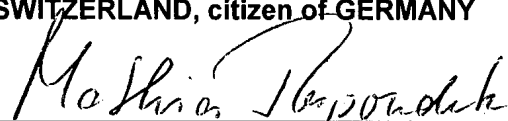
MICROBIOCIDAL HETEROCYCLES

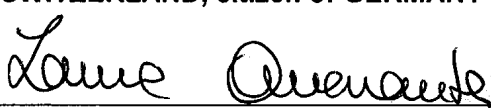
hereby declare (s) that assign (s) all the rights in and to the aforementioned invention to **SYNGENTA PARTICIPATIONS AG**, as far as the Republic of Colombia is concerned.


Sarah SULZER-MOSSE, Syngenta Crop
Protection Münchwilen AG,
Schaffhauserstrasse,
4332 Stein, SWITZERLAND, citizen of FRANCE

FIRMA DEL CEDENTE
domiciliado en


Clemens LAMBERTH, Syngenta Crop
Protection Münchwilen AG,
Schaffhauserstrasse, 4332 Stein,
SWITZERLAND, citizen of GERMANY


Mathias Stephan RESPONDEK, Syngenta Crop
Protection Münchwilen AG,
Schaffhauserstrasse, 4332 Stein,
SWITZERLAND, citizen of GERMANY


Laura QUARANTA, Syngenta Crop Protection
Münchwilen AG, Schaffhauserstrasse, 4332
Stein, SWITZERLAND, citizen of ITALY

ATTESTATION

I, the undersigned Civil Law Notary in Basel, Switzerland, Marius Meier, certify herewith the authenticity of the signatures attached heretofore of **Ms. Sarah Sulzer-Mossé**, French citizen, residing in Maisprach, Switzerland, of **Mr. Clemens Lamberth**, German citizen, residing in Efringen-Kirchen, Germany, of **Mr. Mathias Stephan Respondek**, German citizen, residing in Ballrechten-Dottingen, Germany, and of **Ms. Laura Quaranta**, Italian citizen, residing in Basel, Switzerland.

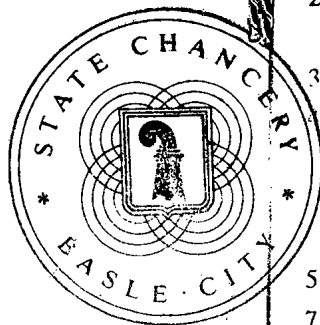
The authenticity of the signatures was established by means of comparison.

BASEL, Switzerland, this 6th (sixth) day of January 2012 (two thousand and twelve)

Leg.Prot.Nr. 37 /2012



M. Meier
Notar



APOSTILLE

(Hague Convention of October 5th, 1961)

1. Country: Switzerland (Schweiz / Suisse)

This official document

2. is signed by lic. iur.

M. Meier

3. in his/her function as notary public

and certified by the seal of the above mentioned

Certified 6. Jan 2012

5. in Basel (Bâle) 6. on

7. by the State Chancery of the Canton of Basel-Stadt

8. no. 137/240

9. Seal /stamp:

10. Signature:

Helena Schaffner

TRADUCCIÓN OFICIAL No. 018-12, DE UN DOCUMENTO ESCRITO EN INGLÉS, SELLADO CON EL SELLO DEL SUSCRITO TRADUCTOR OFICIAL, HOY ENERO 24 DEL 2012, EN LA CIUDAD DE BOGOTÁ D.C., REPÚBLICA DE COLOMBIA.

DOCUMENTO DE CESIÓN

(ESCRITO EN INGLÉS Y ESPAÑOL)

SELLO DE NOTARIO PÚBLICO

CERTIFICACIÓN

Yo, el suscrito Notario de Ley Civil de Basel, Suiza, Marius Meier, por medio del presente certifico la autenticidad de las anteriores firmas de Sarah Sulzer- Mosse, ciudadana francesa, residente en Maisprach, Suiza, de Clemens Iamberth, ciudadano Alemán, residente en Efringen – Kirchen, Alemania, de Mathias Stephan Respondek, ciudadano Alemán, residente en Ballrechten- Dottingen, Alemania y de Laura Quaranta, ciudadana Italiana, residente en Basel, Suiza.

La autenticidad de la firma fue establecida por medio de comparación.

BASEL, Suiza, este día 6 (seis) de Enero del 2012 (dos mil doce).

Firmado

Dr. M. Meier

Notario

Legalización Prot. No. 37/2012

Sergio Eleuterio Latorre Mendoza
Traductor e Interpreté Oficial
Resol. No. 1839 Minjusticia 1991

APOSTILLA

(CONVENCION DE LA HAYE DE 5 OCTOBRE 1961)

1. PAIS: SUIZA
- ESTE DOCUMENTO PUBLICO
2. HA SIDO FIRMADO POR: DR. M. MEIER
3. ACTUANDO EN CAPACIDAD DE: NOTARIO PUBLICO
4. Y CERTIFICADO POR EL SELLO DE: MENCIONADO ANTERIORMENTE

CERTIFICADO

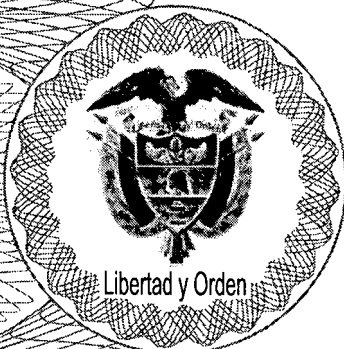
5. EN: BASEL
6. EL 6 DE ENERO DE 2012
7. POR EL CANCELLER DE ESTADO DEL CANTON DE BASEL – STADT
8. No. 137/240
9. SELLO/ESTAMPILLA
10. FIRMA

FIRMADO POR:

HELENA SCHAFFNAR

SELLO DE LA CANCELLERIA

Sergio Eleuterio Platorre Mendoza
Traductor e interprete Oficial
Resol. No. 2839 Minjusticia 1991



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(At: - À:)

El: **1/30/2012 9:27:55 a.m.**
(On: - Le:)

Por: **APOSTILLA Y LEGALIZACIÓN**
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Nombre del Titular: **137/240**
(Name of the holder of document: - Nom du titulaire:)

Tipo de documento: **TRADUCCION APOSTILLA**
(Type of document: - Type du document:)

Número de hojas: **2**
(Number of pages: - Nombre de pages:)

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From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF THE RECORDING
OF A CHANGE

(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

To:

ARUNASALAM, Velautha-Cumaran
Syngenta Crop Protection Münchwilen AG
Patent Department
Schaffhauserstrasse
CH-4332 Stein
SUISSE

Date of mailing (day/month/year) 04 January 2012 (04.01.2012)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference 72584-WO-PCT	
International application No. PCT/EP2010/061381	International filing date (day/month/year) 05 August 2010 (05.08.2010)

1. The following indications appeared on record concerning:

☒ the applicant

☒ the inventor

☐ the agent

☐ the common representative

Name and Address SULZER, Sarah Syngenta Crop Protection Münchwilen AG Schaffhauserstrasse CH-4332 Stein Switzerland	State of Nationality FR	State of Residence CH
	Telephone No.	
	Facsimile No.	
	E-mail address	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person

☒ the name

☐ the address

☐ the nationality

☐ the residence

Name and Address SULZER-MOSSE, Sarah Syngenta Crop Protection Münchwilen AG Schaffhauserstrasse CH-4332 Stein Switzerland	State of Nationality FR	State of Residence CH
	Telephone No.	
	Facsimile No.	
	E-mail address ☐ Notifications by e-mail authorized	

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

☒ the receiving Office

☐ the International Searching Authority

☐ the Authority(ies) specified for supplementary search

☐ the International Preliminary Examining Authority

☒ the designated Offices concerned

☐ the elected Offices concerned

☐ other:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 89 70	Authorized officer Kirchner Maria e-mail pt06.pct@wipo.int Telephone No. +41 22 338 74 06
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(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau(43) International Publication Date
17 February 2011 (17.02.2011)

PCT

(10) International Publication Number
WO 2011/018401 A1

(51) International Patent Classification:

C07D 413/04 (2006.01) A01P 3/00 (2006.01)
 C07D 413/14 (2006.01) A01N 43/78 (2006.01)
 C07D 417/04 (2006.01) A01N 43/76 (2006.01)
 C07D 417/14 (2006.01) A01N 43/836 (2006.01)

(21) International Application Number:

PCT/EP2010/061381

(22) International Filing Date:

5 August 2010 (05.08.2010)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

09167736.9 12 August 2009 (12.08.2009)

EP

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(74) Agent: **ARUNASALAM, Velautha-Cumaran**; Syngenta Crop Protection Münchwilen AG, Patent Department, Schaffhauserstrasse, CH-4332 Stein (CH).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

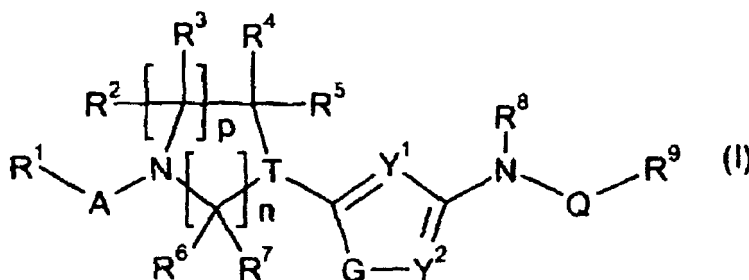
Declarations under Rule 4.17:

— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))

Published:

— with international search report (Art. 21(3))

(54) Title: MICROBIOCIDAL HETEROCYCLES



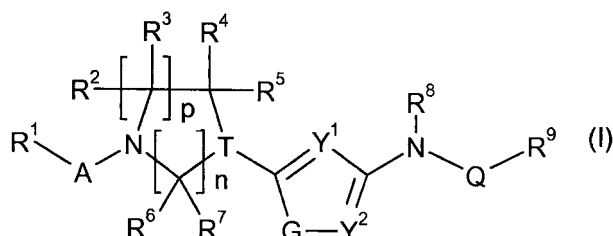
(57) Abstract: The present invention relates to heterocyclic compounds of formula (I) which have microbiocidal activity, in particular fungicidal activity, as well as methods of using the compounds of formula (I) to control microbes.

Microbiocidal Heterocycles

The present invention relates to heterocycles, e.g. as active ingredients, which have microbiocidal activity, in particular fungicidal activity. The invention also relates to preparation of these heterocycles, to heterocyclic derivatives used as intermediates in the preparation of these heterocycles, to preparation of these intermediates, to agrochemical compositions which comprise at least one of the heterocycles, to preparation of these compositions and to use of the heterocycles or compositions in agriculture or horticulture for controlling or preventing infestation of plants, harvested food crops, seeds or non-living materials by phytopathogenic microorganisms, preferably fungi.

- 10 Certain heterocycles for use as fungicides are described in WO 2007/014290, WO 2008/013622, WO 2008/013925, WO 2008/091580, WO 2008/091594 and WO 2009/055514.

The present invention provides compounds of formula I:



- 15 wherein

A is x-C(=O)-, x-C(=S)-, x-C(R¹⁰R¹¹)-C(=O)-, x-C(R¹²R¹³)-C(=S)-, x-O-C(=O)-, x-O-C(=S)-, x-N(R¹⁴)-C(=O)-, x-N(R¹⁵)-C(=S)-, x-C(R¹⁶R¹⁷)-SO₂- or x-N=C(R²⁶)-, in each case x indicates the bond that is connected to R¹;

T is CR¹⁸ or N;

- 20 G is O or S;

Y¹ and Y² are independently CR¹⁹ or N;

Q is -C(=O)-z, -C(=S)-z, -C(=O)-O-z, -C(=S)-O-z, -C(=O)-N(R²⁰)-z, -C(=S)-N(R²¹)-z or -SO₂-z, in each case z indicates the bond that is connected to R⁹;

n is 1 or 2;

- 25 p is 1 or 2, providing that when n is 2, p is 1;

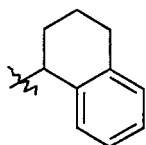
R¹ is phenyl, pyridyl, imidazolyl, or pyrazolyl; wherein the phenyl, pyridyl, imidazolyl and pyrazolyl are each optionally substituted by 1 to 3 substituents independently selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl, halogen, cyano, hydroxy and amino;

R², R³, R⁴, R⁵, R⁶, R⁷, R¹⁰, R¹¹, R¹², R¹³, R¹⁶, R¹⁷, R¹⁸, R¹⁹ and R²⁶ each independently are

- 30 hydrogen, halogen, cyano, C₁-C₄alkyl or C₁-C₄haloalkyl;

R⁸, R¹⁴, R¹⁵, R²⁰ and R²¹ each independently are hydrogen, C₁-C₄alkyl or C₁-C₄alkoxy; and

R⁹ is phenyl, benzyl or group (a):



(a)

- wherein the phenyl, benzyl and group (a) are each optionally substituted with 1 to 3 substituents independently selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkoxy, halogen, cyano, hydroxyl, N(R²⁷)₂, SH, C₁-C₄ alkylthio, nitro, phenylsulfonyl and phenylsulfinyl, wherein the phenylsulfonyl and phenylsulfinyl are optionally substituted by 1 to 3 substituents independently selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkoxy, halogen and cyano;
- each R²⁷ independently is hydrogen, C₁-C₄ alkyl, phenylsulfonyl or phenylsulfinyl, wherein
- 10 the phenylsulfonyl and phenylsulfinyl are optionally substituted by 1 to 3 substituents independently selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkoxy, halogen and cyano; or a salt or a N-oxide thereof.

Where substituents are indicated as being optionally substituted, this means that they may or may not carry one or more identical or different substituents. Normally not more

15 than three such optional substituents are present at the same time.

The term "halogen" refers to fluorine, chlorine, bromine or iodine, preferably fluorine, chlorine or bromine.

The term "amino" refers to -NH₂.

Alkyl substituents may be straight-chained or branched. Alkyl on its own or as part of

20 another substituent is, depending upon the number of carbon atoms mentioned, for example, methyl, ethyl, n-propyl, n-butyl, n-pentyl, n-hexyl and the isomers thereof, for example, iso-propyl, iso-butyl, sec-butyl, tert-butyl, iso-amyl or pivaloyl.

A haloalkyl group may contain one or more identical or different halogen atoms and, for example, may stand for CH₂Cl, CHCl₂, CCl₃, CH₂F, CHF₂, CF₃, CF₃CH₂, CH₃CF₂,

25 CF₃CF₂ or CCl₃CCl₂.

The presence of one or more possible asymmetric carbon atoms in a compound of formula I means that the compounds may occur in optically isomeric forms, i.e. enantiomeric or diastereomeric forms. As a result of the presence of a possible aliphatic C=C double bond, geometric isomerism may occur, i.e. cis-trans or (E)-(Z) isomerism. Also

30 atropisomers may occur as a result of restricted rotation about a single bond. Formula I is intended to include all those possible isomeric forms and mixtures thereof. The present invention includes all those possible isomeric forms and mixtures thereof for a compound of formula I. Likewise, formula I is intended to include all possible tautomers. The present invention includes all possible tautomeric forms for a compound of formula I.

In each case, the compounds of formula I according to the invention are in free form, in oxidized form as a N-oxide or in salt form, e.g. an agronomically usable salt form.

N-oxides are oxidized forms of tertiary amines or oxidized forms of nitrogen containing heteroaromatic compounds. They are described for instance in the book "Heterocyclic N-oxides" by A. Albini and S. Pietra, CRC Press, Boca Raton 1991.

Suitable salts of the compounds of formula I include those resulting after addition of acid such as those with an inorganic mineral acid e.g. hydrochloric, hydrobromic, sulphuric, nitric or phosphoric acid, or an organic carboxylic acid e.g. oxalic, tartaric, lactic, butyric, toluic, hexanoic or phthalic acid, or a sulfonic acid e.g. methane, benzene or toluene sulfonic acid.

Preferably the compound of formula I is a compound wherein:

A is $x\text{-C(=O)-}$, $x\text{-C(=S)-}$, $x\text{-C(R}^{10}\text{R}^{11})\text{-C(=O)-}$, $x\text{-C(R}^{12}\text{R}^{13})\text{-C(=S)-}$, $x\text{-O-C(=O)-}$, $x\text{-O-C(=S)-}$, $x\text{-N(R}^{14})\text{-C(=O)-}$, $x\text{-N(R}^{15})\text{-C(=S)-}$ or $x\text{-C(R}^{16}\text{R}^{17})\text{-SO}_2\text{-}$, in each case x indicates the bond that is connected to R^1 ;

15 T is CR^{18} or N;

G is O or S;

Y^1 and Y^2 are independently CR^{19} or N;

Q is -C(=O)-z , -C(=S)-z , -C(=O)-O-z , -C(=S)-O-z , $\text{-C(=O)-N(R}^{20})\text{-z}$, $\text{-C(=S)-N(R}^{21})\text{-z}$ or $\text{-SO}_2\text{-z}$, in each case z indicates the bond that is connected to R^9 ;

20 n is 1 or 2;

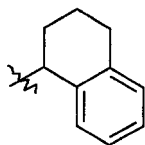
p is 1 or 2, providing that when n is 2, p is 1;

R^1 is phenyl, pyridyl, imidazolyl, or pyrazolyl; wherein the phenyl, pyridyl, imidazolyl and pyrazolyl are each optionally substituted by 1 to 3 substituents independently selected from $\text{C}_1\text{-C}_4$ alkyl, $\text{C}_1\text{-C}_4$ haloalkyl, halogen, cyano, hydroxy and amino;

25 R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^{10} , R^{11} , R^{12} , R^{13} , R^{16} , R^{17} , R^{18} and R^{19} each independently are hydrogen, halogen, cyano, $\text{C}_1\text{-C}_4$ alkyl, or $\text{C}_1\text{-C}_4$ haloalkyl;

R^8 , R^{14} , R^{15} , R^{20} and R^{21} each independently are hydrogen or $\text{C}_1\text{-C}_4$ alkyl; and

R^9 is phenyl, benzyl or group (a):

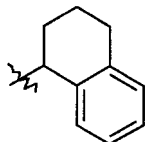


30 (a)

wherein the phenyl, benzyl and group (a) are each optionally substituted with 1 to 3 substituents independently selected from $\text{C}_1\text{-C}_4$ alkyl, $\text{C}_1\text{-C}_4$ haloalkyl, halogen, cyano, hydroxy and amino;

Preferably the compound of formula I is a compound wherein:

- A is $x-C(=O)-$, $x-C(=S)-$, $x-C(R^{10}R^{11})-C(=O)-$, $x-C(R^{12}R^{13})-C(=S)-$, $x-O-C(=O)-$, $x-O-C(=S)-$ or $x-C(R^{16}R^{17})-SO_2-$, in each case x indicates the bond that is connected to R^1 ;
- T is CR^{18} or N;
- 5 G is O or S;
- Y^1 is N;
- Y^2 is CR^{19} or N;
- Q is $-C(=O)-z$, $-C(=S)-z$, $-C(=O)-O-z$, $-C(=S)-O-z$, $-C(=O)-N(R^{20})-z$, $-C(=S)-N(R^{21})-z$ or $-SO_2-z$, in each case z indicates the bond that is connected to R^9 ;
- 10 n is 1 or 2;
- p is 1;
- R^1 is phenyl or pyrazolyl; wherein the phenyl and pyrazolyl are each optionally substituted by 1 to 3 substituents independently selected from C_1 - C_4 alkyl, C_1 - C_4 haloalkyl, halogen, cyano, hydroxy and amino;
- 15 R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^{10} , R^{11} , R^{12} , R^{13} , R^{16} , R^{17} , R^{18} and R^{19} each independently are hydrogen, halogen, C_1 - C_4 alkyl, C_1 - C_4 haloalkyl;
- R^8 , R^{20} and R^{21} each independently are hydrogen or C_1 - C_4 alkyl; and
- R^9 is phenyl, benzyl or group (a):



20 (a)

wherein the phenyl, benzyl and group (a) are each optionally substituted with 1 to 3 substituents independently selected from C_1 - C_4 alkyl, C_1 - C_4 haloalkyl, halogen, cyano, hydroxy, and amino.

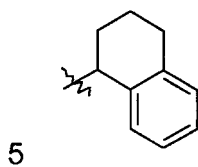
Preferably the compound of formula I is a compound wherein:

- 25 A is $x-C(=O)-$, $-x-CR^{10}R^{11}-C(=O)-$, $x-O-C(=O)-$ or $x-C(R^{16}R^{17})-SO_2-$, in each case x indicates the bond that is connected to R^1 ;
- T is CR^{18} or N;
- G is S;
- Y^1 is N;
- 30 Y^2 is CR^{19} or N;
- Q is $-C(=O)-z$, $-C(=O)-O-z$, $-C(=O)-N(R^{20})-z$ or $-SO_2-z$, in each case z being the bond to R^9 ;
- n is 1 or 2;
- p is 1;
- R^1 is phenyl or pyrazolyl, wherein the phenyl and pyrazolyl are optionally substituted with 1
- 35 to 3 substituents independently selected from C_1 - C_4 alkyl, C_1 - C_4 haloalkyl, and halogen;

R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^{10} , R^{11} , R^{16} , R^{17} , R^{18} and R^{19} each independently are hydrogen, fluoro, or methyl;

R^8 and R^{20} each independently are hydrogen or methyl; and

R^9 is phenyl, benzyl or group (a):



(a)

wherein the phenyl, benzyl and group (a) are each optionally substituted with 1 to 3 substituents independently selected from C_1 - C_4 alkyl, C_1 - C_4 haloalkyl, hydroxy and halogen.

Preferably the compound of formula I is a compound wherein:

- 10 A is $x-C(=O)-$, $x-CH_2-C(=O)-$, $x-O-C(=O)-$ or $x-CH_2-SO_2-$, in each case x indicates the bond that is connected to R^1 ;

T is CH or N;

G is S;

Y^1 is N;

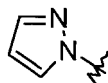
- 15 Y^2 is CH or N;

Q is $-C(=O)-z$, $-C(=O)-O-z$, $-C(=O)-NH-z$ or $-SO_2-z-$, in each case z indicates the bond that is connected to R^9 ;

n is 1 or 2;

p is 1;

- 20 R^1 is phenyl or group (b):



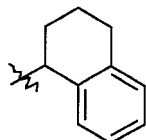
(b)

wherein the phenyl and group (b) are optionally substituted with 1 to 3 substituents independently selected from halogen, C_1 - C_4 alkyl and C_1 - C_4 haloalkyl;

- 25 R^2 , R^3 , R^4 , R^5 , R^6 and R^7 are each hydrogen;

R^8 is hydrogen; and

R^9 is phenyl, benzyl or group (a):



(a)

- 30 wherein the phenyl, benzyl and group (a) are each optionally substituted with 1 to 3 substituents independently selected from C_1 - C_4 alkyl, C_1 - C_4 haloalkyl, hydroxy and halogen.

Preferably the compound of formula I is a compound wherein:

A is $x\text{-CH}_2\text{-C(=O)-}$ wherein x indicates the bond that is connected to R^1 ;

T is CH;

G is S;

5 Y^1 is N;

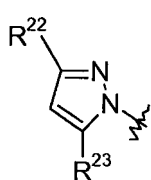
Y^2 is CH;

Q is -C(=O)-z , -C(=O)-O-z or $\text{C(=O)-N(R}^{20}\text{)-z}$, in each case z indicates the bond that is connected to R^9 ;

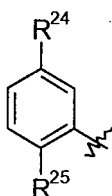
n is 2;

10 p is 1;

R^1 is selected from group (c) or (d):



(c)



(d)

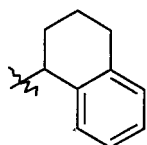
wherein R^{22} , R^{23} , R^{24} and R^{25} are independently selected from hydrogen, methyl

15 and halomethyl;

R_2 , R_3 , R_4 , R_5 , R_6 , and R_7 are each hydrogen;

R_8 is hydrogen;

R^9 is phenyl, benzyl or group (a):



(a)

20

wherein the phenyl, benzyl and group (a) are optionally substituted with 1 to 3 substituents independently selected from halogen, hydroxy, methyl and halomethyl.

The invention also provides a compound of formula I in which:

A is $x\text{-CH}_2\text{C(=O)-}$, $x\text{-CH}_2\text{C(=S)-}$, $x\text{-OC(=O)-}$, $x\text{-C(=O)-}$ or $x\text{-CH}_2\text{-SO}_2\text{-}$, in each case x

25 indicates the bond that is connected to R^1 ;

T is CH or N;

G is O or S;

Y^1 is N;

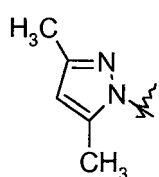
Y^2 is CH or N;

30 Q is -C(=O)-z , -C(=S)-z , -C(=O)O-z , -C(=O)NH-z or $\text{-SO}_2\text{-z}$, in each case z indicates the bond that is connected to R^9 ;

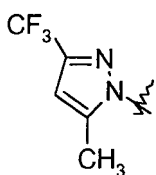
n is 1 or 2;

p is 1 or 2, providing that when n is 2, p is 1;

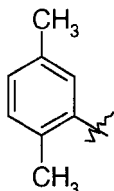
R¹ is group (e), (f), (g), or (h):



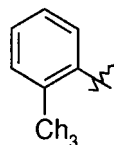
(e)



(f)



(g)

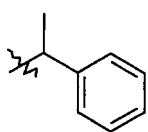


(h)

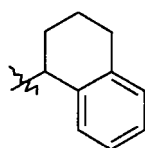
5 R², R³, R⁴, R⁵, R⁶ and R⁷ are H;

R⁸ is H or methyl;

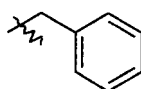
R⁹ is group (i), (j), (k), (l) or (m):



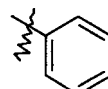
(i)



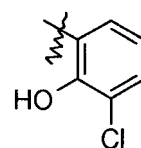
(j)



(k)



(l)



(m)

10 The following list provides definitions, including preferred definitions, for substituents A, T, G, Y¹, Y², Q, n, p, R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹¹, R¹², R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸, R¹⁹, R²⁰, R²¹, R²², R²³, R²⁴, R²⁵, R²⁶ and R²⁷ with reference to compounds of formula I. For any one of these substituents, any of the definitions given below may be combined with any definition of any other substituent given below or elsewhere in this document. The invention includes compounds of formula having all possible combinations of substituent definitions given below. Generally, in this document any substituent definition may be combined with any other substituent definition.

A is x-C(=O)-, x-C(=S)-, x-C(R¹⁰R¹¹)-C(=O)-, x-C(R¹²R¹³)-C(=S)-, x-O-C(=O)-, x-O-C(=S)-, x-N(R¹⁴)-C(=O)-, x-N(R¹⁵)-C(=S)-, x-C(R¹⁶R¹⁷)-SO₂- or x-N=C(R²⁶)-, in each case x indicates the bond that is connected to R¹. Preferably A is x-C(=O)-, x-C(=S)-, x-C(R¹⁰R¹¹)-C(=O)-, x-C(R¹²R¹³)-C(=S)-, x-O-C(=O)-, x-O-C(=S)-, x-N(R¹⁴)-C(=O)-, x-N(R¹⁵)-C(=S)- or x-C(R¹⁶R¹⁷)-SO₂-, in each case x indicates the bond that is connected to R¹. More preferably, A is x-C(=O)-, x-C(=S)-, x-C(R¹⁰R¹¹)-C(=O)-, x-C(R¹²R¹³)-C(=S)-, x-O-C(=O)-, x-O-C(=S)- or x-C(R¹⁶R¹⁷)-SO₂-, in each case x indicates the bond that is connected to R¹. Even more preferably, A is x-C(=O)-, -x-CR¹⁰R¹¹-C(=O)-, x-O-C(=O)- or x-C(R¹⁶R¹⁷)-SO₂-, in each case x indicates the bond that is connected to R¹. Yet more preferably, A is x-CH₂C(=O)-, x-CH₂C(=S)-, x-OC(=O)-, x-C(=O)- or x-CH₂-SO₂-, in each case x indicates the bond that is connected to R¹. Most preferably, A is x-CH₂-C(=O)- wherein x indicates the bond that is connected to R¹.

30 T is CR¹⁸ or N. Preferably, T is CH or N. More preferably, T is CH.

G is O or S. Preferably, G is S.

Y^1 is CR^{19} or N. Preferably, Y^1 is N.

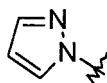
Y^2 is CR^{19} or N. Preferably, Y^2 is CH or N. More preferably, Y^2 is CH.

Q is $-C(=O)-z$, $-C(=S)-z$, $-C(=O)-O-z$, $-C(=S)-O-z$, $-C(=O)-N(R^{20})-z$, $-C(=S)-N(R^{21})-z$ or $-SO_2-z$, in each case z indicates the bond that is connected to R^9 . Preferably, Q is $-C(=O)-z$, $-C(=S)-z$, $-C(=O)-O-z$, $-C(=O)-NH-z$ or $-SO_2-z$, in each case z indicates the bond that is connected to R^9 . Preferably, Q is $-C(=O)-z$, $-C(=O)-O-z$, $-C(=O)-N(R^{20})-z$ or $-SO_2-z$, in each case z indicates the bond that is connected to R^9 . More preferably, Q is $-C(=O)-z$, $-C(=O)-O-z$, $-C(=O)-NH-z$ or $-SO_2-z$, in each case z indicates the bond that is connected to R^9 . Even more preferably, Q is $-C(=O)-z$, $-C(=O)-O-z$ or $-C(=O)-N(R^{20})-z$, in each case z indicates the bond that is connected to R^9 . Most preferably Q is $-C(=O)-z$ wherein z indicates the bond that is connected to R^9 .

n is 1 or 2. Preferably, n is 2.

p is 1 or 2, providing that when n is 2, p is 1. Preferably p is 1.

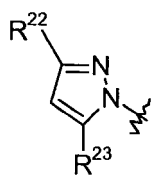
R^1 is phenyl, pyridyl, imidazolyl, or pyrazolyl; wherein the phenyl, pyridyl, imidazolyl and pyrazolyl are each optionally substituted by 1 to 3 substituents independently selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, halogen, cyano, hydroxy and amino. Preferably, R^1 is phenyl or pyrazolyl; wherein the phenyl and pyrazolyl are each optionally substituted by 1 to 3 substituents independently selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, halogen, cyano, hydroxy, and amino. Preferably, R^1 is phenyl or pyrazolyl, wherein the phenyl and pyrazolyl are optionally substituted with 1 to 3 substituents independently selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, and halogen. More preferably, R^1 is phenyl or group (b):



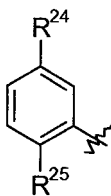
(b)

wherein the phenyl and group (b) are optionally substituted with 1 to 3 substituents independently selected from halogen, C_1-C_4 alkyl and C_1-C_4 haloalkyl.

In one group of compounds R^1 is selected from group (c) or (d):



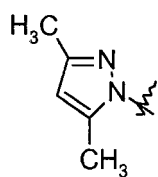
(c)



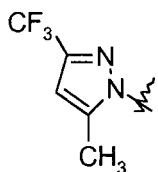
(d)

wherein R^{22} , R^{23} , R^{24} and R^{25} are independently selected from hydrogen, halogen, methyl and halomethyl.

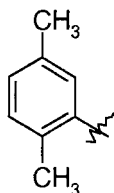
In one group of compounds R^1 is group (e), (f), (g), or (h):



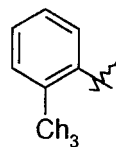
(e)



(f)



(g)

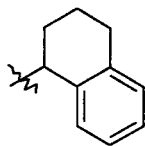


(h).

$R^2, R^3, R^4, R^5, R^6, R^7, R^{10}, R^{11}, R^{12}, R^{13}, R^{16}, R^{17}, R^{18}, R^{19}$ each independently are hydrogen, halogen, cyano, C_1 - C_4 alkyl, or C_1 - C_4 haloalkyl. Preferably, $R^2, R^3, R^4, R^5, R^6, R^7, R^{10}, R^{11}, R^{12}, R^{13}, R^{16}, R^{17}, R^{18}$ and R^{19} each independently are hydrogen, halogen, C_1 - C_4 alkyl, or C_1 - C_4 haloalkyl. More preferably, $R^2, R^3, R^4, R^5, R^6, R^7, R^{10}, R^{11}, R^{12}, R^{13}, R^{16}, R^{17}, R^{18}$ and R^{19} each independently are hydrogen, fluoro, or methyl. Even more preferably, $R^2, R^3, R^4, R^5, R^6, R^7, R^{10}, R^{11}, R^{12}, R^{13}, R^{16}, R^{17}, R^{18}$ and R^{19} each independently are hydrogen.

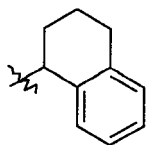
$R^8, R^{14}, R^{15}, R^{20}$, and R^{21} each independently are hydrogen or C_1 - C_4 alkyl. Preferably, $R^8, R^{14}, R^{15}, R^{20}$, and R^{21} each independently are hydrogen or methyl. More preferably, $R^8, R^{14}, R^{15}, R^{20}$, and R^{21} each independently are hydrogen.

R^9 is phenyl, benzyl or group (a):



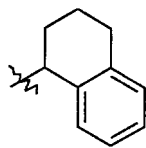
(a)

wherein the phenyl, benzyl and group (a) are each optionally substituted with 1 to 3 substituents independently selected from C_1 - C_4 alkyl, C_1 - C_4 haloalkyl, C_1 - C_4 alkoxy, C_1 - C_4 haloalkoxy, halogen, cyano, hydroxyl, $N(R^{27})_2$, SH, C_1 - C_4 alkylthio, nitro, phenylsulfonyl and phenylsulfinyl, wherein the phenylsulfonyl and phenylsulfinyl are optionally substituted by 1 to 3 substituents independently selected from C_1 - C_4 alkyl, C_1 - C_4 haloalkyl, C_1 - C_4 alkoxy, C_1 - C_4 haloalkoxy, halogen and cyano. Preferably, R^9 is phenyl, benzyl or group (a):



(a)

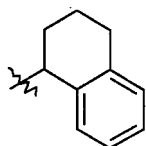
wherein the phenyl, benzyl and group (a) are each optionally substituted with 1 to 3 substituents independently selected from C_1 - C_4 alkyl, C_1 - C_4 haloalkyl, halogen, cyano, hydroxy and amino. Preferably, R^9 is phenyl, benzyl or group (a):



(a)

wherein the phenyl, benzyl and group (a) are each optionally substituted with 1 to 3 substituents independently selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl, hydroxy and halogen.

- 5 More preferably, R⁹ is phenyl, benzyl or group (a):



(a)

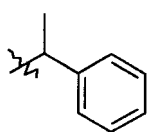
wherein the phenyl, benzyl and group (a) are optionally substituted with 1 to 3 substituents independently selected from halogen, hydroxy, methyl and halomethyl.

- 10 R²⁶ is hydrogen, halogen, cyano, C₁-C₄alkyl, or C₁-C₄haloalkyl. Preferably, R²⁶ is hydrogen, halogen, C₁-C₄alkyl, or C₁-C₄haloalkyl. Preferably, R²⁶ is hydrogen, fluoro, or methyl. More preferably, R²⁶ is hydrogen.

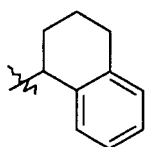
Each R²⁷ independently is hydrogen, C₁-C₄ alkyl, phenylsulfonyl or phenylsulfinyl, wherein the phenylsulfonyl and phenylsulfinyl are optionally substituted by 1 to 3

- 15 substituents independently selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkoxy, halogen and cyano. Preferably, R²⁷ is independently is hydrogen, C₁-C₄ alkyl, phenylsulfonyl or phenylsulfinyl, wherein the phenylsulfonyl and phenylsulfinyl are optionally substituted by 1 to 3 substituents independently selected from halogen, methyl and halomethyl.

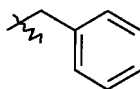
- 20 In one group of compounds R⁹ is group (i), (j), (k), (l) or (m):



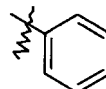
(i)



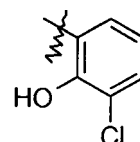
(j)



(k)



(l)



(m)

Preferably R²² is hydrogen or CF₃.

Preferably R²³, R²⁴, and R²⁵ are independently hydrogen or methyl.

- 25 In one group of compounds G is S, Y¹ is N and Y² is CH.

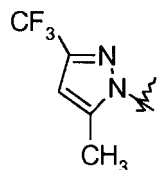
In one group of compounds p is 1 and n is 2.

In one group of compounds R², R³, R⁴, R⁵, R⁶ and R⁷ are H.

In one group of compounds Q is -C(=O)-z, wherein z indicates the bond that is connected to R⁹.

In one group of compounds A is $x\text{-CH}_2\text{-C(=O)-}$, wherein x indicates the bond that is connected to R^1 .

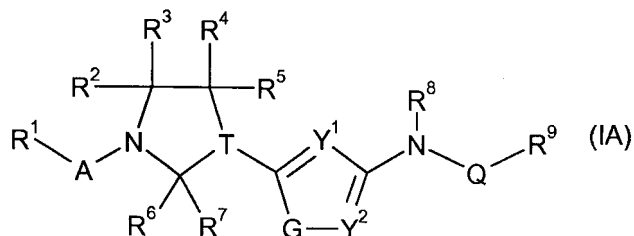
In one group of compounds R^1 is group (f)



5 (f)

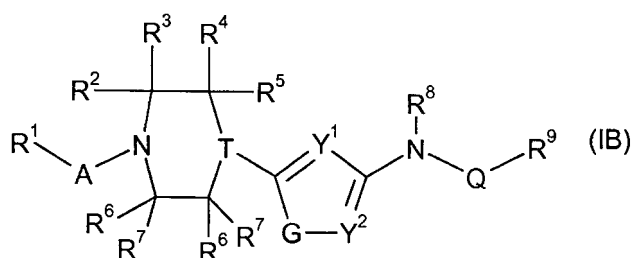
In one group of compounds R^9 is phenyl substituted by hydroxyl, and optionally substituted by one or two further substituents as defined above. Preferably the hydroxy is at the ortho position. Preferably one of the further substituents is halogen and is preferably at the meta position adjacent to the hydroxy.

10 For the avoidance of doubt, when n is 1 and p is 1 compounds of formula I have the formula according to formula IA:



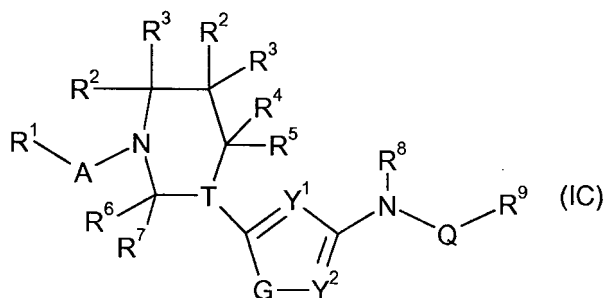
in which A, T, G, Y^1 , Y^2 , Q, R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , and R^9 have the definitions as described for formula I.

15 When n is 2 and p is 1, compounds of formula I have the formula according to formula IB:



in which A, T, G, Y^1 , Y^2 , Q, R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , and R^9 have the definitions as described for formula I.

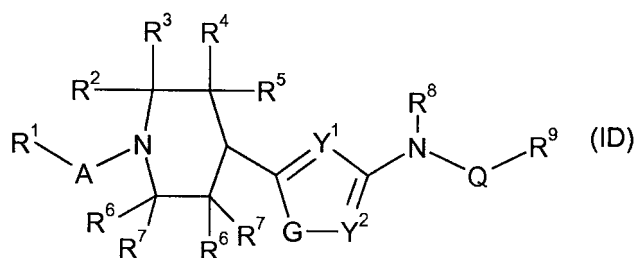
20 When n is 1 and p is 2, compounds of formula I have the formula according to formula IC:



in which A, T, G, Y¹, Y², Q, R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, and R⁹ have the definitions as described for formula I.

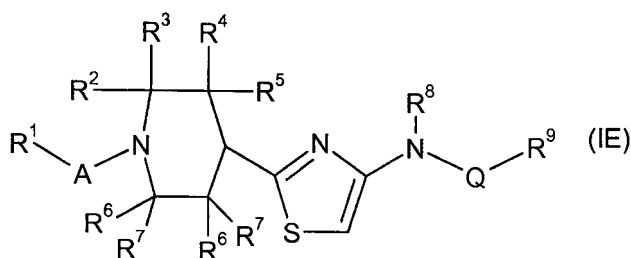
The invention also relates to compounds of formula IA, formula IB and formula IC as shown above.

The invention also relates to compounds of formula ID:



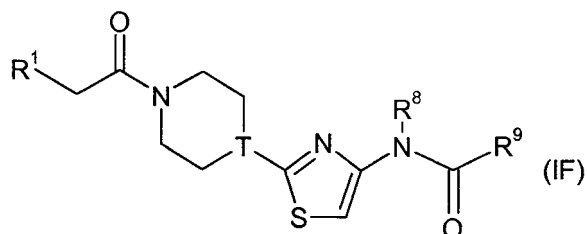
in which A, G, Y¹, Y², Q, R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, and R⁹ have the definitions as described for formula I. Preferred definitions of A, G, Y¹, Y², Q, R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, and R⁹ are as defined for formula I.

The invention also relates to compounds of formula IE:



in which A, Q, R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, and R⁹ have the definitions as described for formula I. Preferred definitions of A, Q, R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, and R⁹ are as defined for formula I.

The invention also relates to compounds of formula IF:

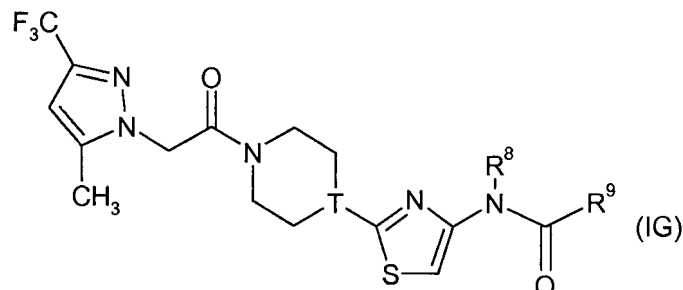


wherein T is CH or N

R⁸ is CH₃ or H; and

R¹ and R⁹ have the definitions as described for formula I. Preferred definitions of R¹ and R⁹ are as defined for formula I.

The invention also relates to compounds of formula IG:

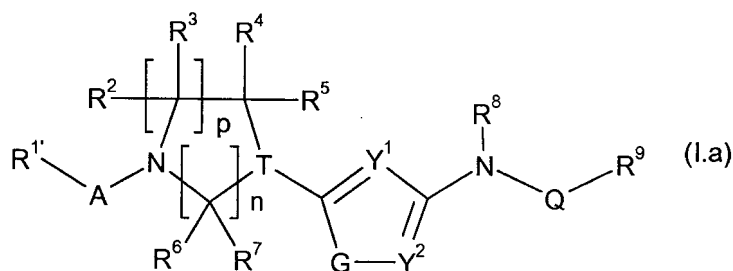


5 wherein T is CH or N

R⁸ is CH₃ or H; and

R⁹ has the definition as described for formula I. Preferred definitions of R⁹ are as defined for formula I.

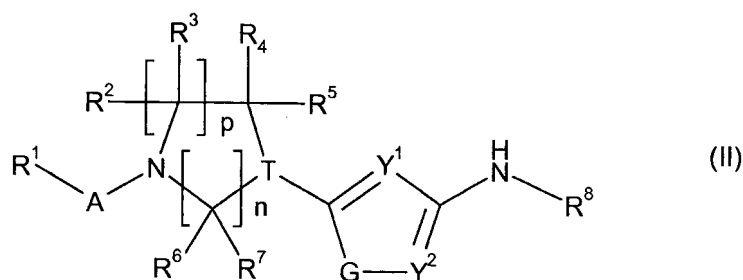
The invention also includes compounds of formula I in which R¹ is a protecting group,
10 such as an alkyl group. Accordingly the invention includes compounds of formula I.a:



in which R¹ is C₁-C₈ alkyl, e.g. C₁-C₄ alkyl, e.g. tert-butyl; and A, T, G, Y¹, Y², Q, n, p, R²,
R³, R⁴, R⁵, R⁶, R⁷, R⁸, and R⁹ have the definitions as described for formula I. Preferably A is
x-O-C(=O)-, x indicating the bond to R¹. Preferred definitions of A, T, G, Y¹, Y², Q, n, p, R²,
15 R³, R⁴, R⁵, R⁶, R⁷, R⁸, and R⁹ are as defined for formula I.

These compounds are useful in the synthesis of compounds of formula I.

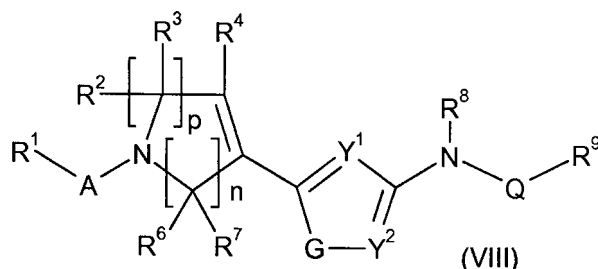
The invention also includes compounds of formula II:



wherein R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, A, T, G, Y¹, Y², p and n are as defined for formula I.

20 Preferred definitions of R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, A, T, G, Y¹, Y², p and n are as defined
for formula I. Compounds of formula II are useful as intermediates in the synthesis of
compounds of formula I.

The invention also includes compounds of formula VIII:



wherein R^1 , R^2 , R^3 , R^4 , R^6 , R^7 , R^8 , A, T, G, Y^1 , Y^2 , p and n are as defined for formula I.

Preferred definitions of R^1 , R^2 , R^3 , R^4 , R^6 , R^7 , R^8 , A, T, G, Y^1 , Y^2 , p and n are as defined for formula I. Compounds of formula VIII are useful as intermediates in the synthesis of

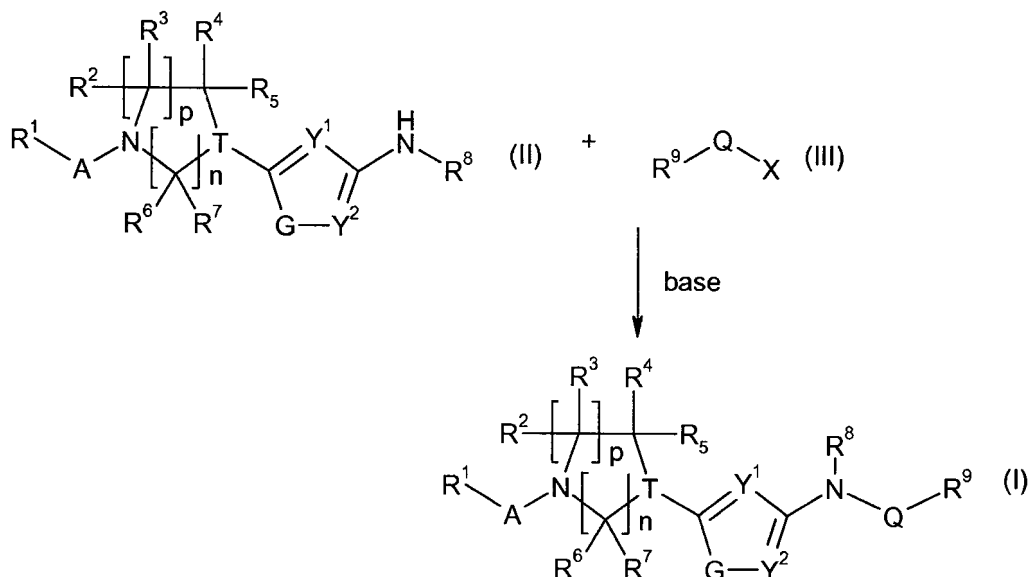
5 compounds of formula I.

Preferred individual compounds are:

- (*R*)-1,2,3,4-tetrahydro-naphthalene-1-carboxylic acid (2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-amide (Compound No. 1.g.001);
- 3-chloro-2-hydroxy-N-(2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-benzamide (Compound No. 1.g.006);
- 1,2,3,4-tetrahydro-naphthalene-1-carboxylic acid (2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-amide (Compound No. 1.g.011);
- (2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-carbamic acid 1,2,3,4-tetrahydro-naphthalen-1-yl ester (Compound No. 1.g.013);
- N-2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-2-phenyl-propionamide (Compound No. 1.g.016);
- N-(2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-carbamic acid 1-phenyl-ethyl ester (Compound No. 1.g.018)
- N-2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-benzamide (Compound No. 1.g.021);
- 2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-carbamic acid phenyl ester (Compound No. 1.g.023);
- 1-(2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-3-phenyl-urea (Compound No. 1.g.024);
- 1,2,3,4-tetrahydro-naphthalene-1-carboxylic acid (2-{1-[2-(2,5-dimethylphenyl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-amide (Compound No. 1.g.136);
- N-(2-{1-[2-(2,5-Dimethyl-phenyl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-2-phenyl-propionamide (Compound No. 1.g.141);
- N-{2-[1-(2,5-Dimethyl-phenylmethanesulfonyl)-piperidin-4-yl]-thiazol-4-yl}-benzamide (Compound No. 1.g. 246)
- 1,2,3,4-tetrahydro-naphthalene-1-carboxylic acid {2-[1-(2-o-tolyl-acetyl)-piperidin-4-yl]-thiazol-4-yl}-amide (Compound No. 1.g. 386)

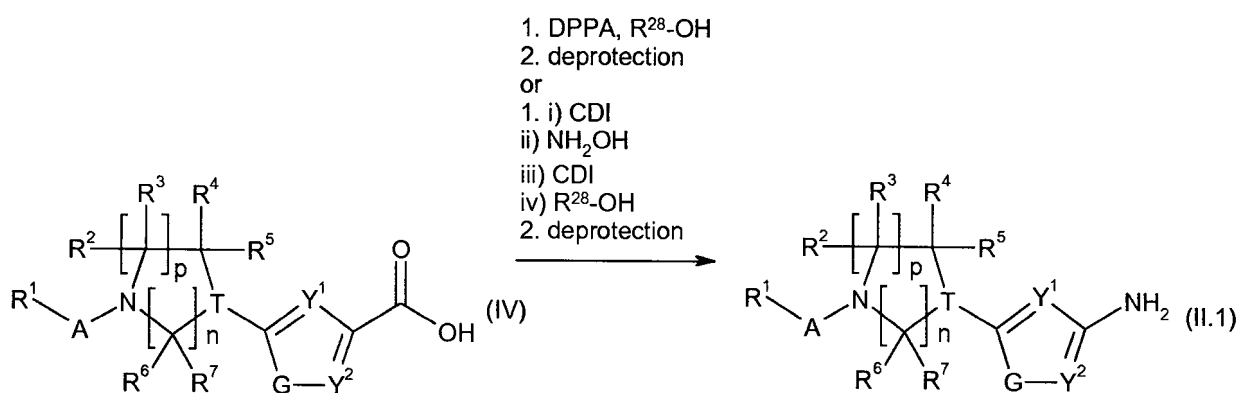
- 3-fluoro-2-hydroxy-N-(2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-benzamide (Compound No. I.g.501);
- 3-bromo-2-hydroxy-N-(2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-benzamide (Compound No. I.g.502);
- 5 2-hydroxy-N-(2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-benzamide (Compound No. I.g.503);
- 2-methoxy-N-(2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-benzamide (Compound No. I.g.506);
- N-(2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-2-(toluene-4-sulfonylamino)-benzamide (Compound No. I.g.508);
- 10 2-methoxy-6-hydroxy-N-(2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-benzamide (Compound No. I.g.509);
- 2-fluoro-6-hydroxy-N-(2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-benzamide (Compound No. I.g.510);
- 15 3-methoxy-2-hydroxy-N-(2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-benzamide (Compound No. I.g.510); 1,2,3,4-tetrahydro-naphthalene-1-carboxylic acid methyl-(2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-amide (Compound No. 1.h.011); and
- N-methyl-N-2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-2-phenyl-propionamide (Compound No. I.h.016).
- 20 1,2,3,4-Tetrahydro-naphthalene-1-carboxylic acid (2-{4-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)acetyl]-piperazin-1-yl}-thiazol-4-yl)-amide (Compound No. I.n.011); and
- N-(2-{4-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperazin-1-yl}-thiazol-4-yl)-benzamide (Compound No. I.n.011).
- 25 Compounds of formula (I) can be made as shown in the following schemes.
- The compounds of formula I, wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , A, T, G, Y^1 , Y^2 , n, p and Q are as defined for formula I can be obtained by transformation of a compound of formula II, wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , A, T, G, Y^1 , Y^2 , n, p and Y are as defined for formula I with a compound of formula III, wherein R^9 and Q are as
- 30 defined for formula I and X is a hydroxy, halogen, preferably fluoro, chloro or bromo or alkoxy, such as methoxy, ethoxy. This is shown in Scheme 1.

Scheme 1



The compounds of formula II.1, wherein R¹, R², R³, R⁴, R⁵, R⁶, R⁷, A, T, G, n, p, Y¹ and Y² are as defined for formula I, can be obtained by transformation of a compound of formula IV, wherein R¹, R², R³, R⁴, R⁵, R⁶, R⁷, A, T, G, n, p, Y¹ and Y² are as defined for formula I with an azide, such as diphenyl phosphoryl azide and subsequent Curtius rearrangement of the resulting acyl azide with an alcohol R²⁸-OH, wherein R²⁸ is C₁-C₆alkyl or optionally substituted aryl and following carbamate cleavage with a mineral acid, such as hydrochloric acid, sulfuric acid or an organic acid, such as trifluoroacetic acid. This is shown in Scheme 2.

Scheme 2

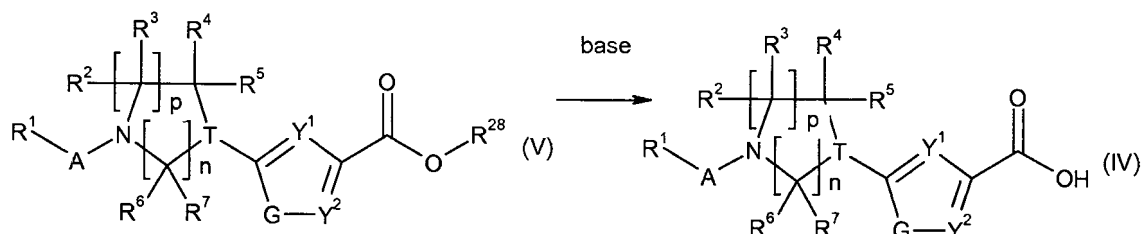


15

The compounds of formula IV, wherein R¹, R², R³, R⁴, R⁵, R⁶, R⁷, A, T, G, n, p, Y¹ and Y² are as defined for formula I can be obtained by saponification of a compound of formula V, wherein R¹, R², R³, R⁴, R⁵, R⁶, R⁷, A, T, G, n, p, Y¹ and Y² are as defined for formula I and R²⁸ is C₁-C₆alkyl or optionally substituted aryl with a base, such as sodium hydroxide, potassium hydroxide or lithium hydroxide. This is shown in Scheme 3.

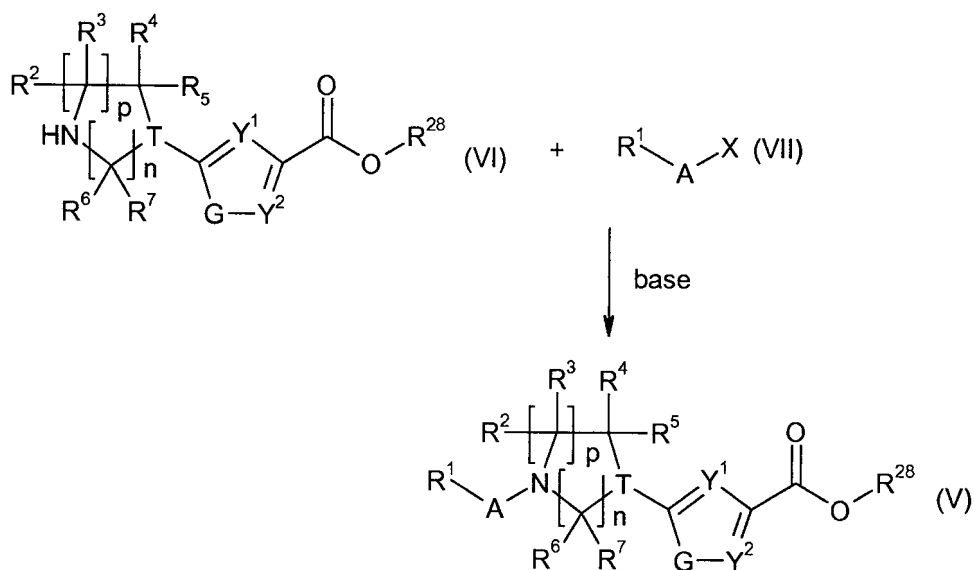
20

Scheme 3



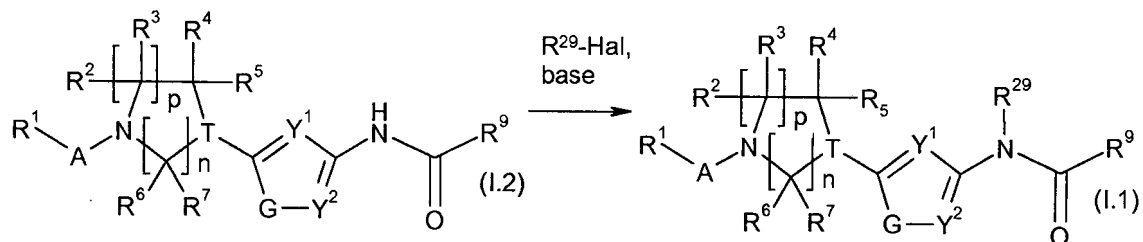
The compounds of formula V, wherein R¹, R², R³, R⁴, R⁵, R⁶, R⁷, A, T, G, n, p, Y¹ and Y² are as defined for formula I and R²⁸ is C₁-C₆alkyl or optionally substituted aryl can be obtained by transformation of a compound of formula VI, wherein R², R³, R⁴, R⁵, R⁶, R⁷, T, G, n, p, Y¹ and Y² are as defined for formula I and R²⁸ is C₁-C₆alkyl or optionally substituted aryl with a compound of formula VII, wherein R¹ and A are as defined for formula I and X is a hydroxy, halogen, preferably fluoro, chloro or bromo or alkoxy, such as methoxy, ethoxy. This is shown in Scheme 4.

10 Scheme 4



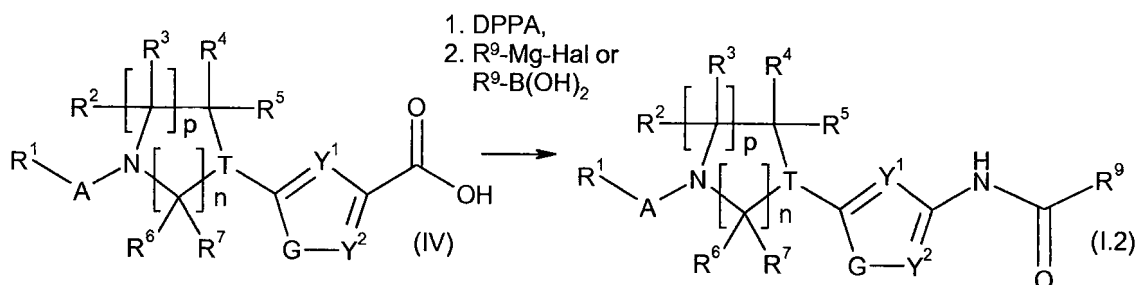
Alternatively, the compounds of formula I.1, wherein R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁹, A, T, G, n, Y¹ and Y² are as defined for formula I and R²⁹ is C₁-C₆alkyl can be obtained by transformation of a compound of formula I.2, wherein R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁹, A, T, G, n, Y¹ and Y² are as defined for formula I with an alkyl halide R²⁹-Hal, wherein R²⁹ is C₁-C₆alkyl and Hal is halogen, preferably chloro or bromo. This is shown in Scheme 5.

Scheme 5



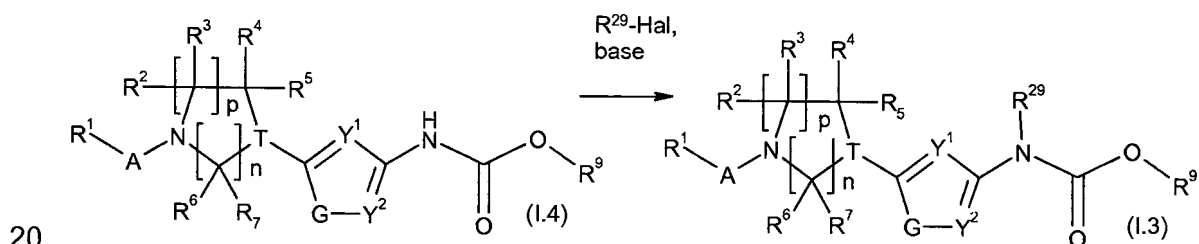
The compounds of formula I.2, wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^9 , A , T , G , n , p , Y^1 and Y^2 are as defined for formula I can be obtained by transformation of a compound of formula IV, wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , A , T , G , n , p , Y^1 and Y^2 are as defined for formula I with an azide, such as diphenyl phosphoryl azide and subsequent Curtius rearrangement of the resulting acyl azide with a Grignard reagent $R^9\text{-Mg-Hal}$, wherein R^9 is as defined for formula I and Hal is halogen, preferably chloro, bromo or iodo, or a boronic acid $R^9\text{-B(OH)}_2$, wherein R^9 is as defined for formula I and a catalyst, such as bis(1,5-cyclooctadiene)rhodium(I) hydroxide. This is shown in Scheme 6.

Scheme 6



Alternatively, the compounds of formula I.3, wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^9 , A , T , G , n , p , Y^1 and Y^2 are as defined for formula I and R^{29} is $C_1\text{-}C_6$ alkyl can be obtained by transformation of a compound of formula I.4, wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^9 , A , T , G , n , p , Y^1 and Y^2 are as defined for formula I with an alkyl halide $R^{29}\text{-Hal}$, wherein R^{29} is $C_1\text{-}C_6$ alkyl and Hal is halogen, preferably chloro or bromo. This is shown in Scheme 7.

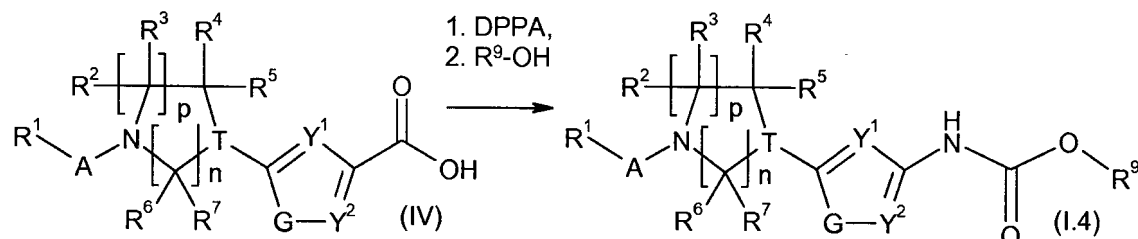
Scheme 7



The compounds of formula I.4, wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^9 , A , T , G , n , p , Y^1 and Y^2 are as defined for formula I can be obtained by transformation of a compound of formula IV, wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , A , T , G , n , p , Y^1 and Y^2 are as defined for formula I with an azide, such as diphenyl phosphoryl azide and subsequent Curtius

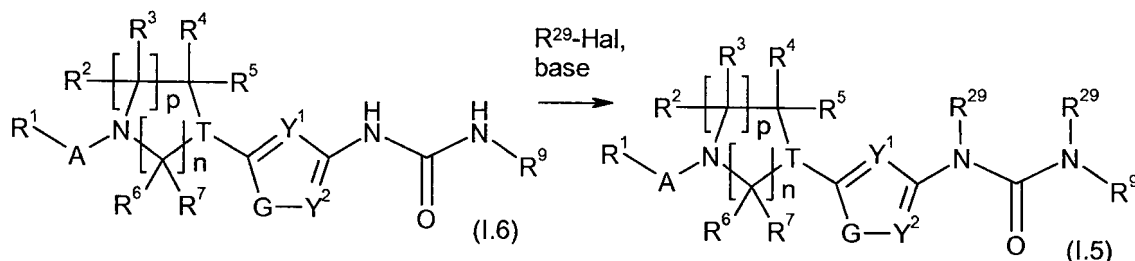
rearrangement of the resulting acyl azide with an alcohol R^9 -OH, wherein R^9 is as defined for formula I as defined for formula I. This is shown in Scheme 8.

Scheme 8



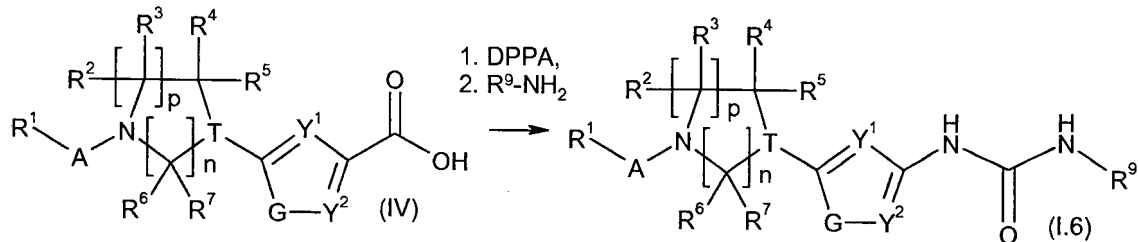
- 5 Alternatively, the compounds of formula I.5, wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^9 , A , T , G , n , Y^1 and Y^2 are as defined for formula I and R^{29} is C_1 - C_6 alkyl can be obtained by transformation of a compound of formula I.6, wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^9 , A , T , G , n , Y^1 and Y^2 are as defined for formula I with an alkyl halide R^{29} -Hal, wherein R^{29} is C_1 - C_6 alkyl and Hal is halogen, preferably chloro or bromo. This is shown in Scheme 9.

10 Scheme 9



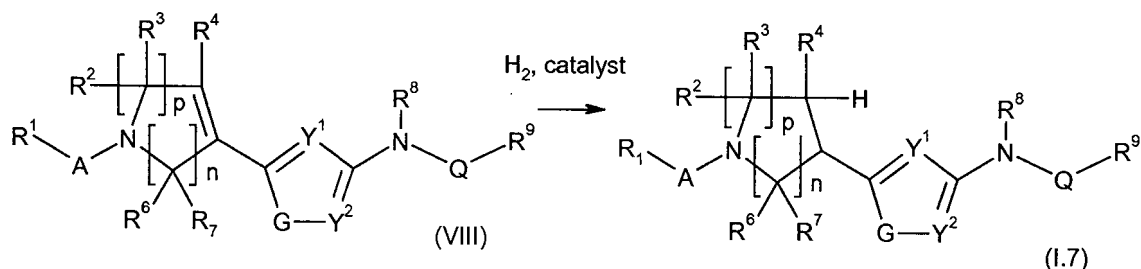
- The compounds of formula I.6, wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^9 , A , T , G , n , p , Y^1 and Y^2 are as defined for formula I can be obtained by transformation of a compound of formula IV, wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , A , T , G , n , p , Y^1 and Y^2 are as defined for formula I with an azide, such as diphenyl phosphoryl azide and subsequent Curtius rearrangement of the resulting acyl azide with an amine R^9 -NH₂, wherein R^9 is as defined for formula I. This is shown in Scheme 10.

Scheme 10



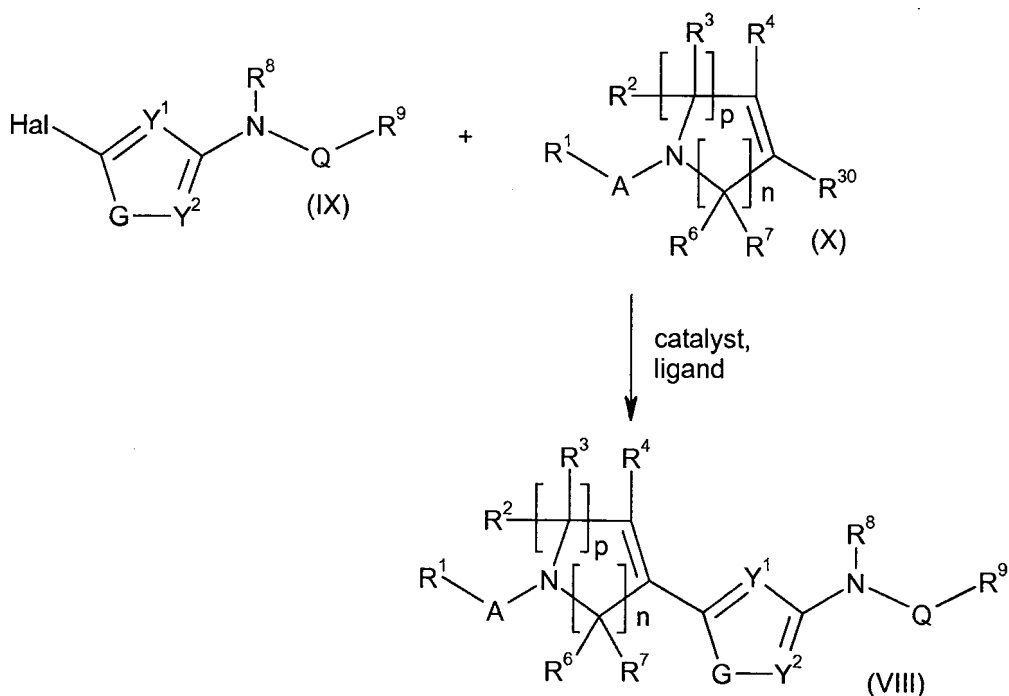
- 20 Alternatively, the compounds of formula I.7, wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , A , G , n , p , Y^1 , Y^2 and Q are as defined for formula I, can be obtained by reduction of a compound of formula VIII, wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , A , G , n , p , Y^1 , Y^2 and Q are as defined for formula I with hydrogen and a catalyst, such as palladium on charcoal, platinum or raney-nickel. This is shown in Scheme 11.

Scheme 11



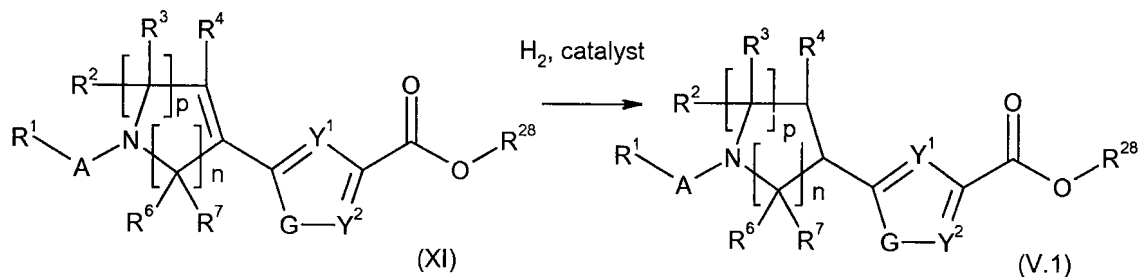
The compounds of formula VIII, wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , A, G, n, p, Y^1 , Y^2 and Q are as defined for formula I can be obtained by cross coupling of a compound
 5 of formula IX, wherein R^8 , R^9 , G, Y^1 , Y^2 and Q are as defined for formula I and Hal is halogen, preferably chloro, bromo or iodo with a compound of formula X, wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 and A are as defined for formula I and R^{30} is $B(OH)_2$ and a transition metal, such as tetrakis(triphenylphosphine)palladium, and a ligand, such as. This is shown in Scheme 12.

10 Scheme 12



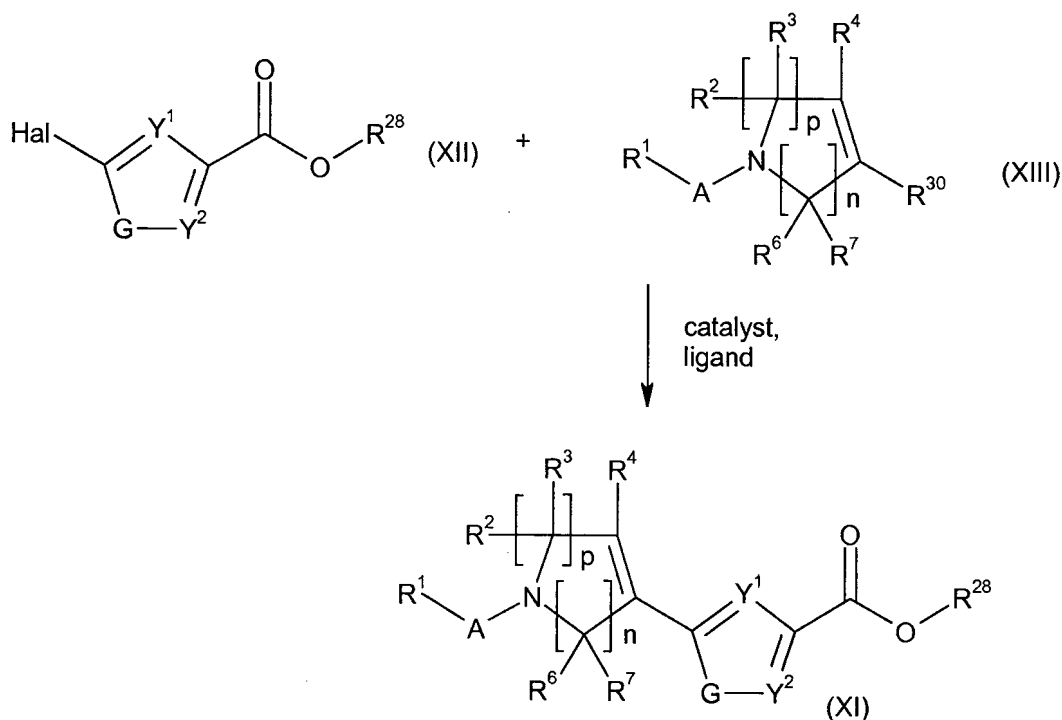
Alternatively, the compounds of formula V.1, wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , A, G, n, p, Y^1 and Y^2 are as defined for formula I and R^{28} is C_1 - C_6 alkyl or optionally substituted aryl can be obtained by reduction of a compound of formula XI, wherein R^1 , R^2 , R^3 , R^4 , R^5 ,
 15 R^6 , R^7 , A, G, n, p, Y^1 and Y^2 are as defined for formula I and R^{28} is C_1 - C_6 alkyl or optionally substituted aryl with hydrogen and a catalyst, such as palladium on charcoal, platinum or raney-nickel. This is shown in Scheme 13.

Scheme 13



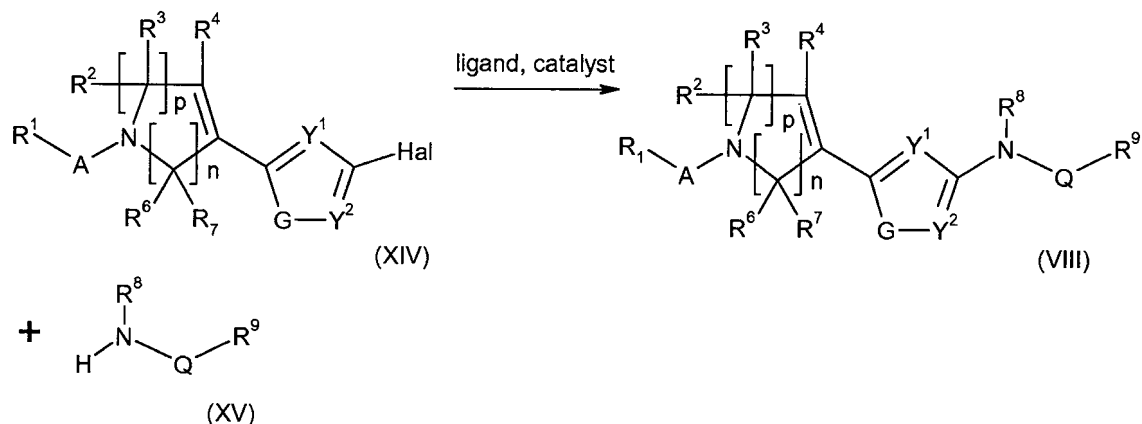
The compounds of formula XI, wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , A , G , n , p , Y^1 and Y^2 are as defined for formula I and R^{28} is C_1 - C_6 alkyl or optionally substituted aryl can be obtained by cross coupling of a compound of formula XII, wherein G , Y^1 and Y^2 are as defined for formula I, R^{28} is C_1 - C_6 alkyl or optionally substituted aryl and Hal is halogen, preferably chloro, bromo or iodo with a compound of formula XIII, wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 and A are as defined for formula I and R^{30} is $B(OH)_2$ and a transition metal, such as bis-(triphenylphosphine)palladium(II) chloride. This is shown in Scheme 14.

10 Scheme 14



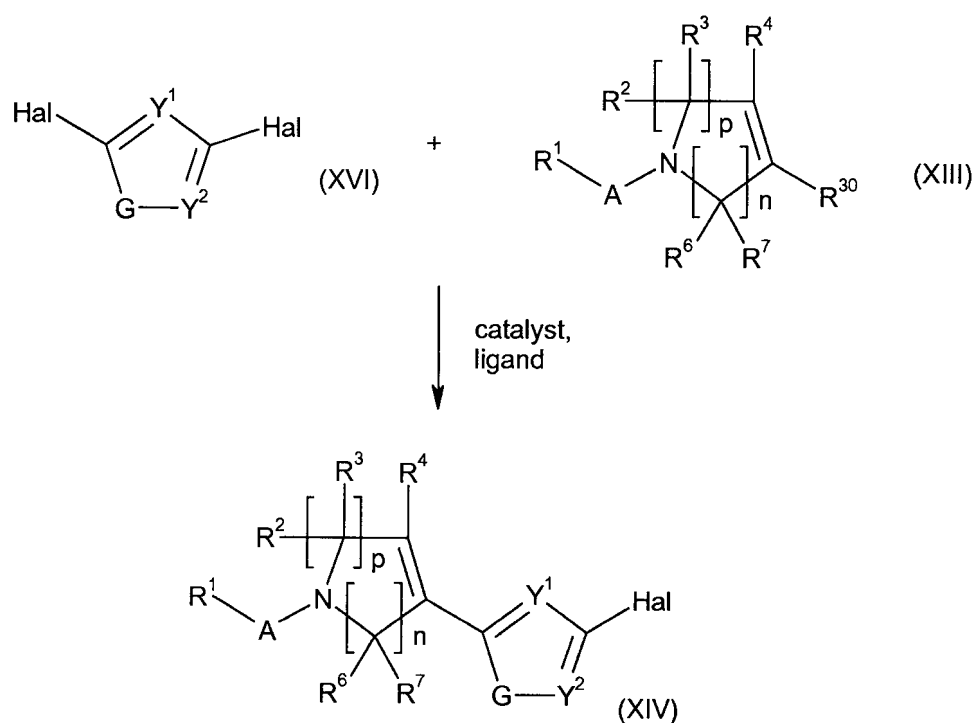
Alternatively, the compounds of formula VIII, wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , A , G , n , p , Y^1 , Y^2 and Q are as defined for formula I, can be obtained by cross coupling of a compound of formula XIV, wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , A , G , n , p , Y^1 , and Y^2 are as defined for formula I with a compound of formula XV, wherein R^8 , R^9 and Q are as defined for formula I and a ligand such as Xantphos or dimethylethylenediamine and a catalyst, such as $Pd(OAc)_2$ or copperiodide. This is shown in Scheme 15.

Scheme 15



The compounds of formula XIV, wherein R¹, R², R³, R⁴, R⁵, R⁶, R⁷, A, G, n, p, Y¹ and Y² are as defined for formula I can be obtained by cross coupling of a compound of formula XVI, wherein G, Y¹ and Y² are as defined for formula I, with a compound of formula XIII, wherein R¹, R², R³, R⁴, R⁵, R⁶, R⁷ and A are as defined for formula I and R³⁰ is B(OH)₂ and a transition metal, such as bis-(triphenylphosphine)palladium(II) chloride. This is shown in Scheme 16.

Scheme 16



Surprisingly, it has now been found that the novel compounds of formula I have, for practical purposes, a very advantageous level of biological activity for protecting plants against diseases that are caused by fungi.

The compounds of formula I can be used in the agricultural sector and related fields of use e.g. as active ingredients for controlling plant pests or on non-living materials for control of spoilage microorganisms or organisms potentially harmful to man. The novel compounds are distinguished by excellent activity at low rates of application, by being well

tolerated by plants and by being environmentally safe. They have very useful curative, preventive and systemic properties and may be used for protecting numerous cultivated plants. The compounds of formula I can be used to inhibit or destroy the pests that occur on plants or parts of plants (fruit, blossoms, leaves, stems, tubers, roots) of different crops of
5 useful plants, while at the same time protecting also those parts of the plants that grow later e.g. from phytopathogenic microorganisms.

It is also possible to use compounds of formula I as dressing agents for the treatment of plant propagation material, e.g., seed, such as fruits, tubers or grains, or plant cuttings (for example rice), for the protection against fungal infections as well as against
10 phytopathogenic fungi occurring in the soil. The propagation material can be treated with a composition comprising a compound of formula I before planting: seed, for example, can be dressed before being sown. The active ingredients according to the invention can also be applied to grains (coating), either by impregnating the seeds in a liquid formulation or by coating them with a solid formulation. The composition can also be applied to the planting
15 site when the propagation material is being planted, for example, to the seed furrow during sowing. The invention relates also to such methods of treating plant propagation material and to the plant propagation material so treated.

Furthermore the compounds according to present invention can be used for controlling fungi in related areas, for example in the protection of technical materials,
20 including wood and wood related technical products, in food storage, in hygiene management.

In addition, the invention could be used to protect non-living materials from fungal attack, e.g. lumber, wall boards and paint.

The compounds of formula I are, for example, effective against the phytopathogenic
25 fungi of the following classes: Fungi imperfecti (e.g. *Alternaria* spp.), Basidiomycetes (e.g. *Corticium* spp., *Ceratobasidium* spp., *Waitea* spp., *Thanatephorus* spp., *Rhizoctonia* spp., *Hemileia* spp., *Puccinia* spp., *Phakopsora* spp., *Ustilago* spp., *Tilletia* spp.), Ascomycetes (e.g. *Venturia* spp., *Blumeria* spp., *Erysiphe* spp., *Podosphaera* spp., *Uncinula* spp., *Monilinia* spp., *Sclerotinia* spp., *Colletotrichum* spp., *Glomerella* spp., *Fusarium* spp.,
30 *Gibberella* spp., *Monographella* spp., *Phaeosphaeria* spp., *Mycosphaerella* spp., *Cercospora* spp., *Pyrenophora* spp., *Rhynchosporium* spp., *Magnaporthe* spp., *Gaeumannomyces* spp., *Oculimacula* spp., *Ramularia* spp., *Botryotinia* spp.) and Oomycetes (e.g. *Phytophthora* spp., *Pythium* spp., *Plasmopara* spp., *Peronospora* spp., *Pseudoperonospora* spp. *Bremia* spp). Outstanding activity is observed against downy
35 mildew (e.g. *Plasmopara viticola*) and late blight (e.g. *Phytophthora infestans*).

Furthermore, the novel compounds of formula I are effective against phytopathogenic gram

negative and gram positive bacteria (e.g. *Xanthomonas* spp, *Pseudomonas* spp, *Erwinia amylovora*, *Ralstonia* spp.) and viruses (e.g. tobacco mosaic virus).

Within the scope of present invention, target crops and/or useful plants to be protected typically comprise the following species of plants: cereal (wheat, barley, rye, oat,
5 rice, maize, sorghum and related species); beet (sugar beet and fodder beet); pomes, drupes and soft fruit (apples, pears, plums, peaches, almonds, cherries, strawberries, raspberries and blackberries); leguminous plants (beans, lentils, peas, soybeans); oil plants (rape, mustard, poppy, olives, sunflowers, coconut, castor oil plants, cocoa beans, groundnuts); cucumber plants (pumpkins, cucumbers, melons); fibre plants (cotton, flax,
10 hemp, jute); citrus fruit (oranges, lemons, grapefruit, mandarins); vegetables (spinach, lettuce, asparagus, cabbages, carrots, onions, tomatoes, potatoes, paprika); lauraceae (avocado, cinnamomum, camphor) or plants such as tobacco, nuts, coffee, eggplants, sugar cane, tea, pepper, vines, hops, bananas and natural rubber plants, as well as turf and ornamentals.

15 The useful plants and / or target crops in accordance with the invention include conventional as well as genetically enhanced or engineered varieties such as, for example, insect resistant (e.g. Bt. and VIP varieties) as well as disease resistant, herbicide tolerant (e.g. glyphosate- and glufosinate-resistant maize varieties commercially available under the trade names RoundupReady® and LibertyLink®) and nematode tolerant varieties. By way
20 of example, suitable genetically enhanced or engineered crop varieties include the Stoneville 5599BR cotton and Stoneville 4892BR cotton varieties.

The term "useful plants" and/or "target crops" is to be understood as including also useful plants that have been rendered tolerant to herbicides like bromoxynil or classes of herbicides (such as, for example, HPPD inhibitors, ALS inhibitors, for example
25 primisulfuron, prosulfuron and trifloxysulfuron, EPSPS (5-enol-pyrovyl-shikimate-3-phosphate-synthase) inhibitors, GS (glutamine synthetase) inhibitors or PPO (protoporphyrinogen-oxidase) inhibitors) as a result of conventional methods of breeding or genetic engineering. An example of a crop that has been rendered tolerant to imidazolinones, e.g. imazamox, by conventional methods of breeding (mutagenesis) is
30 Clearfield® summer rape (Canola). Examples of crops that have been rendered tolerant to herbicides or classes of herbicides by genetic engineering methods include glyphosate- and glufosinate-resistant maize varieties commercially available under the trade names RoundupReady®, Herculex I® and LibertyLink®.

The term "useful plants" and/or "target crops" is to be understood as including also
35 useful plants which have been so transformed by the use of recombinant DNA techniques that they are capable of synthesising one or more selectively acting toxins, such as are known, for example, from toxin-producing bacteria, especially those of the genus *Bacillus*.

The term "useful plants" and/or "target crops" is to be understood as including also useful plants which have been so transformed by the use of recombinant DNA techniques that they are capable of synthesising antipathogenic substances having a selective action, such as, for example, the so-called "pathogenesis-related proteins" (PRPs, see e.g. EP-A-0 5 392 225). Examples of such antipathogenic substances and transgenic plants capable of synthesising such antipathogenic substances are known, for example, from EP-A-0 392 225, WO 95/33818, and EP-A-0 353 191. The methods of producing such transgenic plants are generally known to the person skilled in the art and are described, for example, in the publications mentioned above.

10 The term "locus" of a plant as used herein is intended to embrace the place on which the plants are growing, where the plant propagation materials of the plants are sown or where the plant propagation materials of the plants will be placed into the soil. An example for such a locus is a field, on which crop plants are growing.

The term "plant propagation material" is understood to denote generative parts of the 15 plant, such as seeds, which can be used for the multiplication of the latter, and vegetative material, such as cuttings or tubers, for example potatoes. There may be mentioned for example seeds (in the strict sense), roots, fruits, tubers, bulbs, rhizomes and parts of plants. Germinated plants and young plants which are to be transplanted after germination or after emergence from the soil, may also be mentioned. These young plants may be 20 protected before transplantation by a total or partial treatment by immersion. Preferably "plant propagation material" is understood to denote seeds.

The compounds of formula I may be used in unmodified form or, preferably, together with the adjuvants conventionally employed in the art of formulation. To this end they may be conveniently formulated in known manner to emulsifiable concentrates, coatable pastes, 25 directly sprayable or dilutable solutions or suspensions, dilute emulsions, wettable powders, soluble powders, dusts, granulates, and also encapsulations e.g. in polymeric substances. As with the type of the compositions, the methods of application, such as spraying, atomising, dusting, scattering, coating or pouring, are chosen in accordance with the intended objectives and the prevailing circumstances. The compositions may also contain 30 further adjuvants such as stabilizers, antifoams, viscosity regulators, binders or tackifiers as well as fertilizers, micronutrient donors or other formulations for obtaining special effects.

Suitable carriers and adjuvants, e.g. for agricultural use, can be solid or liquid and are substances useful in formulation technology, e.g. natural or regenerated mineral substances, solvents, dispersants, wetting agents, tackifiers, thickeners, binders or 35 fertilizers. Such carriers are for example described in WO 97/33890.

The compounds of formula I are normally used in the form of compositions and can be applied to the crop area or plant to be treated, simultaneously or in succession with

further compounds. These further compounds can be e.g. fertilizers or micronutrient donors or other preparations, which influence the growth of plants. They can also be selective herbicides or non-selective herbicides as well as insecticides, fungicides, bactericides, nematocides, molluscicides or mixtures of several of these preparations, if desired together
5 with further carriers, surfactants or application promoting adjuvants customarily employed in the art of formulation.

The compounds of formula I may be used in the form of fungicidal compositions for controlling or protecting against phytopathogenic microorganisms, comprising as active ingredient at least one compound of formula I or of at least one preferred individual
10 compound as above-defined, in free form or in agrochemically usable salt form, and at least one of the above-mentioned adjuvants.

The invention provides a fungicidal composition comprising at least one compound formula I an agriculturally acceptable carrier and optionally an adjuvant. An agricultural acceptable carrier is for example a carrier that is suitable for agricultural use. Agricultural
15 carriers are well known in the art. Preferably said fungicidal compositions may comprise an additional fungicidal active ingredient in addition to the compound of formula I.

The compound of formula (I) may be the sole active ingredient of a composition or it may be admixed with one or more additional active ingredients such as an insecticide, fungicide, synergist, herbicide or plant growth regulator where appropriate. An additional
20 active ingredient may, in some cases, result in unexpected synergistic activities. Examples of suitable additional active ingredients include the following: Azoxystrobin (131860-33-8), Dimoxystrobin (149961-52-4), Enestrobin (238410-11-2), Fluoxastrobin (193740-76-0), Kresoxim-methyl (143390-89-0), Metominostrobin (133408-50-1), Orysastrobin (248593-16-0), Picoxystrobin (117428-22-5), Pyraclostrobin (175013-18-0), Azaconazole (60207-31-0),
25 Bromuconazole (116255-48-2), Cyproconazole (94361-06-5), Difenconazole (119446-68-3), Diniconazole (83657-24-3), Diniconazole-M (83657-18-5), Epoxiconazole (13385-98-8), Fenbuconazole (114369-43-6), Fluquinconazole (136426-54-5), Flusilazole (85509-19-9), Flutriafol (76674-21-0), Hexaconazole (79983-71-4), Imazalil (58594-72-2), Imibenconazole (86598-92-7), Ipconazole (125225-28-7), Metconazole (125116-23-6), Myclobutanil (88671-
30 89-0), Oxpconazole (174212-12-5), Pefurazoate (58011-68-0), Penconazole (66246-88-6), Prochloraz (67747-09-5), Propiconazole (60207-90-1), Prothioconazole (178928-70-6), Simeconazole (149508-90-7), Tebuconazole (107534-96-3), Tetraconazole (112281-77-3), Triadimefon (43121-43-3), Triadimenol (55219-65-3), Triflumizole (99387-89-0), Triticonazole (131983-72-7), Diclobutrazol (76738-62-0), Etaconazole (60207-93-4),
35 Fluconazole (86386-73-4), Fluconazole-cis (112839-32-4), Thiabendazole (148-79-8), Quinconazole (103970-75-8), Fenpiclonil (74738-17-3), Fludioxonil (131341-86-1), Cyprodinil (121552-61-2), Mepanipyrim (110235-47-7), Pyrimethanil (53112-28-0),

Aldimorph (91315-15-0), Dodemorph (1593-77-7), Fenpropimorph (67564-91-4),
 Tridemorph (81412-43-3), Fenpropidin (67306-00-7), Spiroxamine (118134-30-8),
 Isopyrazam (881685-58-1), Sedaxane (874967-67-6), Bixafen (581809-46-3), Penthiopyrad
 (183675-82-3), Fluxapyroxad (907204-31-3), Boscalid (188425-85-6), Penflufen (494793-
 5 67-8), Fluopyram (658066-35-4), Mandipropamid (374726-62-2), Benthiavalicarb (413615-
 35-7), Dimethomorph (110488-70-5), Chlorothalonil (1897-45-6), Fluazinam (79622-59-6),
 Dithianon (3347-22-6), Metrafenone (220899-03-6), Tricyclazole (41814-78-2), Mefenoxam
 (70630-17-0), Metalaxyl (57837-19-1), Acibenzolar (126448-41-7) (Acibenzolar-S-methyl
 (126448-41-7)), Mancozeb (8018-01-7), Ametoctridine (865318-97-4) Ipconazole (125225-
 10 28-7), Amisulbrom (348635-87-0), Cyflufenamid (180409-60-3), Ethaboxam (16650-77-3),
 Fluopicolide (239110-15-7), Fluthianil (304900-25-2), Isotianil (224049-04-1), Proquinazid
 (189278-12-4), Valiphenal (283159-90-0), 1-methyl-cyclopropene (3100-04-7),
 Trifloxystrobin (141517-21-7), Sulfur (7704-34-9), Copper ammoniumcarbonate (CAS
 33113-08-5); Copper oleate (CAS 1120-44-1); Folpet (133-07-3), Quinoxifen (124495-18-
 15 7), Captan (133-06-2), Fenhexamid (126833-17-8), Glufosinate and its salts (51276-47-2,
 35597-44-5 (S-isomer)), Glyphosate (1071-83-6) and its salts (69254-40-6 (Diammonium),
 34494-04-7 (Dimethylammonium), 38641-94-0 (Isopropylammonium), 40465-66-5
 (Monoammonium), 70901-20-1 (Potassium), 70393-85-0 (Sesquisodium), 81591-81-3
 (Trimesium)), 1,3-Dimethyl-1H-pyrazole-4-carboxylic acid (2-dichloromethylene-3-ethyl-1-
 20 methyl-indan-4-yl)-amide, 1,3-Dimethyl-1H-pyrazole-4-carboxylic acid (4'-methylsulfanyl-
 biphenyl-2-yl)-amide, 1,3-Dimethyl-4H-pyrazole-4-carboxylic acid [2-(2,4-dichloro-phenyl)-2-
 methoxy-1-methyl-ethyl]-amide, (5-Chloro-2,4-dimethyl-pyridin-3-yl)-(2,3,4-trimethoxy-6-
 methyl-phenyl)-methanone, (5-Bromo-4-chloro-2-methoxy-pyridin-3-yl)-(2,3,4-trimethoxy-6-
 methyl-phenyl)-methanone, 2-{2-[(E)-3-(2,6-Dichloro-phenyl)-1-methyl-prop-2-en-(E)-
 25 ylideneaminoxymethyl]-phenyl}-2-[(Z)-methoxyimino]-N-methyl-acetamide, 3-[5-(4-Chloro-
 phenyl)-2,3-dimethyl-isoxazolidin-3-yl]-pyridine.

Another aspect of invention is related to the use of a compound of formula I or of a
 preferred individual compound as above-defined, of a composition comprising at least one
 compound of formula I or at least one preferred individual compound as above-defined, or
 30 of a fungicidal mixture comprising at least one compound of formula I or at least one
 preferred individual compound as above-defined, in admixture with other fungicides, as
 described above, for controlling or preventing infestation of plants, e.g. useful plants such
 as crop plants, propagation material thereof, e.g. seeds, harvested crops, e.g. harvested
 food crops, or non-living materials by phytopathogenic microorganisms, preferably fungal
 35 organisms.

A further aspect of invention is related to a method of controlling or preventing an
 infestation of plants, e.g. useful plants such as crop plants, propagation material thereof,

e.g. seeds, harvested crops, e.g. harvested food crops, or of non-living materials by phytopathogenic or spoilage microorganisms or organisms potentially harmful to man, especially fungal organisms, which comprises the application of a compound of formula I or of a preferred individual compound as above-defined as active ingredient to the plants, to parts of the plants or to the locus thereof, to the propagation material thereof, or to any part of the non-living materials.

Controlling or preventing means reducing infestation by phytopathogenic or spoilage microorganisms or organisms potentially harmful to man, especially fungal organisms, to such a level that an improvement is demonstrated.

10 A preferred method of controlling or preventing an infestation of crop plants by phytopathogenic microorganisms, especially fungal organisms, which comprises the application of a compound of formula I, or an agrochemical composition which contains at least one of said compounds, is foliar application. The frequency of application and the rate of application will depend on the risk of infestation by the corresponding pathogen.

15 However, the compounds of formula I can also penetrate the plant through the roots via the soil (systemic action) by drenching the locus of the plant with a liquid formulation, or by applying the compounds in solid form to the soil, e.g. in granular form (soil application). In crops of water rice such granulates can be applied to the flooded rice field. The compounds of formula I may also be applied to seeds (coating) by impregnating the seeds or tubers
20 either with a liquid formulation of the fungicide or coating them with a solid formulation.

A formulation, e.g. a composition containing the compound of formula I, and, if desired, a solid or liquid adjuvant or monomers for encapsulating the compound of formula I, may be prepared in a known manner, typically by intimately mixing and/or grinding the compound with extenders, for example solvents, solid carriers and, optionally, surface
25 active compounds (surfactants).

The agrochemical formulations and/or compositions will usually contain from 0.1 to 99% by weight, preferably from 0.1 to 95% by weight, of the compound of formula I, 99.9 to 1% by weight, preferably 99.8 to 5% by weight, of a solid or liquid adjuvant, and from 0 to 25% by weight, preferably from 0.1 to 25% by weight, of a surfactant.

30 Advantageous rates of application are normally from 5g to 2kg of active ingredient (a.i.) per hectare (ha), preferably from 10g to 1kg a.i./ha, most preferably from 20g to 600g a.i./ha. When used as seed drenching agent, convenient dosages are from 10mg to 1g of active substance per kg of seeds.

Whereas it is preferred to formulate commercial products as concentrates, the end
35 user will normally use dilute formulations.

The following non-limiting examples illustrate the above-described invention in more detail.

Example 1: This example illustrates the preparation of 1,2,3,4-tetrahydro-naphthalene-1-carboxylic acid (2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-amide (Compound No. 1.g.011)

- 5 a) Preparation of 2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazole-4-carboxylic acid ethyl ester

To a solution of (5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetic acid (9.1 g, 36.1 mmol) in DMF (100 mL) is added diisopropylethylamine (45 mL, 216 mmol), followed by O-(benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium tetrafluoroborate (15.5 g, 39.7 mmol). After
10 stirring 15 min at RT, 2-piperidin-4-yl-thiazole-4-carboxylic acid ethyl ester hydrochloride (10 g, 36.1 mmol) is added to the reaction mixture. After stirring overnight at RT, solvent is evaporated and the resulting yellow oil is dissolved in ethylacetate (300 mL), washed with saturated aqueous sodium bicarbonate solution (300 mL), 1M HCl solution (300 mL), and brine (100 mL). The organic layer is dried over sodium sulfate, filtered, and evaporated
15 under reduced pressure. The crude mixture is purified by column chromatography on silica gel (dichloromethane/methanol 10:1) to give 2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazole-4-carboxylic acid ethyl ester (13.6 g, 88 %). ¹H-NMR (400 MHz, CDCl₃): δ = 1.40 (t, 3H), 1.70-1.85 (m, 2H), 2.16-2.30 (m, 2H), 2.32 (s, 3H), 2.79-2.89 (m, 1H), 3.22-3.43 (m, 1H), 4.03-4.12 (m, 1H), 4.42 (q, 3H), 4.54-4.69 (m, 1H), 4.93-5.08
20 (2d, 2H (diastereotopic)), 6.35 (s, 1H), 8.10 (br, 1H). MS: m/z = 209 (M+1).

- b) Preparation of 2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazole-4-carboxylic acid

To a solution of 2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-
25 thiazole-4-carboxylic acid ethyl ester (2.67 g, 6.2 mmol) in THF (20 mL) is added aqueous solution of sodium hydroxide (2 M, 4.65 mL, 9.3 mmol) at RT. After stirring 3 h at RT, the reaction mixture is acidified with 2M aqueous solution of HCl until pH 2-3, and the solution is extracted with ethylacetate (20 mL). The aqueous layer is re-extracted with ethylacetate (20 mL) and the combined organic layers are washed with brine (10 mL), dried over sodium
30 sulfate, filtered, and evaporated under reduced pressure to give 2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazole-4-carboxylic acid (2.33 g, 94 %), which can be used in the next step without further purification. ¹H-NMR (400 MHz, d₆-acetone): δ = 1.69-1.82 (m, 1H), 1.87-2.02 (m, 1H), 2.16-2.37 (m, 2H), 2.38 (s, 3H), 2.89-2.99 (m, 1H), 3.38-3.48 (m, 2H), 4.14-4.22 (m, 1H), 4.50-4.69 (m, 1H), 5.20-5.36 (2d, 2H
35 (diastereotopic)), 6.41, (s, 1H), 8.34 (s, 1H). MS: m/z = 403 (M+1).

c) Preparation of 2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-carbamic acid tert-butyl ester

To a solution of 2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazole-4-carboxylic acid (9.95 g, 24.74 mmol) in *tert*-butanol (90 mL) is added
5 triethylamine (8.2 mL, 56.9 mmol). After stirring 30 min. at RT, diphenylphosphoryl azide (10.9 mL, 49.5 mmol) is added and the reaction mixture is divided in 6 portions and each portion was irradiated under microwave (100 °C, 15 min.). After cooling to RT, all portions are combined and water (3 mL) is added to the reaction mixture and stirred for 30 minutes. Acetonitrile (40 mL) is then added, followed by addition of basic Amberlyst A21. After
10 stirring overnight at RT, the resin is filtered off, and solvents are evaporated under reduced pressure. The residue is purified by column chromatography on silica gel (ethyl acetate/cyclohexane 7:3) to give 2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-carbamic acid tert-butyl ester (9.6 g, 82 %). ¹H-NMR (400 MHz, CDCl₃): δ = 1.53 (s, 9H), 1.68-1.78 (m, 2H), 2.08-2.19 (m, 2H), 2.32 (s, 3H), 2.85-2.95 (m,
15 1H), 3.10-3.20 (m, 1H), 3.23-3.34 (m, 1H), 3.97-4.04 (m, 1H), 4.50-4.58 (m, 1H), 4.93-5.05 (2d, 2H, diastereotopic protons), 6.33 (s, 1H), 7.10 (br, 1H), 7.30 (s, 1H). MS: m/z = 474 (M+1).

d) Preparation of 1-[4-(4-amino-thiazol-2-yl)-piperidin-1-yl]-2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-ethanone
20

To a solution of 2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-carbamic acid tert-butyl ester (9.6 g, 20.3 mmol) is added a solution of 4M HCl in dioxane (50 mL, 203 mmol) at RT. After stirring 2 days at RT, the solvent is evaporated under reduced pressure. The resulting yellowish foam is triturated with diethylether, and
25 filtered to give 1-[4-(4-Amino-thiazol-2-yl)-piperidin-1-yl]-2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-ethanone hydrochloride salt, which is suspended in aqueous saturated sodium bicarbonate (500 mL). After stirring 30 min. at RT, the reaction mixture is extracted with ethylacetate (500 mL). The combined organic layers are washed with water (100 mL) and brine (100 mL), filtered, dried over sodium sulfate, and evaporated under reduced pressure
30 to give 1-[4-(4-amino-thiazol-2-yl)-piperidin-1-yl]-2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-ethanone (5.63 g, 74 %). ¹H-NMR (400 MHz, CDCl₃): δ = 1.65-1.80 (m, 2H), 2.08-2.20 (m, 2H), 2.31 (s, 3H), 2.81-2.91 (m, 1H), 3.08-3.18 (m, 1H), 3.21-3.32 (m, 1H), 3.95-4.08 (m, 3H), 4.50-4.59 (m, 1H), 4.93-5.04 (2d, 2H, diastereotopic protons), 5.84 (s, 1H), 6.32 (s, 1H). MS: m/z = 374 (M+1).

e) Preparation of 1,2,3,4-tetrahydro-naphthalene-1-carboxylic acid (2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-amide (Compound No. I.g.011)

- To a solution of 1-[4-(4-amino-thiazol-2-yl)-piperidin-1-yl]-2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-ethanone (120 mg, 0.32 mmol) and diisopropylethylamine (0.2 mL, 0.96 mmol) in dichloromethane (5 mL) is added dropwise a solution of 1,2,3,4-tetrahydro-naphthalene-1-carbonyl chloride (74 mg, 0.38 mmol) in dichloromethane (3 mL) at 0°C. After stirring overnight at RT, the solvent is evaporated and the residue is purified by flash chromatography on silica gel (ethylacetate/cyclohexane 1:1) to give 1,2,3,4-tetrahydro-naphthalene-1-carboxylic acid (2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-amide (Compound No. I.g.011, 82 mg, 48%). M.p. = 179.2-181.3 °C. ¹H-NMR (400 MHz, CDCl₃): δ = 1.60-1.75 (m, 3H), 1.81-1.89 (m, 2H), 2.05-2.15 (m, 2H), 2.31 (s, 3H), 2.32-2.40 (m, 1H), 2.77-2.94 (m, 3H), 3.05-3.18 (m, 1H), 3.19-3.29 (m, 1H), 3.87 (t, 1H), 3.95-4.04 (m, 1H), 4.50-4.59 (m, 1H), 4.90-5.06 (2d, 2H, diastereotopic protons), 6.32 (s, 1H), 7.25-7.30 (m, 4H), 7.49 (s, 1H), 7.79 (br, 1H). MS: m/z = 532 (M+1).

Example 2: This example illustrates the preparation of 2-{1-[2-(5-Methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-carbamic acid phenyl ester (Compound No. I.g.023)

a) Preparation of 2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-carbamic acid phenyl ester (Compound No. I.g.023)

- To a solution of 1-[4-(4-amino-thiazol-2-yl)-piperidin-1-yl]-2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-ethanone (80 mg, 0.21 mmol) in dichloromethane (5 mL) is added diisopropylethylamine (0.053 mL, 0.25 mmol), and subsequently phenylchloroformate (0.033 mL, 0.21 mmol) at 0°C. After stirring overnight at RT, solvents are evaporated under reduced pressure and the residue is purified by column chromatography on silica gel (ethyl acetate/heptane 7:3) to give 2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-carbamic acid phenyl ester (Compound No. I.g.023, 71 mg, 67 %). ¹H-NMR (400 MHz, CDCl₃): δ = 1.57-1.78 (m, 2H), 2.08-2.19 (m, 2H), 2.22 (s, 3H), 2.75-2.81 (m, 1H), 3.05-3.20 (m, 2H), 3.95-3.99 (m, 1H), 4.44-4.52 (m, 1H), 4.83-4.98 (2d, 2H, diastereotopic protons), 6.25 (s, 1H), 7.05-7.20 (m, 3H), 7.29-7.38 (m, 2H), 7.95 (br, 1H). MS: m/z = 494 (M+1).

Example 3: This example illustrates the preparation of 1-(2-{1-[2-(5-Methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-3-phenyl-urea (Compound No. I.g.024)

- 5 a) Preparation of 1-(2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-3-phenyl-urea (Compound No. I.g.024)

To a solution of 1-[4-(4-amino-thiazol-2-yl)-piperidin-1-yl]-2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-ethanone (100 mg, 0.27 mmol) in THF (5 mL) is added dropwise a solution of phenylisocyanate (30 μ L, 0.28 mmol) in THF (1 mL) at 0°C. After
10 stirring overnight at RT, methanol (1 mL) is added to the reaction mixture. After stirring 15 min. at RT, the solvents are evaporated and the residue was triturated with diethylether (5 mL) to induce precipitation. The resulting solid is filtered and dried under vacuum to give 1-(2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-3-phenyl-urea as beige solid (Compound No. I.g.024, 105 mg, 79%). M.p. = 192.6 °C. ¹H-
15 NMR (400 MHz, CDCl₃): δ = ¹H-NMR (MeOD): d = 1.65 (m, 1H), 1.80 (m, 1H), 2.40 (m, 2H), 2.30 (s, 3H), 2.98 (m, 1H), 3.30 (m, 1H), 3.39 (m, 1H), 4.10 (m, 1H), 4.52 (m, 1H), 5.22 (2d, 2H, diastereotopic), 6.42 (s, 1H), 7.05 (t, 1H), 7.09 (s, 1H), 7.26 – 7.45 (m, 6H). MS: m/z = 494 (M+1).

- 20 Example 4: This example illustrates the preparation of N-(2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-C-phenyl-methanesulfonamide (Compound No. I.g.025)

- a) Preparation of N-(2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-benzenesulfonamide (Compound No. I.g.025)

To a solution of 1-[4-(4-amino-thiazol-2-yl)-piperidin-1-yl]-2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-ethanone (100 mg, 0.04 mmol) in dimethylacetamide (0.8 mL) is added diisopropylethylamine (8.6 μ L, 0.28 mmol), followed by benzenesulfonyl chloride (8.8 mg, 0.05 mmol) at RT. After stirring 15 min at 60 °C, the reaction mixture is purified
30 directly by preparative HPLC to give N-(2-{1-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-benzenesulfonamide (Compound No. I.g.025). MS: m/z = 514 (M+1).

- Example 5: This example illustrates the preparation of N-(2-{1-[2-(2,5-Dimethyl-phenyl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-2-phenyl-propionamide (Compound No. I.g.141)

a) Preparation of 2-{1-[2-(2,5-dimethyl-phenyl)-acetyl]-piperidin-4-yl}-thiazole-4-carboxylic acid ethyl ester

To a solution of 2,5-dimethylphenylacetic acid (5.45 g, 27.4 mmol) in DMF (80 mL) is added diisopropylethylamine (85.4 mL, 411.32 mmol), followed by O-(benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium tetrafluoroborate (12.8 g, 32.9 mmol) at 0 °C. After stirring 15 min at RT, 2-piperidin-4-yl-thiazole-4-carboxylic acid ethyl ester (6.59 g, 27.4 mmol) is added to the reaction mixture. After stirring overnight at RT, solvent is evaporated and the resulting yellow oil is dissolved in ethylacetate (500 mL), washed with aqueous saturated sodium bicarbonate solution (500 mL) and the aqueous phase is re-extracted with ethylacetate (100 mL). The combined organic layers are washed with 0.5M HCl solution (400 mL) and brine (400 mL), dried over sodium sulfate, filtered, and evaporated under reduced pressure to give 2-{1-[2-(2,5-dimethyl-phenyl)-acetyl]-piperidin-4-yl}-thiazole-4-carboxylic acid ethyl ester (10.46 g, 98 %), which can be used in the next step without further purification. ¹H-NMR (400 MHz, CDCl₃): δ = 1.41 (t, 3H), 1.52-1.82 (m, 2H), 2.10-2.22 (m, 2H), 2.25 (s, 3H), 2.30 (s, 3H), 2.73-2.86 (m, 1H), 3.08-3.22 (m, 1H), 3.29-3.40 (m, 1H), 3.68 (s, 2H), 3.8-3.95 (m, 1H), 4.38-4.42 (q, 2H), 4.73-4.88 (m, 1H), 6.96 (s, 1H), 6.98-7.01 (d, 1H), 7.08 (d, 1H), 8.10 (s, 1H). MS: m/z = 387 (M+1).

b) Preparation of 2-{1-[2-(2,5-dimethyl-phenyl)-acetyl]-piperidin-4-yl}-thiazole-4-carboxylic acid

To a solution of 2-{1-[2-(2,5-dimethyl-phenyl)-acetyl]-piperidin-4-yl}-thiazole-4-carboxylic acid ethyl ester (10.46 g, 27.06 mmol) in THF (30 mL) is added aqueous solution of sodium hydroxide (2 M, 20.3 mL) at RT. After stirring 3h at RT, the reaction mixture is acidified with aqueous solution of HCl (2 M) until pH 2-3, and ethylacetate (30 mL) is added to the reaction mixture, and layers are separated. The aqueous layer is extracted with ethyl acetate (20 mL) and the combined organic layers are washed with brine (10 mL), dried over sodium sulfate, filtered, and evaporated under reduced pressure to give 2-{1-[2-(2,5-dimethyl-phenyl)-acetyl]-piperidin-4-yl}-thiazole-4-carboxylic acid (5.9 g, 60.8 %), which can be used in the next step without further purification. ¹H-NMR (400 MHz, d₆-DMSO): δ = 1.55-1.65 (m, 2H), 2.01-2.12 (m, 2H), 2.15 (s, 3H), 2.22 (s, 3H), 2.77-2.86 (m, 1H), 3.18-3.29 (m, 1H), 3.65 (d, 2H), 3.98-4.07 (m, 1H), 4.45-4.53 (m, 1H), 6.90 (s, 1H), 6.92 (s, 1H), 6.93 (s, 1H), 7.04 (d, 1H), 8.49 (br, 1H), 12.95 (s, 1H). MS: m/z = 359 (M+1).

c) Preparation of (2-{1-[2-(2,5-dimethyl-phenyl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-carbamic acid tert-butyl ester

To a solution of 2-{1-[2-(2,5-dimethyl-phenyl)-acetyl]-piperidin-4-yl}-thiazole-4-carboxylic acid (5.65 g, 15.76 mmol) in *tert*-butanol (60 mL) is added triethylamine (5.2 mL,

36.2 mmol). After stirring 30 min. at RT, diphenylphosphoryl azide (6.9 mL, 31.5 mmol) is added and the reaction mixture is divided in 4 portions and each portion is irradiated under microwave (100 °C, 15 min.). After cooling to RT, all portions are combined and water (1 mL) is added to the reaction mixture and stirred for 30 minutes. Acetonitrile (50 mL) is then added, followed by addition of basic Amberlyst A21. After stirring overnight at RT, the resin is filtered off, and solvents are evaporated under reduced pressure. The remainder is purified by column chromatography on silica gel (ethyl acetate/cyclohexane 7:3) to give (2-{1-[2-(2,5-dimethyl-phenyl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-carbamic acid tert-butyl ester (4.93 g, 73 %). ¹H-NMR (400 MHz, CDCl₃): δ = 1.53 (s, 9H), 1.53-1.61 (m, 1H), 1.67-1.79 (m, 1H), 1.95-2.04 (m, 1H), 2.08-2.14 (m, 1H), 2.25 (s, 3H), 2.30 (s, 3H), 2.80-2.90 (m, 1H), 3.06-3.20 (m, 2H), 3.68 (s, 2H), 3.80-3.89 (m, 1H), 4.68-4.74 (m, 1H), 6.95 (s, 1H), 6.98 (d, 1H), 7.07 (d, 1H), 7.23 (s, 1H). MS: m/z = 430 (M+1).

d) Preparation of 1-[4-(4-amino-thiazol-2-yl)-piperidin-1-yl]-2-(2,5-dimethyl-phenyl)-ethanone

To a solution of (2-{1-[2-(2,5-dimethyl-phenyl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-carbamic acid tert-butyl ester (5.65 g, 13.15 mmol) is added a solution of 4M HCl in dioxane (35 mL) at RT. After stirring 3 days at RT, the solvent is evaporated under reduce pressure. The resulting solid is triturated with diethylether, and filtered to give 1-[4-(4-amino-thiazol-2-yl)-piperidin-1-yl]-2-(2,5-dimethyl-phenyl)-ethanone hydrochloride salt, which is suspended in aqueous saturated sodium bicarbonate (500 mL). After stirring 30 min at RT, the reaction mixture is extracted with ethyl acetate (500 mL). The combined organic layers are washed with water (100 mL) and brine (100 mL), filtered, dried over sodium sulfate, and evaporated under reduced pressure to give 1-[4-(4-amino-thiazol-2-yl)-piperidin-1-yl]-2-(2,5-dimethyl-phenyl)-ethanone (3.27 g, 75 %). ¹H-NMR (400 MHz, CDCl₃): δ = 1.53-1.61 (m, 1H), 1.67-1.79 (m, 1H), 1.95-2.04 (m, 1H), 2.08-2.13 (m, 1H), 2.25 (s, 3H), 2.30 (s, 3H), 2.78-2.88 (m, 1H), 3.06-3.20 (m, 2H), 3.68 (s, 2H), 3.80-3.89 (m, 1H), 4.05 (s, 1H), 4.68-4.74 (m, 1H), 6.95 (s, 1H), 6.98 (d, 1H), 7.07 (d, 1H), 7.23 (s, 1H). MS: m/z = 330 (M+1). MS: m/z = 330 (M+1).

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e) Preparation of N-(2-{1-[2-(2,5-dimethyl-phenyl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-2-phenyl-propionamide (Compound No. I.g.141)

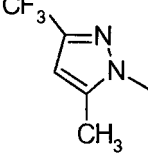
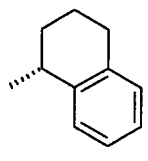
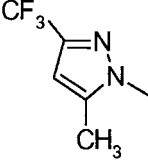
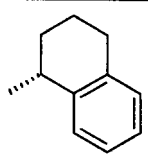
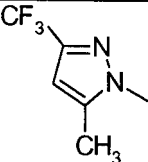
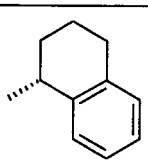
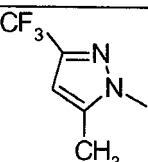
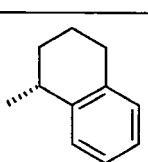
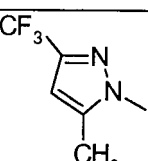
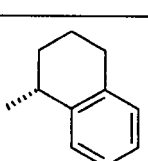
To a solution of (rac.)-2-phenylpropionic acid (46 mg, 0.30 mmol) and diisopropylethylamine (0.15 mL, 0.9 mmol) in acetonitrile (2 mL) is added benzotriazole-1-yl-oxy-tris-(dimethylamino)-phosphonium hexafluorophosphate (322 mg, 0.73 mmol) at RT. After stirring 30 min at RT, 1-[4-(4-amino-thiazol-2-yl)-piperidin-1-yl]-2-(2,5-dimethyl-phenyl)-ethanone (100 mg, 0.30 mmol) is added to the reaction mixture. After stirring

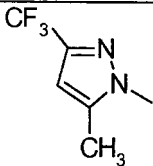
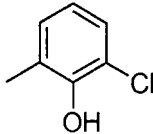
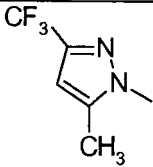
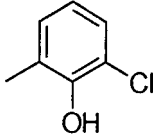
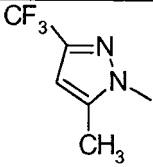
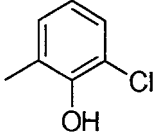
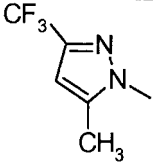
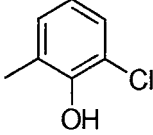
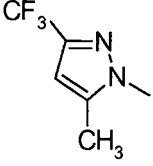
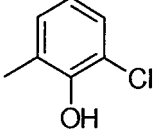
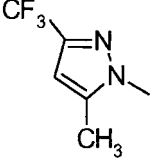
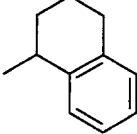
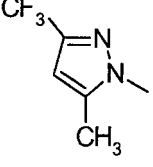
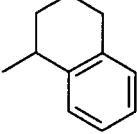
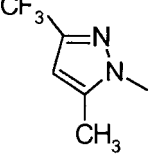
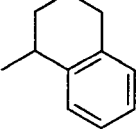
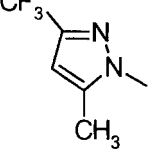
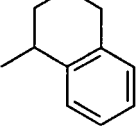
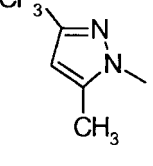
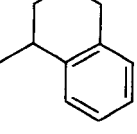
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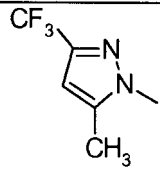
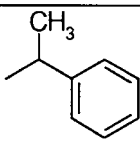
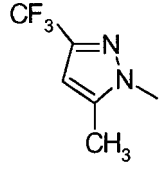
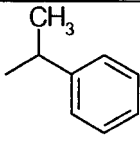
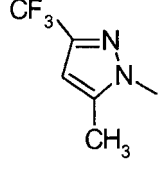
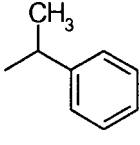
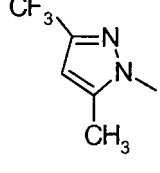
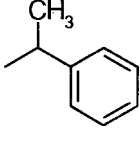
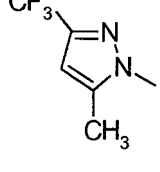
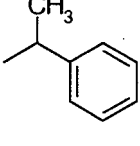
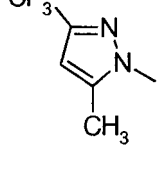
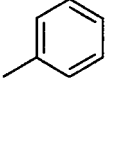
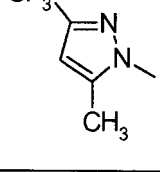
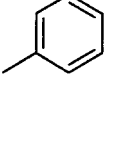
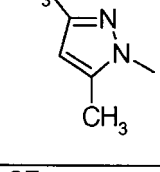
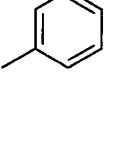
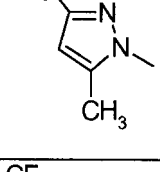
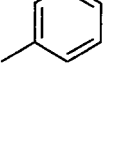
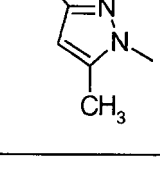
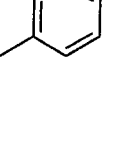
overnight at RT, the solvent is evaporated and the residue is purified by flash chromatography on silica gel (ethylacetate/cyclohexane 1:1) to give N-(2-{1-[2-(2,5-dimethyl-phenyl)-acetyl]-piperidin-4-yl}-thiazol-4-yl)-2-phenyl-propionamide (Compound No. 1.g.141, 19 mg, 13.4%). ¹H-NMR (400 MHz, CDCl₃): δ = 1.46-1.39 (m, 1H), 1.52 (d, 3H), 1.68-1.56 (m, 1H), 1.89-1.83 (m, 1H), 2.01-1.97 (m, 1H), 2.15 (s, 3H), 2.19 (s, 3H), 2.73-2.67 (m, 1H), 3.18-2.92 (m, 2H), 3.59 (s, 2H), 3.68-3.63 (q, 1H), 3.78-3.71 (m, 1H), 4.65-4.62 (m, 1H), 6.91-6.82 (m, 2H), 7.02-6.98 (m, 1H), 7.31-7.15 (m, 5H), 7.42 (s, 1H), 8.05 (br, 1H). MS: m/z = 462 (M+1).

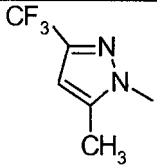
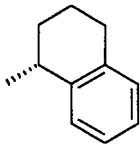
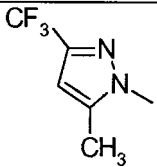
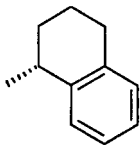
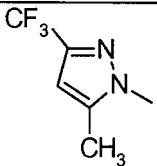
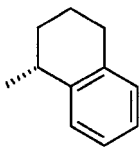
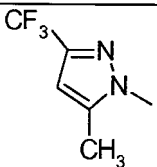
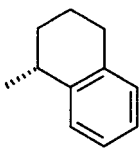
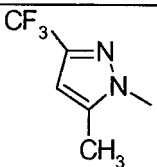
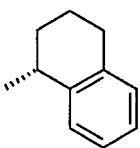
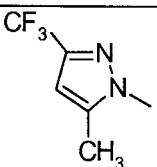
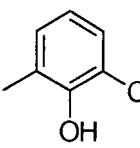
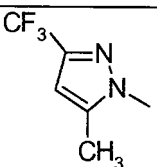
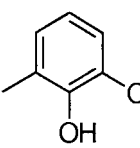
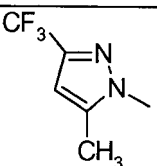
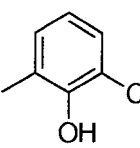
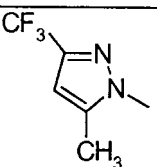
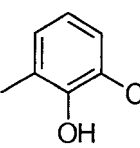
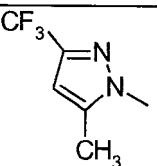
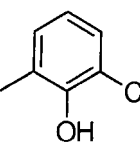
- 10 Table 1 below illustrates examples of individual compounds of formula I according to the invention.

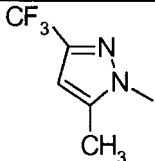
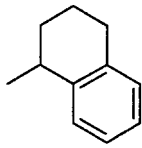
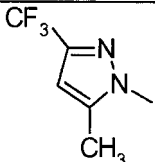
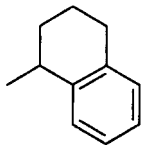
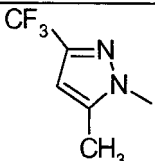
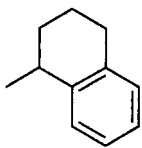
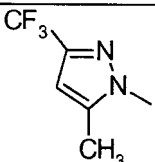
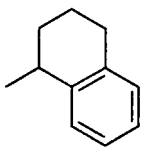
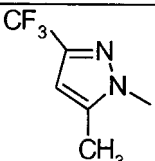
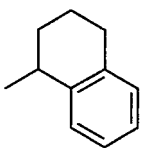
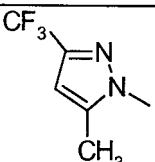
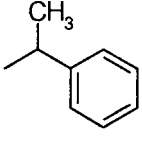
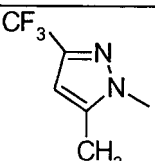
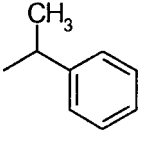
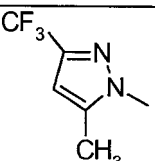
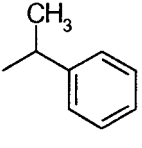
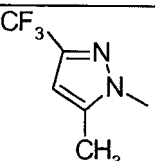
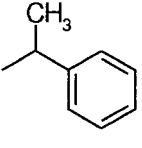
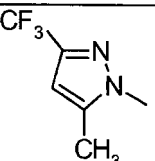
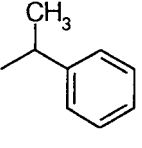
Table 1: individual compounds of formula I according to the invention

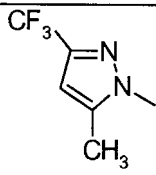
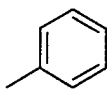
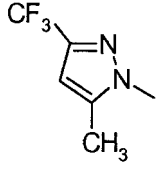
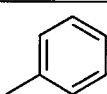
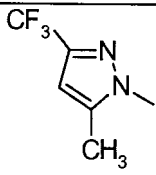
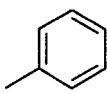
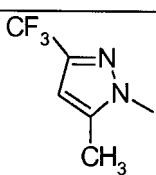
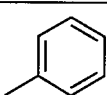
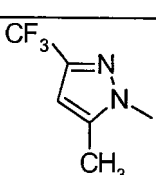
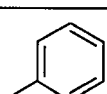
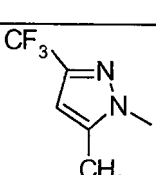
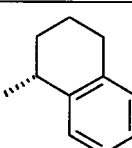
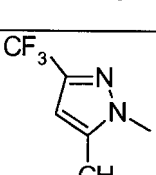
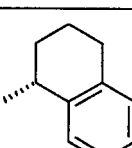
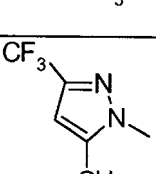
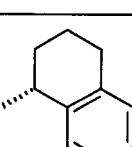
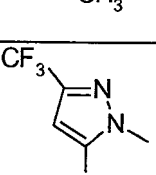
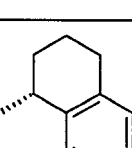
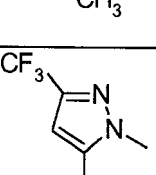
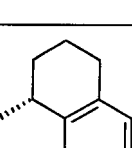
Compound No.	R ¹	A	Q	R ⁹
001		-CH ₂ C(=O)-	-C(=O)-	
002		-CH ₂ C(=O)-	-C(=S)-	
003		-CH ₂ C(=O)-	-C(=O)O-	
004		-CH ₂ C(=O)-	-C(=O)NH-	
005		-CH ₂ C(=O)-	-SO ₂ -	

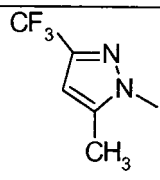
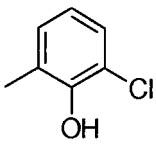
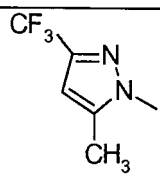
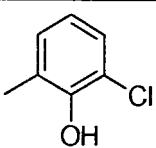
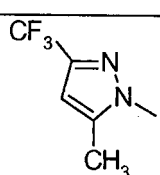
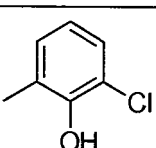
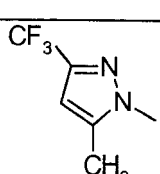
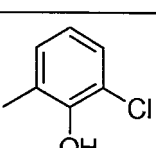
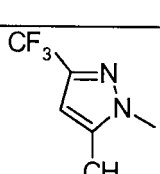
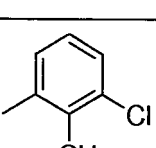
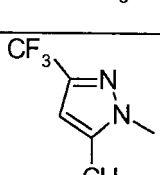
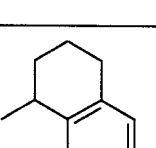
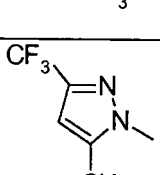
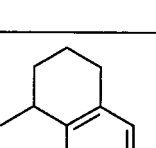
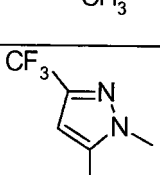
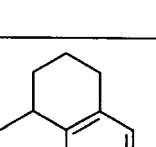
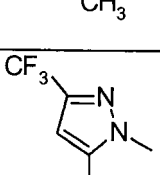
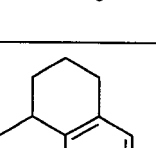
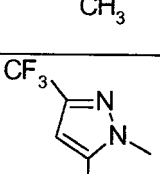
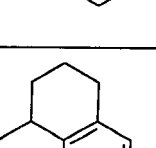
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007		-CH ₂ C(=O)-	-C(=S)-	
008		-CH ₂ C(=O)-	-C(=O)O-	
009		-CH ₂ C(=O)-	-C(=O)NH-	
010		-CH ₂ C(=O)-	-SO ₂ -	
011		-CH ₂ C(=O)-	-C(=O)-	
012		-CH ₂ C(=O)-	-C(=S)-	
013		-CH ₂ C(=O)-	-C(=O)O-	
014		-CH ₂ C(=O)-	-C(=O)NH-	
015		-CH ₂ C(=O)-	-SO ₂ -	

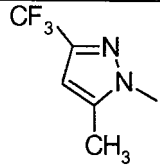
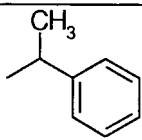
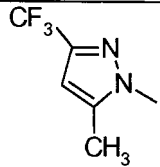
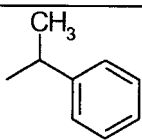
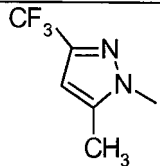
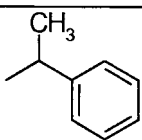
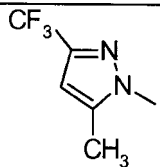
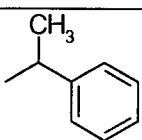
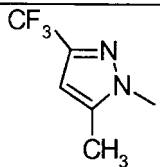
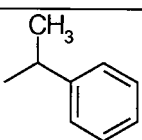
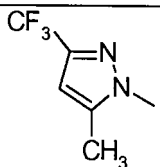
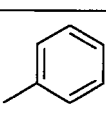
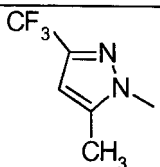
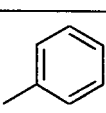
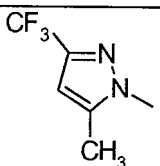
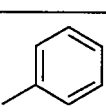
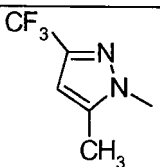
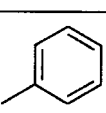
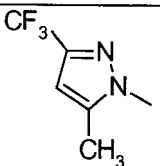
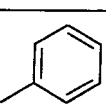
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017		-CH ₂ C(=O)-	-C(=S)-	
018		-CH ₂ C(=O)-	-C(=O)O-	
019		-CH ₂ C(=O)-	-C(=O)NH-	
020		-CH ₂ C(=O)-	-SO ₂ -	
021		-CH ₂ C(=O)-	-C(=O)-	
022		-CH ₂ C(=O)-	-C(=S)-	
023		-CH ₂ C(=O)-	-C(=O)O-	
024		-CH ₂ C(=O)-	-C(=O)NH-	
025		-CH ₂ C(=O)-	-SO ₂ -	

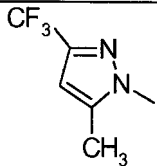
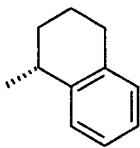
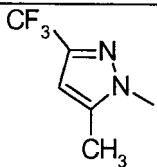
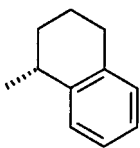
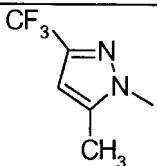
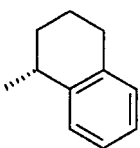
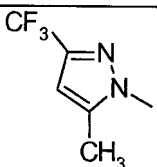
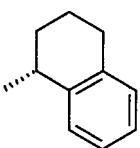
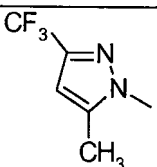
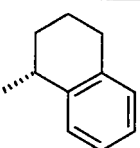
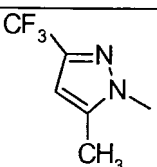
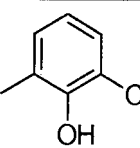
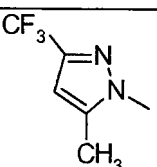
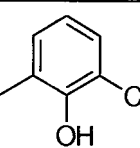
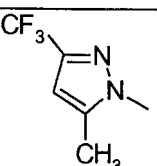
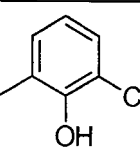
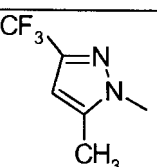
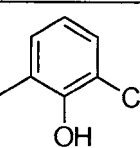
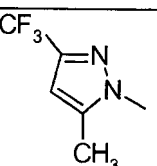
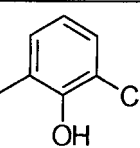
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027		-CH ₂ C(=S)-	-C(=S)-	
028		-CH ₂ C(=S)-	-C(=O)O-	
029		-CH ₂ C(=S)-	-C(=O)NH-	
030		-CH ₂ C(=S)-	-SO ₂ -	
031		-CH ₂ C(=S)-	-C(=O)-	
032		-CH ₂ C(=S)-	-C(=S)-	
033		-CH ₂ C(=S)-	-C(=O)O-	
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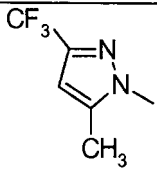
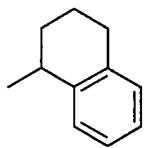
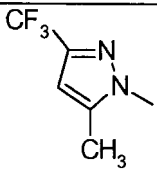
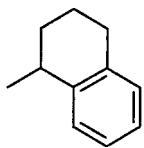
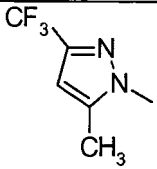
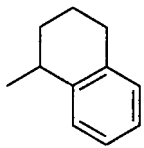
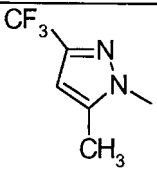
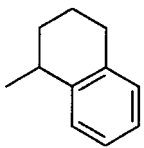
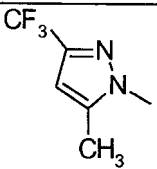
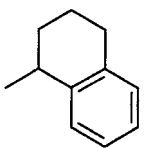
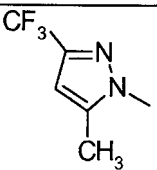
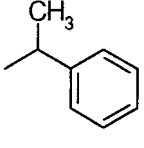
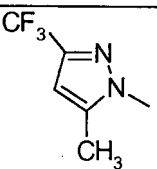
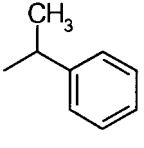
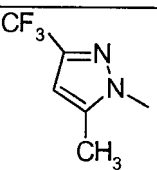
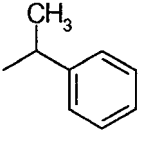
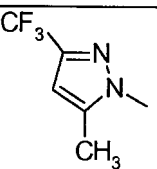
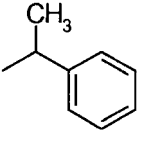
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037		-CH ₂ C(=S)-	-C(=S)-	
038		-CH ₂ C(=S)-	-C(=O)O-	
039		-CH ₂ C(=S)-	-C(=O)NH-	
040		-CH ₂ C(=S)-	-SO ₂ -	
041		-CH ₂ C(=S)-	-C(=O)-	
042		-CH ₂ C(=S)-	-C(=S)-	
043		-CH ₂ C(=S)-	-C(=O)O-	
044		-CH ₂ C(=S)-	-C(=O)NH-	
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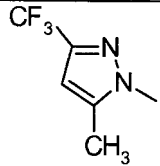
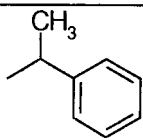
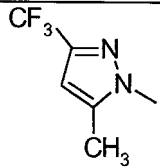
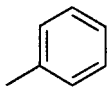
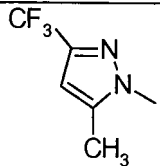
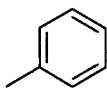
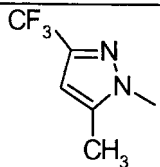
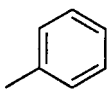
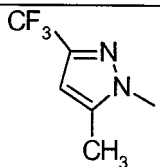
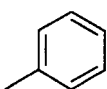
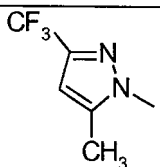
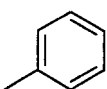
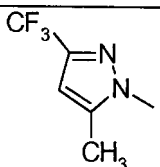
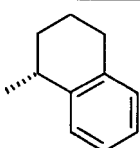
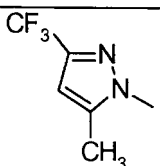
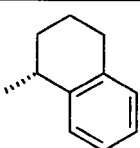
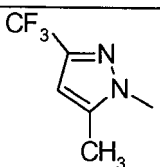
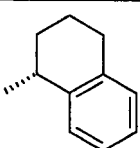
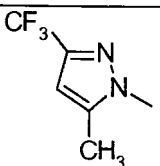
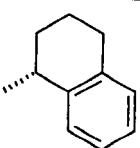
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047		-CH ₂ C(=S)-	-C(=S)-	
048		-CH ₂ C(=S)-	-C(=O)O-	
049		-CH ₂ C(=S)-	-C(=O)NH-	
050		-CH ₂ C(=S)-	-SO ₂ -	
051		-OC(=O)-	-C(=O)-	
052		-OC(=O)-	-C(=S)-	
053		-OC(=O)-	-C(=O)O-	
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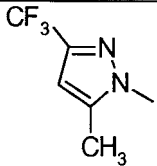
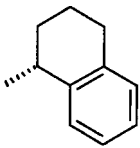
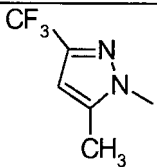
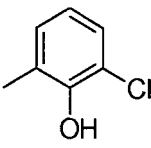
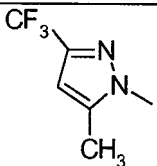
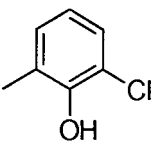
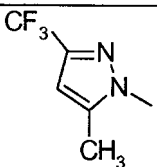
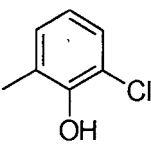
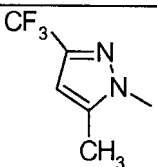
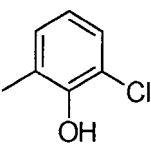
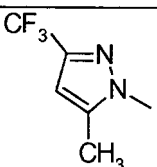
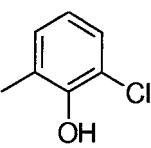
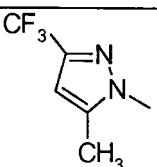
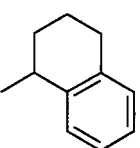
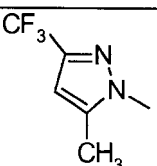
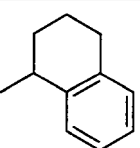
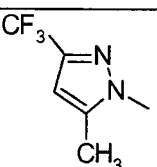
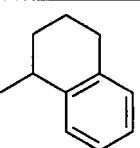
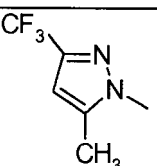
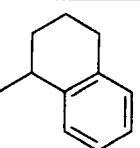
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058		-OC(=O)-	-C(=O)O-	
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060		-OC(=O)-	-SO ₂ -	
061		-OC(=O)-	-C(=O)-	
062		-OC(=O)-	-C(=S)-	
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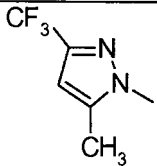
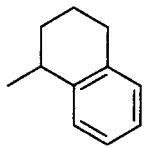
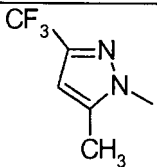
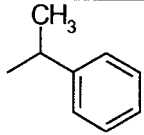
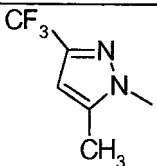
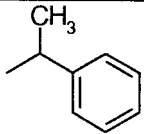
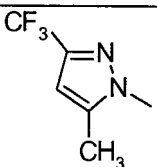
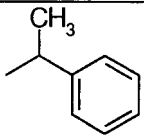
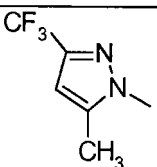
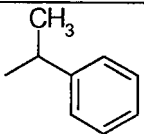
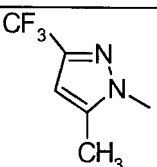
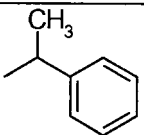
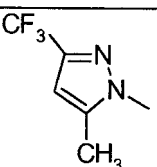
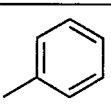
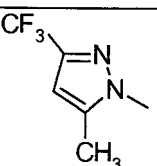
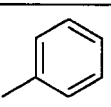
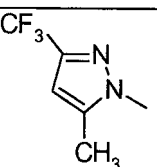
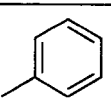
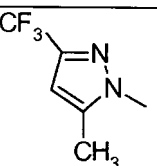
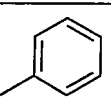
066		-OC(=O)-	-C(=O)-	
067		-OC(=O)-	-C(=S)-	
068		-OC(=O)-	-C(=O)O-	
069		-OC(=O)-	-C(=O)NH-	
070		-OC(=O)-	-SO ₂ -	
071		-OC(=O)-	-C(=O)-	
072		-OC(=O)-	-C(=S)-	
073		-OC(=O)-	-C(=O)O-	
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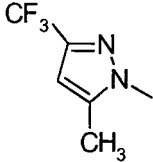
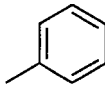
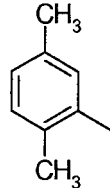
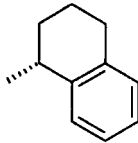
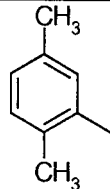
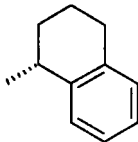
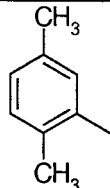
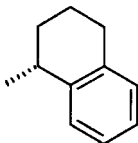
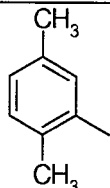
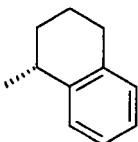
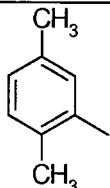
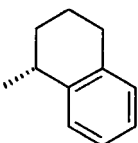
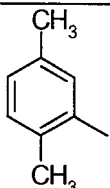
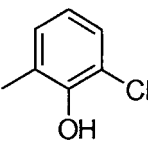
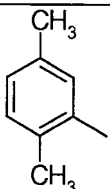
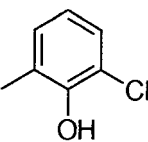
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078		-C(=O)-	-C(=O)O-	
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080		-C(=O)-	-SO ₂ -	
081		-C(=O)-	-C(=O)-	
082		-C(=O)-	-C(=S)-	
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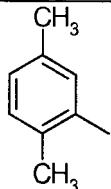
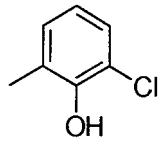
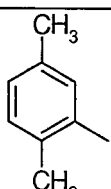
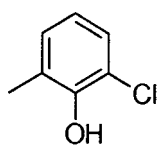
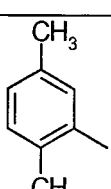
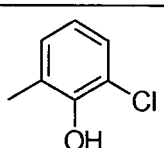
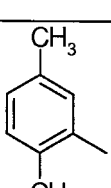
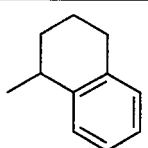
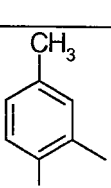
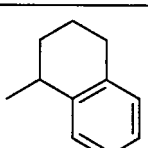
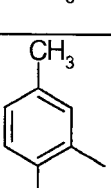
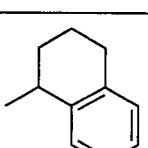
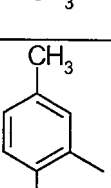
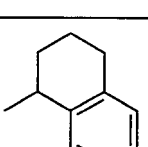
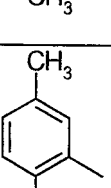
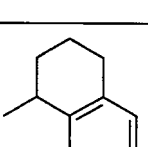
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088		-C(=O)-	-C(=O)O-	
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090		-C(=O)-	-SO ₂ -	
091		-C(=O)-	-C(=O)-	
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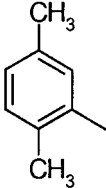
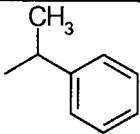
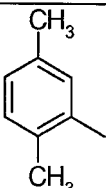
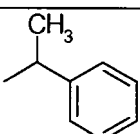
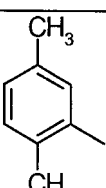
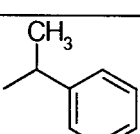
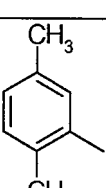
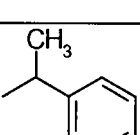
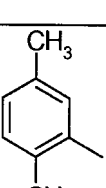
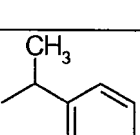
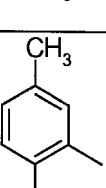
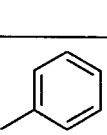
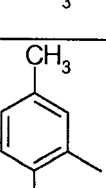
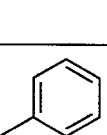
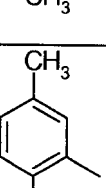
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098		-C(=O)-	-C(=O)O-	
099		-C(=O)-	-C(=O)NH-	
100		-C(=O)-	-SO ₂ -	
101		-CH ₂ SO ₂ -	-C(=O)-	
102		-CH ₂ SO ₂ -	-C(=S)-	
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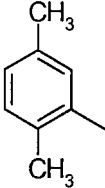
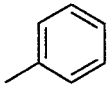
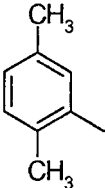
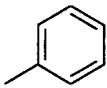
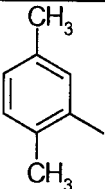
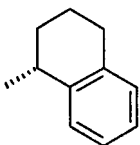
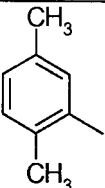
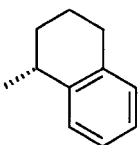
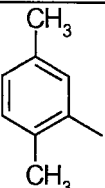
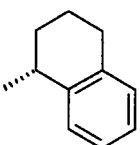
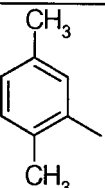
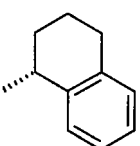
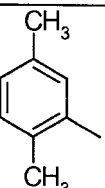
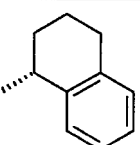
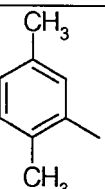
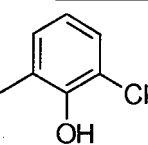
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107		-CH ₂ SO ₂ -	-C(=S)-	
108		-CH ₂ SO ₂ -	-C(=O)O-	
109		-CH ₂ SO ₂ -	-C(=O)NH-	
110		-CH ₂ SO ₂ -	-SO ₂ -	
111		-CH ₂ SO ₂ -	-C(=O)-	
112		-CH ₂ SO ₂ -	-C(=S)-	
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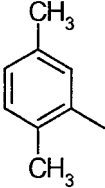
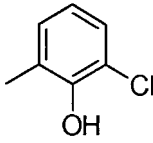
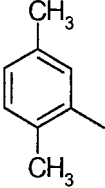
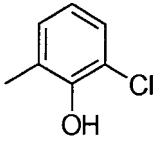
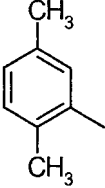
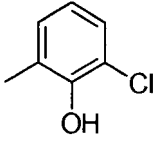
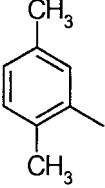
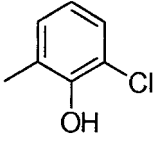
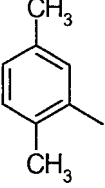
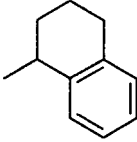
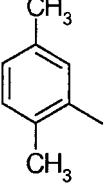
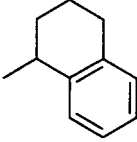
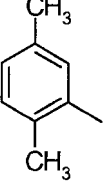
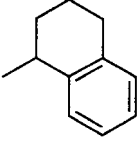
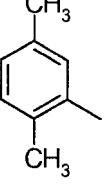
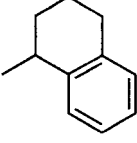
115		-CH ₂ SO ₂ -	-SO ₂ -	
116		-CH ₂ SO ₂ -	-C(=O)-	
117		-CH ₂ SO ₂ -	-C(=S)-	
118		-CH ₂ SO ₂ -	-C(=O)O-	
119		-CH ₂ SO ₂ -	-C(=O)NH-	
120		-CH ₂ SO ₂ -	-SO ₂ -	
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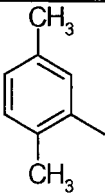
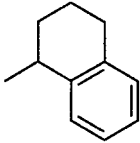
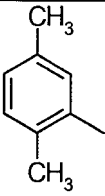
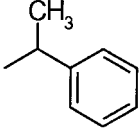
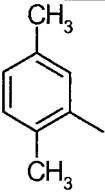
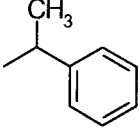
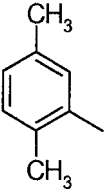
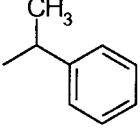
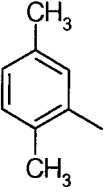
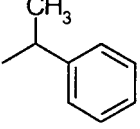
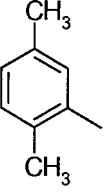
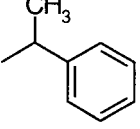
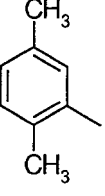
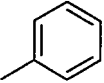
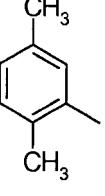
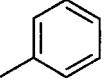
125		-CH ₂ SO ₂ -	-SO ₂ -	
126		-CH ₂ C(=O)-	-C(=O)-	
127		-CH ₂ C(=O)-	-C(=S)-	
128		-CH ₂ C(=O)-	-C(=O)O-	
129		-CH ₂ C(=O)-	-C(=O)NH-	
130		-CH ₂ C(=O)-	-SO ₂ -	
131		-CH ₂ C(=O)-	-C(=O)-	
132		-CH ₂ C(=O)-	-C(=S)-	

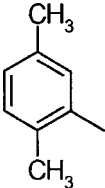
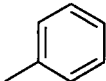
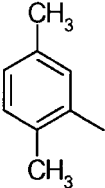
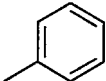
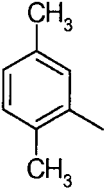
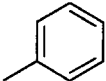
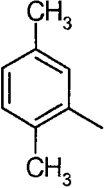
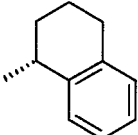
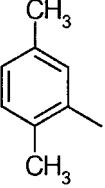
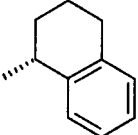
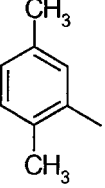
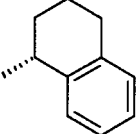
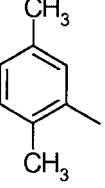
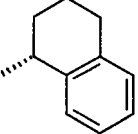
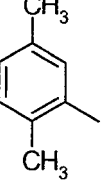
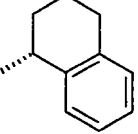
133		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{O})\text{O}-$	
134		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{O})\text{NH}-$	
135		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{SO}_2-$	
136		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{O})-$	
137		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{S})-$	
138		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{O})\text{O}-$	
139		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{O})\text{NH}-$	
140		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{SO}_2-$	

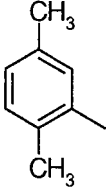
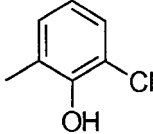
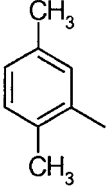
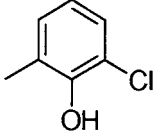
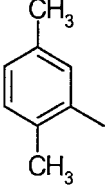
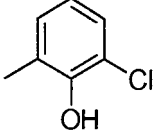
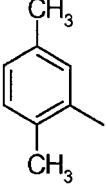
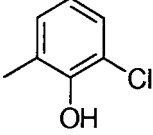
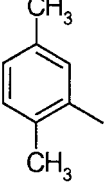
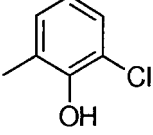
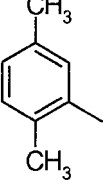
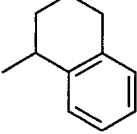
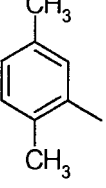
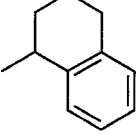
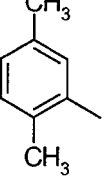
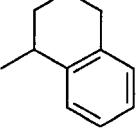
141		-CH ₂ C(=O)-	-C(=O)-	
142		-CH ₂ C(=O)-	-C(=S)-	
143		-CH ₂ C(=O)-	-C(=O)O-	
144		-CH ₂ C(=O)-	-C(=O)NH-	
145		-CH ₂ C(=O)-	-SO ₂ -	
146		-CH ₂ C(=O)-	-C(=O)-	
147		-CH ₂ C(=O)-	-C(=S)-	
148		-CH ₂ C(=O)-	-C(=O)O-	

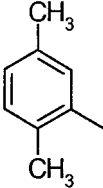
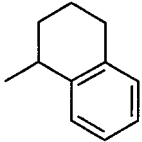
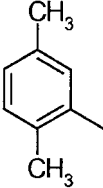
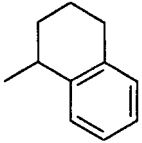
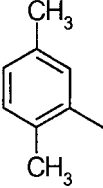
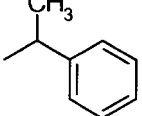
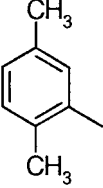
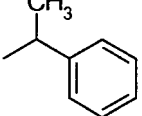
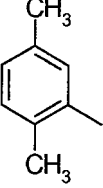
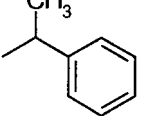
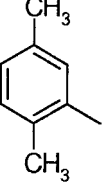
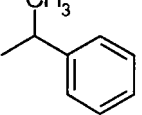
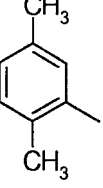
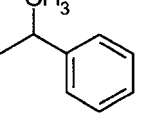
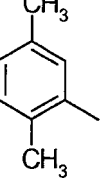
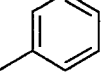
149		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{O})\text{NH}-$	
150		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{SO}_2-$	
151		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})-$	
152		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{S})-$	
153		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})\text{O}-$	
154		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})\text{NH}-$	
155		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{SO}_2-$	
156		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})-$	

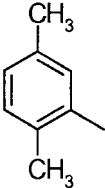
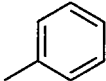
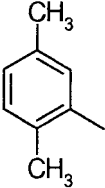
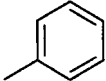
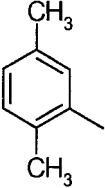
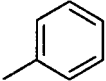
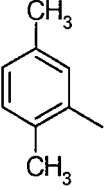
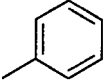
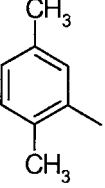
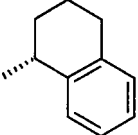
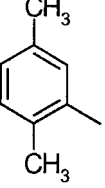
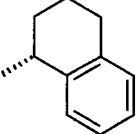
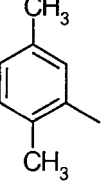
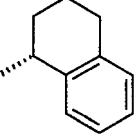
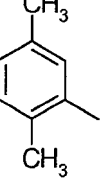
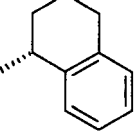
157		-CH ₂ C(=S)-	-C(=S)-	
158		-CH ₂ C(=S)-	-C(=O)O-	
159		-CH ₂ C(=S)-	-C(=O)NH-	
160		-CH ₂ C(=S)-	-SO ₂ -	
161		-CH ₂ C(=S)-	-C(=O)-	
162		-CH ₂ C(=S)-	-C(=S)-	
163		-CH ₂ C(=S)-	-C(=O)O-	
164		-CH ₂ C(=S)-	-C(=O)NH-	

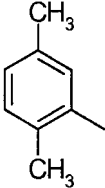
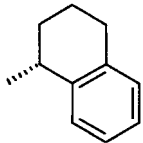
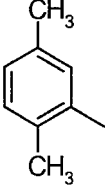
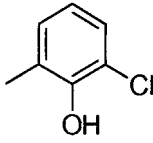
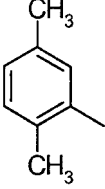
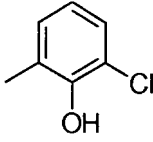
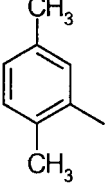
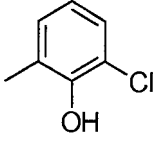
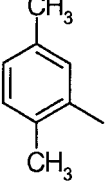
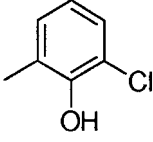
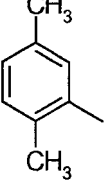
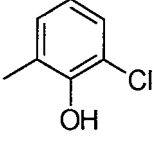
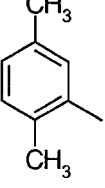
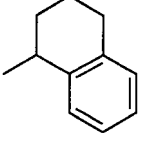
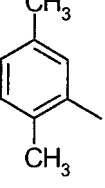
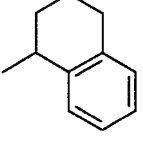
165		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{SO}_2-$	
166		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})-$	
167		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{S})-$	
168		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})\text{O}-$	
169		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})\text{NH}-$	
170		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{SO}_2-$	
171		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})-$	
172		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{S})-$	

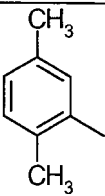
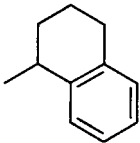
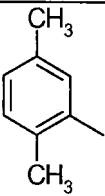
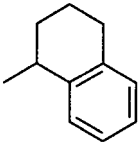
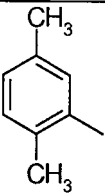
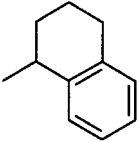
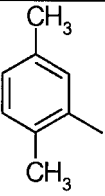
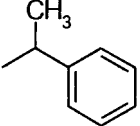
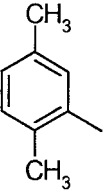
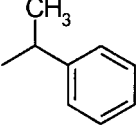
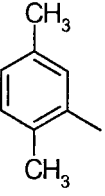
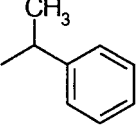
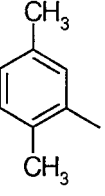
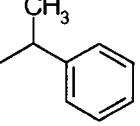
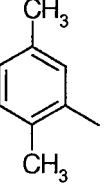
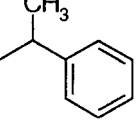
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174		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})\text{NH}-$	
175		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{SO}_2-$	
176		$-\text{OC}(=\text{O})-$	$-\text{C}(=\text{O})-$	
177		$-\text{OC}(=\text{O})-$	$-\text{C}(=\text{S})-$	
178		$-\text{OC}(=\text{O})-$	$-\text{C}(=\text{O})\text{O}-$	
179		$-\text{OC}(=\text{O})-$	$-\text{C}(=\text{O})\text{NH}-$	
180		$-\text{OC}(=\text{O})-$	$-\text{SO}_2-$	

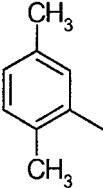
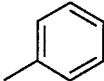
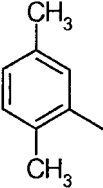
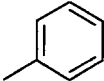
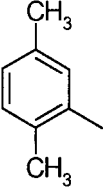
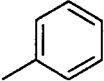
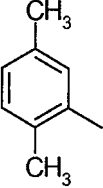
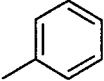
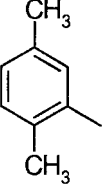
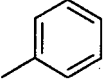
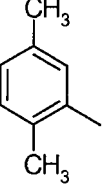
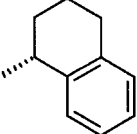
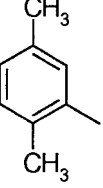
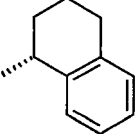
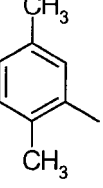
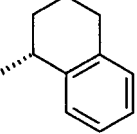
181		-OC(=O)-	-C(=O)-	
182		-OC(=O)-	-C(=S)-	
183		-OC(=O)-	-C(=O)O-	
184		-OC(=O)-	-C(=O)NH-	
185		-OC(=O)-	-SO ₂ -	
186		-OC(=O)-	-C(=O)-	
187		-OC(=O)-	-C(=S)-	
188		-OC(=O)-	-C(=O)O-	

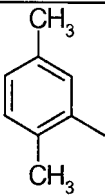
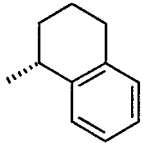
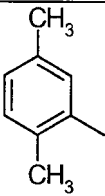
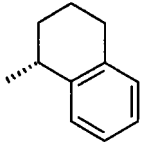
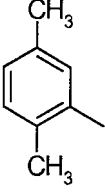
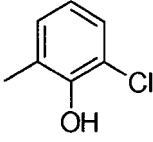
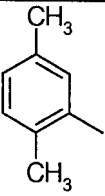
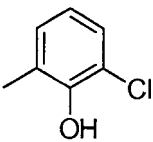
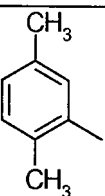
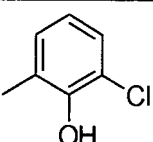
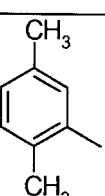
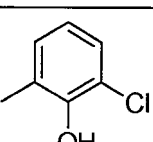
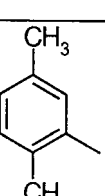
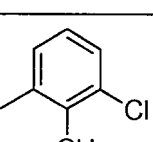
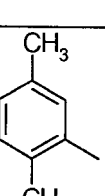
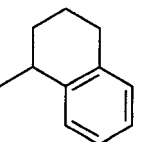
189		-OC(=O)-	-C(=O)NH-	
190		-OC(=O)-	-SO ₂ -	
191		-OC(=O)-	-C(=O)-	
192		-OC(=O)-	-C(=S)-	
193		-OC(=O)-	-C(=O)O-	
194		-OC(=O)-	-C(=O)NH-	
195		-OC(=O)-	-SO ₂ -	
196		-OC(=O)-	-C(=O)-	

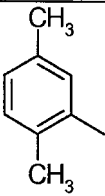
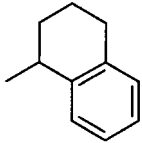
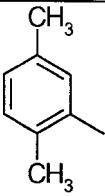
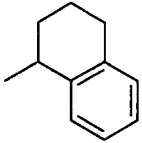
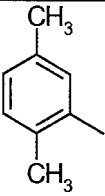
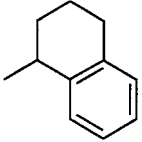
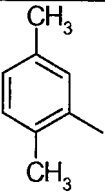
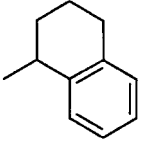
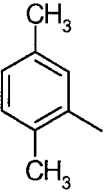
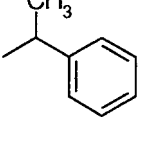
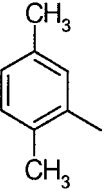
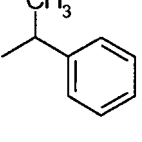
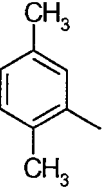
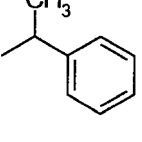
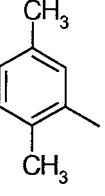
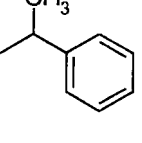
197		-OC(=O)-	-C(=S)-	
198		-OC(=O)-	-C(=O)O-	
199		-OC(=O)-	-C(=O)NH-	
200		-OC(=O)-	-SO ₂ -	
201		-C(=O)-	-C(=O)-	
202		-C(=O)-	-C(=S)-	
203		-C(=O)-	-C(=O)O-	
204		-C(=O)-	-C(=O)NH-	

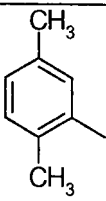
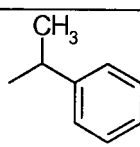
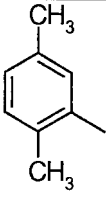
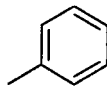
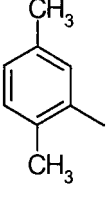
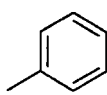
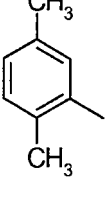
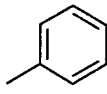
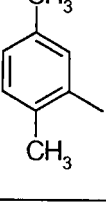
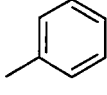
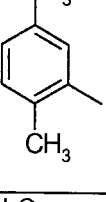
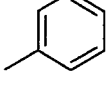
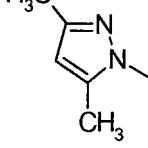
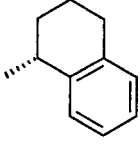
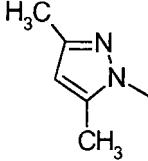
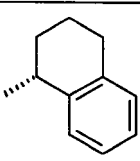
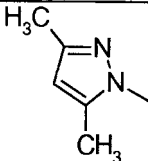
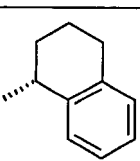
205		-C(=O)-	-SO ₂ -	
206		-C(=O)-	-C(=O)-	
207		-C(=O)-	-C(=S)-	
208		-C(=O)-	-C(=O)O-	
209		-C(=O)-	-C(=O)NH-	
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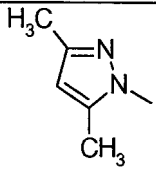
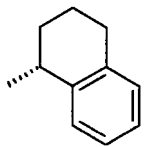
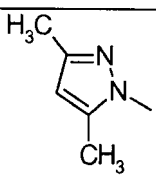
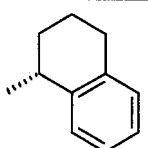
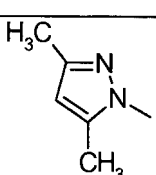
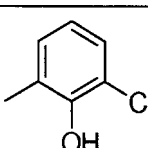
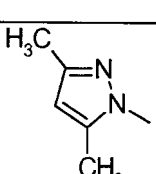
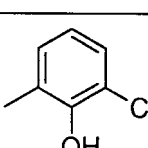
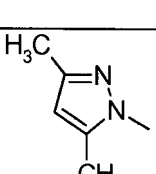
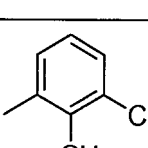
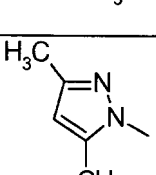
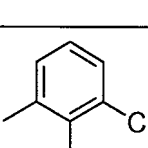
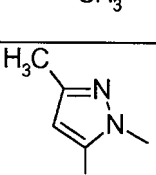
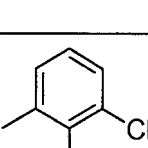
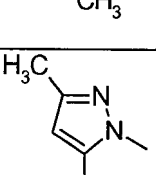
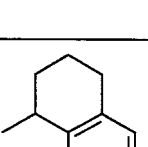
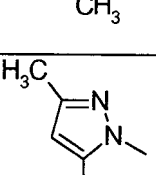
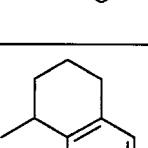
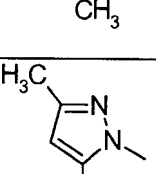
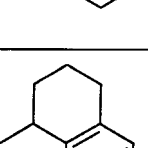
213		-C(=O)-	-C(=O)O-	
214		-C(=O)-	-C(=O)NH-	
215		-C(=O)-	-SO ₂ -	
216		-C(=O)-	-C(=O)-	
217		-C(=O)-	-C(=S)-	
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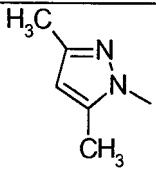
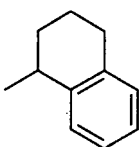
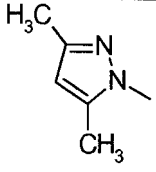
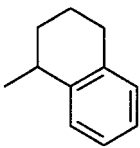
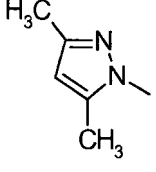
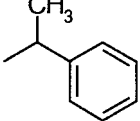
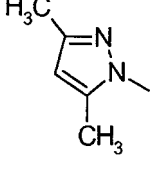
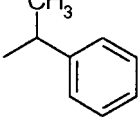
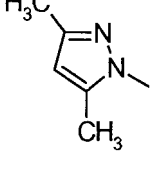
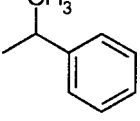
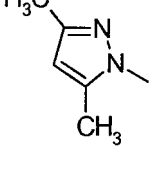
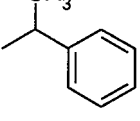
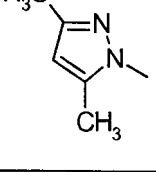
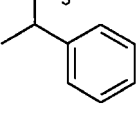
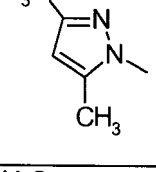
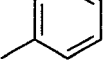
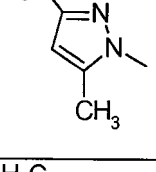
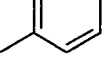
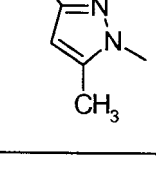
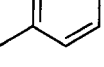
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222		-C(=O)-	-C(=S)-	
223		-C(=O)-	-C(=O)O-	
224		-C(=O)-	-C(=O)NH-	
225		-C(=O)-	-SO ₂ -	
226		-CH ₂ SO ₂ -	-C(=O)-	
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228		-CH ₂ SO ₂ -	-C(=O)O-	

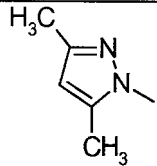
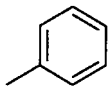
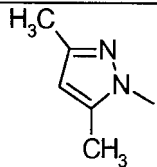
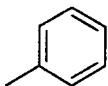
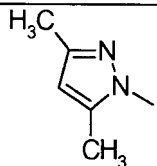
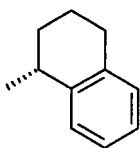
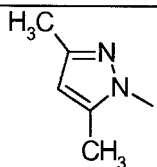
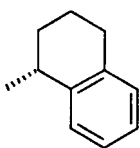
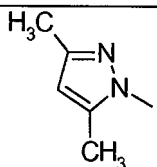
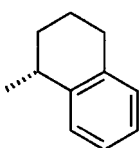
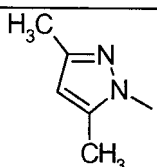
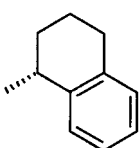
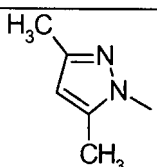
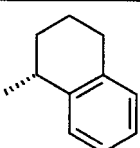
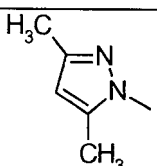
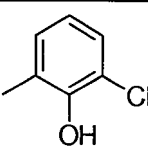
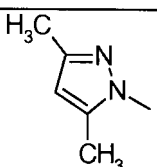
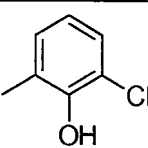
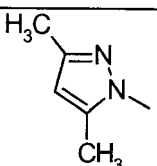
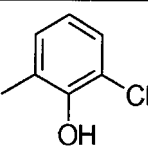
229		-CH ₂ SO ₂ -	-C(=O)NH-	
230		-CH ₂ SO ₂ -	-SO ₂ -	
231		-CH ₂ SO ₂ -	-C(=O)-	
232		-CH ₂ SO ₂ -	-C(=S)-	
233		-CH ₂ SO ₂ -	-C(=O)O-	
234		-CH ₂ SO ₂ -	-C(=O)NH-	
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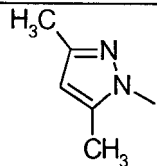
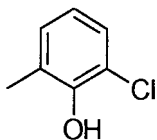
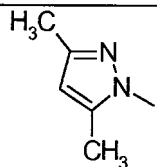
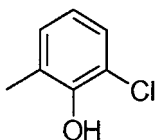
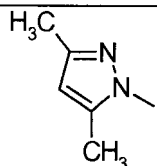
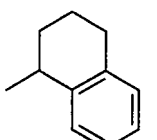
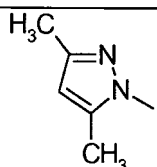
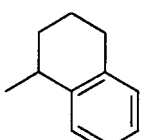
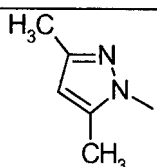
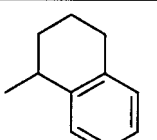
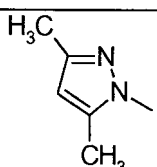
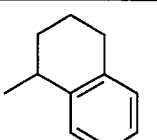
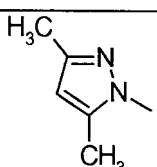
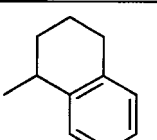
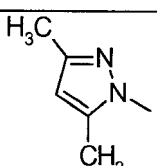
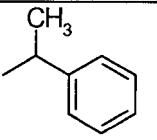
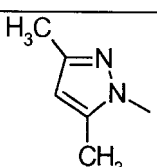
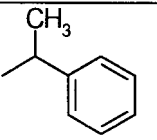
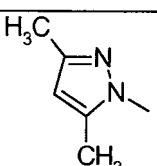
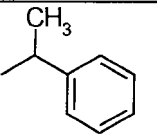
237		- CH ₂ SO ₂ -	-C(=S)-	
238		- CH ₂ SO ₂ -	-C(=O)O-	
239		- CH ₂ SO ₂ -	-C(=O)NH-	
240		- CH ₂ SO ₂ -	-SO ₂ -	
241		- CH ₂ SO ₂ -	-C(=O)-	
242		- CH ₂ SO ₂ -	-C(=S)-	
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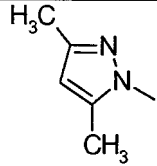
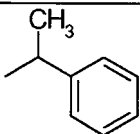
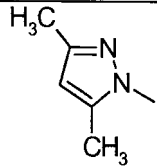
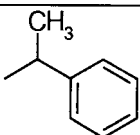
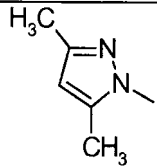
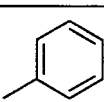
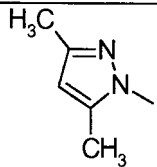
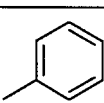
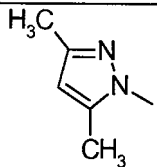
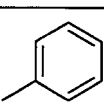
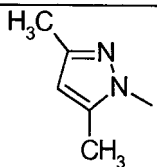
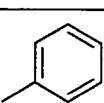
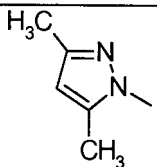
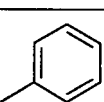
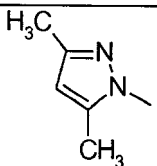
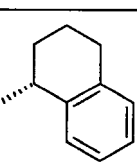
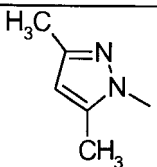
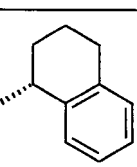
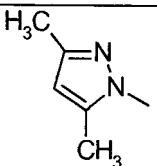
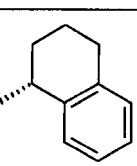
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247		-CH ₂ SO ₂ -	-C(=S)-	
248		-CH ₂ SO ₂ -	-C(=O)O-	
249		-CH ₂ SO ₂ -	-C(=O)NH-	
250		-CH ₂ SO ₂ -	-SO ₂ -	
251		-CH ₂ C(=O)-	-C(=O)-	
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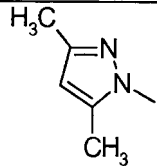
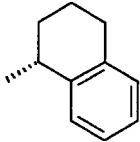
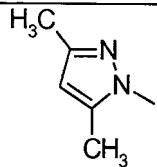
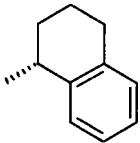
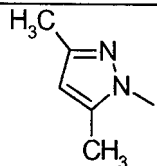
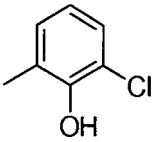
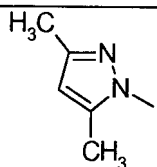
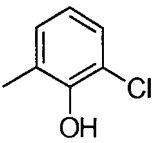
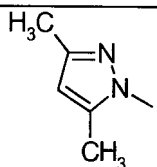
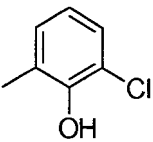
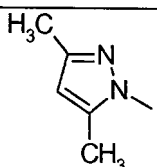
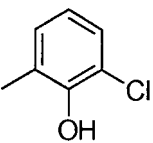
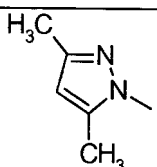
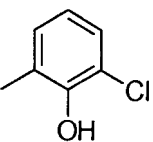
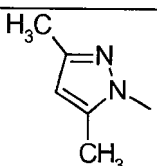
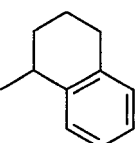
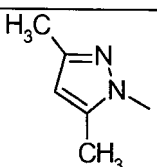
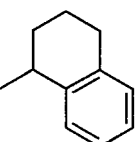
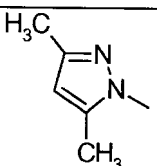
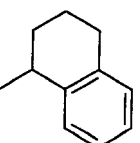
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257		-CH ₂ C(=O)-	-C(=S)-	
258		-CH ₂ C(=O)-	-C(=O)O-	
259		-CH ₂ C(=O)-	-C(=O)NH-	
260		-CH ₂ C(=O)-	-SO ₂ -	
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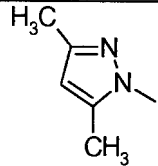
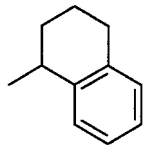
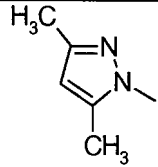
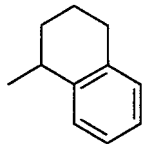
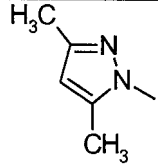
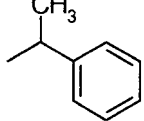
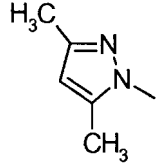
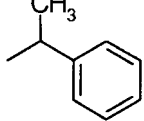
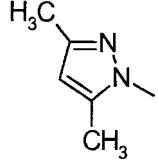
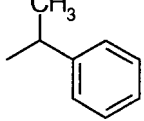
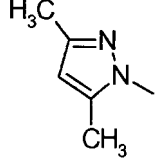
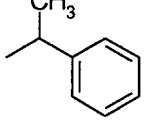
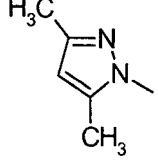
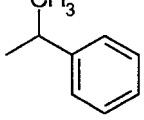
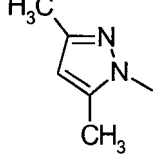
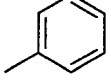
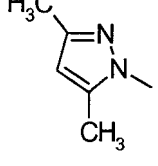
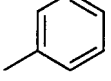
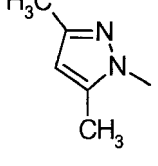
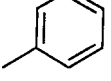
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267		-CH ₂ C(=O)-	-C(=S)-	
268		-CH ₂ C(=O)-	-C(=O)O-	
269		-CH ₂ C(=O)-	-C(=O)NH-	
270		-CH ₂ C(=O)-	-SO ₂ -	
271		-CH ₂ C(=O)-	-C(=O)-	
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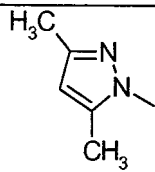
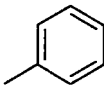
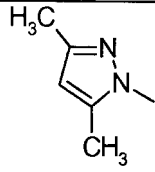
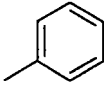
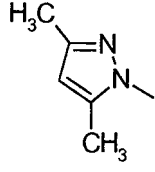
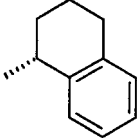
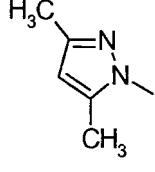
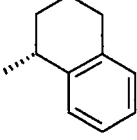
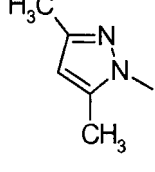
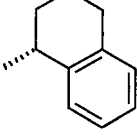
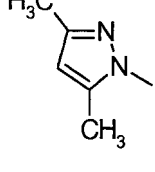
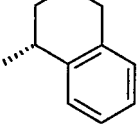
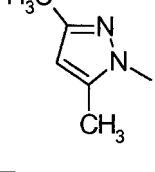
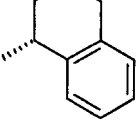
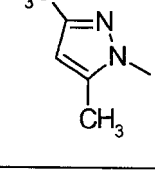
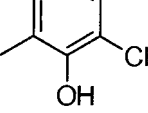
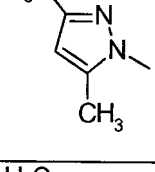
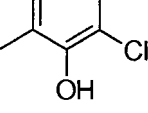
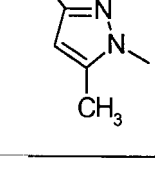
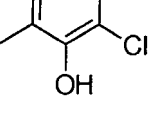
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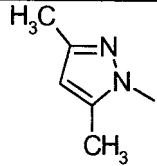
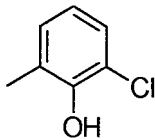
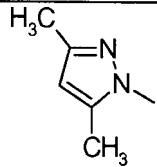
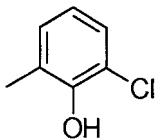
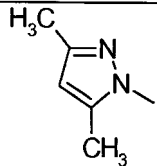
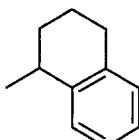
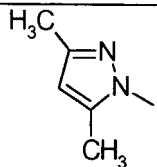
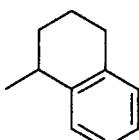
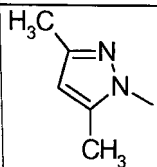
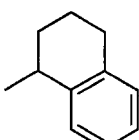
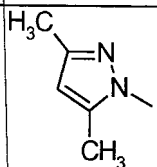
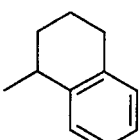
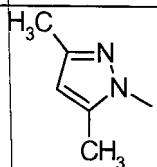
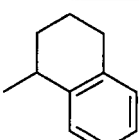
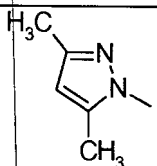
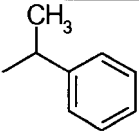
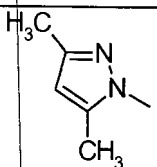
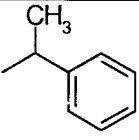
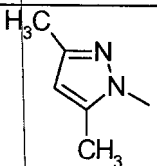
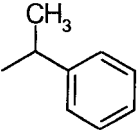
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289		-CH ₂ C(=S)-	-C(=O)NH-	
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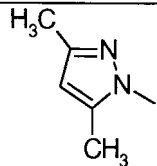
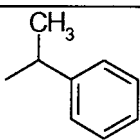
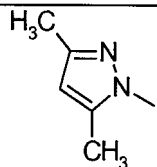
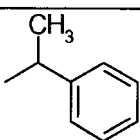
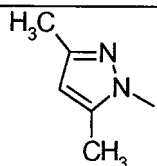
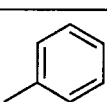
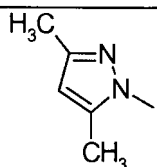
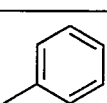
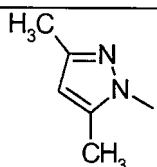
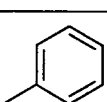
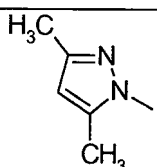
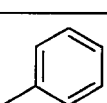
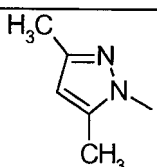
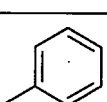
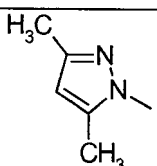
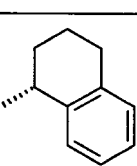
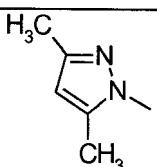
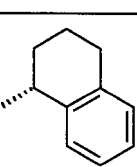
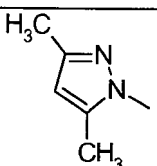
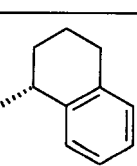
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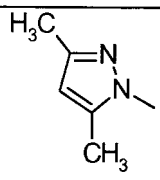
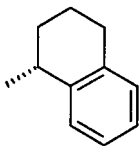
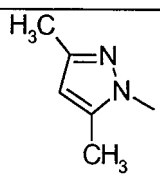
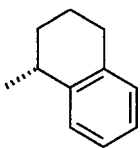
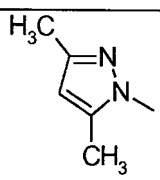
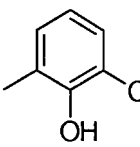
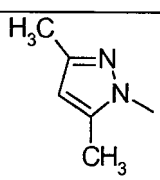
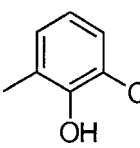
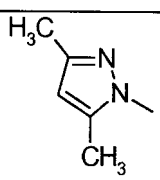
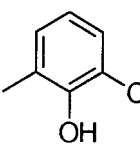
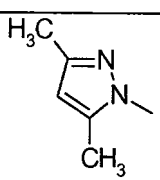
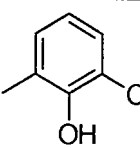
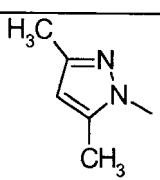
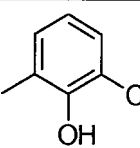
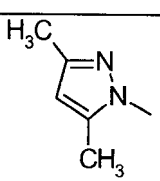
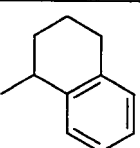
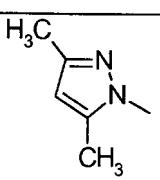
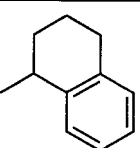
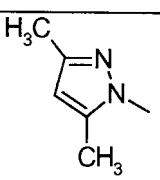
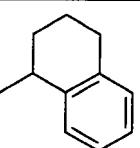
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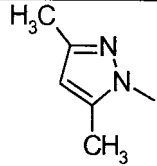
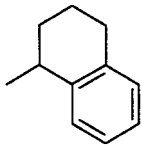
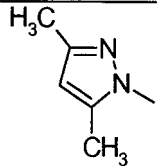
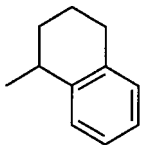
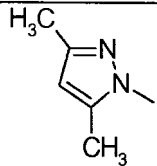
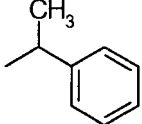
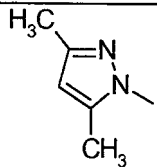
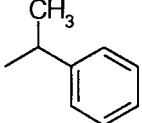
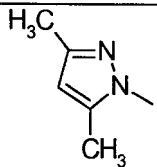
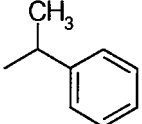
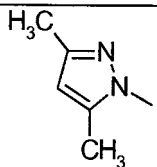
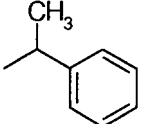
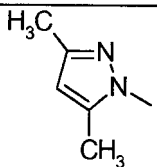
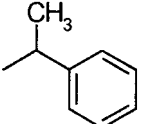
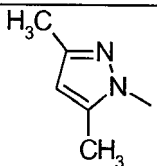
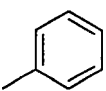
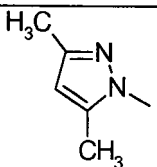
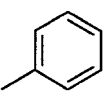
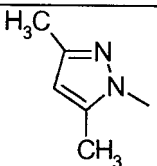
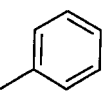
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319		-OC(=O)-	-C(=O)NH-	
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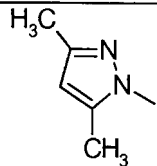
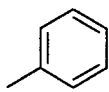
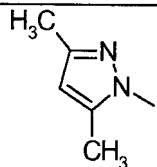
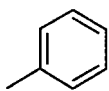
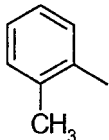
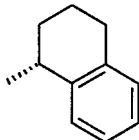
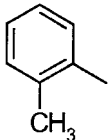
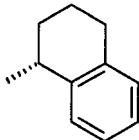
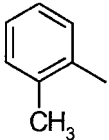
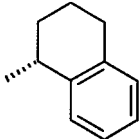
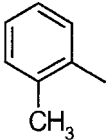
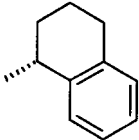
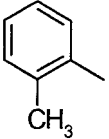
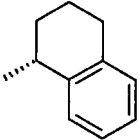
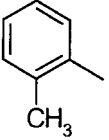
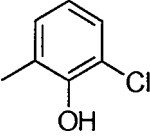
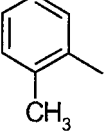
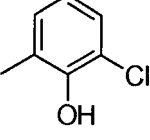
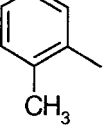
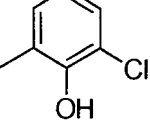
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330		-C(=O)-	-SO ₂ -	
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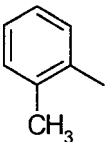
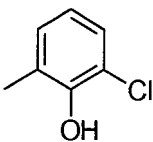
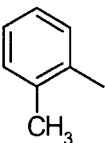
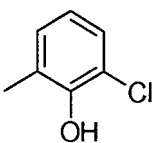
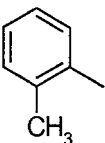
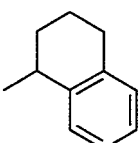
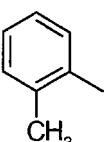
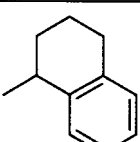
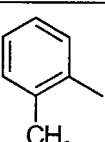
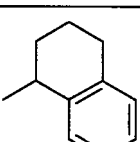
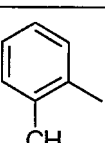
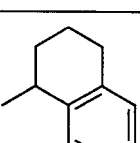
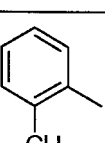
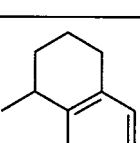
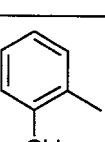
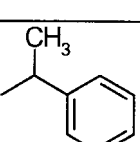
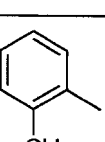
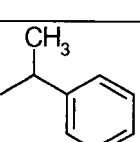
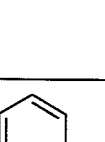
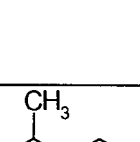
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338		-C(=O)-	-C(=O)O-	
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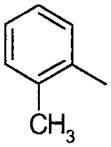
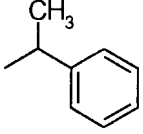
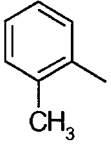
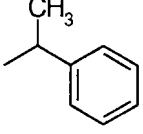
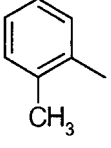
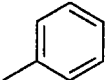
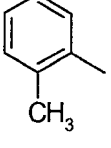
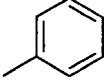
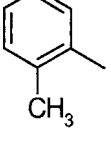
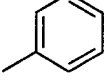
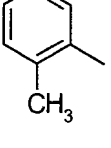
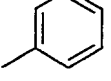
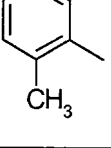
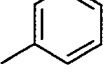
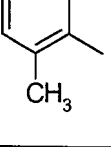
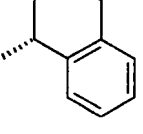
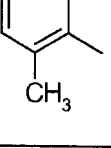
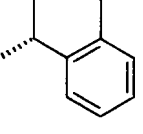
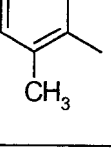
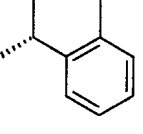
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348		-C(=O)-	-C(=O)O-	
349		-C(=O)-	-C(=O)NH-	
350		-C(=O)-	-SO ₂ -	
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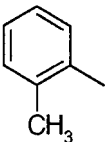
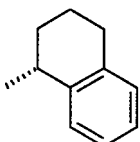
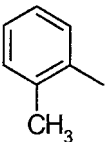
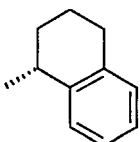
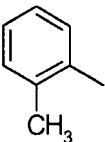
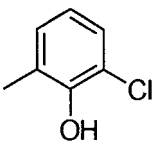
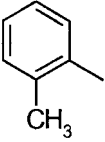
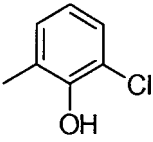
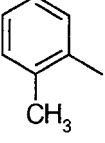
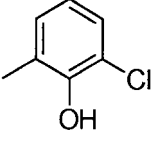
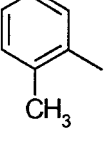
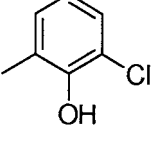
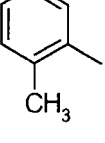
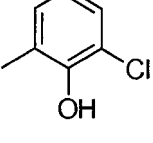
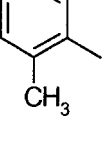
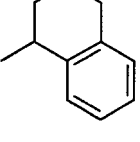
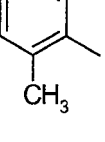
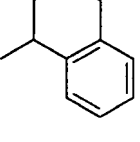
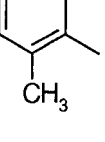
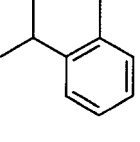
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357			- CH ₂ SO ₂ ⁻	-C(=S)-	
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359			- CH ₂ SO ₂ ⁻	-C(=O)NH-	
360			- CH ₂ SO ₂ ⁻	-SO ₂ ⁻	
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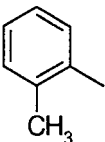
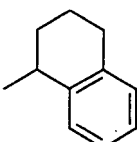
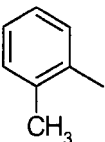
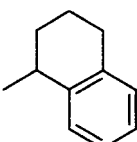
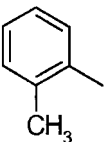
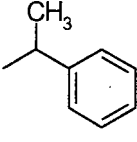
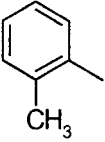
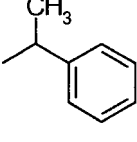
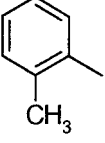
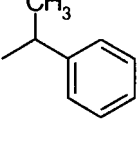
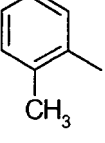
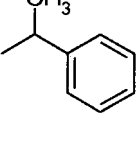
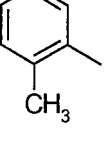
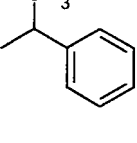
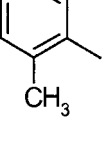
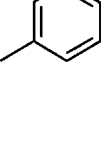
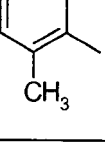
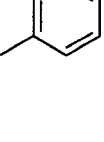
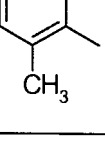
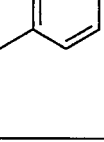
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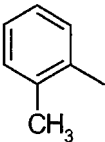
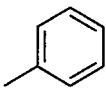
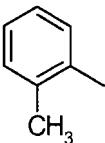
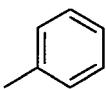
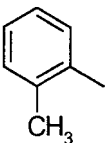
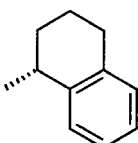
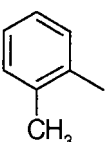
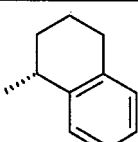
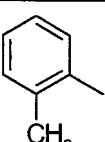
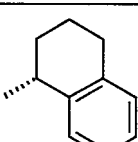
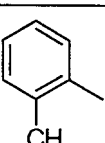
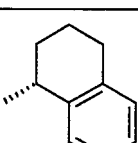
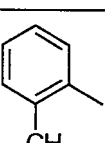
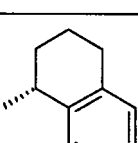
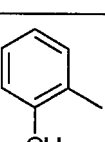
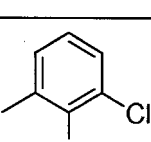
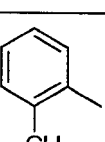
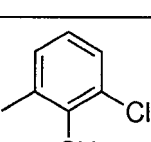
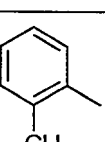
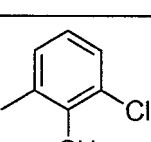
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375		-CH ₂ SO ₂ -	-SO ₂ -	
376		-CH ₂ C(=O)-	-C(=O)-	
377		-CH ₂ C(=O)-	-C(=S)-	
378		-CH ₂ C(=O)-	-C(=O)O-	
379		-CH ₂ C(=O)-	-C(=O)NH-	
380		-CH ₂ C(=O)-	-SO ₂ -	
381		-CH ₂ C(=O)-	-C(=O)-	
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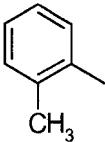
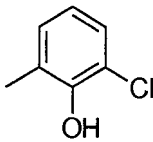
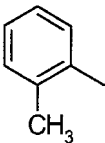
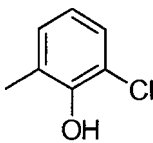
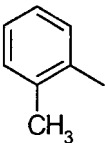
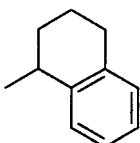
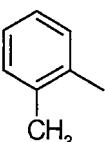
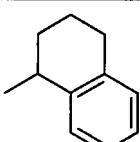
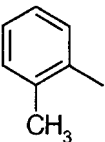
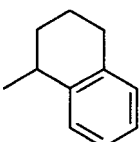
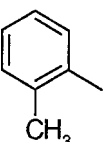
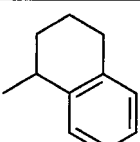
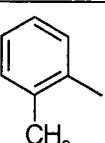
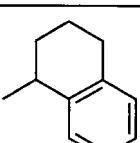
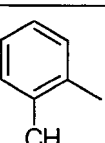
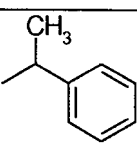
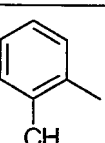
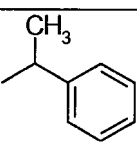
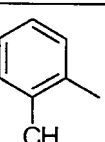
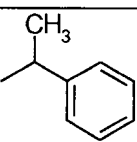
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387			-CH ₂ C(=O)-	-C(=S)-	
388			-CH ₂ C(=O)-	-C(=O)O-	
389			-CH ₂ C(=O)-	-C(=O)NH-	
390			-CH ₂ C(=O)-	-SO ₂ -	
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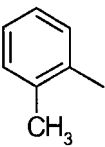
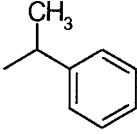
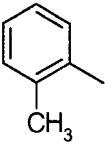
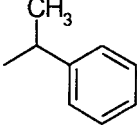
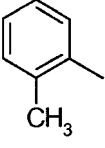
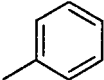
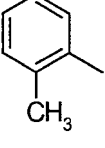
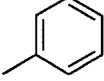
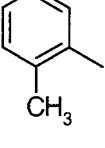
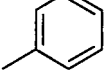
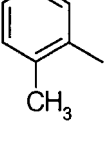
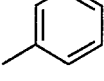
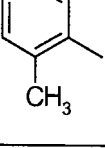
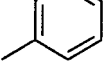
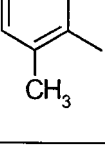
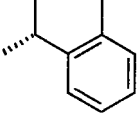
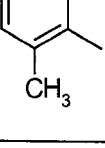
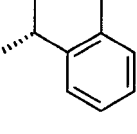
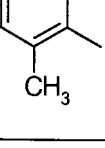
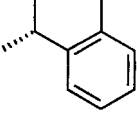
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396		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{O})-$	
397		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{S})-$	
398		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{O})\text{O}-$	
399		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{O})\text{NH}-$	
400		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{SO}_2-$	
401		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})-$	
402		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{S})-$	
403		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})\text{O}-$	

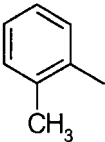
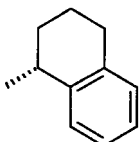
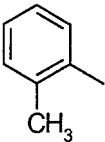
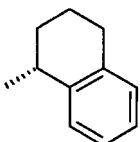
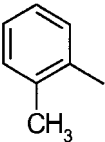
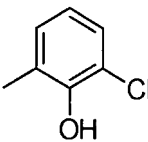
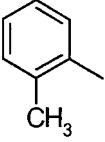
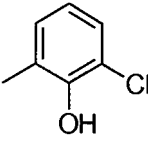
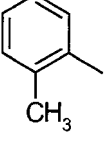
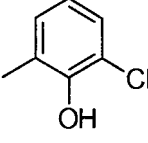
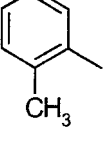
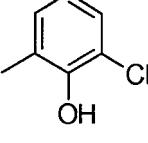
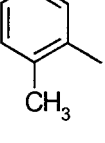
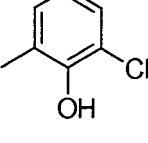
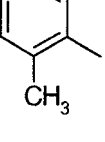
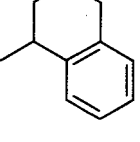
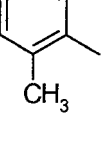
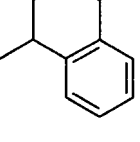
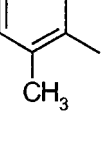
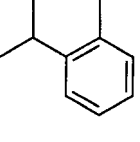
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409		-CH ₂ C(=S)-	-C(=O)NH-	
410		-CH ₂ C(=S)-	-SO ₂ -	
411		-CH ₂ C(=S)-	-C(=O)-	
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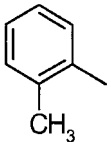
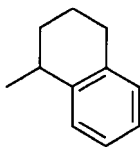
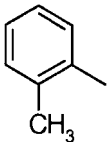
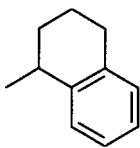
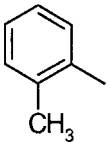
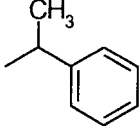
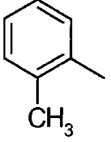
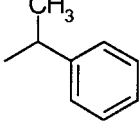
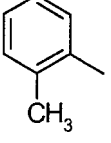
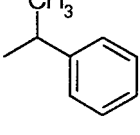
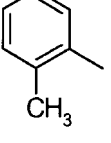
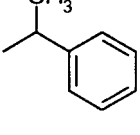
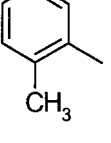
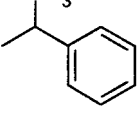
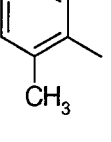
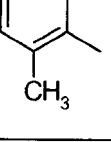
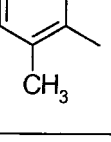
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416		-CH ₂ C(=S)-	-C(=O)-	
417		-CH ₂ C(=S)-	-C(=S)-	
418		-CH ₂ C(=S)-	-C(=O)O-	
419		-CH ₂ C(=S)-	-C(=O)NH-	
420		-CH ₂ C(=S)-	-SO ₂ -	
421		-CH ₂ C(=S)-	-C(=O)-	
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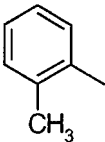
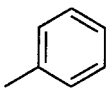
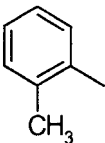
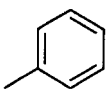
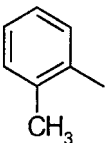
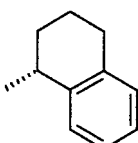
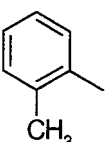
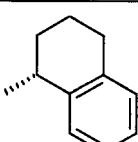
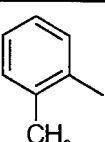
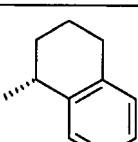
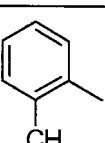
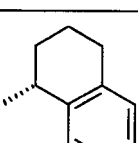
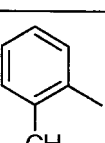
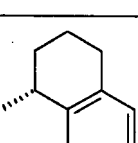
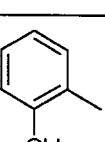
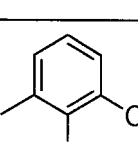
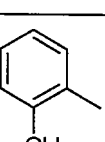
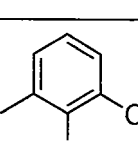
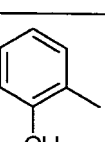
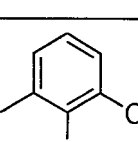
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426		$-\text{OC}(=\text{O})-$	$-\text{C}(=\text{O})-$	
427		$-\text{OC}(=\text{O})-$	$-\text{C}(=\text{S})-$	
428		$-\text{OC}(=\text{O})-$	$-\text{C}(=\text{O})\text{O}-$	
429		$-\text{OC}(=\text{O})-$	$-\text{C}(=\text{O})\text{NH}-$	
430		$-\text{OC}(=\text{O})-$	$-\text{SO}_2-$	
431		$-\text{OC}(=\text{O})-$	$-\text{C}(=\text{O})-$	
432		$-\text{OC}(=\text{O})-$	$-\text{C}(=\text{S})-$	
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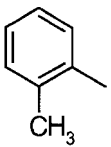
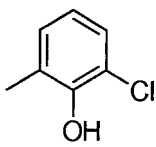
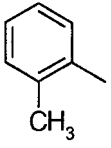
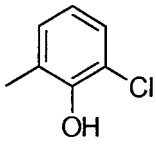
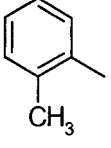
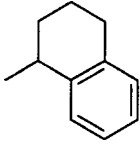
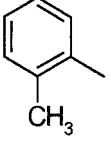
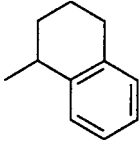
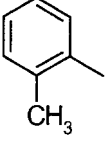
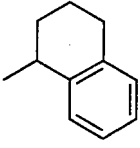
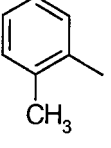
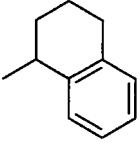
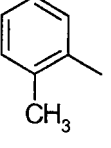
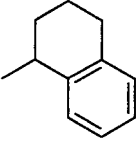
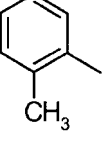
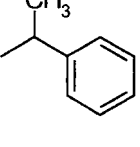
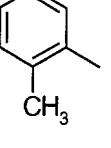
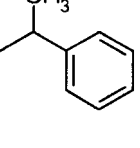
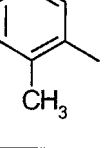
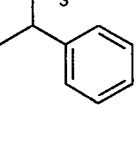
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435		-OC(=O)-	-SO ₂ -	
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437		-OC(=O)-	-C(=S)-	
438		-OC(=O)-	-C(=O)O-	
439		-OC(=O)-	-C(=O)NH-	
440		-OC(=O)-	-SO ₂ -	
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443		-OC(=O)-	-C(=O)O-	

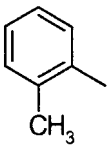
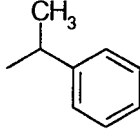
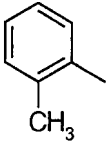
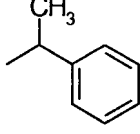
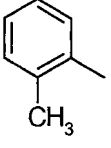
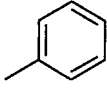
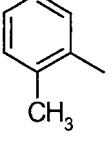
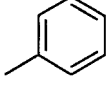
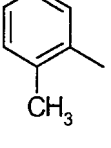
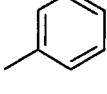
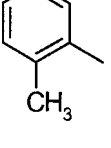
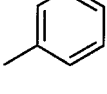
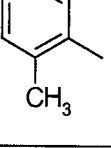
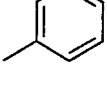
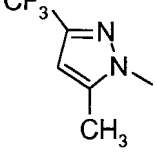
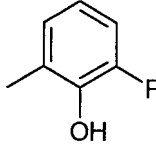
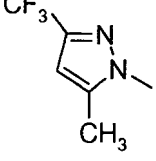
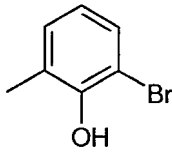
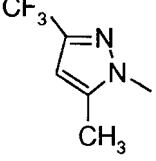
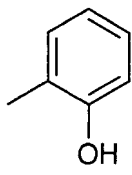
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448		-OC(=O)-	-C(=O)O-	
449		-OC(=O)-	-C(=O)NH-	
450		-OC(=O)-	-SO ₂ -	
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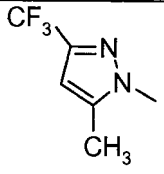
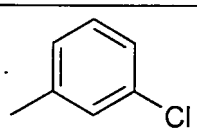
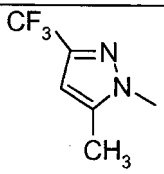
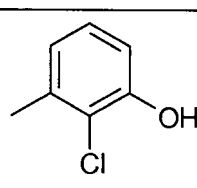
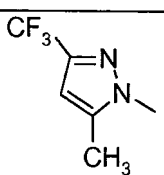
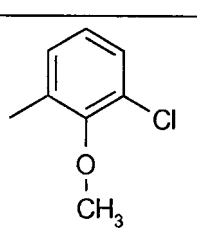
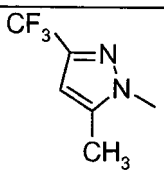
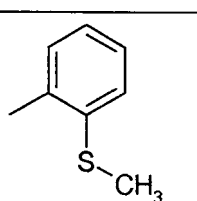
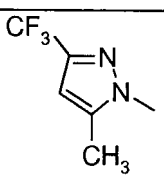
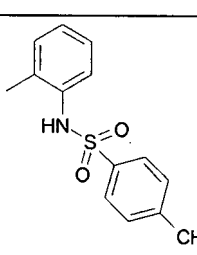
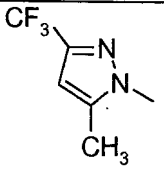
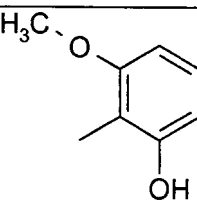
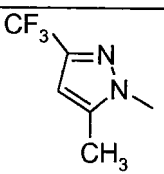
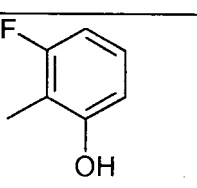
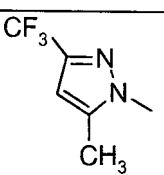
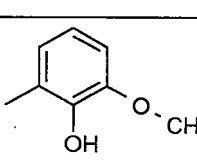
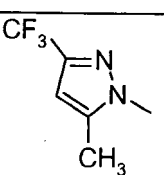
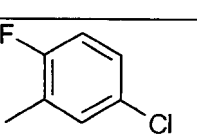
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455		-C(=O)-	-SO ₂ -	
456		-C(=O)-	-C(=O)-	
457		-C(=O)-	-C(=S)-	
458		-C(=O)-	-C(=O)O-	
459		-C(=O)-	-C(=O)NH-	
460		-C(=O)-	-SO ₂ -	
461		-C(=O)-	-C(=O)-	
462		-C(=O)-	-C(=S)-	
463		-C(=O)-	-C(=O)O-	

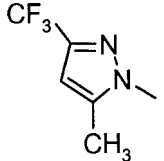
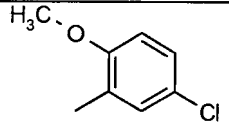
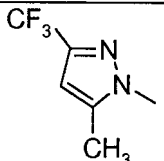
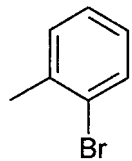
464		-C(=O)-	-C(=O)NH-	
465		-C(=O)-	-SO ₂ -	
466		-C(=O)-	-C(=O)-	
467		-C(=O)-	-C(=S)-	
468		-C(=O)-	-C(=O)O-	
469		-C(=O)-	-C(=O)NH-	
470		-C(=O)-	-SO ₂ -	
471		-C(=O)-	-C(=O)-	
472		-C(=O)-	-C(=S)-	
473		-C(=O)-	-C(=O)O-	

474		-C(=O)-	-C(=O)NH-	
475		-C(=O)-	-SO ₂ -	
476		-CH ₂ SO ₂ -	-C(=O)-	
477		-CH ₂ SO ₂ -	-C(=S)-	
478		-CH ₂ SO ₂ -	-C(=O)O-	
479		-CH ₂ SO ₂ -	-C(=O)NH-	
480		-CH ₂ SO ₂ -	-SO ₂ -	
481		-CH ₂ SO ₂ -	-C(=O)-	
482		-CH ₂ SO ₂ -	-C(=S)-	
483		-CH ₂ SO ₂ -	-C(=O)O-	

484		- CH ₂ SO ₂ -	-C(=O)NH-	
485		- CH ₂ SO ₂ -	-SO ₂ -	
486		- CH ₂ SO ₂ -	-C(=O)-	
487		- CH ₂ SO ₂ -	-C(=S)-	
488		- CH ₂ SO ₂ -	-C(=O)O-	
489		- CH ₂ SO ₂ -	-C(=O)NH-	
490		- CH ₂ SO ₂ -	-SO ₂ -	
491		- CH ₂ SO ₂ -	-C(=O)-	
492		- CH ₂ SO ₂ -	-C(=S)-	
493		- CH ₂ SO ₂ -	-C(=O)O-	

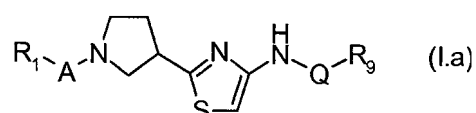
494		-CH ₂ SO ₂ -	-C(=O)NH-	
495		-CH ₂ SO ₂ -	-SO ₂ -	
496		-CH ₂ SO ₂ -	-C(=O)-	
497		-CH ₂ SO ₂ -	-C(=S)-	
498		-CH ₂ SO ₂ -	-C(=O)O-	
499		-CH ₂ SO ₂ -	-C(=O)NH-	
500		-CH ₂ SO ₂ -	-SO ₂ -	
501		-CH ₂ C(=O)-	-C(=O)-	
502		-CH ₂ C(=O)-	-C(=O)-	
503		-CH ₂ C(=O)-	-C(=O)-	

504		-CH ₂ C(=O)-	-C(=O)-	
505		-CH ₂ C(=O)-	-C(=O)-	
506		-CH ₂ C(=O)-	-C(=O)-	
507		-CH ₂ C(=O)-	-C(=O)-	
508		-CH ₂ C(=O)-	-C(=O)-	
509		-CH ₂ C(=O)-	-C(=O)-	
510		-CH ₂ C(=O)-	-C(=O)-	
511		-CH ₂ C(=O)-	-C(=O)-	
512		-CH ₂ C(=O)-	-C(=O)-	

513		-CH ₂ C(=O)-	-C(=O)-	
514		-CH ₂ C(=O)-	-C(=O)-	

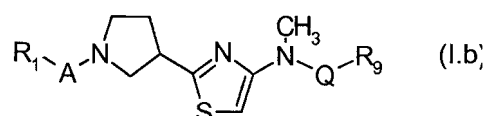
where

a) 514 compounds of formula (I.a):



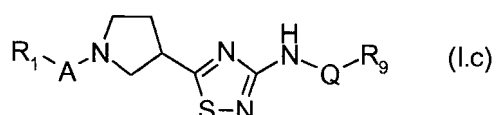
5 wherein A, Q, R¹ and R⁹ are as defined in Table 1.

b) 514 compounds of formula (I.b):



10 wherein A, Q, R¹ and R⁹ are as defined in Table 1.

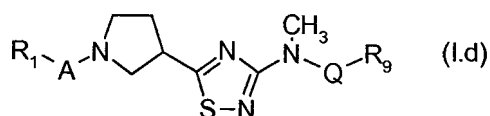
c) 514 compounds of formula (I.c):



wherein A, Q, R¹ and R⁹ are as defined in Table 1.

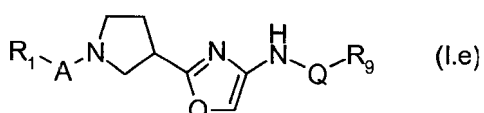
15

d) 514 compounds of formula (I.d):



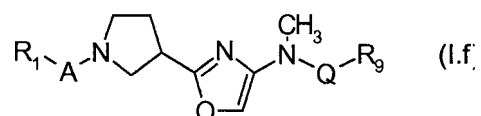
wherein A, Q, R¹ and R⁹ are as defined in Table 1.

20 e) 514 compounds of formula (I.e):



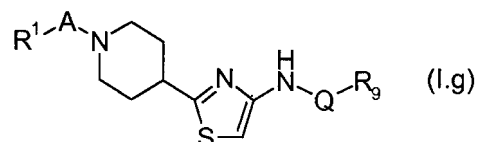
wherein A, Q, R¹ and R⁹ are as defined in Table 1.

f) 514 compounds of formula (I.f):



5 wherein A, Q, R¹ and R⁹ are as defined in Table 1.

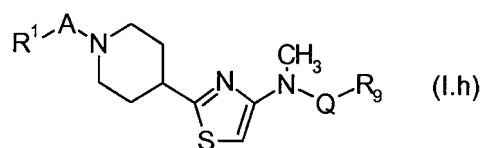
g) 514 compounds of formula (I.g):



wherein A, Q, R¹ and R⁹ are as defined in Table 1.

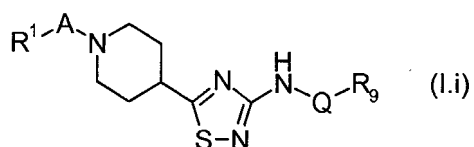
10

h) 514 compounds of formula (I.h):



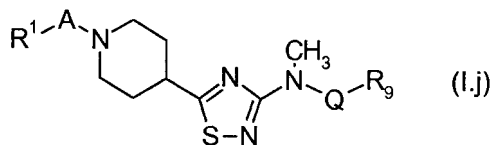
wherein A, Q, R¹ and R⁹ are as defined in Table 1.

15 i) 514 compounds of formula (I.i):



wherein A, Q, R¹ and R⁹ are as defined in Table 1.

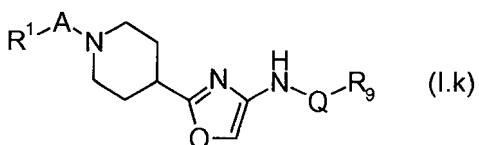
j) 514 compounds of formula (I.j):



20

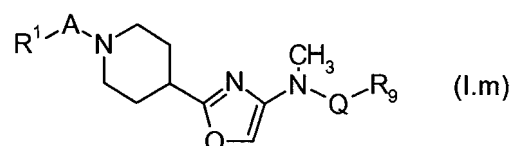
wherein A, Q, R¹ and R⁹ are as defined in Table 1.

k) 514 compounds of formula (I.k):



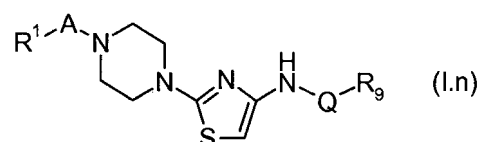
wherein A, Q, R¹ and R⁹ are as defined in Table 1.

m) 514 compounds of formula (l.m):



5 wherein A, Q, R¹ and R⁹ are as defined in Table 1.

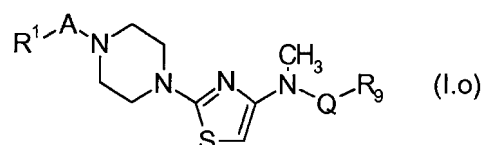
n) 514 compounds of formula (l.n):



wherein A, Q, R¹ and R⁹ are as defined in Table 1.

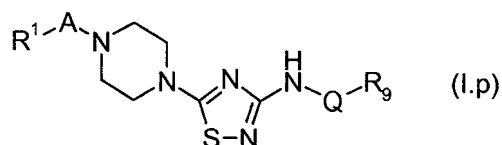
10

o) 514 compounds of formula (l.o):



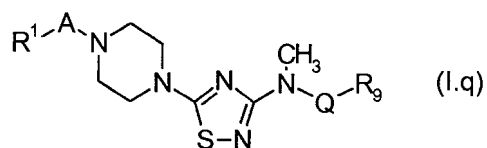
wherein A, Q, R¹ and R⁹ are as defined in Table 1.

15 p) 514 compounds of formula (l.p):



wherein A, Q, R¹ and R⁹ are as defined in Table 1.

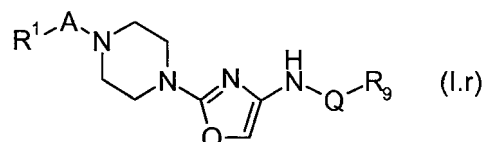
q) 514 compounds of formula (l.q):



20

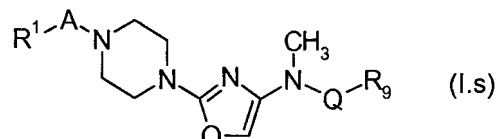
wherein A, Q, R¹ and R⁹ are as defined in Table 1.

r) 514 compounds of formula (l.r):



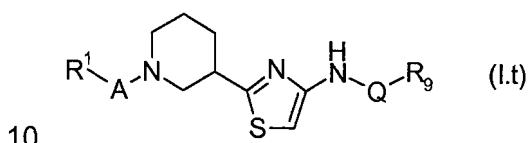
wherein A, Q, R¹ and R⁹ are as defined in Table 1.

5 s) 514 compounds of formula (l.s):



wherein A, Q, R¹ and R⁹ are as defined in Table 1.

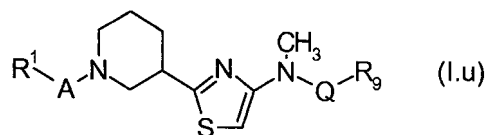
t) 514 compounds of formula (l.t):



10

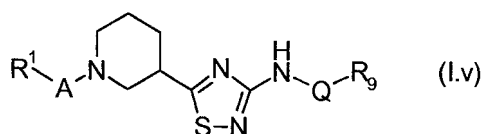
wherein A, Q, R¹ and R⁹ are as defined in Table 1.

u) 514 compounds of formula (l.u):



15 wherein A, Q, R¹ and R⁹ are as defined in Table 1.

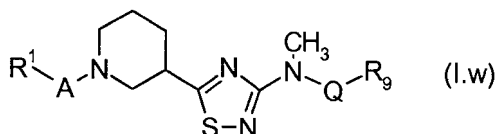
v) 514 compounds of formula (l.v):



wherein A, Q, R¹ and R⁹ are as defined in Table 1.

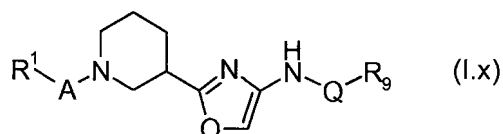
20

w) 514 compounds of formula (l.w):



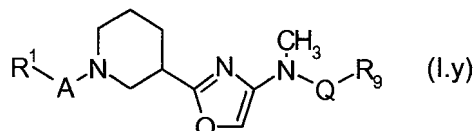
wherein A, Q, R¹ and R⁹ are as defined in Table 1.

x) 514 compounds of formula (I.x):



wherein A, Q, R¹ and R⁹ are as defined in Table 1.

5 y) 514 compounds of formula (I.y):



wherein A, Q, R¹ and R⁹ are as defined in Table 1.

Throughout this description, temperatures are given in degrees Celsius and "m.p." means melting point. LC/MS means Liquid Chromatography Mass Spectroscopy and the description of the apparatus and the method is: (HP 1100 HPLC from Agilent, Phenomenex Gemini C18, 3 µm particle size, 110 Angström, 30 x 3 mm column, 1.7mL/min., 60 °C, H₂O + 0.05% HCOOH (95%) / CH₃CN/MeOH 4:1 + 0.04% HCOOH (5%) – 2 min. – CH₃CN/MeOH 4:1 + 0.04% HCOOH (5%) – 0.8 min., ZQ Mass Spectrometer from Waters, ionization method: electrospray (ESI), Polarity: positive ions, Capillary (kV) 3.00, Cone (V) 30.00, Extractor (V) 2.00, Source Temperature (°C) 100, Desolvation Temperature (°C) 250, Cone Gas Flow (L/Hr) 50, Desolvation Gas Flow (L/Hr) 400)).

Table 2 shows selected m.p. data and selected LC/MS data for compounds of Table 1.

Table 2: Melting point and LC/MS data for compounds of Table 1

Compound No.	Melting point (°C)	LC/MS
I.g.001	175	
I.g.006		Rt = 3.27 min. ; MS: m/z = 527 (M+1)
I.g.011	179 - 181	
I.g.013		Rt = 2.02 min. ; MS: m/z = 570 (M+23)
I.g.016		Rt = 1.9 min. ; MS: m/z = 506 (M+1)
I.g.018		Rt = 1.91 min. ; MS: m/z = 522 (M+23)
I.g.021 ¹		Rt = 2.77 min ; MS: m/z = 478 (M+1)
I.g.023	154 - 156	Rt = 1.94 min ; MS: m/z = 508 (M+1)
I.g.024		Rt = 1.85 min ; MS: m/z = 494 (M+1)
I.g.025 ¹		Rt = 2.75 min ; MS: m/z = 514 (M+1)

I.g.136		Rt = 2.01 min ; MS: m/z = 488 (M+1)
I.g.141		Rt = 1.98 min ; MS: m/z = 462 (M+1)
I.g.196		Rt = 2.17 min ; MS: m/z = 490 (M+1)
I.g.211	233-234	
I.g.246	173-175	
I.g.386	174-175	
I.g.501		Rt = 1.88 min ; MS: m/z = 512 (M+1)
I.g.502	193-195	
I.g.503		Rt = 1.85 min ; MS: m/z = 494 (M+1)
I.g.504		Rt = 1.95 min ; MS: m/z = 512 (M+1)
I.g.505		Rt = 1.70 min ; MS: m/z = 528(M+1)
I.g.506		Rt = 1.97 min ; MS: m/z = 542 (M+1)
I.g.507		Rt = 1.85 min ; MS: m/z = 524 (M+1)
I.g.508		Rt = 1.98 min ; MS: m/z = 647 (M+1)
I.g.509		Rt = 2.03 min ; MS: m/z = 524 (M+1)
I.g.510		Rt = 1.94 min ; MS: m/z = 512 (M+1)
I.g.511		Rt = 1.85 min ; MS: m/z = 524 (M+1)
I.g.512		Rt = 1.96 min ; MS: m/z = 530 (M+1)
I.g.513		Rt = 2.03 min ; MS: m/z = 542 (M+1)
I.g.514		Rt = 1.86 min ; MS: m/z = 558 (M+2)
I.h.011		Rt = 1.90 min ; MS: m/z = 546 (M+1)
I.n.011	207-209	
I.n.021		Rt = 1.78 min ; MS: m/z = 479 (M+1)
I.n. 023		Rt = 1.83 min ; MS: m/z = 495 (M+1)
I.n. 024	175-178	

The compounds according to the present invention can be prepared according to the above-mentioned reaction schemes, in which, unless otherwise stated, the definition of each variable is as defined above for a compound of formula (I).

5

Biological examples

Phytophthora infestans / tomato / leaf disc preventative (tomato late blight)

Tomato leaf disks are placed on water agar in multiwell plates (24-well format) and sprayed
 10 with the formulated test compound diluted in water. The leaf disks are inoculated with a spore suspension of the fungus 1 day after application. The inoculated leaf disks are

incubated at 16°C and 75% rh under a light regime of 24 h darkness followed by 12 h light / 12 h darkness in a climate cabinet and the activity of a compound is assessed as percent disease control compared to untreated when an appropriate level of disease damage appears in untreated check leaf disks (5 – 7 days after application).

- 5 Compounds I.g.001, I.g.006, I.g.011, I.g.013, I.g.016, I.g.018, I.g.021, I.g.023, I.g.024, I.g.136, I.g.386, I.g.501, I.g.503, I.g.506, I.g.508, I.g.509, I.g.510, I.g.511, I.h.011, I.n.011 and I.n.021 at 200 ppm give at least 80% disease control in this test when compared to untreated control leaf disks under the same conditions, which show extensive disease development.

10

Phytophthora infestans / potato / preventative (potato late blight)

- 2-week old potato plants cv. Bintje are sprayed in a spray chamber with the formulated test compound diluted in water. The test plants are inoculated by spraying them with a sporangia suspension 2 days after application. The inoculated test plants are incubated at 15 18° C with 14 h light/day and 100 % rh in a growth chamber and the percentage leaf area covered by disease is assessed when an appropriate level of disease appears on untreated check plants (5 – 7 days after application).

- Compounds I.g.001, I.g.006, I.g.011, I.g.016, I.g.023, I.g.024, I.g.136, I.g.501, I.g.502 and I.g.511 at 200 ppm give at least 80% disease control in this test when compared to 20 untreated control leaf disks under the same conditions, which show extensive disease development.

Phytophthora infestans / potato / long lasting (potato late blight)

- 2-week old potato plants cv. Bintje are sprayed in a spray chamber with the formulated test 25 compound diluted in water. The test plants are inoculated by spraying them with a sporangia suspension 6 days after application. The inoculated test plants are incubated at 18° C with 14 h light/day and 100 % rh in a growth chamber and the percentage leaf area covered by disease is assessed when an appropriate level of disease appears on untreated check plants (9 – 11 days after application).

- 30 Compounds I.g.001, I.g.006, I.g.011, I.g.016, I.g.023, I.g.024, I.g.501 and I.g.502 at 200 ppm give at least 80% disease control in this test when compared to untreated control leaf disks under the same conditions, which show extensive disease development.

Phytophthora infestans / potato / curative (potato late blight)

- 35 2-week old potato plants cv. Bintje are inoculated by spraying them with a sporangia suspension one day before application. The inoculated plants are sprayed in a spray chamber with the formulated test compound diluted in water. The inoculated test plants are

incubated at 18° C with 14 h light/day and 100 % rh in a growth chamber and the percentage leaf area covered by disease is assessed when an appropriate level of disease appears on untreated check plants (3 – 4 days after application).

Compounds I.g.001, I.g.011 and I.g.023 at 200 ppm give at least 80% disease control in this test when compared to untreated control leaf disks under the same conditions, which show extensive disease development.

Plasmopara viticola / grape / leaf disc preventative (grape downy mildew)

Grape vine leaf disks are placed on water agar in multiwell plates (24-well format) and sprayed with the formulated test compound diluted in water. The leaf disks are inoculated with a spore suspension of the fungus 1 day after application. The inoculated leaf disks are incubated at 19°C and 80% rh under a light regime of 12 h light / 12 h darkness in a climate cabinet and the activity of a compound is assessed as percent disease control compared to untreated when an appropriate level of disease damage appears in untreated check leaf disks (6 – 8 days after application).

Compounds I.g.001, I.g.011, I.g.013, I.g.016, I.g.018, I.g.021, I.g.023, I.g.024, I.g.246 I.g.386, I.g.501, I.g.503, I.g.506, I.g.508, I.g.509, I.g.510, I.n.011 and I.n.021 at 200 ppm give at least 80% disease control in this test when compared to untreated control leaf disks under the same conditions, which show extensive disease development.

Plasmopara viticola / grape / preventative (grape downy mildew)

5-week old grape seedlings cv. Gutedel are sprayed in a spray chamber with the formulated test compound diluted in water. The test plants are inoculated by spraying a sporangia suspension on their lower leaf surface one day after application. The inoculated test plants are incubated at 22° C and 100% rh in a greenhouse and the percentage leaf area covered by disease is assessed when an appropriate level of disease appears on untreated check plants (6 – 8 days after application).

Compounds I.g.001, I.g.006, I.g.011, I.g.016, I.g.023 and I.g.024, I.g.501, I.g.502 and I.g.503 at 200 ppm give at least 80% disease control in this test when compared to untreated control leaf disks under the same conditions, which show extensive disease development.

Plasmopara viticola / grape / long lasting (grape downy mildew)

5-week old grape seedlings cv. Gutedel are sprayed in a spray chamber with the formulated test compound diluted in water. The test plants are inoculated by spraying a sporangia suspension on their lower leaf surface 6 days after application. The inoculated test plants are incubated at 22° C and 100% rh in a greenhouse and the percentage leaf area covered

by disease is assessed when an appropriate level of disease appears on untreated check plants (11 – 13 days after application).

Compounds I.g.001, I.g.006, I.g.011, I.g.023 and I.g.024, I.g.501 and I.g.502 at 200 ppm give at least 80% disease control in this test when compared to untreated control leaf disks under the same conditions, which show extensive disease development.

Plasmopara viticola / grape / curative (grape downy mildew)

5-week-old grape seedlings cv. Gutedel are inoculated by spraying a sporangia suspension on their lower leaf surface one day before application. The inoculated grape plants are sprayed in a spray chamber with the formulated test compound diluted in water. The inoculated test plants are incubated at 22° C and 100% rh in a greenhouse and the percentage leaf area covered by disease is assessed when an appropriate level of disease appears on untreated check plants (4 – 6 days after application).

Compounds I.g.001, I.g.006, I.g.011 and I.g.023 at 200 ppm give at least 80% disease control in this test when compared to untreated control leaf disks under the same conditions, which show extensive disease development.

Pythium ultimum / liquid culture (seedling damping off)

Mycelia fragments and oospores of a newly grown liquid culture of the fungus are directly mixed into nutrient broth (PDB potato dextrose broth). After placing a (DMSO) solution of test compound into a microtiter plate (96-well format), the nutrient broth containing the fungal mycelia/spore mixture is added. The test plates are incubated at 24°C and the inhibition of growth is determined photometrically 2-3 days after application.

Compounds I.g.006, I.g.501, I.g.502, I.g.503 and I.g.511 at 200 ppm give at least 80% disease control in this test when compared to untreated control leaf disks under the same conditions, which show extensive disease development.

Pythium ultimum / cotton / soil drench (seedling damping off)

The test is carried out in plastic containers (650 ml volume) using a mixture of (50% Vermiculit + sterile 50% Cugy soil) + 10% v/v water. 10 seeds (cotton, cv. Sure Grow 747) are sown in 2 rows of 5 seeds per container (3 replicates for evaluation of the activity, 3 replicates for evaluation of phytotox). Application is carried out directly after sowing by pouring 10 ml compound diluted in water per row over the seeds. Just afterwards the seeds are covered with a thin layer of the same soil and the inoculation is happening. *Pythium ultimum* is cultivated for 14 days on carrot slices in Roux bottles. For inoculation, the content of the Roux bottles is mixed and homogenously dispensed over the plastic containers without further filtering (70ml suspension per container). Incubation conditions:

20°C, 12h/12h day/night period in the greenhouse. The activity of a compound is assessed as percent disease control relative to untreated check plants when an appropriate level of disease damage appears in untreated check plants (13 – 16 days after application).

- Compounds l.g.006, l.g.501, l.g.502 and l.g.511 at 200 ppm give at least 80%
5 disease control in this test when compared to untreated control leaf disks under the same conditions, which show extensive disease development.

30 phenylsulfinyl, wherein the phenylsulfonyl and phenylsulfinyl are optionally substituted by 1

to 3 substituents independently selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkoxy, halogen and cyano;

each R²⁷ independently is hydrogen, C₁-C₄ alkyl, phenylsulfonyl or phenylsulfinyl, wherein the phenylsulfonyl and phenylsulfinyl are optionally substituted by 1 to 3 substituents

- 5 independently selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkoxy, halogen and cyano;
or a salt or a N-oxide thereof.

2. The compound according to claim 1, wherein

- 10 A is x-C(=O)-, x-C(=S)-, x-C(R¹⁰R¹¹)-C(=O)-, x-C(R¹²R¹³)-C(=S)-, x-O-C(=O)-, x-O-C(=S)-, x-N(R¹⁴)-C(=O)-, x-N(R¹⁵)-C(=S)- or x-C(R¹⁶R¹⁷)-SO₂-, in each case x indicates the bond that is connected to R¹;

T is CR¹⁸ or N;

G is O or S;

- 15 Y¹ and Y² are independently CR¹⁹ or N;

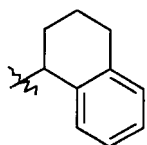
Q is -C(=O)-z-, -C(=S)-z-, -C(=O)-O-z-, -C(=S)-O-z-, -C(=O)-N(R²⁰)-z-, -C(=S)-N(R²¹)-z or -SO₂-z-, in each case z indicates the bond that is connected to R⁹;

n is 1 or 2;

p is 1 or 2, providing that when n is 2, p is 1;

- 20 R¹ is phenyl, pyridyl, imidazolyl or pyrazolyl; wherein the phenyl, pyridyl, imidazolyl and pyrazolyl are each optionally substituted by 1 to 3 substituents independently selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl, halogen, cyano, hydroxy and amino;
R², R³, R⁴, R⁵, R⁶, R⁷, R¹⁰, R¹¹, R¹², R¹³, R¹⁶, R¹⁷, R¹⁸ and R¹⁹ each independently are hydrogen, halogen, cyano, C₁-C₄alkyl or C₁-C₄haloalkyl;

- 25 R⁸, R¹⁴, R¹⁵, R²⁰, and R²¹ each independently are hydrogen or C₁-C₄alkyl; and
R⁹ is phenyl, benzyl or group (a):



(a)

wherein the phenyl, benzyl and group (a) are each optionally substituted with 1 to 3

- 30 substituents independently selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl, halogen, cyano, hydroxy and amino.

3. The compound according to claim 1, wherein

A is x-C(=O)-, x-C(=S)-, x-C(R¹⁰R¹¹)-C(=O)-, x-C(R¹²R¹³)-C(=S)-, x-O-C(=O)-, x-O-C(=S)- or

- 35 x-C(R¹⁶R¹⁷)-SO₂-, in each case x indicates the bond that is connected to R¹;

T is CR¹⁸ or N;

G is O or S;

Y¹ is N;

Y² is CR¹⁹ or N;

5 Q is -C(=O)-z, -C(=S)-z, -C(=O)-O-z, -C(=S)-O-z, -C(=O)-N(R²⁰)-z, -C(=S)-N(R²¹)-z or -SO₂-z-, in each case z indicates the bond that is connected to R⁹;

n is 1 or 2;

p is 1;

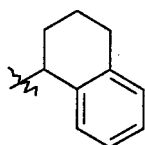
R¹ is phenyl or pyrazolyl; wherein the phenyl and pyrazolyl are each optionally substituted

10 by 1 to 3 substituents independently selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl, halogen, cyano, hydroxy, and amino;

R², R³, R⁴, R⁵, R⁶, R⁷, R¹⁰, R¹¹, R¹², R¹³, R¹⁶, R¹⁷, R¹⁸ and R¹⁹ each independently are hydrogen, halogen, C₁-C₄alkyl or C₁-C₄haloalkyl;

R⁸, R²⁰ and R²¹ each independently are hydrogen or C₁-C₄alkyl; and

15 R⁹ is phenyl, benzyl or group (a):



(a)

wherein the phenyl, benzyl and group (a) are each optionally substituted with 1 to 3 substituents independently selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl, halogen, cyano,

20 hydroxy and amino.

4. The compound according to claim 1, wherein

A is x-C(=O)-, -x-CR¹⁰R¹¹-C(=O)-, x-O-C(=O)- or x-C(R¹⁶R¹⁷)-SO₂-, in each case x indicates the bond that is connected to R¹;

25 T is CR¹⁸ or N;

G is S;

Y¹ is N;

Y² is CR¹⁹ or N;

Q is -C(=O)-z, -C(=O)-O-z, -C(=O)-N(R²⁰)-z or -SO₂-z-, in each case z being the bond to R⁹;

30 n is 1 or 2;

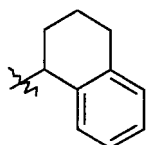
p is 1;

R¹ is phenyl or pyrazolyl, wherein the phenyl and pyrazolyl are each optionally substituted with 1 to 3 substituents independently selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl and halogen;

$R^2, R^3, R^4, R^5, R^6, R^7, R^{10}, R^{11}, R^{16}, R^{17}, R^{18}$, and R^{19} each independently are hydrogen, fluoro or methyl;

R^8 and R^{20} each independently are hydrogen or methyl; and

R^9 is phenyl, benzyl or group (a):



5

(a)

wherein the phenyl, benzyl and group (a) are each optionally substituted with 1 to 3 substituents independently selected from C_1 - C_4 alkyl, C_1 - C_4 haloalkyl, hydroxy and halogen.

10 5. The compound according to claim 1, wherein

A is $x-C(=O)-$, $x-CH_2-C(=O)-$, $x-O-C(=O)-$ or $x-CH_2-SO_2-$, in each case x indicates the bond that is connected to R^1 ;

T is CH or N;

G is S;

15 Y^1 is N;

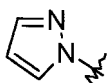
Y^2 is CH or N;

Q is $-C(=O)-z$, $-C(=O)-O-z$, $-C(=O)-NH-z$ or $-SO_2-z$, in each case z indicates the bond that is connected to R^9 ;

n is 1 or 2;

20 p is 1;

R^1 is phenyl or group (b):



(b)

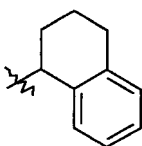
wherein the phenyl and group (b) are optionally substituted with 1 to 3 substituents

25 independently selected from halogen, C_1 - C_4 alkyl and C_1 - C_4 haloalkyl;

R^2, R^3, R^4, R^5, R^6 and R^7 are each hydrogen;

R^8 is hydrogen; and

R^9 is phenyl, benzyl or group (a):



30

(a)

wherein the phenyl, benzyl and group (a) are each optionally substituted with 1 to 3 substituents independently selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl, hydroxy and halogen.

6. The compound according to claim 1, wherein

5 A is x-CH₂-C(=O)- wherein x indicates the bond that is connected to R¹;

T is CH;

G is S;

Y¹ is N;

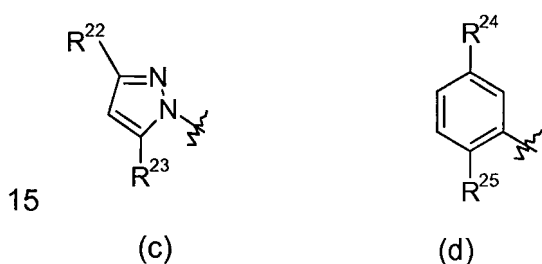
Y² is CH;

10 Q is -C(=O)-z, -C(=O)-O-z or C(=O)-N(R²⁰)-z, in each case z indicates the bond that is connected to R⁹;

n is 2;

p is 1;

R¹ is selected from group (c) or (d):

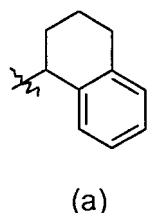


wherein R²², R²³, R²⁴ and R²⁵ are independently selected from hydrogen, halogen, methyl and halomethyl;

R₂, R₃, R₄, R₅, R₆, and R₇ are each hydrogen;

20 R₈ is hydrogen;

R⁹ is phenyl, benzyl or group (a):



wherein the phenyl, benzyl and group (a) are optionally substituted with 1 to 3 substituents

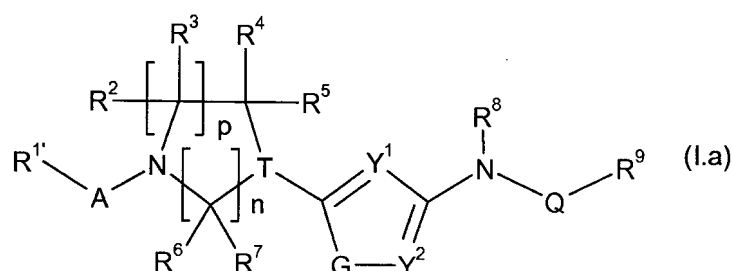
25 independently selected from halogen, hydroxy, methyl and halomethyl.

7. The compound according to any one of claims 1 to 6, wherein G is S, Y¹ is N and Y² is CH.

30 8. The compound according to any one of claims 1 to 7, wherein p is 1 and n is 2.

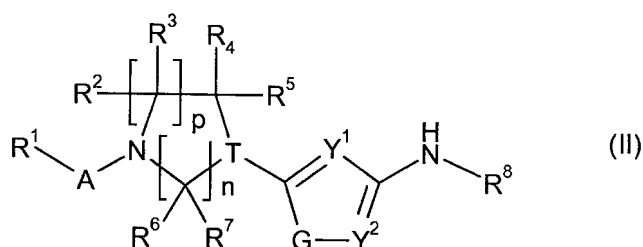
9. The compound according to any one of the claims 1 to 8, wherein R^2 , R^3 , R^4 , R^5 , R^6 and R^7 are H.
10. The compound according to any one of claims 1 to 9, wherein Q is $-C(=O)-z$, wherein
5 z indicates the bond that is connected to R^9 .
11. The compound according to any one of claims 1 to 10, wherein R^9 is phenyl substituted by hydroxy and optionally substituted by one or two further substituents.
- 10 12. The compound according to claim 11, wherein the hydroxy is at the ortho position.

13 A compound of formula I.a:



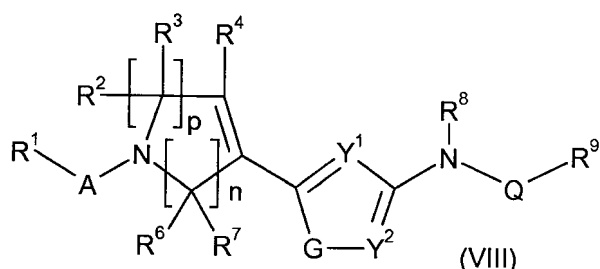
in which R^1 is C_1 - C_8 alkyl and A, T, G, Y^1 , Y^2 , Q, n, p, R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 and R^9 have
15 the definitions as defined for formula I in any one of claims 1 to 12;

or a compound of formula II:



wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , A, T, G, Y^1 , Y^2 , n and p are as defined for formula I in
20 any one of claims 1 to 12;

or a compound of formula VIII:



wherein R^1 , R^2 , R^3 , R^4 , R^6 , R^7 , R^8 , A, T, G, Y^1 , Y^2 , p and n are as defined for formula I in any one of claims 1 to 12.

14. A fungicidal composition comprising at least one compound as defined in any one of
5 claims 1 to 12 and an agriculturally acceptable carrier, optionally comprising an adjuvant, and optionally comprising at least one additional fungicidally active compound.

15. A method of controlling or preventing an infestation of plants, propagation material thereof, harvested crops or non-living materials by phytopathogenic or spoilage
10 microorganisms or organisms potentially harmful to man, which comprises the application of a compound as defined in any one of claims 1 to 12, to the plant, to parts of the plants or to the locus thereof, to propagation material thereof or to any part of the non-living materials; wherein the phytopathogenic microorganisms are preferably fungal organisms.

15

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2010/061381

A. CLASSIFICATION OF SUBJECT MATTER

INV. C07D413/04 C07D413/14 C07D417/04 C07D417/14 A01P3/00
A01N43/78 A01N43/76 A01N43/836

ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07D A01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2007/014290 A2 (DU PONT [US]; BISAHA JOHN JOSEPH [US]; KOVACS PATRICK RYAN [US]; LETT) 1 February 2007 (2007-02-01) cited in the application claim 1 examples page 241 - page 251	1-15
A	PATANI G A ET AL: "BIOISOSTERISM: A RATIONAL APPROACH IN DRUG DESIGN" CHEMICAL REVIEWS, ACS, WASHINGTON, DC, US LNKD- DOI:10.1021/CR950066Q, vol. 96, no. 8, 1 January 1996 (1996-01-01), pages 3147-3176, XP000652176 ISSN: 0009-2665 page 3170; table 48 ----- -/-	1-15

☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

11 November 2010

Date of mailing of the international search report

23/11/2010

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Miniejew, Catherine

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2010/061381

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2009/094445 A2 (DU PONT [US]; KAMIREDDY BALREDDY [US]; PASTERIS ROBERT JAMES [US]; HAN) 30 July 2009 (2009-07-30) claim 1 examples page 226 - page 229 -----	1-15

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2010/061381

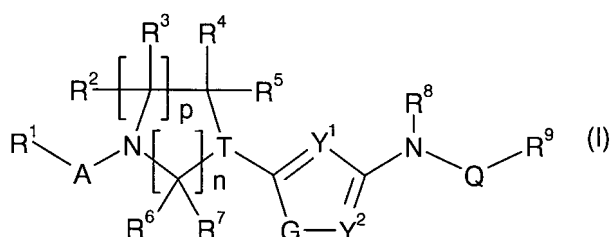
Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 2007014290	A2	01-02-2007	AR 057688 A1	12-12-2007
			AU 2006272551 A1	01-02-2007
			CA 2614288 A1	01-02-2007
			CN 101228156 A	23-07-2008
			EC SP088112 A	20-02-2008
			EP 1948649 A2	30-07-2008
			GT 200600329 A	26-03-2007
			JP 2009502948 T	29-01-2009
			KR 20080031030 A	07-04-2008
			NZ 564017 A	29-01-2010
			UY 29695 A1	28-02-2007
			ZA 200711055 A	26-08-2009
WO 2009094445	A2	30-07-2009	AU 2009206468 A1	30-07-2009

HETEROCICLOS MICROBICIDAS

La presente invención trata acerca de heterociclos, por ejemplo como ingredientes activos, los cuales tienen actividad microbicida, en particular actividad fungicida. También, la invención trata acerca de la preparación de estos heterociclos, de derivados heterocíclicos utilizados como intermediarios en la preparación de estos heterociclos, de la preparación de estos intermediarios, de composiciones agroquímicas las cuales comprenden al menos uno de los heterociclos, de la preparación de estas composiciones y del uso de los heterociclos o de las composiciones, en la agricultura o la horticultura, para controlar o evitar la infestación de plantas, cultivos comestibles cosechados, semillas o materiales no vivientes, por parte de microorganismos fitopatógenos, preferiblemente hongos.

Ciertos heterociclos utilizados como fungicidas son descritos en los documentos WO 2007/014290, WO 2008/013622, WO 2008/013925, WO 2008/091580, WO 2008/091594 y WO 2009/055514.

La presente invención provee compuestos de fórmula I:



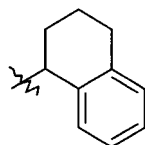
en donde

- A es $x-C(=O)-$, $x-C(=S)-$, $x-C(R^{10}R^{11})-C(=O)-$, $x-C(R^{12}R^{13})-C(=S)-$, $x-O-C(=O)-$, $x-O-C(=S)-$, $x-N(R^{14})-C(=O)-$, $x-N(R^{15})-C(=S)-$, $x-C(R^{16}R^{17})-SO_2-$ o $x-N=C(R^{26})-$, en cada caso x representa el enlace que está conectado a R^1 ;
- T es CR^{18} o N;
- G es O o S;
- Y^1 y Y^2 son independientemente CR^{19} o N;
- Q es $-C(=O)-z$, $-C(=S)-z$, $-C(=O)-O-z$, $-C(=S)-O-z$, $-C(=O)-N(R^{20})-z$, $-C(=S)-N(R^{21})-z$ o $-SO_2-z-$, en cada caso z representa el enlace que está conectado a R^9 ;
- n es 1 o 2;
- p es 1 o 2, con la condición de que cuando n es 2, p es 1;
- R^1 es fenilo, piridilo, imidazolilo, o pirazolilo; en donde cada uno de los fenilo, piridilo, imidazolilo y pirazolilo están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre alquilo C_1-C_4 , haloalquilo C_1-C_4 , halógeno, ciano, hidroxi y amino;

R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^{10} , R^{11} , R^{12} , R^{13} , R^{16} , R^{17} , R^{18} , R^{19} y R^{26} son, cada uno independientemente, hidrógeno, halógeno, ciano, alquilo C_1-C_4 o haloalquilo C_1-C_4 ;

R^8 , R^{14} , R^{15} , R^{20} y R^{21} son, cada uno independientemente, hidrógeno, alquilo C_1-C_4 o alcoxi C_1-C_4 ; y

- 5 R^9 es fenilo, bencilo o el grupo (a):



(a)

- 10 en donde cada uno de fenilo, bencilo y el grupo (a) están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre alquilo C_1-C_4 , haloalquilo C_1-C_4 , alcoxi C_1-C_4 , haloalcoxi C_1-C_4 , halógeno, ciano, hidroxilo, $N(R^{27})_2$, SH, alquiltio C_1-C_4 , nitro, fenilsulfonilo y fenilsulfinilo, en donde el fenilsulfonilo y el fenilsulfinilo están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente

- 15 entre alquilo C_1-C_4 , haloalquilo C_1-C_4 , alcoxi C_1-C_4 , haloalcoxi C_1-C_4 , halógeno y ciano; cada R^{27} es independientemente hidrógeno, alquilo C_1-C_4 , fenilsulfonilo o fenilsulfinilo, en donde el fenilsulfonilo y el fenilsulfinilo están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre alquilo C_1-C_4 , haloalquilo C_1-C_4 , alcoxi C_1-C_4 , haloalcoxi C_1-C_4 , halógeno y ciano; o una sal o un N-óxido de los mismos.

- 20 Cuando se indica que los sustituyentes están sustituidos opcionalmente, esto significa que puede que los mismos incluyan, o no incluyan, uno o más sustituyentes idénticos o diferentes. Normalmente, no más de tres de tales sustituyentes opcionales están presentes al mismo tiempo.

- El término "halógeno" se refiere a flúor, cloro, bromo o yodo, preferiblemente flúor,
25 cloro o bromo.

El término "amino" se refiere a $-NH_2$.

- Los sustituyentes alquilo pueden ser lineales o ramificados. Como sustituyente individual o como parte de otro sustituyente, alquilo es, dependiendo del número de átomos de carbono mencionados, por ejemplo, metilo, etilo, n-propilo, n-butilo, n-pentilo,
30 n-hexilo y los isómeros de los mismos, por ejemplo, iso-propilo, iso-butilo, sec-butilo, terc-butilo, iso-amilo o pivaloilo.

Un grupo haloalquilo puede contener uno o más átomos de halógeno, idénticos o diferentes y, por ejemplo, puede corresponder a CH_2Cl , CHCl_2 , CCl_3 , CH_2F , CHF_2 , CF_3 , CF_3CH_2 , CH_3CF_2 , CF_3CF_2 o CCl_3CCl_2 .

La presencia de uno o más átomos asimétricos de carbono posibles en un
 5 compuesto de fórmula I significa que los compuestos pueden existir en formas isoméricas ópticas, es decir formas enantioméricas o diastereoisoméricas. Como un resultado de la presencia de un enlace doble alifático $\text{C}=\text{C}$ posible, se puede presentar isomería geométrica, es decir isomería cis-trans o (*E*)-(*Z*). Se pueden presentar también atropoisómeros como resultado de la rotación restringida con respecto a un enlace
 10 sencillo. Se pretende que la Fórmula I incluya todas aquellas formas isoméricas y mezclas de las mismas que sean posibles. La presente invención incluye a todas aquellas formas isoméricas y mezclas de las mismas que sean posibles para un compuesto de fórmula I. De forma similar, se pretende que la Fórmula I incluya a todos los tautómeros posibles. La presente invención incluye a todas las formas tautoméricas posibles para un compuesto
 15 de fórmula I.

En cada caso, los compuestos de fórmula I de conformidad con la invención están en forma libre, en forma oxidada como un N-óxido o en forma de sal, por ejemplo una forma de sal utilizable agronómicamente.

Los N-óxidos son formas oxidadas de aminas terciarias o formas oxidadas de
 20 compuestos heteroaromáticos nitrogenados. Por ejemplo, son descritos en el libro "Heterocyclic N-oxides" por A. Albini y S. Pietra, CRC Press, Boca Raton 1991.

Las sales adecuadas de los compuestos de fórmula I incluyen a aquellas que se producen tras la adición de ácido, tales como aquellas formadas con un ácido inorgánico mineral, por ejemplo ácido clorhídrico, bromhídrico, sulfúrico, nítrico o fosfórico, o un ácido
 25 carboxílico orgánico, por ejemplo ácido oxálico, tartárico, láctico, butírico, toluico, hexanoico o ftálico, o un ácido sulfónico, por ejemplo ácido metano, benceno o tolueno sulfónico.

Preferiblemente el compuesto de fórmula I es un compuesto en donde:

A es x-C(=O)- , x-C(=S)- , $\text{x-C(R}^{10}\text{R}^{11}\text{)-C(=O)-}$, $\text{x-C(R}^{12}\text{R}^{13}\text{)-C(=S)-}$, x-O-C(=O)- , x-O-C(=S)- ,
 30 $\text{x-N(R}^{14}\text{)-C(=O)-}$, $\text{x-N(R}^{15}\text{)-C(=S)-}$ o $\text{x-C(R}^{16}\text{R}^{17}\text{)-SO}_2\text{-}$, en cada caso x representa el enlace que está conectado a R^1 ;
 T es CR^{18} o N;
 G es O o S;
 Y^1 y Y^2 son independientemente CR^{19} o N;
 35 Q es -C(=O)-z , -C(=S)-z , -C(=O)-O-z , -C(=S)-O-z , $\text{-C(=O)-N(R}^{20}\text{)-z}$, $\text{-C(=S)-N(R}^{21}\text{)-z}$ o $\text{-SO}_2\text{-z}$, en cada caso z representa el enlace que está conectado a R^9 ;

n es 1 o 2;

p es 1 o 2, con la condición de que cuando n es 2, p es 1;

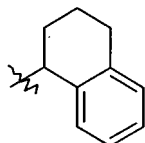
R¹ es fenilo, piridilo, imidazolilo, o pirazolilo; en donde cada uno de los fenilo, piridilo, imidazolilo y pirazolilo están sustituidos opcionalmente con entre 1 y 3 sustituyentes

5 escogidos independientemente entre alquilo C₁-C₄, haloalquilo C₁-C₄, halógeno, ciano, hidroxi y amino;

R², R³, R⁴, R⁵, R⁶, R⁷, R¹⁰, R¹¹, R¹², R¹³, R¹⁶, R¹⁷, R¹⁸ y R¹⁹ son, cada uno independientemente, hidrógeno, halógeno, ciano, alquilo C₁-C₄, o haloalquilo C₁-C₄;

R⁸, R¹⁴, R¹⁵, R²⁰ y R²¹ son, cada uno independientemente, hidrógeno o alquilo C₁-C₄; y

10 R⁹ es fenilo, bencilo o el grupo (a):



(a)

en donde cada uno de fenilo, bencilo y el grupo (a) están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre alquilo C₁-C₄, haloalquilo

15 C₁-C₄, halógeno, ciano, hidroxi y amino;

Preferiblemente el compuesto de fórmula I es un compuesto en donde:

A es x-C(=O)-, x-C(=S)-, x-C(R¹⁰R¹¹)-C(=O)-, x-C(R¹²R¹³)-C(=S)-, x-O-C(=O)-, x-O-C(=S)- o x-C(R¹⁶R¹⁷)-SO₂-, en cada caso x representa el enlace que está conectado a R¹;

T es CR¹⁸ o N;

20 G es O o S;

Y¹ es N;

Y² es CR¹⁹ o N;

Q es -C(=O)-z, -C(=S)-z, -C(=O)-O-z, -C(=S)-O-z, -C(=O)-N(R²⁰)-z, -C(=S)-N(R²¹)-z o -SO₂-z-, en cada caso z representa el enlace que está conectado a R⁹;

25 n es 1 o 2;

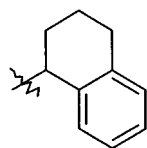
p es 1;

R¹ es fenilo o pirazolilo; en donde cada uno de los fenilo y pirazolilo están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre alquilo C₁-C₄, haloalquilo C₁-C₄, halógeno, ciano, hidroxi y amino;

30 R², R³, R⁴, R⁵, R⁶, R⁷, R¹⁰, R¹¹, R¹², R¹³, R¹⁶, R¹⁷, R¹⁸ y R¹⁹ son, cada uno independientemente, hidrógeno, halógeno, alquilo C₁-C₄, haloalquilo C₁-C₄;

R⁸, R²⁰ y R²¹ son, cada uno independientemente, hidrógeno o alquilo C₁-C₄; y

R⁹ es fenilo, bencilo o el grupo (a):



(a)

en donde cada uno de fenilo, bencilo y el grupo (a) están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre alquilo C_1-C_4 , haloalquilo C_1-C_4 , halógeno, ciano, hidroxilo, y amino.

Preferiblemente el compuesto de fórmula I es un compuesto en donde:

A es $x-C(=O)-$, $-x-CR^{10}R^{11}-C(=O)-$, $x-O-C(=O)-$ o $x-C(R^{16}R^{17})-SO_2-$, en cada caso x representa el enlace que está conectado a R^1 ;

T es CR^{18} o N;

10 G es S;

Y^1 es N;

Y^2 es CR^{19} o N;

Q es $-C(=O)-z$, $-C(=O)-O-z$, $-C(=O)-N(R^{20})-z$ o $-SO_2-z$, en cada caso siendo z el enlace con R^9 ;

15 n es 1 o 2;

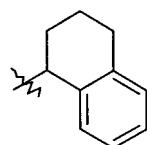
p es 1;

R^1 es fenilo o pirazolilo, en donde el fenilo y pirazolilo están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre alquilo C_1-C_4 , haloalquilo C_1-C_4 , y halógeno;

20 R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^{10} , R^{11} , R^{16} , R^{17} , R^{18} y R^{19} son, cada uno independientemente, hidrógeno, fluoro, o metilo;

R^8 y R^{20} son, cada uno independientemente, hidrógeno o metilo; y

R^9 es fenilo, bencilo o el grupo (a):



(a)

25

en donde cada uno de fenilo, bencilo y el grupo (a) están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre alquilo C_1-C_4 , haloalquilo C_1-C_4 , hidroxilo y halógeno.

Preferiblemente el compuesto de fórmula I es un compuesto en donde:

30 A es $x-C(=O)-$, $x-CH_2-C(=O)-$, $x-O-C(=O)-$ o $x-CH_2-SO_2-$, en cada caso x representa el enlace que está conectado a R^1 ;

T es CH o N;

G es S;

Y^1 es N;

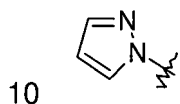
Y^2 es CH o N;

- 5 Q es $-C(=O)-z$, $-C(=O)-O-z$, $-C(=O)-NH-z$ o $-SO_2-z$, en cada caso z representa el enlace que está conectado a R^9 ;

n es 1 o 2;

p es 1;

R^1 es fenilo o el grupo (b):



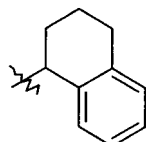
(b)

en donde el fenilo y el grupo (b) están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre halógeno, alquilo C_1-C_4 y haloalquilo C_1-C_4 ;

- 15 R^2 , R^3 , R^4 , R^5 , R^6 y R^7 son, cada uno, hidrógeno;

R^8 es hidrógeno; y

R^9 es fenilo, bencilo o el grupo (a):



(a)

- 20 en donde cada uno de fenilo, bencilo y el grupo (a) están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre alquilo C_1-C_4 , haloalquilo C_1-C_4 , hidroxi y halógeno.

Preferiblemente el compuesto de fórmula I es un compuesto en donde:

A es $x-CH_2-C(=O)-$ en donde x representa el enlace que está conectado a R^1 ;

- 25 T es CH;

G es S;

Y^1 es N;

Y^2 es CH;

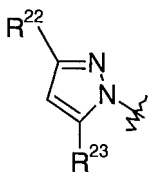
Q es $-C(=O)-z$, $-C(=O)-O-z$ o $C(=O)-N(R^{20})-z$, en cada caso z representa el enlace que

- 30 está conectado a R^9 ;

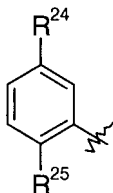
n es 2;

p es 1;

R^1 es escogido entre los grupos (c) o (d):



(c)



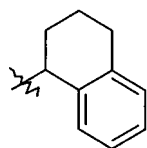
(d)

en donde R^{22} , R^{23} , R^{24} y R^{25} son escogidos independientemente entre hidrógeno, halógeno, metilo y halometilo;

R_2 , R_3 , R_4 , R_5 , R_6 , y R_7 son, cada uno, hidrógeno;

R_8 , es hidrógeno;

R^9 es fenilo, bencilo o el grupo (a):



(a)

10

en donde el fenilo, bencilo y el grupo(a) están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre halógeno, hidroxi, metilo y halometilo.

También, la invención provee un compuesto de fórmula I en el cual:

A es $x\text{-CH}_2\text{C(=O)-}$, $x\text{-CH}_2\text{C(=S)-}$, $x\text{-OC(=O)-}$, $x\text{-C(=O)-}$ o $x\text{-CH}_2\text{-SO}_2\text{-}$, en cada caso x representa el enlace que está conectado a R^1 ;

15

T es CH o N;

G es O o S;

Y^1 es N;

Y^2 es CH o N;

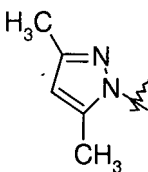
Q es $-\text{C(=O)-z}$, $-\text{C(=S)-z}$, $-\text{C(=O)O-z}$, $-\text{C(=O)NH-z}$ o $-\text{SO}_2\text{-z}$, en cada caso z representa el enlace que está conectado a R^9 ;

20

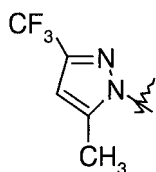
n es 1 o 2;

p es 1 o 2, con la condición de que cuando n es 2, p es 1;

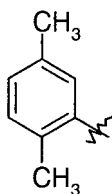
R^1 es el grupo (e), (f), (g), o (h):



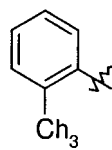
(e)



(f)



(g)



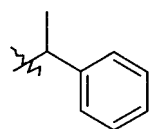
(h)

25

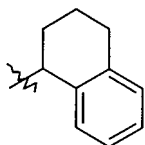
R^2 , R^3 , R^4 , R^5 , R^6 y R^7 son H;

R^8 es H o metilo;

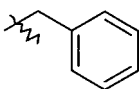
R^9 es el grupo (i), (j), (k), (l) o (m):



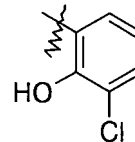
(i)



(j)



(k)



(l)

5

(m)

La lista siguiente provee definiciones, incluyendo a las definiciones preferidas, de los sustituyentes A, T, G, Y^1 , Y^2 , Q, n, p, R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , R^{10} , R^{11} , R^{12} , R^{13} , R^{14} , R^{15} , R^{16} , R^{17} , R^{18} , R^{19} , R^{20} , R^{21} , R^{22} , R^{23} , R^{24} , R^{25} , R^{26} y R^{27} con respecto a los compuestos de fórmula I. Para cualesquiera de estos sustituyentes, cualesquiera de las definiciones dadas más adelante pueden ser combinadas con cualquier definición de cualquier otro sustituyente, dada más adelante o en cualquier otro lugar de este documento. La invención incluye compuestos de fórmula, los cuales tienen todas las combinaciones posibles de las definiciones de sustituyentes dadas más adelante. Por lo general, en este documento cualquier definición de sustituyente puede ser combinada con cualquier otra definición de sustituyente.

A es $x-C(=O)-$, $x-C(=S)-$, $x-C(R^{10}R^{11})-C(=O)-$, $x-C(R^{12}R^{13})-C(=S)-$, $x-O-C(=O)-$, $x-O-C(=S)-$, $x-N(R^{14})-C(=O)-$, $x-N(R^{15})-C(=S)-$, $x-C(R^{16}R^{17})-SO_2-$ o $x-N=C(R^{26})-$, en cada caso x representa el enlace que está conectado a R^1 . Preferiblemente A es $x-C(=O)-$, $x-C(=S)-$, $x-C(R^{10}R^{11})-C(=O)-$, $x-C(R^{12}R^{13})-C(=S)-$, $x-O-C(=O)-$, $x-O-C(=S)-$, $x-N(R^{14})-C(=O)-$, $x-N(R^{15})-C(=S)-$ o $x-C(R^{16}R^{17})-SO_2-$, en cada caso x representa el enlace que está conectado a R^1 . Más preferiblemente, A es $x-C(=O)-$, $x-C(=S)-$, $x-C(R^{10}R^{11})-C(=O)-$, $x-C(R^{12}R^{13})-C(=S)-$, $x-O-C(=O)-$, $x-O-C(=S)-$ o $x-C(R^{16}R^{17})-SO_2-$, en cada caso x representa el enlace que está conectado a R^1 . Aún más preferiblemente, A es $x-C(=O)-$, $-x-CR^{10}R^{11}-C(=O)-$, $x-O-C(=O)-$ o $x-C(R^{16}R^{17})-SO_2-$, en cada caso x representa el enlace que está conectado a R^1 . Todavía más preferiblemente, A es $x-CH_2C(=O)-$, $x-CH_2C(=S)-$, $x-OC(=O)-$, $x-C(=O)-$ o $x-CH_2-SO_2-$, en cada caso x representa el enlace que está conectado a R^1 . Lo más preferible es que A sea $x-CH_2-C(=O)-$ en donde x representa el enlace que está conectado a R^1 .

T es CR^{18} o N. Preferiblemente, T es CH o N. Más preferiblemente, T es CH.

G es O o S. Preferiblemente, G es S.

Y^1 es CR^{19} o N. Preferiblemente, Y^1 es N.

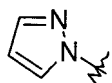
Y^2 es CR^{19} o N. Preferiblemente, Y^2 es CH o N. Más preferiblemente, Y^2 es CH.

Q es $-C(=O)-z$, $-C(=S)-z$, $-C(=O)-O-z$, $-C(=S)-O-z$, $-C(=O)-N(R^{20})-z$, $-C(=S)-N(R^{21})-z$ o $-SO_2-z$, en cada caso z representa el enlace que está conectado a R^9 . Preferiblemente, Q es $-C(=O)-z$, $-C(=S)-z$, $-C(=O)O-z$, $-C(=O)NH-z$ o $-SO_2-z$, en cada caso z representa el enlace que está conectado a R^9 . Preferiblemente, Q es $-C(=O)-z$, $-C(=O)-O-z$, $-C(=O)-N(R^{20})-z$ o $-SO_2-z$, en cada caso z representa el enlace que está conectado a R^9 . Más preferiblemente, Q es $-C(=O)-z$, $-C(=O)-O-z$, $-C(=O)-NH-z$ o $-SO_2-z$, en cada caso z representa el enlace que está conectado a R^9 . Aún más preferiblemente, Q es $-C(=O)-z$, $-C(=O)-O-z$ o $-C(=O)-N(R^{20})-z$, en cada caso z representa el enlace que está conectado a R^9 . Lo más preferible es que Q sea $-C(=O)-z$ en donde z representa el enlace que está

n es 1 o 2. Preferiblemente, n es 2.

p es 1 o 2, con la condición de que cuando n es 2, p es 1. Preferiblemente p es 1.

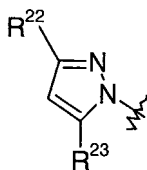
R^1 es fenilo, piridilo, imidazolilo, o pirazolilo; en donde cada uno de los fenilo, piridilo, imidazolilo y pirazolilo están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre alquilo C_1-C_4 , haloalquilo C_1-C_4 , halógeno, ciano, hidroxilo y amino. Preferiblemente, R^1 es fenilo o pirazolilo; en donde cada uno de los fenilo y pirazolilo están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre alquilo C_1-C_4 , haloalquilo C_1-C_4 , halógeno, ciano, hidroxilo, y amino. Preferiblemente, R^1 es fenilo o pirazolilo, en donde el fenilo y el pirazolilo están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre alquilo C_1-C_4 , haloalquilo C_1-C_4 , y halógeno. Más preferiblemente, R^1 es fenilo o el grupo (b):



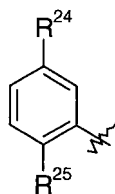
(b)

en donde el fenilo y el grupo (b) están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre halógeno, alquilo C_1-C_4 y haloalquilo C_1-C_4 .

En un grupo de compuestos R^1 es escogido entre los grupos (c) o (d):



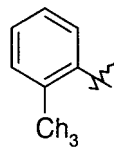
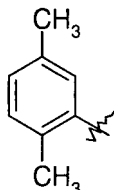
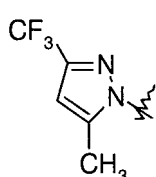
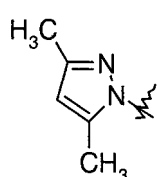
(c)



(d)

en donde R^{22} , R^{23} , R^{24} y R^{25} son escogidos independientemente entre hidrógeno, halógeno, metilo y halometilo.

En un grupo de compuestos R^1 es el grupo (e), (f), (g), o (h):



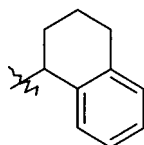
5 (e) (f) (g) (h)

R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^{10} , R^{11} , R^{12} , R^{13} , R^{16} , R^{17} , R^{18} , R^{19} son, cada uno independientemente, hidrógeno, halógeno, ciano, alquilo C_1 - C_4 , o haloalquilo C_1 - C_4 . Preferiblemente, R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^{10} , R^{11} , R^{12} , R^{13} , R^{16} , R^{17} , R^{18} y R^{19} son, cada uno independientemente, hidrógeno, halógeno, alquilo C_1 - C_4 , o haloalquilo C_1 - C_4 . Más
10 preferiblemente, R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^{10} , R^{11} , R^{12} , R^{13} , R^{16} , R^{17} , R^{18} y R^{19} son, cada uno independientemente, hidrógeno, fluoro, o metilo. Aún más preferiblemente, R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^{10} , R^{11} , R^{12} , R^{13} , R^{16} , R^{17} , R^{18} y R^{19} son, cada uno independientemente, hidrógeno.

R^8 , R^{14} , R^{15} , R^{20} , y R^{21} son, cada uno independientemente, hidrógeno o alquilo C_1 -
15 C_4 . Preferiblemente, R^8 , R^{14} , R^{15} , R^{20} , y R^{21} son, cada uno independientemente, hidrógeno o metilo.

Más preferiblemente, R^8 , R^{14} , R^{15} , R^{20} , y R^{21} son, cada uno independientemente, hidrógeno.

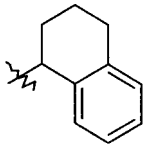
R^9 es fenilo, bencilo o el grupo (a):



20

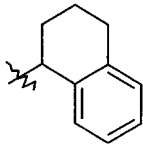
(a)

en donde cada uno de fenilo, bencilo y el grupo (a) están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre alquilo C_1 - C_4 , haloalquilo C_1 - C_4 , alcoxi C_1 - C_4 , haloalcoxi C_1 - C_4 , halógeno, ciano, hidroxilo, $N(R^{27})_2$, SH,
25 alquiltio C_1 - C_4 , nitro, fenilsulfonilo y fenilsulfinilo, en donde el fenilsulfonilo y el fenilsulfinilo están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre alquilo C_1 - C_4 , haloalquilo C_1 - C_4 , alcoxi C_1 - C_4 , haloalcoxi C_1 - C_4 , halógeno y ciano. Preferiblemente, R^9 es fenilo, bencilo o el grupo (a):



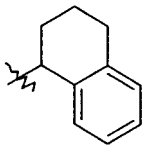
(a)

en donde cada uno de fenilo, bencilo y el grupo (a) están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre alquilo C₁-C₄, haloalquilo C₁-C₄, halógeno, ciano, hidroxí y amino. Preferiblemente, R⁹ es fenilo, bencilo o el grupo (a):



(a)

en donde cada uno de fenilo, bencilo y el grupo (a) están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre alquilo C₁-C₄, haloalquilo C₁-C₄, hidroxí y halógeno. Más preferiblemente, R⁹ es fenilo, bencilo o el grupo (a):



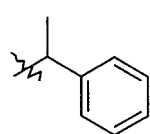
(a)

en donde el fenilo, bencilo y el grupo(a) están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre halógeno, hidroxí, metilo y halometilo.

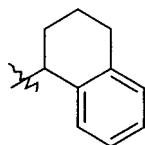
R²⁶ es hidrógeno, halógeno, ciano, alquilo C₁-C₄, o haloalquilo C₁-C₄. Preferiblemente, R²⁶ es hidrógeno, halógeno, alquilo C₁-C₄, o haloalquilo C₁-C₄. Preferiblemente, R²⁶ es hidrógeno, fluoro, o metilo. Más preferiblemente, R²⁶ es hidrógeno.

Cada R²⁷ es independientemente hidrógeno, alquilo C₁-C₄, fenilsulfonilo o fenilsulfinilo, en donde el fenilsulfonilo y el fenilsulfinilo están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre alquilo C₁-C₄, haloalquilo C₁-C₄, alcoxi C₁-C₄, haloalcoxi C₁-C₄, halógeno y ciano. Preferiblemente, R²⁷ es independientemente hidrógeno, alquilo C₁-C₄, fenilsulfonilo o fenilsulfinilo, en donde el fenilsulfonilo y el fenilsulfinilo están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre halógeno, metilo y halometilo.

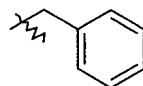
En un grupo de compuestos R⁹ es el grupo (i), (j), (k), (l) o (m):



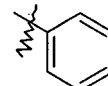
(i)



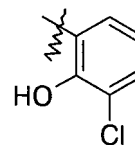
(m)



(j)



(k)



(l)

Preferiblemente R^{22} es hidrógeno o CF_3 .

5 Preferiblemente R^{23} , R^{24} , y R^{25} son independientemente hidrógeno o metilo.

En un grupo de compuestos G es S, Y^1 es N y Y^2 es CH.

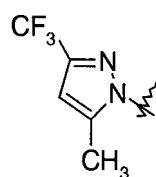
En un grupo de compuestos p es 1 y n es 2.

En un grupo de compuestos R^2 , R^3 , R^4 , R^5 , R^6 y R^7 son H

10 En un grupo de compuestos Q es $-C(=O)-z$, en donde z representa el enlace que está conectado a R^9 .

En un grupo de compuestos A es $x-CH_2-C(=O)-$, en donde x representa el enlace que está conectado a R^1 .

En un grupo de compuestos R^1 es el grupo (f)

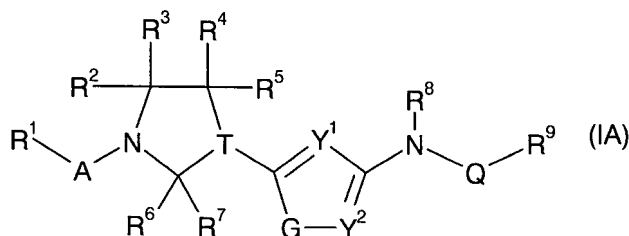


15 (f)

En un grupo de compuestos R^9 es fenilo sustituido con hidroxilo, y sustituido opcionalmente con uno o dos sustituyentes adicionales, tal y como se definieron anteriormente. Preferiblemente el hidroxilo está en la posición orto. Preferiblemente uno de los sustituyentes adicionales es halógeno y está preferiblemente en la posición meta

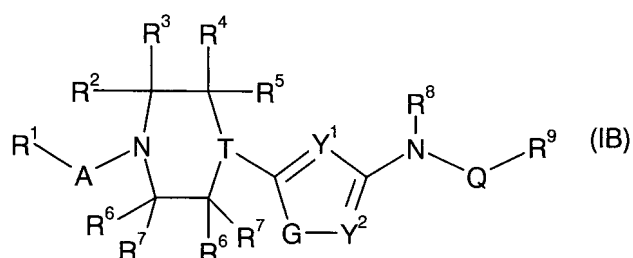
20 adyacente al hidroxilo.

Para evitar dudas, cuando n es 1 y p es 1, los compuestos de fórmula I tienen la fórmula de conformidad con la fórmula IA:



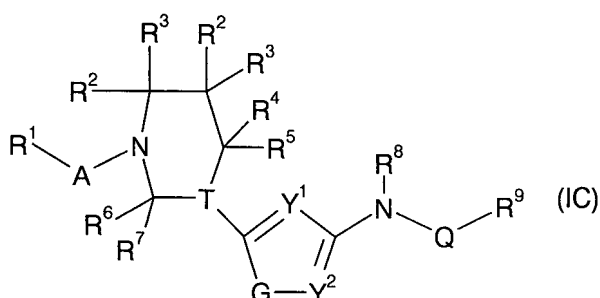
25 en la cual A, T, G, Y^1 , Y^2 , Q, R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , y R^9 tienen las definiciones tales como fueron descritas para la fórmula I.

Cuando n es 2 y p es 1, los compuestos de fórmula I tienen la fórmula de conformidad con la fórmula IB:



en la cual A, T, G, Y¹, Y², Q, R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, y R⁹ tienen las definiciones 5 tales como fueron descritas para la fórmula I.

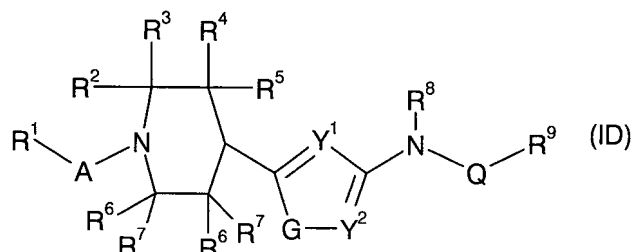
Cuando n es 1 y p es 2, los compuestos de fórmula I tienen la fórmula de conformidad con la fórmula IC:



en la cual A, T, G, Y¹, Y², Q, R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, y R⁹ tienen las definiciones 10 tales como fueron descritas para la fórmula I.

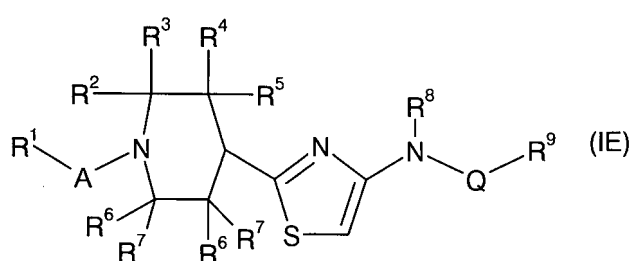
También, la invención trata acerca de compuestos de fórmula IA, fórmula IB y fórmula IC, tal y como se mostró anteriormente.

La invención trata también acerca de compuestos de fórmula ID:



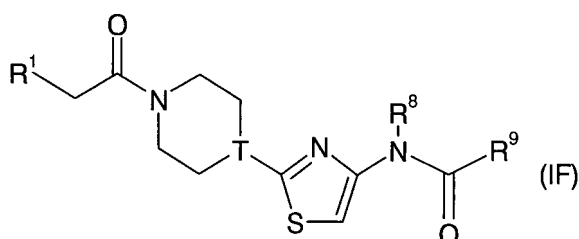
15 en la cual A, G, Y¹, Y², Q, R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, y R⁹ tienen las definiciones tales como fueron descritas para la fórmula I. Las definiciones preferidas de A, G, Y¹, Y², Q, R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, y R⁹ son tales como las definidas para la fórmula I.

También, la invención trata acerca de compuestos de fórmula IE:



en la cual A, Q, R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, y R⁹ tienen las definiciones tales como fueron descritas para la fórmula I. Las definiciones preferidas de A, Q, R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, y R⁹ son tales como las definidas para la fórmula I.

5 También, la invención trata acerca de compuestos de fórmula IF:

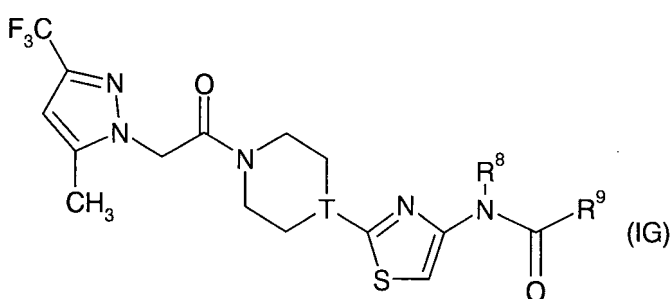


en donde T es CH o N

R⁸ es CH₃ o H; y

R¹ y R⁹ tienen las definiciones tales como fueron descritas para la fórmula I. Las definiciones preferidas de R¹ y R⁹ son tales como las definidas para la fórmula I.

También, la invención trata acerca de compuestos de fórmula IG:

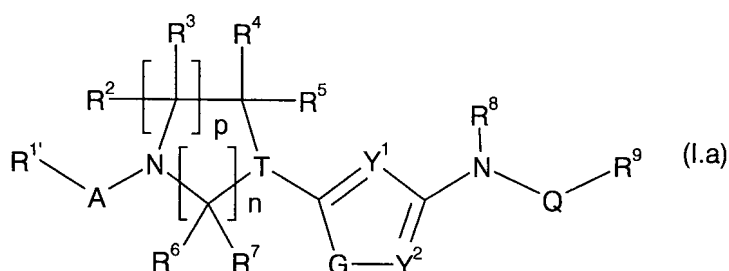


en donde T es CH o N

R⁸ es CH₃ o H; y

15 R⁹ tiene la definición tal y como la descrita para la fórmula I. Las definiciones preferidas de R⁹ son tales como las definidas para la fórmula I.

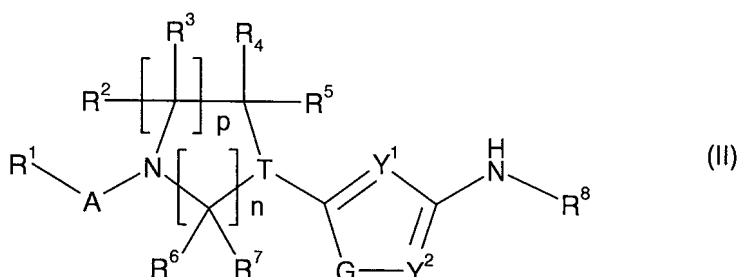
También, la invención incluye compuestos de fórmula I en los cuales R¹ es un grupo protector, tal y como un grupo alquilo. Por consiguiente, la invención incluye compuestos de fórmula I.a:



en la cual R^1 es alquilo C_1 - C_8 , por ejemplo alquilo C_1 - C_4 , por ejemplo terc-butilo; y A, T, G, Y^1 , Y^2 , Q, n, p, R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , y R^9 tienen las definiciones tales como fueron descritas para la fórmula I. Preferiblemente A es $x-O-C(=O)-$, x representa el enlace con R^1 . Las definiciones preferidas de A, T, G, Y^1 , Y^2 , Q, n, p, R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , y R^9 son tales como las definidas para la fórmula I.

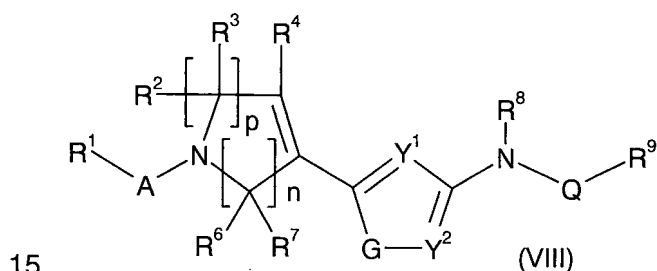
Estos compuestos son útiles para la síntesis de los compuestos de fórmula I.

También, la invención incluye compuestos de fórmula II:



en donde R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , A, T, G, Y^1 , Y^2 , p y n son tales como los definidos para la fórmula I. Las definiciones preferidas de R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , A, T, G, Y^1 , Y^2 , p y n son tales como las definidas para la fórmula I. Los compuestos de fórmula II son útiles como intermediarios en la síntesis de los compuestos de fórmula I.

La invención incluye también compuestos de fórmula VIII:



en donde R^1 , R^2 , R^3 , R^4 , R^6 , R^7 , R^8 , A, T, G, Y^1 , Y^2 , p y n son tales como los definidos para la fórmula I. Las definiciones preferidas de R^1 , R^2 , R^3 , R^4 , R^6 , R^7 , R^8 , A, T, G, Y^1 , Y^2 , p y n son tales como las definidas para la fórmula I. Los compuestos de fórmula VIII son útiles como intermediarios en la síntesis de los compuestos de fórmula I.

Los compuestos individuales preferidos son:

(2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-amida del ácido (*R*)-1,2,3,4-tetrahidro-naftalen-1-carboxílico (Compuesto No. 1.g.001);

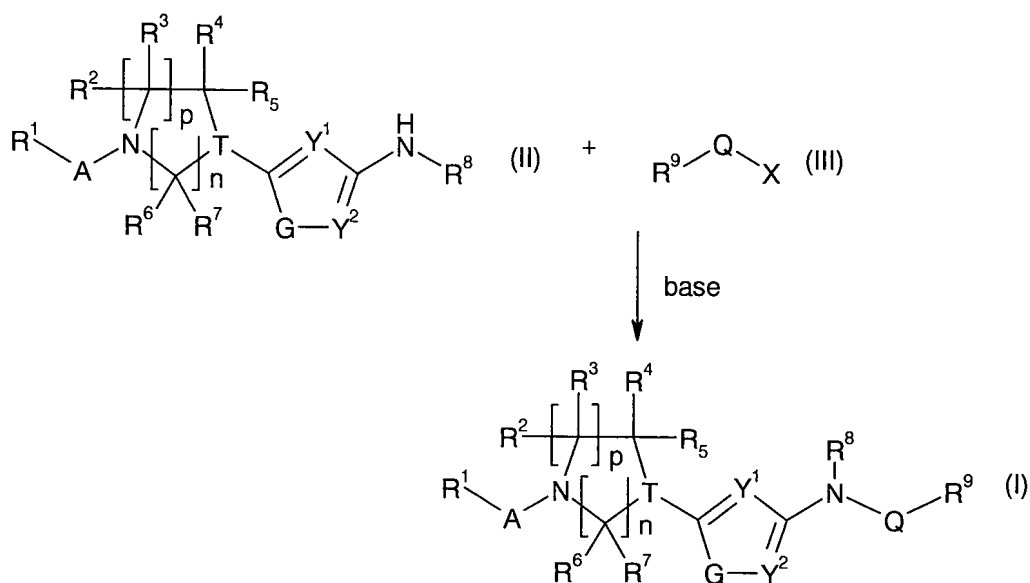
- 3-cloro-2-hidroxi-N-(2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-benzamida (Compuesto No. I.g.006);
- (2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-amida del ácido 1,2,3,4-tetrahidro-naftalen-1-carboxílico (Compuesto No. 1.g.011);
- 5 Éster 1,2,3,4-tetrahidro-naftalen-1-ílico del ácido (2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-carbámico (Compuesto No. I.g.013);
- N-2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-2-fenil-propionamida (Compuesto No. I.g.016);
- Éster 1-fenil-etílico del ácido N-(2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-carbámico (Compuesto No. I.g.018)
- 10 N-2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-benzamida (Compuesto No. I.g.021);
- Éster fenílico del ácido 2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-carbámico (Compuesto No. I.g.023);
- 15 1-(2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-3-fenil-urea (Compuesto No. I.g.024);
- (2-{1-[2-(2,5-dimetilfenil)-acetil]-piperidin-4-il}-tiazol-4-il)-amida del ácido 1,2,3,4-tetrahidro-naftalen-1-carboxílico (Compuesto No. 1.g.136);
- N-(2-{1-[2-(2,5-dimetil-fenil)-acetil]-piperidin-4-il}-tiazol-4-il)-2-fenil-propionamida
- 20 (Compuesto No. I.g.141);
- N-{2-[1-(2,5-dimetil-fenilmetansulfonil)-piperidin-4-il]-tiazol-4-il)-benzamida (Compuesto No. I.g. 246)
- {2-[1-(2-o-tolil-acetil)-piperidin-4-il]-tiazol-4-il)-amida del ácido 1,2,3,4-tetrahidro-naftalen-1-carboxílico (Compuesto No. I.g. 386)
- 25 3-fluoro-2-hidroxi-N-(2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-benzamida (Compuesto No. I.g.501);
- 3-bromo-2-hidroxi-N-(2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-benzamida (Compuesto No. I.g.502);
- 2-hidroxi-N-(2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-benzamida (Compuesto No. I.g.503);
- 30 2-metoxi-N-(2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-benzamida (Compuesto No. I.g.506);
- N-(2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-2-(toluen-4-sulfonilamino)-benzamida (Compuesto No. I.g.508);
- 35 2-metoxi-6-hidroxi-N-(2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-benzamida (Compuesto No. I.g.509);

- 2-fluoro-6-hidroxi-N-(2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-benzamida (Compuesto No. I.g.510);
- 3-metoxi-2-hidroxi-N-(2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-benzamida (Compuesto No. I.g.510);
- 5 metil-(2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-amida del ácido 1,2,3,4-tetrahidro-naftalen-1-carboxílico (Compuesto No. I.h.011); y
- N-metil-N-2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-2-fenil-propionamida (Compuesto No. I.h.016).
- (2-{4-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperazin-1-il}-tiazol-4-il)-amida del ácido
- 10 1,2,3,4-tetrahidro-naftalen-1-carboxílico (Compuesto No. I.n.011); y
- N-(2-{4-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperazin-1-il}-tiazol-4-il)-benzamida (Compuesto No. I.n.011).

Los compuestos de fórmula (I) pueden ser preparados según lo mostrado en los esquemas siguientes.

- 15 Los compuestos de fórmula I, en donde R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , A, T, G, Y^1 , Y^2 , n, p y Q son tales como los definidos para la fórmula I; pueden ser obtenidos mediante la transformación de un compuesto de fórmula II, en donde R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , A, T, G, Y^1 , Y^2 , n, p y Y son tales como los definidos para la fórmula I con un compuesto de fórmula III, en donde R^9 y Q son tales como los definidos para la fórmula I y X es a
- 20 hidroxi, halógeno, preferiblemente fluoro, cloro o bromo o alcoxi, tal y como metoxi, etoxi. Esto se muestra en el Esquema 1.

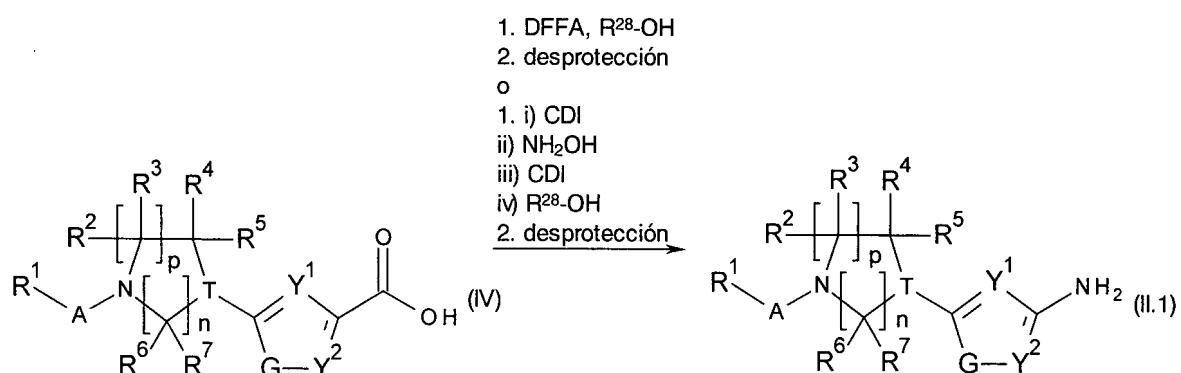
Esquema 1



Los compuestos de fórmula II.1, en donde R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , A, T, G, n, p, Y^1 y Y^2 son tales como los definidos para la fórmula I; pueden ser obtenidos mediante la transformación de un compuesto de fórmula IV, en donde R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , A, T, G, n, p, Y^1 y Y^2 son tales como los definidos para la fórmula I con una azida, tal y como

5 difenil fosforil azida y el reordenamiento de Curtius subsiguiente de la acil azida resultante con un alcohol R^{28} -OH, en donde R^{28} es alquilo C_1 - C_6 o arilo sustituido opcionalmente y descomposición posterior del carbamato con un ácido mineral, tal y como el ácido clorhídrico, ácido sulfúrico o un ácido orgánico, tal y como el ácido trifluoroacético. Esto se muestra en el Esquema 2.

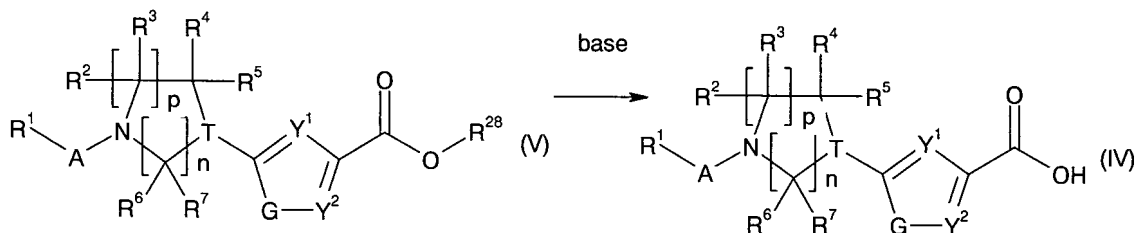
10 Esquema 2



Los compuestos de fórmula IV, en donde R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , A, T, G, n, p, Y^1 y

15 Y^2 son tales como los definidos para la fórmula I; pueden ser obtenidos mediante la saponificación de un compuesto de fórmula V, en donde R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , A, T, G, n, p, Y^1 y Y^2 son tales como los definidos para la fórmula I y R^{28} es alquilo C_1 - C_6 o arilo sustituido opcionalmente con una base, tal y como el hidróxido de sodio, hidróxido de potasio o hidróxido de litio. Esto se muestra en el Esquema 3.

20 Esquema 3



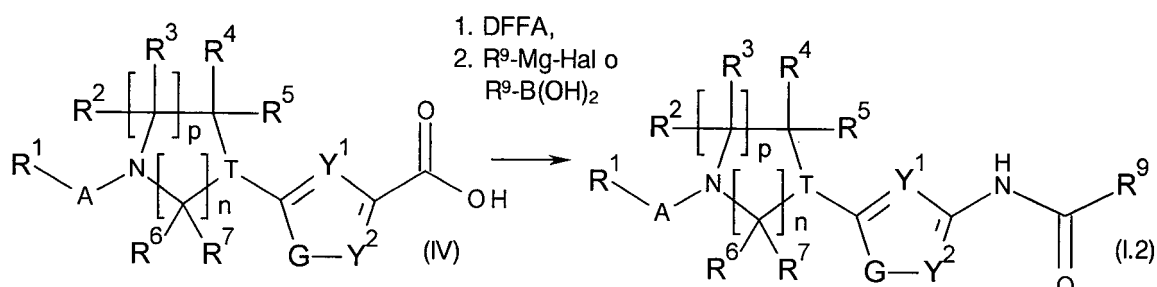
Los compuestos de fórmula V, en donde R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , A, T, G, n, p, Y^1 y Y^2 son tales como los definidos para la fórmula I y R^{28} es alquilo C_1 - C_6 o arilo sustituido opcionalmente; pueden ser obtenidos mediante la transformación de un compuesto de

25 fórmula VI, en donde R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , T, G, n, p, Y^1 y Y^2 son tales como los definidos para la fórmula I y R^{28} es alquilo C_1 - C_6 o arilo sustituido opcionalmente con un compuesto

Los compuestos de fórmula I.2, en donde R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^9 , A, T, G, n, p, Y^1 y Y^2 son tales como los definidos para la fórmula I; pueden ser obtenidos mediante la transformación de un compuesto de fórmula IV, en donde R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , A, T, G, n, p, Y^1 y Y^2 son tales como los definidos para la fórmula I con una azida, tal y como difenil fosforil azida y el reordenamiento de Curtius subsiguiente de la acil azida resultante con un reactivo de Grignard R^9 -Mg-Hal, en donde R^9 es tal y como se definió para la fórmula I y Hal es halógeno, preferiblemente cloro, bromo o yodo, o un ácido borónico R^9 -

$B(OH)_2$, en donde R^9 es tal y como se definió para la fórmula I y un catalizador, tal y como el hidróxido de bis(1,5-ciclooctadieno)rodio (I). Esto se muestra en el Esquema 6.

Esquema 6

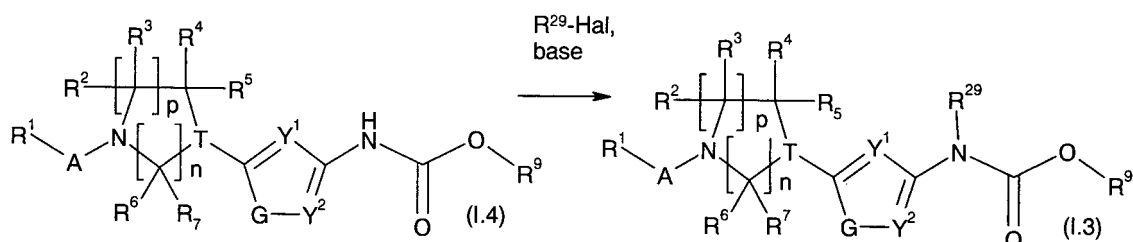


5

Alternativamente, los compuestos de fórmula I.3, en donde R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^9 , A, T, G, n, p, Y^1 y Y^2 son tales como los definidos para la fórmula I y R^{29} es alquilo C_1 - C_6 ; pueden ser obtenidos mediante la transformación de un compuesto de fórmula I.4, en donde R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^9 , A, T, G, n, p, Y^1 y Y^2 son tales como los definidos para la fórmula I con un haluro de alquilo $R^{29}\text{-Hal}$, en donde R^{29} es alquilo C_1 - C_6 y Hal es halógeno, preferiblemente cloro o bromo. Esto se muestra en el Esquema 7.

10

Esquema 7

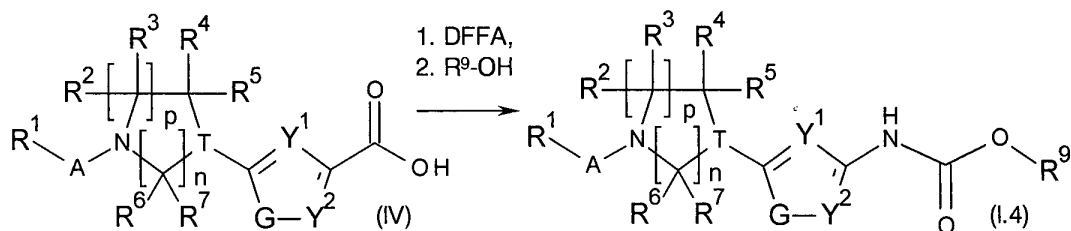


15

Los compuestos de fórmula I.4, en donde R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^9 , A, T, G, n, p, Y^1 y Y^2 son tales como los definidos para la fórmula I; pueden ser obtenidos mediante la transformación de un compuesto de fórmula IV, en donde R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , A, T, G, n, p, Y^1 y Y^2 son tales como los definidos para la fórmula I con una azida, tal y como difenil fosforil azida y el reordenamiento de Curtius subsiguiente de la acil azida resultante con un alcohol $R^9\text{-OH}$, en donde R^9 es tal y como se definió para la fórmula I. Esto se muestra en el Esquema 8.

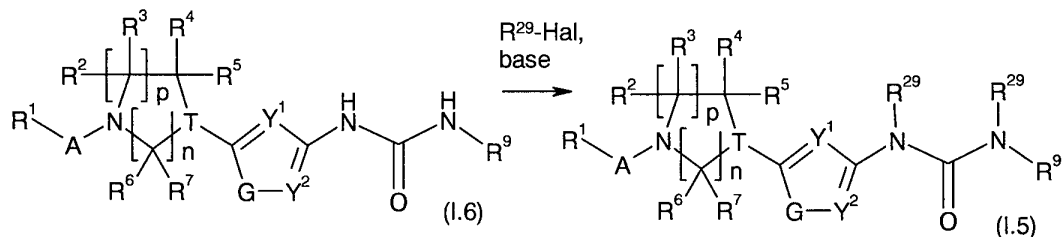
20

Esquema 8



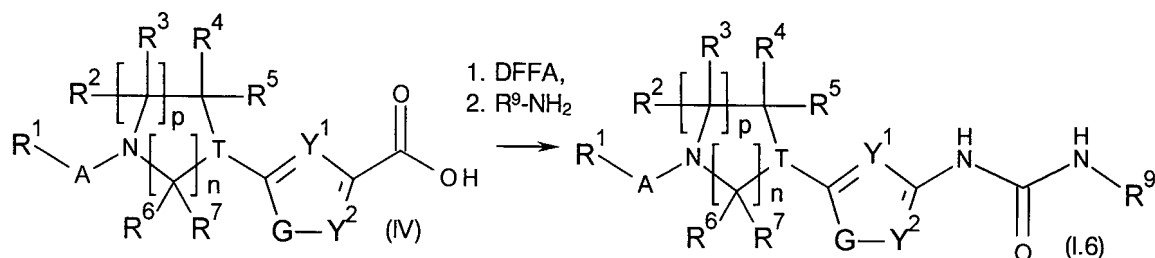
Alternativamente, los compuestos de fórmula I.5, en donde R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁹, A, T, G, n, Y¹ y Y² son tales como los definidos para la fórmula I y R²⁹ es alquilo C₁-C₆; pueden ser obtenidos mediante la transformación de un compuesto de fórmula I.6, en donde R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁹, A, T, G, n, Y¹ y Y² son tales como los definidos para la fórmula I con un haluro de alquilo R²⁹-Hal, en donde R²⁹ es alquilo C₁-C₆ y Hal es halógeno, preferiblemente cloro o bromo. Esto se muestra en el Esquema 9.

10 Esquema 9



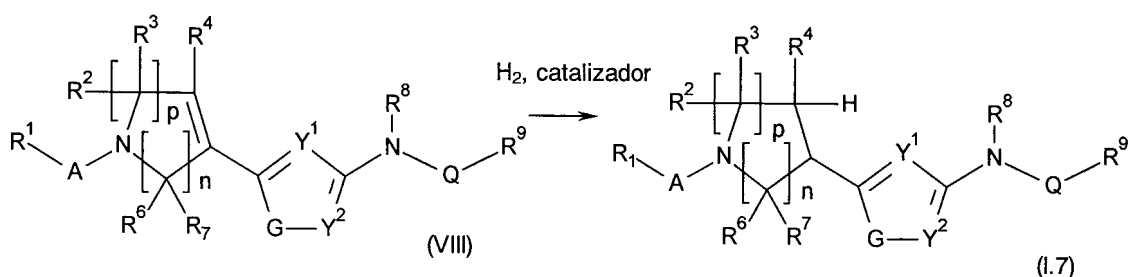
Los compuestos de fórmula I.6, en donde R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁹, A, T, G, n, p, Y¹ y Y² son tales como los definidos para la fórmula I; pueden ser obtenidos mediante la transformación de un compuesto de fórmula IV, en donde R¹, R², R³, R⁴, R⁵, R⁶, R⁷, A, T, G, n, p, Y¹ y Y² son tales como los definidos para la fórmula I con una azida, tal y como difenil fosforil azida y el reordenamiento de Curtius subsiguiente de la acil azida resultante con una amina R⁹-NH₂, en donde R⁹ es tal y como se definió para la fórmula I. Esto se muestra en el Esquema 10.

Esquema 10



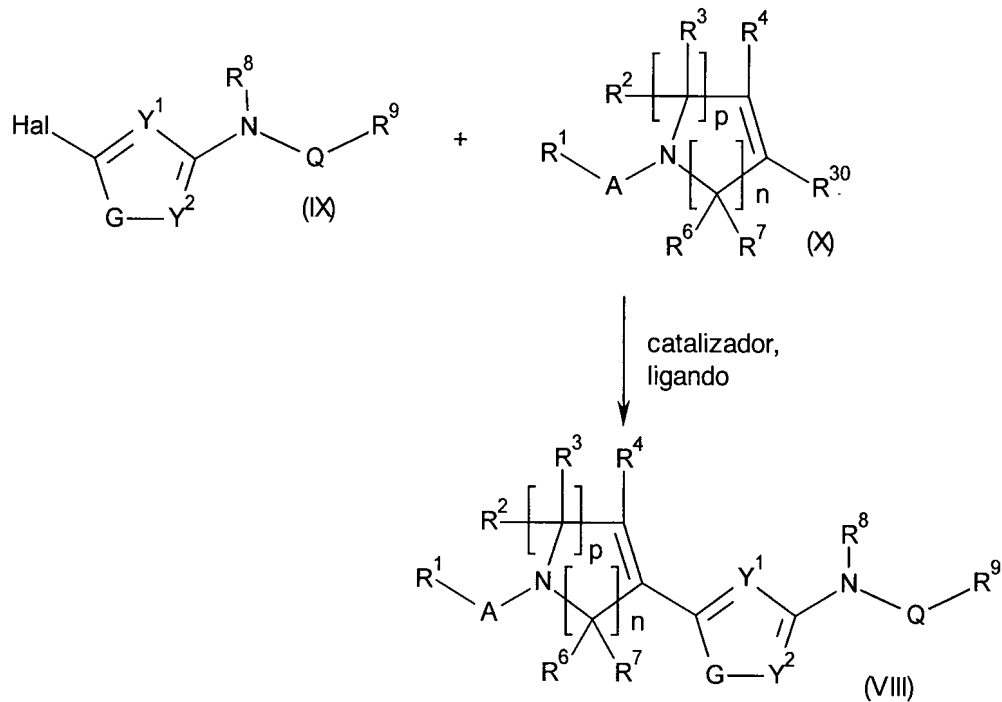
Alternativamente, los compuestos de fórmula I.7, en donde R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, A, G, n, p, Y¹, Y² y Q son tales como los definidos para la fórmula I; pueden ser obtenidos mediante la reducción de un compuesto de fórmula VIII, en donde R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, A, G, n, p, Y¹, Y² y Q son tales como los definidos para la fórmula I con hidrógeno y un catalizador, paladio sobre carbono, platino o níquel Raney. Esto se muestra en el Esquema 11.

10 Esquema 11



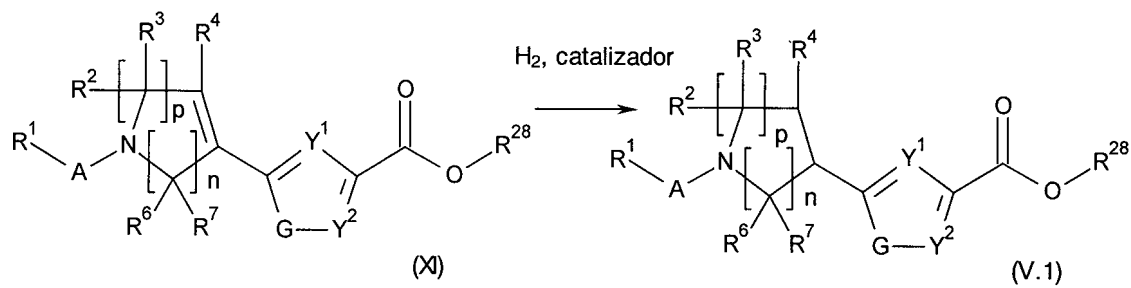
Los compuestos de fórmula VIII, en donde R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, A, G, n, p, Y¹, Y² y Q son tales como los definidos para la fórmula I; pueden ser obtenidos mediante el acoplamiento cruzado de un compuesto de fórmula IX, en donde R⁸, R⁹, G, Y¹, Y² y Q son tales como los definidos para la fórmula I y Hal es halógeno, preferiblemente cloro, bromo o yodo con un compuesto de fórmula X, en donde R¹, R², R³, R⁴, R⁵, R⁶, R⁷ y A son tales como los definidos para la fórmula I y R³⁰ es B(OH)₂ y un metal de transición, tal y como el tetrakis(trifenilfosfina)paladio, y un ligando, tal y como. Esto se muestra en el Esquema 12.

Esquema 12



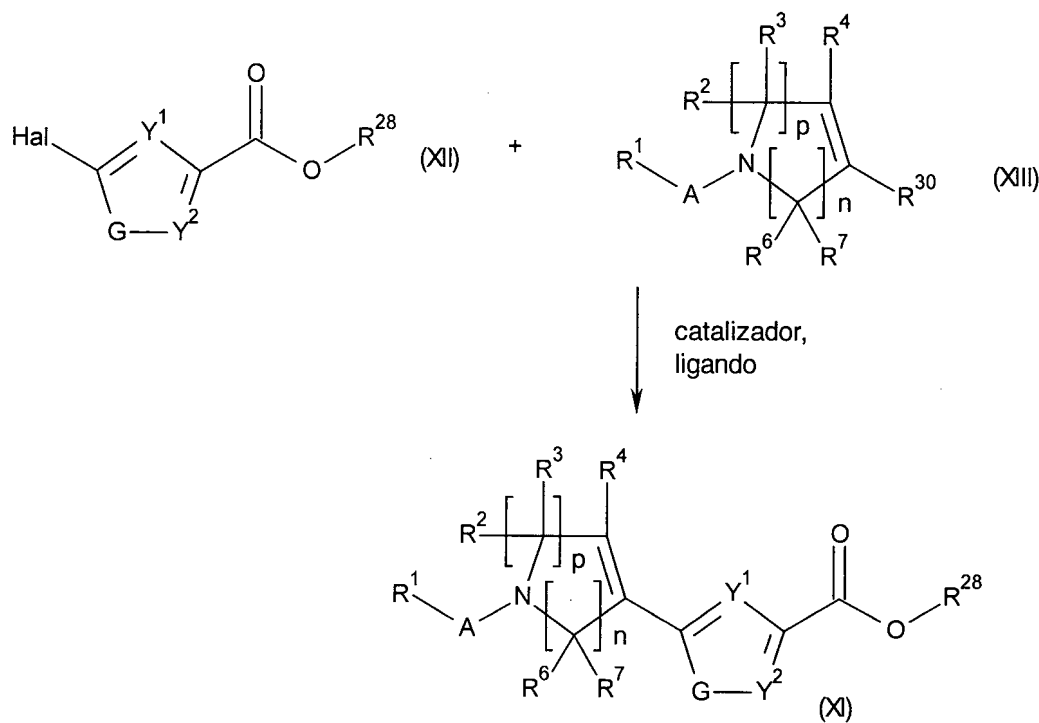
Alternativamente, los compuestos de fórmula V.1, en donde R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , A , G , n , p , Y^1 y Y^2 son tales como los definidos para la fórmula I y R^{28} es alquilo C_1-C_6 5 o arilo sustituido opcionalmente; pueden ser obtenidos mediante la reducción de un compuesto de fórmula XI, en donde R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , A , G , n , p , Y^1 y Y^2 son tales como los definidos para la fórmula I y R^{28} es alquilo C_1-C_6 o arilo sustituido opcionalmente con hidrógeno y un catalizador, paladio sobre carbono, platino o níquel Raney. Esto se muestra en el Esquema 13.

Esquema 13



Los compuestos de fórmula XI, en donde $R^1, R^2, R^3, R^4, R^5, R^6, R^7, A, G, n, p, Y^1$ y Y^2 son tales como los definidos para la fórmula I y R^{28} es alquilo C_1-C_6 o arilo sustituido
 5 opcionalmente; pueden ser obtenidos mediante el acoplamiento cruzado de un compuesto de fórmula XII, en donde G, Y^1 y Y^2 son tales como los definidos para la fórmula I, R^{28} es alquilo C_1-C_6 o arilo sustituido opcionalmente y Hal es halógeno, preferiblemente cloro, bromo o yodo con un compuesto de fórmula XIII, en donde $R^1, R^2, R^3, R^4, R^5, R^6, R^7$ y A
 son tales como los definidos para la fórmula I y R^{30} es $B(OH)_2$ y un metal de transición, tal
 10 y como el cloruro de bis-(trifenilfosfina)paladio(II). Esto se muestra en el Esquema 14.

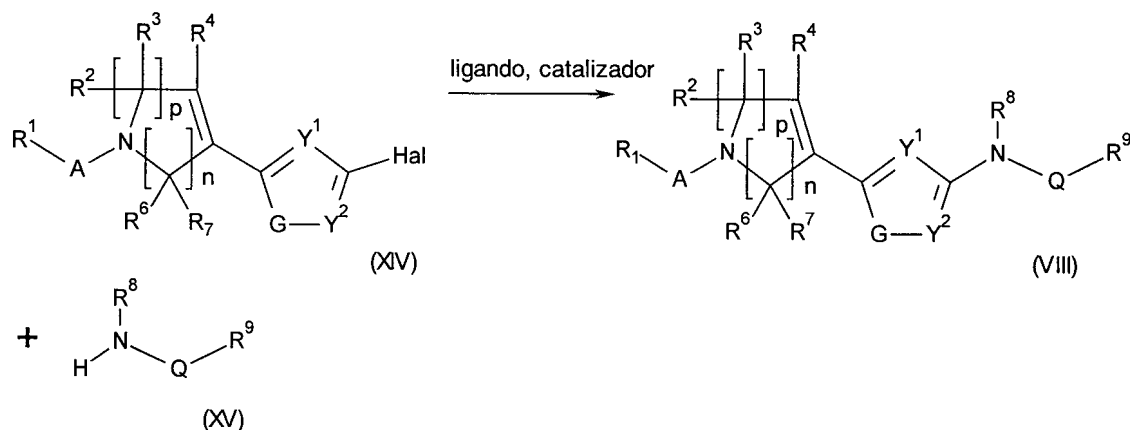
Esquema 14



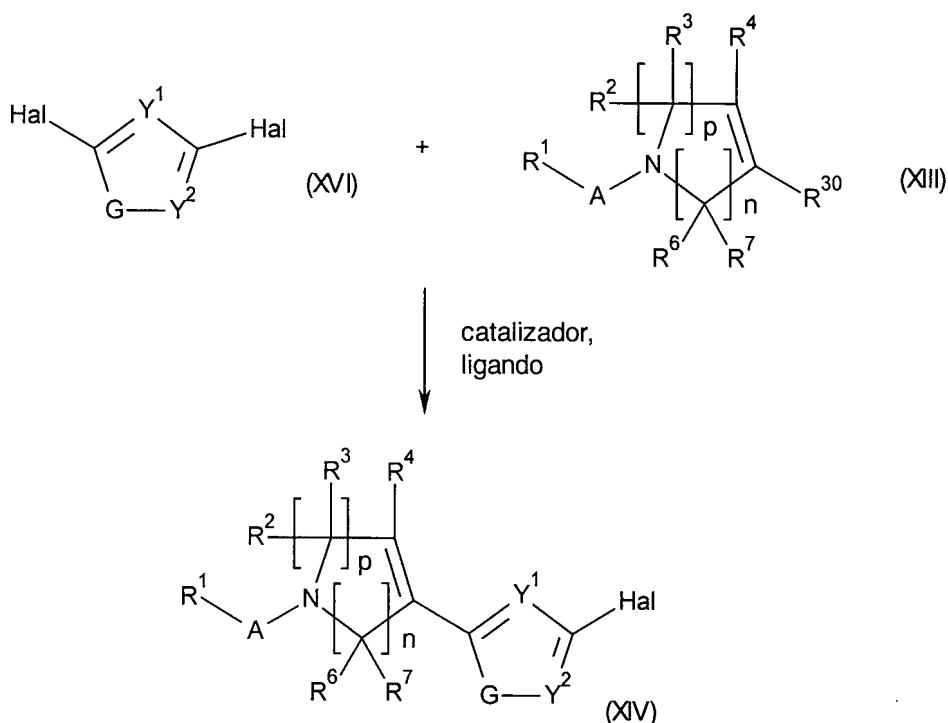
Alternativamente, los compuestos de fórmula VIII, en donde $R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, A, G, n, p, Y^1, Y^2$ y Q son tales como los definidos para la fórmula I; pueden ser

obtenidos mediante el acoplamiento cruzado de un compuesto de fórmula XIV, en donde R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , A, G, n, p, Y^1 , y Y^2 son tales como los definidos para la fórmula I con un compuesto de fórmula XV, en donde R^8 , R^9 y Q son tales como los definidos para la fórmula I y un ligando tal y como Xantphos o dimetiletilendiamina y un catalizador, tal y como el $Pd(OAc)_2$ o yoduro de cobre. Esto se muestra en el Esquema 15.

Esquema 15



Los compuestos de fórmula XIV, en donde R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , A, G, n, p, Y^1 y Y^2 son tales como los definidos para la fórmula I; pueden ser obtenidos mediante el acoplamiento cruzado de un compuesto de fórmula XVI, en donde G, Y^1 y Y^2 son tales como los definidos para la fórmula I, con un compuesto de fórmula XIII, en donde R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 y A son tales como los definidos para la fórmula I y R^{30} es $B(OH)_2$ y un metal de transición, tal y como el cloruro de bis-(trifenilfosfina)paladio(II). Esto se muestra en el Esquema 16.

Esquema 16

Sorprendentemente, se ha descubierto que los compuestos novedosos de fórmula I tienen, para propósitos prácticos, un grado muy ventajoso de actividad biológica para la
5 protección de plantas contra enfermedades que son provocadas por hongos.

Los compuestos de fórmula I pueden ser utilizados en el sector agrícola y en campos de utilización relacionados, por ejemplo como ingredientes activos para el control de plagas de plantas o en materiales no vivientes, para el control de microorganismos causantes de deterioro o de organismos potencialmente dañinos para el hombre. Los
10 compuestos novedosos se distinguen por tener una excelente actividad con tasas de aplicación bajas, por ser bien tolerados por las plantas y por ser ambientalmente seguros. Tienen propiedades curativas, preventivas y sistémicas, muy útiles y pueden ser utilizados para la protección de muchas plantas cultivadas. Los compuestos de fórmula I pueden ser utilizados para inhibir o destruir las plagas que se presentan en plantas o partes de
15 plantas (frutos, flores, hojas, tallos, tubérculos, raíces) de diferentes cultivos de plantas útiles, mientras que al mismo tiempo se protege también a aquellas partes de las plantas que crecen posteriormente, por ejemplo, de microorganismos fitopatógenos.

Es posible también utilizar los compuestos de fórmula I como agentes de recubrimiento para el tratamiento de material de propagación de plantas, *por ejemplo*, por
20 *ejemplo*, semillas, tales como frutas, tubérculos o granos o esquejes (por ejemplo arroz), para la protección contra infecciones fúngicas, así como contra hongos fitopatógenos presentes en el suelo. El material de propagación puede ser tratado con una composición

que comprende un compuesto de fórmula I antes de ser plantado: la semilla, por ejemplo, puede ser impregnada antes de ser plantada. Los ingredientes activos de conformidad con la invención pueden ser aplicados también a granos (recubrimiento), ya sea mediante la impregnación de las semillas en una formulación líquida o mediante el recubrimiento de
 5 las mismas con una formulación sólida. La composición puede ser aplicada también al sitio de plantación cuando el material de propagación está siendo plantado, por ejemplo, al surco de las semillas durante la siembra. También, la invención trata acerca de tales métodos para el tratamiento del material de propagación de plantas y acerca del material de propagación de plantas tratado de tal forma.

10 Adicionalmente, los compuestos de conformidad con la presente invención pueden ser utilizados para el control de hongos en áreas relacionadas, por ejemplo en la protección de materiales técnicos, incluyendo a madera y productos técnicos relacionados con madera, en almacenamiento de alimentos, en gestión de higiene.

Además, la invención podría ser utilizada para proteger materiales no vivientes del
 15 ataque por hongos, por ejemplo madera, paneles de madera laminada y pintura.

Los compuestos de fórmula I son, por ejemplo, efectivos contra los hongos fitopatógenos de las clases siguientes: Hongos imperfectos (por ejemplo *Alternaria* spp.), Basidiomicetes (por ejemplo *Corticium* spp., *Ceratobasidium* spp., *Waitea* spp., *Thanatephorus* spp., *Rhizoctonia* spp., *Hemileia* spp., *Puccinia* spp., *Phakopsora* spp.,
 20 *Ustilago* spp., *Tilletia* spp.), Ascomicetes (por ejemplo *Venturia* spp., *Blumeria* spp., *Erysiphe* spp., *Podosphaera* spp., *Uncinula* spp., *Monilinia* spp., *Sclerotinia* spp., *Colletotrichum* spp., *Glomerella* spp., *Fusarium* spp., *Gibberella* spp., *Monographella* spp., *Phaeosphaeria* spp., *Mycosphaerella* spp., *Cercospora* spp., *Pyrenophora* spp., *Rhynchosporium* spp., *Magnaporthe* spp., *Gaeumannomyces* spp., *Oculimacula* spp.,
 25 *Ramularia* spp., *Botryotinia* spp.) y Oomicetes (por ejemplo *Phytophthora* spp., *Pythium* spp., *Plasmopara* spp., *Peronospora* spp., *Pseudoperonospora* spp. *Bremia* spp). Se observa una actividad sobresaliente contra el moho o mildíu (en inglés, downy mildew) (por ejemplo *Plasmopara viticola*) y el tizón tardío (por ejemplo *Phytophthora infestans*). Adicionalmente, los compuestos novedosos de fórmula I son efectivos contra bacterias
 30 fitopatógenas gram negativas y gram positivas (por ejemplo *Xanthomonas* spp., *Pseudomonas* spp., *Erwinia amylovora*, *Ralstonia* spp.) y virus (por ejemplo el virus del mosaico del tabaco).

Dentro del alcance de la presente invención, los cultivos objetivo y/o plantas útiles que van a ser protegidos comprenden típicamente a las siguientes especies de plantas:
 35 cereal (trigo, cebada, centeno, avena, arroz, maíz, sorgo y las especies relacionadas); remolacha (remolacha azucarera y remolacha forrajera); pomos, drupas y frutas suaves

(manzanas, peras, ciruelas, melocotones, almendras, cerezas, fresas, frambuesas y moras); plantas leguminosas (frijoles, lentejas, guisantes, frijoles de soya); plantas oleaginosas (colza, mostaza, amapola, aceitunas, girasoles, coco, ricino, granos de cacao, cacahuates); plantas cucurbitáceas (calabazas, pepinos, melones); plantas de fibra 5 (algodón, lino, cáñamo, yute); frutas cítricas (naranjas, limones, toronjas, mandarinas); vegetales (espinaca, lechuga, espárrago, repollos, zanahorias, cebollas, tomates, papas, pimentón dulce); lauráceas (aguacate, canela, alcanfor) o plantas tales como el tabaco, nueces, café, berenjena, caña de azúcar, té, pimienta, vides, lúpulo, bananos y plantas de hule natural, así como césped y plantas ornamentales.

10 Las plantas útiles y / o cultivos objetivo de conformidad con la invención incluyen a variedades convencionales así como variedades mejoradas o modificadas genéticamente tales como, por ejemplo, variedades resistentes a insectos (por ejemplo las variedades Bt. y VIP) así como resistentes a enfermedades, tolerantes a herbicidas (por ejemplo por ejemplo, variedades de maíz resistentes al glifosato y al glufosinato, disponibles 15 comercialmente bajo las marcas comerciales RoundupReady® y LibertyLink®) y tolerantes a nematodos. A manera de ejemplo, las variedades de cultivos mejoradas o modificadas genéticamente incluyen a las variedades de algodón Stoneville 5599BR y Stoneville 4892BR.

El término "plantas útiles" y/o "cultivos objetivo" debe ser entendido también como si 20 incluyera a plantas útiles que han sido hechas tolerantes a herbicidas tales como bromoxinilo o clases de herbicidas (tales como, por ejemplo, inhibidores de la HPPD, inhibidores de la ALS, por ejemplo primisulfurón, prosulfurón y trifloxisulfurón, inhibidores de la EPSPS (siglas en inglés de la 5-enol-piruvil-shikimato-3-fosfato-sintasa), inhibidores de la GS (glutamina sintetasa) o Inhibidores de la PPO (protoporfirinogen-oxidasa)) como 25 un resultado de métodos convencionales de reproducción o de ingeniería genética. Un ejemplo de un cultivo que ha sido hecho tolerante a las imidazolinonas, por ejemplo imazamox, mediante métodos convencionales de reproducción (mutagénesis) es la colza (Canola) Clearfield®. Ejemplos de cultivos que han sido hechos tolerantes mediante métodos de ingeniería genética incluyen por ejemplo, variedades de maíz resistentes al 30 glifosato y al glufosinato, disponibles comercialmente bajo las marcas comerciales RoundupReady®, Herculex I® y LibertyLink®.

El término "plantas útiles" y/o "cultivos objetivo" debe ser entendido también como si incluyera a plantas útiles las cuales han sido transformadas mediante el uso de técnicas de ADN recombinante y que son capaces de sintetizar una o más toxinas de acción 35 selectiva, tales como las conocidas, por ejemplo, de bacterias productoras de toxinas, especialmente aquellas del género Bacillus.

El término "plantas útiles" y/o "cultivos objetivo" debe ser entendido también como si incluyera a plantas útiles las cuales han sido transformadas mediante el uso de técnicas de ADN recombinante y que son capaces de sintetizar sustancias antipatogénicas que tienen acción selectiva, tales como, por ejemplo, las denominadas "proteínas relacionadas con patogénesis" (PRP, véase por ejemplo EP-A-0 392 225). Ejemplos de tales sustancias antipatogénicas y plantas transgénicas capaces de sintetizar tales sustancias antipatogénicas son conocidos, por ejemplo, a partir de los documentos EP-A-0 392 225, WO 95/33818, y EP-A-0 353 191. Por lo general, los métodos para la producción de tales plantas transgénicas son conocidos por las personas con conocimientos de la técnica y son descritos, por ejemplo, en las publicaciones mencionadas anteriormente.

Tal y como se emplea en este documento, se pretende que el término "locus" de una planta abarque el lugar en el cual están creciendo las plantas, en donde los materiales de propagación de plantas son sembrados o en donde los materiales de propagación de plantas van a ser colocados dentro del suelo. Un ejemplo de tal locus es un campo, en el cual están creciendo las plantas.

Se entiende que el término "material de propagación de plantas" denota partes generativas de la planta, tales como semillas, las cuales pueden ser utilizadas para la multiplicación de aquellas, y material vegetativo, tal y como esquejes y tubérculos, por ejemplo papas o patatas. Se pueden mencionar por ejemplo semillas (en el sentido estricto), raíces, frutos, tubérculos, bulbos, rizomas y partes de plantas. Se pueden mencionar también plantas germinadas y plántulas que van a ser trasplantadas después de la germinación o después de brotar del suelo. Estas plántulas pueden ser protegidas antes del trasplante mediante inmersión total o parcial. Preferiblemente se entiende que "material de propagación de plantas" denota a las semillas.

Los compuestos de fórmula I pueden ser utilizados en forma no modificada, preferiblemente, junto con los adyuvantes que son empleados convencionalmente en el campo de la formulación. Para tal fin, pueden ser formulados convenientemente de manera conocida para producir concentrados que se pueden emulsificar, pastas para recubrimientos, disoluciones o suspensiones para aspersión directa o para ser diluidas, emulsiones diluidas, polvos humectables, polvos solubles, polvos, granulados y también encapsulados por ejemplo en sustancias poliméricas. Al igual que con el tipo de composiciones, los métodos de aplicación, tales como aspersión, atomización, espolvoreo, dispersión, recubrimiento o vertido, son escogidos según los objetivos deseados y las circunstancias existentes. Las composiciones pueden contener también adyuvantes adicionales, tales como estabilizadores, antiespumantes, reguladores de

viscosidad, aglutinantes o promotores de adhesividad, así como fertilizantes, donadores de micronutrientes u otras formulaciones para la obtención de efectos especiales.

Los vehículos y adyuvantes adecuados, por ejemplo para ser utilizados en agricultura, pueden ser sólidos o líquidos y son sustancias útiles en las tecnologías de formulación, por ejemplo sustancias minerales naturales o regeneradas, disolventes, dispersantes, agentes humectantes, promotores de adhesividad, espesantes, aglutinantes o fertilizantes. Tales vehículos son descritos, por ejemplo, en el documento WO 97/33890.

Normalmente, los compuestos de fórmula I son utilizados en forma de composiciones y pueden ser aplicados al área de cultivo o a la planta que va a ser tratada, en forma simultánea, o sucesiva, con compuestos adicionales. Por ejemplo, estos compuestos adicionales pueden ser fertilizantes, donadores de micronutrientes u otras preparaciones, los cuales ejercen influencia sobre el crecimiento de las plantas. Pueden ser también herbicidas selectivos o herbicidas no selectivos, así como insecticidas, fungicidas, bactericidas, nematocidas, molusquicidas o mezclas de varias de estas preparaciones, si se desea junto con vehículos, surfactantes o adyuvantes promotores de aplicación adicionales, los cuales son empleados comúnmente en el campo de la formulación.

Los compuestos de fórmula I pueden ser utilizados en forma de composiciones fungicidas para el control de, o la protección contra, microorganismos fitopatógenos, las cuales comprenden como ingrediente activo al menos un compuesto de fórmula I o de al menos un compuesto individual preferido, tal y como uno de los definidos anteriormente, en forma libre o en forma de sal utilizable agroquímicamente, y al menos uno de los adyuvantes mencionados anteriormente.

La invención provee una composición fungicida que comprende al menos un compuesto de fórmula I, un vehículo aceptable para ser utilizado en agricultura y opcionalmente un adyuvante. Por ejemplo, un vehículo aceptable para ser utilizado en agricultura es un vehículo que es adecuado para ser utilizado en agricultura. Los vehículos para agricultura son ampliamente conocidos en la técnica. Preferiblemente dichas composiciones fungicidas pueden comprender un ingrediente activo fungicida adicional además del compuesto de fórmula I.

El compuesto de fórmula (I) puede ser el único ingrediente activo de una composición o puede ser mezclado con uno o más ingredientes activos adicionales, tales como un insecticida, fungicida, sinérgico, herbicida o regulador del crecimiento de plantas, donde sea apropiado. En algunos casos, un ingrediente activo adicional puede producir actividades sinérgicas inesperadas. Ejemplos de ingredientes activos adicionales incluyen a los siguientes: Azoxistrobin(131860-33-8), Dimoxistrobin(149961-52-4), Enestrobin

- (238410-11-2), Fluoxastrobin (193740-76-0), Kresoxim-metilo (143390-89-0), Metominostrobin (133408-50-1), Orisastrobin (248593-16-0), Picoxistrobin(117428-22-5), Piraclostrobin (175013-18-0), Azaconazol (60207-31-0), Bromuconazol (116255-48-2), Ciproconazol (94361-06-5), Difenoconazol (119446-68-3), Diniconazol (83657-24-3),
- 5 Diniconazol-M (83657-18-5), Epoxiconazol (13385-98-8), Fenbuconazol (114369-43-6), Fluquinconazol (136426-54-5), Flusilazol (85509-19-9), Flutriafol (76674-21-0), Hexaconazol (79983-71-4), Imazalil (58594-72-2), Imibenconazol (86598-92-7), Ipconazol (125225-28-7), Metconazol (125116-23-6), Miclobutanil (88671-89-0), Oxpoconazol (174212-12-5), Pefurazoato (58011-68-0), Penconazol (66246-88-6), Procloraz (67747-09-
- 10 5), Propiconazol (60207-90-1), Protioconazol (178928-70-6), Simeconazol (149508-90-7), Tebuconazol (107534-96-3), Tetraconazol (112281-77-3), Triadimefon (43121-43-3), Triadimenol (55219-65-3), Triflumizol (99387-89-0), Triticónazol (131983-72-7), Diclobutrazol (76738-62-0), Etaconazol (60207-93-4), Fluconazol (86386-73-4), Fluconazol-cis (112839-32-4), Tiabendazol (148-79-8), Quinconazol (103970-75-8),
- 15 Fenpiclonil (74738-17-3), Fludioxonil (131341-86-1), Ciprodinil (121552-61-2), Mepanipirim (110235-47-7), Pirimetanil (53112-28-0), Aldimorf (91315-15-0), Dodemorf (1593-77-7), Fenpropimorf (67564-91-4), Tridemorf (81412-43-3), Fenpropidin (67306-00-7), Espiroxamina (118134-30-8), Isopirazam (881685-58-1), Sedaxano (874967-67-6), Bixafen (581809-46-3), Pentiopirad (183675-82-3), Fluxapiroxad (907204-31-3), Boscalid
- 20 (188425-85-6), Penflufen (494793-67-8), Fluopiram (658066-35-4), Mandipropamid (374726-62-2), Bentiavalicarb (413615-35-7), Dimetomorf (110488-70-5), Clorotalonilo (1897-45-6), Fluazinam (79622-59-6), Ditianon (3347-22-6), Metrafenona (220899-03-6), Triciclazol (41814-78-2), Mefenoxam (70630-17-0), Metalaxilo (57837-19-1), Acibenzolar (126448-41-7) (Acibenzolar-S-metilo (126448-41-7)), Mancozeb (8018-01-7),
- 25 Ametoctradina (865318-97-4) Ipconazol (125225-28-7), Amisulbrom (348635-87-0), Ciflufenamid (180409-60-3), Etaboxam (16650-77-3), Fluopicolide (239110-15-7), Flutianil (304900-25-2), Isotianil (224049-04-1), Proquinazid (189278-12-4), Valifenal (283159-90-0), 1-metil-ciclopropeno (3100-04-7), Trifloxistrobin(141517-21-7), azufre (7704-34-9), Amoniocarbonato de cobre (CAS 33113-08-5); Oleato de cobre (CAS 1120-44-1); Folpet
- 30 (133-07-3), Quinoxifen (124495-18-7), Captan (133-06-2), Fenhexamid (126833-17-8), Glufosinato y su sales (51276-47-2, 35597-44-5 (Isómero S)), Glifosato (1071-83-6) y su sales (69254-40-6 (Diamonio), 34494-04-7 (Dimetilamonio), 38641-94-0 (Isopropilamonio), 40465-66-5 (Monoamonio), 70901-20-1 (Potasio), 70393-85-0 (Sesquisodio), 81591-81-3 (Trimesio)), (2-diclorometilen-3-etil-1-metil-indan-4-il)-amida del ácido 1,3-dimetil-1H-
- 35 pirazol-4-carboxílico, (4'-metilsulfanil-bifenil-2-il)-amida del ácido 1,3-dimetil-1H-pirazol-4-carboxílico, [2-(2,4-dicloro-fenil)-2-metoxi-1-metil-etil]-amida del ácido 1,3-dimetil-4H-

pirazol-4-carboxílico, (5-Cloro-2,4-dimetil-piridin-3-il)-(2,3,4-trimetoxi-6-metil-fenil)-metanona, (5-Bromo-4-cloro-2-metoxi-piridin-3-il)-(2,3,4-trimetoxi-6-metil-fenil)-metanona, 2-{2-[(E)-3-(2,6-Dicloro-fenil)-1-metil-prop-2-en-(E)-ilideneaminooximetil]-fenil}-2-[(Z)-metoxiimino]-N-metil-acetamida, 3-[5-(4-Cloro-fenil)-2,3-dimetil-isoxazolidin-3-il]-piridina.

- 5 Otra faceta de la invención trata acerca del uso de un compuesto de fórmula I o de un compuesto individual preferido tal y como uno de los definidos anteriormente, de una composición que comprende al menos un compuesto de fórmula I o al menos un compuesto individual preferido tal y como uno de los definidos anteriormente, o una mezcla fungicida que comprende al menos un compuesto de fórmula I o al menos un
- 10 compuesto individual preferido tal y como uno de los definidos anteriormente, mezclado con otros fungicidas, tal y como se describió anteriormente, para controlar o evitar la infestación de plantas, por ejemplo plantas útiles tales como plantas de cultivo, material de propagación de las mismas, por ejemplo semillas, cultivos cosechados, por ejemplo cultivos comestibles cosechados, o materiales no vivientes, por parte de microorganismos
- 15 fitopatógenos, preferiblemente organismos fúngicos.

Una faceta adicional de la invención trata acerca de un método para controlar o evitar una infestación de plantas, por ejemplo plantas útiles tales como plantas de cultivo, material de propagación de las mismas, por ejemplo semillas, cultivos cosechados, por ejemplo cultivos comestibles cosechados, o materiales no vivientes por parte de

20 microorganismos fitopatógenos o causantes de deterioro o de organismos potencialmente dañinos para el hombre, especialmente organismos fúngicos, el cual incluye la aplicación de un compuesto de fórmula I o de un compuesto individual preferido tal y como uno de los definidos anteriormente como ingrediente activo a las plantas, a partes de las plantas o al locus de las mismas, al material de propagación de las mismas, o a cualquier parte de

25 los materiales no vivientes.

Controlar o prevenir significa reducir la infestación por parte de microorganismos fitopatógenos o causantes de deterioro o de organismos potencialmente dañinos para el hombre, especialmente organismos fúngicos, hasta un nivel tal que se demuestre una mejoría.

- 30 Un método preferido para controlar o evitar una infestación de plantas de cultivo por parte de microorganismos fitopatógenos, especialmente organismos fúngicos, el cual incluye la aplicación de un compuesto de fórmula I, o una composición agroquímica que contiene al menos uno de tales compuestos, es la aplicación foliar. La frecuencia de aplicación y la tasa de aplicación van a depender del riesgo de infestación por parte del
- 35 patógeno correspondiente. Sin embargo, los compuestos de fórmula I pueden también penetrar la planta a través de las raíces, por medio del suelo (acción sistémica) al

impregnar el locus de la planta con una formulación líquida, o al aplicar los compuestos en forma sólida en el suelo, por ejemplo en forma granular (aplicación en suelo). En los cultivos de arroz anegado, tales granulados pueden ser aplicados al campo de arroz inundado. Los compuestos de fórmula I pueden ser aplicados también a las semillas
5 (recubrimiento) al impregnar las semillas o tubérculos, ya sea con una formulación líquida del fungicida o recubriéndolos con una formulación sólida.

Una formulación, por ejemplo una composición que contiene al compuesto de fórmula I, y, si se desea, un adyuvante sólido o líquido o monómeros para encapsular al compuesto de fórmula I, pueden ser preparados en una manera conocida, típicamente al
10 mezclar muy bien y/o moler el compuesto con diluyentes, por ejemplo disolventes, vehículos sólidos y, opcionalmente, compuestos tensoactivos (surfactantes).

Usualmente las formulaciones agroquímicas y/o composiciones van a contener entre 0.1 y 99% por masa, preferiblemente entre 0.1 y 95% por masa, del compuesto de fórmula I, entre 99.9 y 1% por masa, preferiblemente entre 99.8 y 5% por masa, de un
15 adyuvante sólido o líquido, y entre 0 y 25% por masa, preferiblemente entre 0.1 y 25% por masa, de un surfactante.

Normalmente, las tasas de aplicación que son ventajosas están entre 5g y 2kg de ingrediente activo (i.a.) por hectárea (ha), preferiblemente entre 10g y 1kg i.a./ha, lo más preferible es que estén entre 20g y 600g i.a./ha. Cuando son utilizados como agentes
20 para aplicación en semillas mediante impregnación, las dosis convenientes son entre 10mg y 1g de sustancia activa por kg de semillas.

Aunque es preferible formular a los productos comerciales como concentrados, el usuario final normalmente va a utilizar formulaciones diluidas.

Los siguientes ejemplos no limitantes ilustran con mayor detalle a la invención
25 descrita anteriormente.

Ejemplo 1: Este ejemplo ilustra la preparación de la (2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-amida del ácido 1,2,3,4-tetrahidro-naftalen-1-carboxílico (Compuesto No. 1.g.011)

30 a) Preparación del éster etílico del ácido 2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-carboxílico

A una disolución de ácido (5-metil-3-trifluorometil-pirazol-1-il)-acético (9.1 g, 36.1 mmol) en DMF (100 mL) se añade diisopropiletilamina (45 mL, 216 mmol), seguida por tetrafluoroborato de O-(benzotriazol-1-il)-N,N,N',N'-tetrametiluronio (15.5 g, 39.7 mmol).
35 Después de agitar por 15 min a temperatura ambiente, el clorhidrato del éster etílico del ácido 2-piperidin-4-il-tiazol-4-carboxílico (10 g, 36.1 mmol) es añadido a la mezcla de

reacción. Después de agitar durante toda la noche a temperatura ambiente, el disolvente es evaporado y el aceite amarillo resultante es disuelto en acetato de etilo (300 mL), lavado con una disolución saturada acuosa de bicarbonato de sodio (300 mL), disolución de HCl 1M (300 mL) y disolución acuosa saturada de cloruro de sodio (100 mL). La capa
5 orgánica es secada sobre sulfato de sodio, filtrada y evaporada bajo presión reducida. La mezcla cruda es purificada mediante cromatografía de columna en gel de sílice (diclorometano/metanol 10:1) para dar el éster etílico del ácido 2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-carboxílico (13.6 g, 88 %). ¹H-RMN (400 MHz, CDCl₃): δ = 1.40 (t, 3H), 1.70-1.85 (m, 2H), 2.16-2.30 (m, 2H), 2.32 (s, 3H),
10 2.79-2.89 (m, 1H), 3.22-3.43 (m, 1H), 4.03-4.12 (m, 1H), 4.42 (q, 3H), 4.54-4.69 (m, 1H), 4.93-5.08 (2d, 2H (diastereotópicos)), 6.35 (s, 1H), 8.10 (br, 1H). EM: m/z = 209 (M+1).

b) Preparación del ácido 2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-carboxílico

15 A una disolución del éster etílico del ácido 2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-carboxílico (2.67 g, 6.2 mmol) en THF (20 mL) se añade una disolución acuosa de hidróxido de sodio (2 M, 4.65 mL, 9.3 mmol) a temperatura ambiente. Después de agitar por 3 h a temperatura ambiente, la mezcla de reacción es acidificada con una disolución acuosa 2M de HCl hasta alcanzar un pH entre 2 y 3 y la
20 disolución es extraída con acetato de etilo (20 mL). La capa acuosa es re-extraída con acetato de etilo (20 mL) y las capas orgánicas combinadas son lavadas con disolución saturada de NaCl (10 mL), secadas sobre sulfato de sodio, filtradas y evaporadas bajo presión reducida para dar el ácido 2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-carboxílico (2.33 g, 94 %), el cual puede ser utilizado en el paso
25 siguiente sin purificación adicional. ¹H-RMN (400 MHz, d₆-acetona): δ = 1.69-1.82 (m, 1H), 1.87-2.02 (m, 1H), 2.16-2.37 (m, 2H), 2.38 (s, 3H), 2.89-2.99 (m, 1H), 3.38-3.48 (m, 2H), 4.14-4.22 (m, 1H), 4.50-4.69 (m, 1H), 5.20-5.36 (2d, 2H (diastereotópicos)), 6.41, (s, 1H), 8.34 (s, 1H). EM: m/z = 403 (M+1).

30 c) Preparación del éster terc-butílico del ácido 2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-carbámico

A una disolución del ácido 2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-carboxílico (9.95 g, 24.74 mmol) en terc-butanol (90 mL) se añade trietilamina (8.2 mL, 56.9 mmol). Después de agitar por 30 min. a temperatura ambiente,
35 difenilfosforil azida (10.9 mL, 49.5 mmol) es añadida y la mezcla de reacción es dividida en 6 porciones y cada porción fue irradiada con microondas (100 °C, 15 min.). Después

de enfriar a temperatura ambiente, todas las porciones fueron combinadas y se añadió agua (3 mL) a la mezcla de reacción y se agitó 30 minutos. Luego, se añade acetonitrilo (40 mL), seguido por adición de Amberlyst A21 básica. Después de agitar durante toda la noche a temperatura ambiente, la resina es removida por filtración y los disolventes son
 5 evaporados bajo presión reducida. El residuo es purificado mediante cromatografía de columna en gel de sílice (acetato de etilo/ciclohexano 7:3) para dar el éster terc-butílico del ácido 2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-carbámico (9.6 g, 82 %). ¹H-RMN (400 MHz, CDCl₃): δ = 1.53 (s, 9H), 1.68-1.78 (m, 2H), 2.08-2.19 (m, 2H), 2.32 (s, 3H), 2.85-2.95 (m, 1H), 3.10-3.20 (m, 1H), 3.23-3.34 (m, 1H),
 10 3.97-4.04 (m, 1H), 4.50-4.58 (m, 1H), 4.93-5.05 (2d, 2H, protones diasterotópicos), 6.33 (s, 1H), 7.10 (br, 1H), 7.30 (s, 1H). EM: m/z = 474 (M+1).

d) Preparación de 1-[4-(4-amino-tiazol-2-il)-piperidin-1-il]-2-(5-metil-3-trifluorometil-pirazol-1-il)-etanona

15 A una disolución del éster terc-butílico del ácido 2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-carbámico (9.6 g, 20.3 mmol) se añade una disolución de HCl 4M en dioxano (50 mL, 203 mmol), a temperatura ambiente. Después de agitar por 2 días a temperatura ambiente, el disolvente es evaporado bajo presión reducida. La espuma amarillenta resultante es triturada con éter dietílico y filtrada para dar
 20 el clorhidrato de la 1-[4-(4-Amino-tiazol-2-il)-piperidin-1-il]-2-(5-metil-3-trifluorometil-pirazol-1-il)-etanona, el cual es suspendido en bicarbonato de sodio acuoso saturado (500 mL). Después de agitar por 30 min. a temperatura ambiente, la mezcla de reacción es extraída con acetato de etilo (500 mL). Las capas orgánicas combinadas son lavadas con agua (100 mL) y cloruro de sodio saturado (100 mL), filtradas, secadas sobre sulfato de sodio y
 25 evaporadas bajo presión reducida para dar la 1-[4-(4-amino-tiazol-2-il)-piperidin-1-il]-2-(5-metil-3-trifluorometil-pirazol-1-il)-etanona (5.63 g, 74 %). ¹H-RMN (400 MHz, CDCl₃): δ = 1.65-1.80 (m, 2H), 2.08-2.20 (m, 2H), 2.31 (s, 3H), 2.81-2.91 (m, 1H), 3.08-3.18 (m, 1H), 3.21-3.32 (m, 1H), 3.95-4.08 (m, 3H), 4.50-4.59 (m, 1H), 4.93-5.04 (2d, 2H, protones diasterotópicos), 5.84 (s, 1H), 6.32 (s, 1H). EM: m/z = 374 (M+1).

30

e) Preparación de la (2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-amida del ácido 1,2,3,4-tetrahidro-naftalen-1-carboxílico (Compuesto No. I.g.011)

A una disolución de 1-[4-(4-amino-tiazol-2-il)-piperidin-1-il]-2-(5-metil-3-trifluorometil-pirazol-1-il)-etanona (120 mg, 0.32 mmol) y diisopropiletilamina (0.2 mL, 0.96
 35 mmol) en diclorometano (5 mL) se añade gota a gota una disolución de cloruro de 1,2,3,4-

tetrahidro-naftalen-1-carbonilo (74 mg, 0.38 mmol) en diclorometano (3 mL) a 0°C. Después de agitar durante toda la noche a temperatura ambiente, el disolvente es evaporado y el residuo es purificado mediante cromatografía "flash" con gel de sílice (acetato de etilo/ciclohexano 1:1) para dar la (2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-amida del ácido 1,2,3,4-tetrahidro-naftalen-1-carboxílico (Compuesto No. 1.g.011, 82 mg, 48%). P.f. = 179.2-181.3 °C. ¹H-RMN (400 MHz, CDCl₃): □ = 1.60-1.75 (m, 3H), 1.81-1.89 (m, 2H), 2.05-2.15 (m, 2H), 2.31 (s, 3H), 2.32-2.40 (m, 1H), 2.77-2.94 (m, 3H), 3.05-3.18 (m, 1H), 3.19-3.29 (m, 1H), 3.87 (t, 1H), 3.95-4.04 (m, 1H), 4.50-4.59 (m, 1H), 4.90-5.06 (2d, 2H, protones diasterotópicos), 6.32 (s, 1H), 7.25-7.30 (m, 4H), 7.49 (s, 1H), 7.79 (br, 1H). EM: m/z = 532 (M+1).

Ejemplo 2: Este ejemplo ilustra la preparación del éster fenílico del ácido 2-{1-[2-(5-Metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-carbámico (Compuesto No. 1.g.023)

15

a) Preparación del éster fenílico del ácido 2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-carbámico (Compuesto No. 1.g.023)

A una disolución de 1-[4-(4-amino-tiazol-2-il)-piperidin-1-il]-2-(5-metil-3-trifluorometil-pirazol-1-il)-etanona (80 mg, 0.21 mmol) en diclorometano (5 mL) se añade diisopropiletilamina (0.053 mL, 0.25 mmol y subsiguientemente cloroformato de fenilo (0.033 mL, 0.21 mmol) a 0°C. Después de agitar durante toda la noche a temperatura ambiente, los disolventes son evaporados bajo presión reducida y el residuo es purificado mediante cromatografía de columna en gel de sílice (acetato de etilo/heptano 7:3) para dar el éster fenílico del ácido 2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-carbámico (Compuesto No. 1.g.023, 71 mg, 67 %). ¹H-RMN (400 MHz, CDCl₃): □ = 1.57-1.78 (m, 2H), 2.08-2.19 (m, 2H), 2.22 (s, 3H), 2.75-2.81 (m, 1H), 3.05-3.20 (m, 2H), 3.95-3.99 (m, 1H), 4.44-4.52 (m, 1H), 4.83-4.98 (2d, 2H, protones diasterotópicos), 6.25 (s, 1H), 7.05-7.20 (m, 3H), 7.29-7.38 (m, 2H), 7.95 (br, 1H). EM: m/z = 494 (M+1).

30

Ejemplo 3: Este ejemplo ilustra la preparación de la 1-(2-{1-[2-(5-Metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-3-fenil-urea (Compuesto No. 1.g.024)

a) Preparación de 1-(2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-3-fenil-urea (Compuesto No. 1.g.024)

35

A una disolución de 1-[4-(4-amino-tiazol-2-il)-piperidin-1-il]-2-(5-metil-3-trifluorometil-pirazol-1-il)-etanona (100 mg, 0.27 mmol) en THF (5 mL) se añade gota a gota una disolución de fenilisocianato (30 μ L, 0.28 mmol) en THF (1 mL) a 0°C. Después de agitar durante toda la noche a temperatura ambiente, se añade metanol (1 mL) a la
 5 mezcla de reacción. Después de agitar por 15 min. a temperatura ambiente, los disolventes son evaporados y el residuo fue triturado con éter dietílico (5 mL) para inducir la precipitación. El sólido resultante es filtrado y secado al vacío para dar la 1-(2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-3-fenil-urea en forma de un sólido beige (Compuesto No. I.g.024, 105 mg, 79%). P.f. = 192.6 °C. ¹H-RMN (400 MHz,
 10 CDCl₃): δ = ¹H-RMN (MeOD): δ = 1.65 (m, 1H), 1.80 (m, 1H), 2.40 (m, 2H), 2.30 (s, 3H), 2.98 (m, 1H), 3.30 (m, 1H), 3.39 (m, 1H), 4.10 (m, 1H), 4.52 (m, 1H), 5.22 (2d, 2H, diastereotópicos), 6.42 (s, 1H), 7.05 (t, 1H), 7.09 (s, 1H), 7.26 – 7.45 (m, 6H). EM: m/z = 494 (M+1).

15 Ejemplo 4: Este ejemplo ilustra la preparación de la N-(2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-C-fenil-metansulfonamida (Compuesto No. I.g.025)

a) Preparación de la N-(2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-
 20 tiazol-4-il)-bencensulfonamida (Compuesto No. I.g.025)

A una disolución de la 1-[4-(4-amino-tiazol-2-il)-piperidin-1-il]-2-(5-metil-3-trifluorometil-pirazol-1-il)-etanona (100 mg, 0.04 mmol) en dimetilacetamida (0.8 mL) se añade diisopropiletilamina (8.6 μ L, 0.28 mmol), seguida por cloruro de bencensulfonilo (8.8 mg, 0.05 mmol) a temperatura ambiente. Después de agitar por 15 min a 60 °C, la
 25 mezcla de reacción es purificada directamente por HPLC preparativa para dar la N-(2-{1-[2-(5-metil-3-trifluorometil-pirazol-1-il)-acetil]-piperidin-4-il}-tiazol-4-il)-bencensulfonamida (Compuesto No. I.g.025). EM: m/z = 514 (M+1).

Ejemplo 5: Este ejemplo ilustra la preparación de la N-(2-{1-[2-(2,5-Dimetil-fenil)-acetil]-
 30 piperidin-4-il}-tiazol-4-il)-2-fenil-propionamida (Compuesto No. I.g.141)

a) Preparación del éster etílico del ácido 2-{1-[2-(2,5-dimetil-fenil)-acetil]-piperidin-4-il}-tiazol-4-carboxílico

A una disolución de ácido 2,5-dimetilfenilacético (5.45 g, 27.4 mmol) en DMF (80
 35 mL) se añade diisopropiletilamina (85.4 mL, 411.32 mmol), seguida por tetrafluoroborato de O-(benzotriazol-1-il)-N,N,N',N'-tetrametiluronio (12.8 g, 32.9 mmol) a 0 °C. Después de

agitar por 15 min a temperatura ambiente, el éster etílico del ácido 2-piperidin-4-il-tiazol-4-carboxílico (6.59 g, 27.4 mmol) es añadido a la mezcla de reacción. Después de agitar durante toda la noche a temperatura ambiente, el disolvente es evaporado y el aceite amarillo resultante es disuelto en acetato de etilo (500 mL), lavado con disolución acuosa saturada de bicarbonato de sodio (500 mL) y la fase acuosa es re-extraída con acetato de etilo (100 mL). Las capas orgánicas combinadas son lavadas con disolución 0.5M de HCl (400 mL) y cloruro de sodio saturado (400 mL), secadas sobre sulfato de sodio, filtradas y evaporadas bajo presión reducida para dar el éster etílico del ácido 2-{1-[2-(2,5-dimetil-fenil)-acetil]-piperidin-4-il}-tiazol-4-carboxílico (10.46 g, 98 %), el cual puede ser utilizado en el paso siguiente sin purificación adicional. $^1\text{H-RMN}$ (400 MHz, CDCl_3): δ = 1.41 (t, 3H), 1.52-1.82 (m, 2H), 2.10-2.22 (m, 2H), 2.25 (s, 3H), 2.30 (s, 3H), 2.73-2.86 (m, 1H), 3.08-3.22 (m, 1H), 3.29-3.40 (m, 1H), 3.68 (s, 2H), 3.8-3.95 (m, 1H), 4.38-4.42 (q, 2H), 4.73-4.88 (m, 1H), 6.96 (s, 1H), 6.98-7.01 (d, 1H), 7.08 (d, 1H), 8.10 (s, 1H). EM: m/z = 387 (M+1).

15

b) Preparación del ácido 2-{1-[2-(2,5-dimetil-fenil)-acetil]-piperidin-4-il}-tiazol-4-carboxílico

A una disolución del éster etílico del ácido 2-{1-[2-(2,5-dimetil-fenil)-acetil]-piperidin-4-il}-tiazol-4-carboxílico (10.46 g, 27.06 mmol) en THF (30 mL) se añade una disolución acuosa de hidróxido de sodio (2 M, 20.3 mL) a temperatura ambiente. Después de agitar por 3h a temperatura ambiente, la mezcla de reacción es acidificada con una disolución acuosa de HCl (2 M) hasta alcanzar un pH entre 2 y 3, y se añade acetato de etilo (30 mL) a la mezcla de reacción y las capas son separadas. La capa acuosa es extraída con acetato de etilo (20 mL) y las capas orgánicas combinadas son lavadas con disolución saturada de NaCl (10 mL), secadas sobre sulfato de sodio, filtradas y evaporadas bajo presión reducida para dar el ácido 2-{1-[2-(2,5-dimetil-fenil)-acetil]-piperidin-4-il}-tiazol-4-carboxílico (5.9 g, 60.8 %), el cual puede ser utilizado en el paso siguiente sin purificación adicional. $^1\text{H-RMN}$ (400 MHz, $d_6\text{-DMSO}$): δ = 1.55-1.65 (m, 2H), 2.01-2.12 (m, 2H), 2.15 (s, 3H), 2.22 (s, 3H), 2.77-2.86 (m, 1H), 3.18-3.29 (m, 1H), 3.65 (d, 2H), 3.98-4.07 (m, 1H), 4.45-4.53 (m, 1H), 6.90 (s, 1H), 6.92 (s, 1H), 6.93 (s, 1H), 7.04 (d, 1H), 8.49 (br, 1H), 12.95 (s, 1H). EM: m/z = 359 (M+1).

30

c) Preparación del éster terc-butílico del ácido (2-{1-[2-(2,5-dimetil-fenil)-acetil]-piperidin-4-il}-tiazol-4-il)-carbámico

A una disolución del ácido 2-{1-[2-(2,5-dimetil-fenil)-acetil]-piperidin-4-il}-tiazol-4-carboxílico (5.65 g, 15.76 mmol) en terc-butanol (60 mL) se añade trietilamina (5.2 mL, 36.2 mmol). Después de agitar por 30 min. a temperatura ambiente, difenilfosforil azida

35

(6.9 mL, 31.5 mmol) es añadida y la mezcla de reacción es dividida en 4 porciones y cada porción es irradiada con microondas (100 °C, 15 min.). Después de enfriar a temperatura ambiente, todas las porciones son combinadas y se añade agua (1 mL) a la mezcla de reacción y se agita por 30 minutos. Luego, se añade acetonitrilo (50 mL), seguido por
5 adición de Amberlyst A21 básica. Después de agitar durante toda la noche a temperatura ambiente, la resina es removida por filtración y los disolventes son evaporados bajo presión reducida. El residuo es purificado mediante cromatografía de columna en gel de sílice (acetato de etilo/ciclohexano 7:3) para dar el éster terc-butílico del ácido (2-{1-[2-(2,5-dimetil-fenil)-acetil]-piperidin-4-il}-tiazol-4-il)-carbámico (4.93 g, 73 %). ¹H-RMN (400
10 MHz, CDCl₃): δ = 1.53 (s, 9H), 1.53-1.61 (m, 1H), 1.67-1.79 (m, 1H), 1.95-2.04 (m, 1H), 2.08-2.14 (m, 1H), 2.25 (s, 3H), 2.30 (s, 3H), 2.80-2.90 (m, 1H), 3.06-3.20 (m, 2H), 3.68 (s, 2H), 3.80-3.89 (m, 1H), 4.68-4.74 (m, 1H), 6.95 (s, 1H), 6.98 (d, 1H), 7.07 (d, 1H), 7.23 (s, 1H). EM: m/z = 430 (M+1).

15 d) Preparación de 1-[4-(4-amino-tiazol-2-il)-piperidin-1-il]-2-(2,5-dimetil-fenil)-etanona

A una disolución del éster terc-butílico del ácido (2-{1-[2-(2,5-dimetil-fenil)-acetil]-piperidin-4-il}-tiazol-4-il)-carbámico (5.65 g, 13.15 mmol) se añade una disolución de HCl 4M en dioxano (35 mL) a temperatura ambiente. Después de agitar por 3 días a temperatura ambiente, el disolvente es evaporado bajo presión reducida. El sólido
20 resultante es triturado con éter dietílico y filtrado para dar el clorhidrato de 1-[4-(4-amino-tiazol-2-il)-piperidin-1-il]-2-(2,5-dimetil-fenil)-etanona, el cual es suspendido en bicarbonato de sodio acuoso saturado (500 mL). Después de agitar por 30 min a temperatura ambiente, la mezcla de reacción es extraída con acetato de etilo (500 mL). Las capas orgánicas combinadas son lavadas con agua (100 mL) y cloruro de sodio saturado (100
25 mL), filtradas, secadas sobre sulfato de sodio y evaporadas bajo presión reducida para dar a la 1-[4-(4-amino-tiazol-2-il)-piperidin-1-il]-2-(2,5-dimetil-fenil)-etanona (3.27 g, 75 %). ¹H-RMN (400 MHz, CDCl₃): δ = 1.53-1.61 (m, 1H), 1.67-1.79 (m, 1H), 1.95-2.04 (m, 1H), 2.08-2.13 (m, 1H), 2.25 (s, 3H), 2.30 (s, 3H), 2.78-2.88 (m, 1H), 3.06-3.20 (m, 2H), 3.68 (s, 2H), 3.80-3.89 (m, 1H), 4.05 (s, 1H), 4.68-4.74 (m, 1H), 6.95 (s, 1H), 6.98 (d, 1H), 7.07 (d,
30 1H), 7.23 (s, 1H). EM: m/z = 330 (M+1). EM: m/z = 330 (M+1).

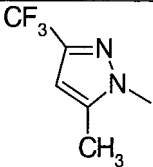
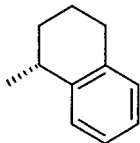
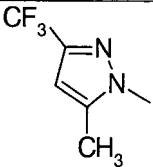
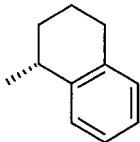
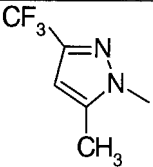
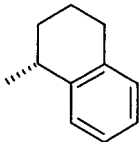
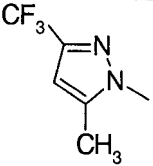
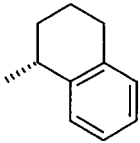
e) Preparación de la N-(2-{1-[2-(2,5-dimetil-fenil)-acetil]-piperidin-4-il}-tiazol-4-il)-2-fenil-propionamida (Compuesto No. I.g.141)

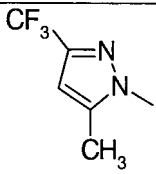
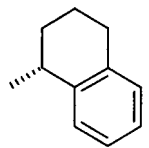
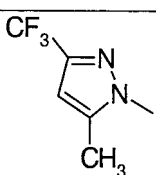
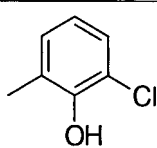
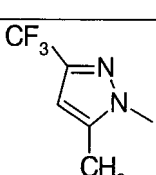
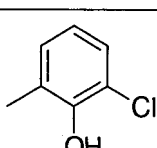
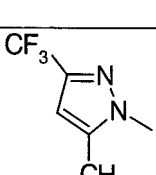
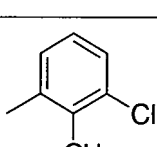
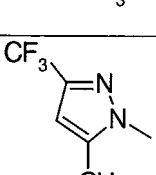
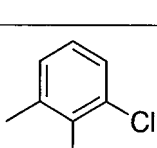
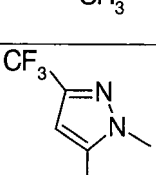
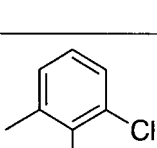
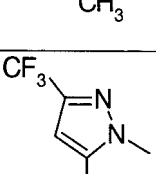
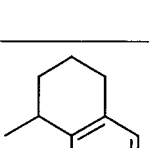
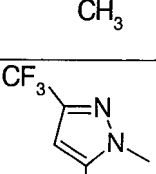
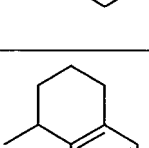
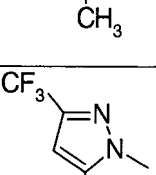
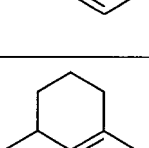
A una disolución del ácido (rac)-2-fenilpropiónico (46 mg, 0.30 mmol) y
35 diisopropiletilamina (0.15 mL, 0.9 mmol) en acetonitrilo (2 mL) se añade hexafluorofosfato de benzotriazol-1-il-oxi-tris-(dimetilamino)-fosfonio (322 mg, 0.73 mmol) a temperatura

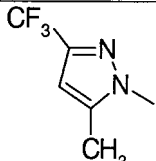
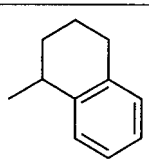
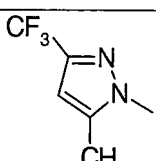
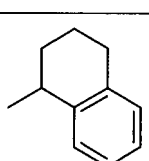
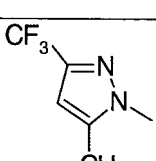
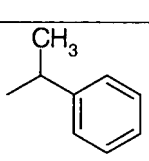
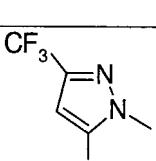
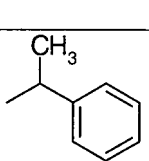
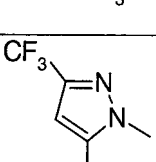
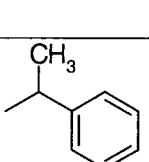
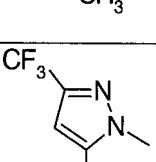
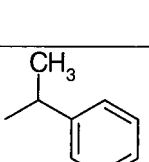
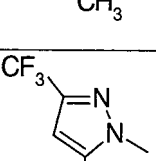
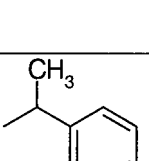
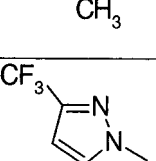
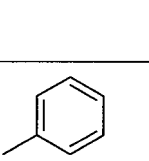
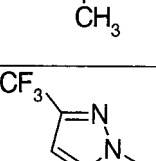
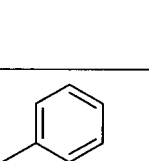
ambiente. Después de agitar por 30 min a temperatura ambiente, se añadió 1-[4-(4-amino-tiazol-2-il)-piperidin-1-il]-2-(2,5-dimetil-fenil)-etanona (100 mg, 0.30 mmol) a la mezcla de reacción. Después de agitar durante toda la noche a temperatura ambiente, el disolvente es evaporado y el residuo es purificado mediante cromatografía “flash” con gel 5 de sílice (acetato de etilo/ciclohexano 1:1) para dar N-(2-{1-[2-(2,5-dimetil-fenil)-acetil]-piperidin-4-il}-tiazol-4-il)-2-fenil-propionamida (Compuesto No. I.g.141, 19 mg, 13.4%). ¹H-RMN (400 MHz, CDCl₃): δ = 1.46-1.39 (m, 1H), 1.52 (d, 3H), 1.68-1.56 (m, 1H), 1.89-1.83 (m, 1H), 2.01-1.97 (m, 1H), 2.15 (s, 3H), 2.19 (s, 3H), 2.73-2.67 (m, 1H), 3.18-2.92 (m, 2H), 3.59 (s, 2H), 3.68-3.63 (q, 1H), 3.78-3.71 (m, 1H), 4.65-4.62 (m, 1H), 6.91-6.82 (m, 10 2H), 7.02-6.98 (m, 1H), 7.31-7.15 (m, 5H), 7.42 (s, 1H), 8.05 (br, 1H). EM: m/z = 462 (M+1).

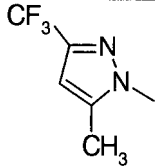
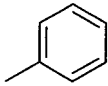
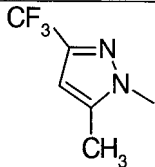
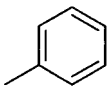
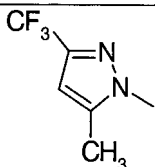
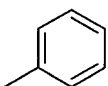
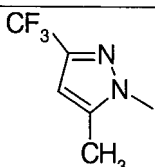
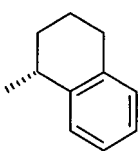
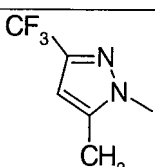
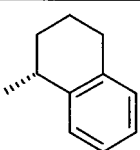
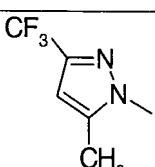
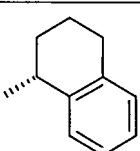
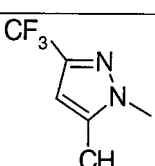
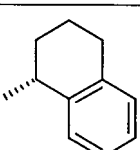
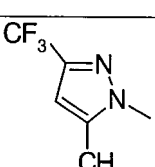
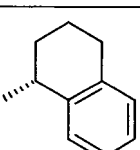
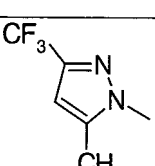
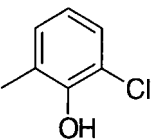
La Tabla 1, mostrada a continuación, ilustra ejemplos de compuestos individuales de fórmula I de conformidad con la invención.

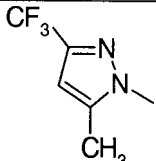
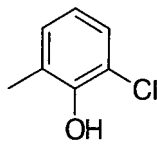
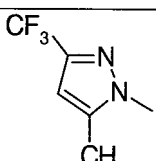
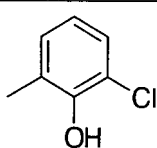
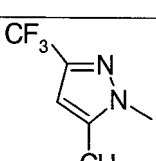
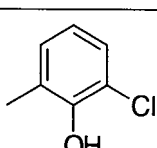
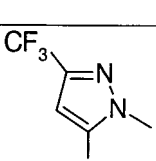
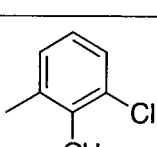
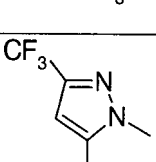
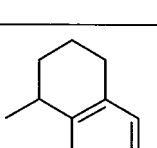
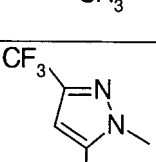
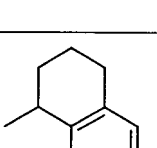
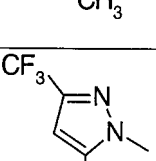
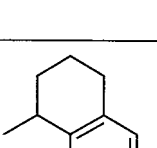
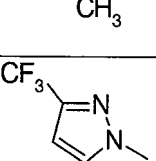
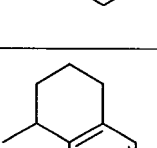
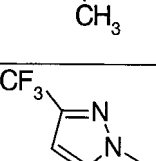
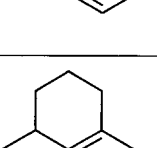
15 Tabla 1: compuestos individuales de fórmula I de conformidad con la invención

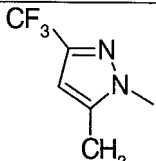
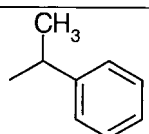
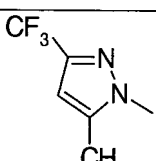
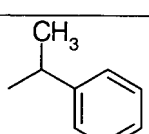
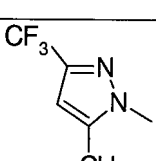
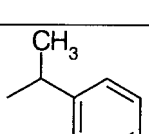
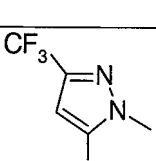
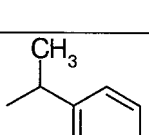
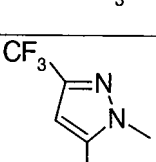
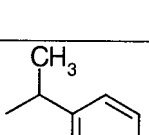
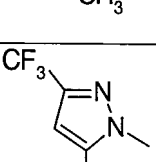
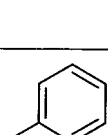
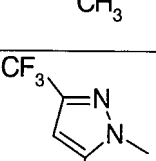
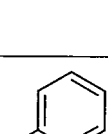
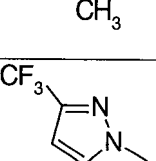
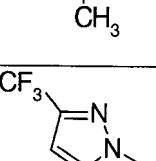
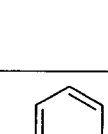
Compuesto No.	R ¹	A	Q	R ⁹
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002		-CH ₂ C(=O)-	-C(=S)-	
003		-CH ₂ C(=O)-	-C(=O)O-	
004		-CH ₂ C(=O)-	-C(=O)NH-	

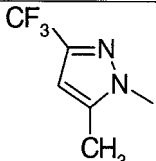
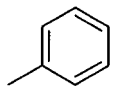
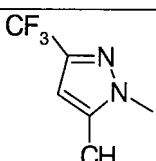
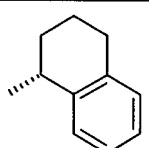
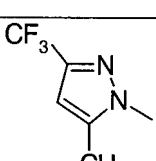
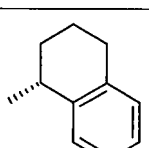
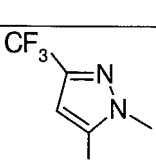
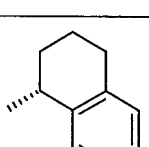
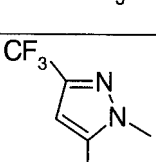
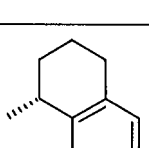
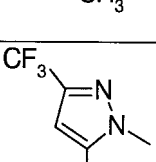
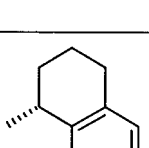
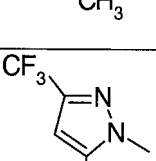
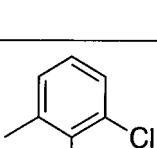
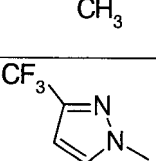
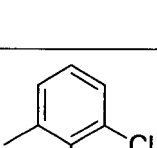
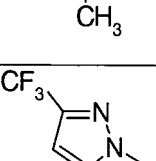
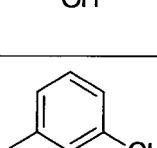
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006		-CH ₂ C(=O)-	-C(=O)-	
007		-CH ₂ C(=O)-	-C(=S)-	
008		-CH ₂ C(=O)-	-C(=O)O-	
009		-CH ₂ C(=O)-	-C(=O)NH-	
010		-CH ₂ C(=O)-	-SO ₂ -	
011		-CH ₂ C(=O)-	-C(=O)-	
012		-CH ₂ C(=O)-	-C(=S)-	
013		-CH ₂ C(=O)-	-C(=O)O-	

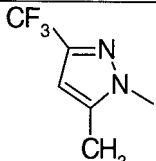
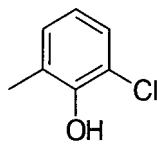
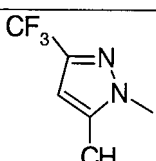
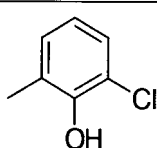
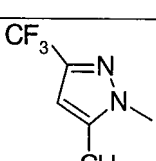
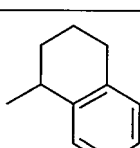
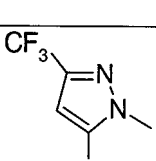
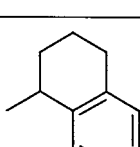
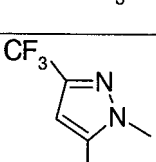
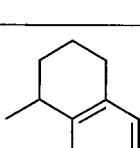
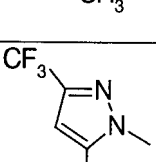
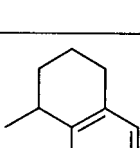
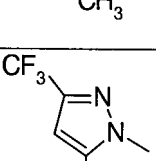
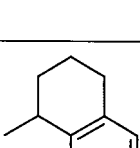
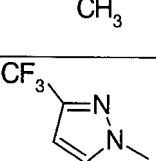
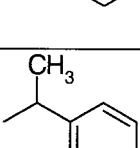
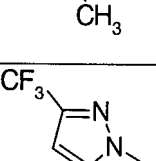
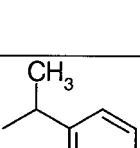
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015		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{SO}_2-$	
016		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{O})-$	
017		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{S})-$	
018		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{O})\text{O}-$	
019		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{O})\text{NH}-$	
020		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{SO}_2-$	
021		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{O})-$	
022		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{S})-$	

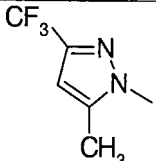
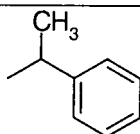
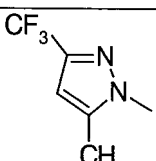
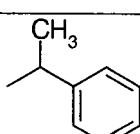
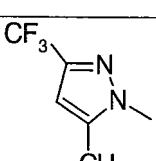
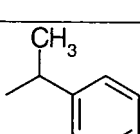
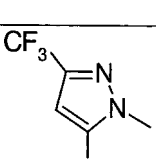
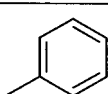
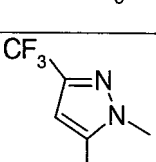
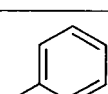
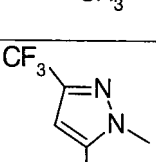
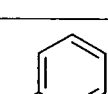
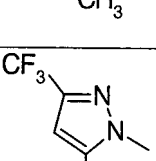
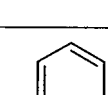
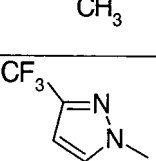
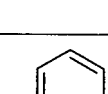
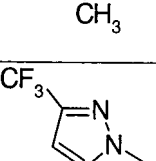
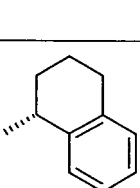
023		-CH ₂ C(=O)-	-C(=O)O-	
024		-CH ₂ C(=O)-	-C(=O)NH-	
025		-CH ₂ C(=O)-	-SO ₂ -	
026		-CH ₂ C(=S)-	-C(=O)-	
027		-CH ₂ C(=S)-	-C(=S)-	
028		-CH ₂ C(=S)-	-C(=O)O-	
029		-CH ₂ C(=S)-	-C(=O)NH-	
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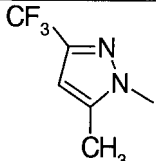
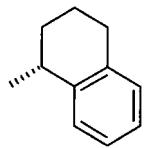
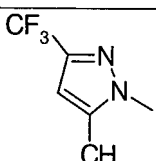
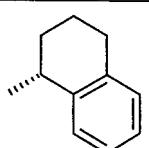
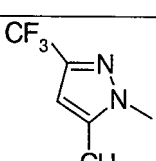
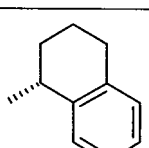
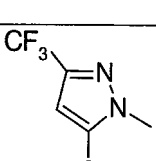
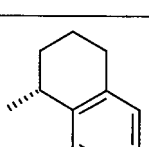
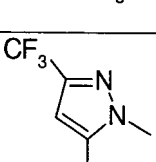
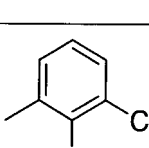
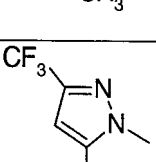
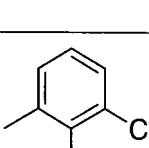
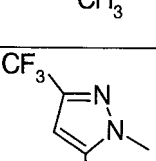
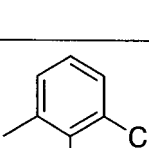
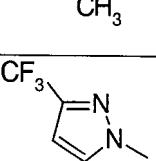
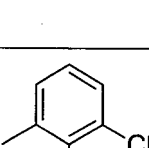
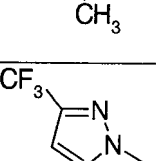
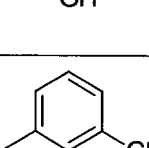
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033		-CH ₂ C(=S)-	-C(=O)O-	
034		-CH ₂ C(=S)-	-C(=O)NH-	
035		-CH ₂ C(=S)-	-SO ₂ -	
036		-CH ₂ C(=S)-	-C(=O)-	
037		-CH ₂ C(=S)-	-C(=S)-	
038		-CH ₂ C(=S)-	-C(=O)O-	
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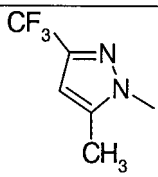
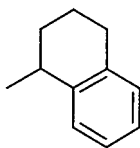
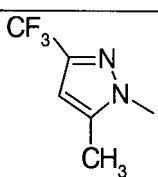
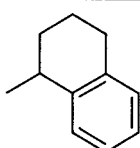
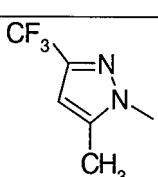
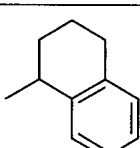
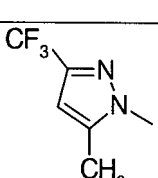
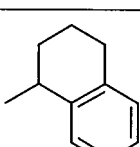
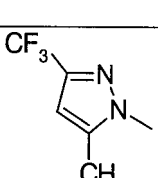
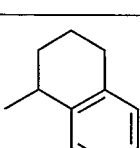
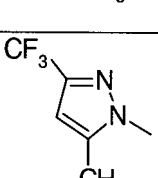
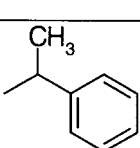
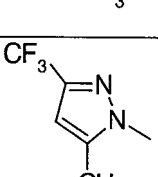
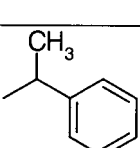
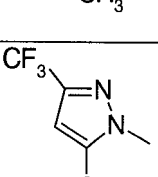
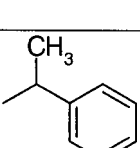
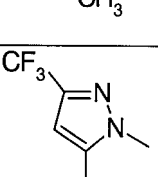
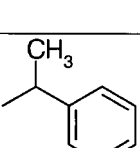
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042		-CH ₂ C(=S)-	-C(=S)-	
043		-CH ₂ C(=S)-	-C(=O)O-	
044		-CH ₂ C(=S)-	-C(=O)NH-	
045		-CH ₂ C(=S)-	-SO ₂ -	
046		-CH ₂ C(=S)-	-C(=O)-	
047		-CH ₂ C(=S)-	-C(=S)-	
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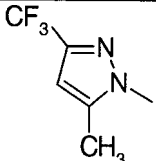
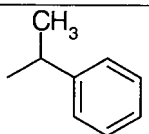
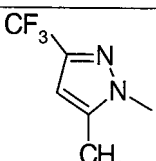
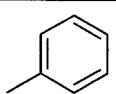
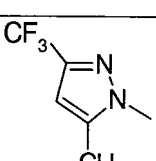
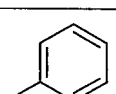
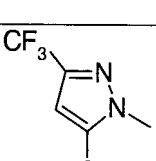
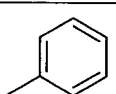
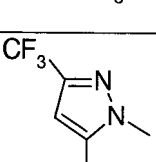
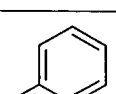
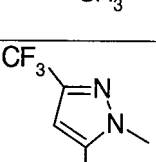
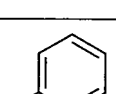
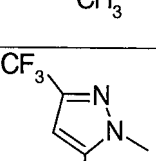
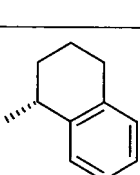
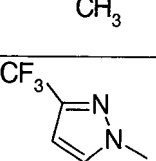
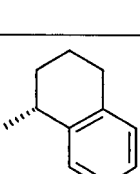
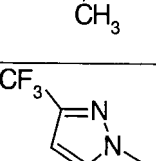
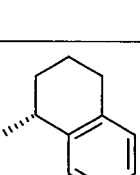
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051		$-\text{OC}(=\text{O})-$	$-\text{C}(=\text{O})-$	
052		$-\text{OC}(=\text{O})-$	$-\text{C}(=\text{S})-$	
053		$-\text{OC}(=\text{O})-$	$-\text{C}(=\text{O})\text{O}-$	
054		$-\text{OC}(=\text{O})-$	$-\text{C}(=\text{O})\text{NH}-$	
055		$-\text{OC}(=\text{O})-$	$-\text{SO}_2-$	
056		$-\text{OC}(=\text{O})-$	$-\text{C}(=\text{O})-$	
057		$-\text{OC}(=\text{O})-$	$-\text{C}(=\text{S})-$	
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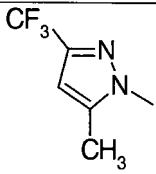
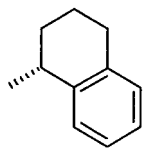
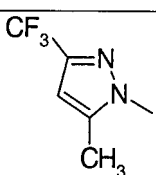
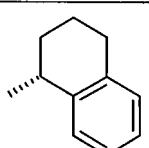
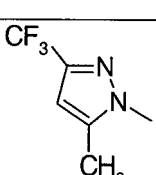
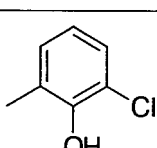
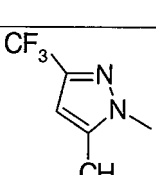
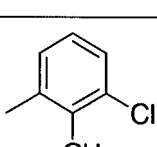
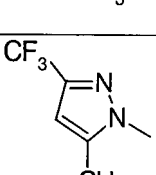
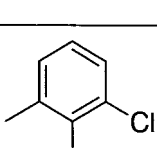
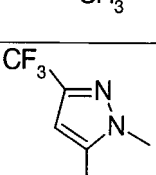
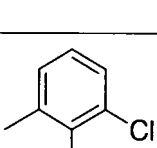
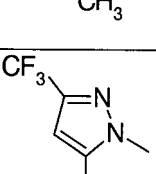
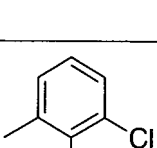
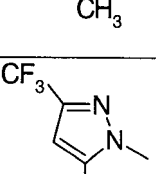
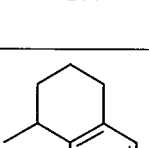
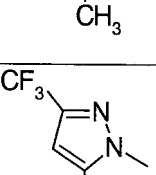
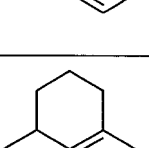
059		-OC(=O)-	-C(=O)NH-	
060		-OC(=O)-	-SO ₂ -	
061		-OC(=O)-	-C(=O)-	
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063		-OC(=O)-	-C(=O)O-	
064		-OC(=O)-	-C(=O)NH-	
065		-OC(=O)-	-SO ₂ -	
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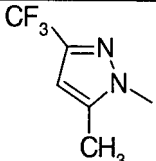
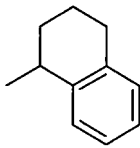
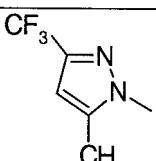
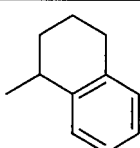
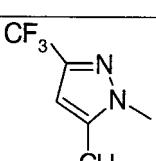
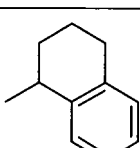
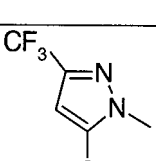
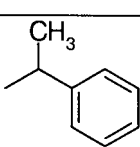
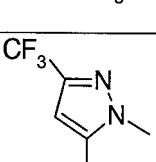
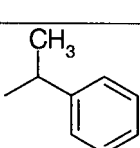
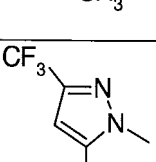
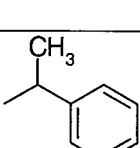
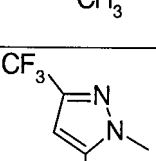
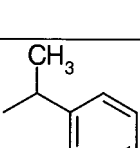
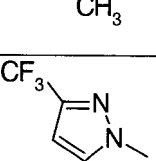
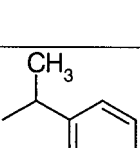
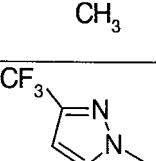
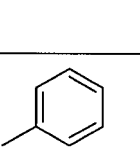
068		-OC(=O)-	-C(=O)O-	
069		-OC(=O)-	-C(=O)NH-	
070		-OC(=O)-	-SO ₂ -	
071		-OC(=O)-	-C(=O)-	
072		-OC(=O)-	-C(=S)-	
073		-OC(=O)-	-C(=O)O-	
074		-OC(=O)-	-C(=O)NH-	
075		-OC(=O)-	-SO ₂ -	
076		-C(=O)-	-C(=O)-	

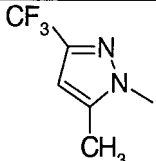
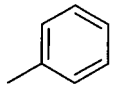
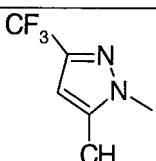
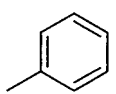
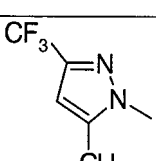
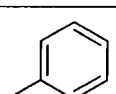
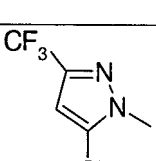
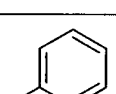
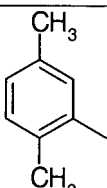
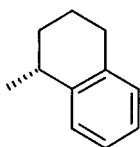
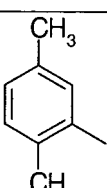
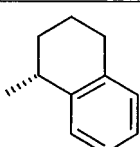
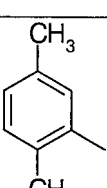
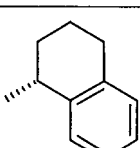
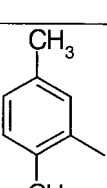
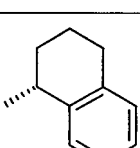
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078		-C(=O)-	-C(=O)O-	
079		-C(=O)-	-C(=O)NH-	
080		-C(=O)-	-SO ₂ -	
081		-C(=O)-	-C(=O)-	
082		-C(=O)-	-C(=S)-	
083		-C(=O)-	-C(=O)O-	
084		-C(=O)-	-C(=O)NH-	
085		-C(=O)-	-SO ₂ -	

086		-C(=O)-	-C(=O)-	
087		-C(=O)-	-C(=S)-	
088		-C(=O)-	-C(=O)O-	
089		-C(=O)-	-C(=O)NH-	
090		-C(=O)-	-SO ₂ -	
091		-C(=O)-	-C(=O)-	
092		-C(=O)-	-C(=S)-	
093		-C(=O)-	-C(=O)O-	
094		-C(=O)-	-C(=O)NH-	

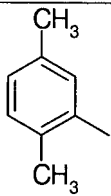
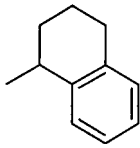
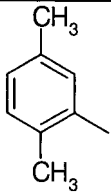
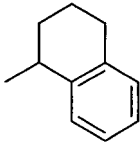
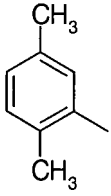
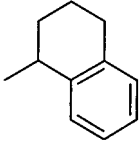
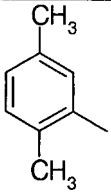
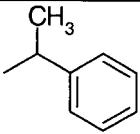
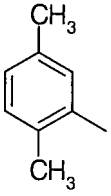
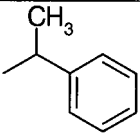
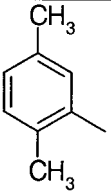
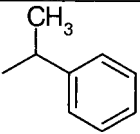
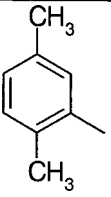
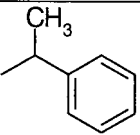
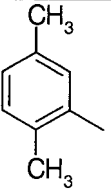
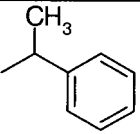
095		-C(=O)-	-SO ₂ -	
096		-C(=O)-	-C(=O)-	
097		-C(=O)-	-C(=S)-	
098		-C(=O)-	-C(=O)O-	
099		-C(=O)-	-C(=O)NH-	
100		-C(=O)-	-SO ₂ -	
101		-CH ₂ SO ₂ -	-C(=O)-	
102		-CH ₂ SO ₂ -	-C(=S)-	
103		-CH ₂ SO ₂ -	-C(=O)O-	

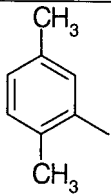
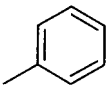
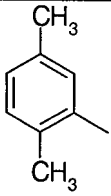
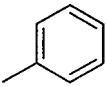
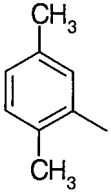
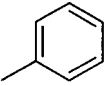
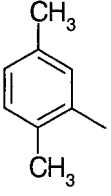
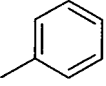
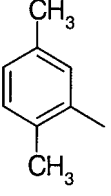
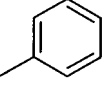
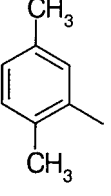
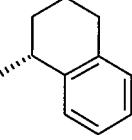
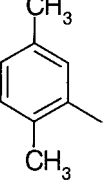
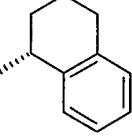
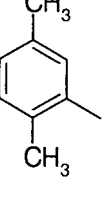
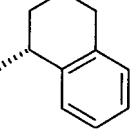
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105		-CH ₂ SO ₂ -	-SO ₂ -	
106		-CH ₂ SO ₂ -	-C(=O)-	
107		-CH ₂ SO ₂ -	-C(=S)-	
108		-CH ₂ SO ₂ -	-C(=O)O-	
109		-CH ₂ SO ₂ -	-C(=O)NH-	
110		-CH ₂ SO ₂ -	-SO ₂ -	
111		-CH ₂ SO ₂ -	-C(=O)-	
112		-CH ₂ SO ₂ -	-C(=S)-	

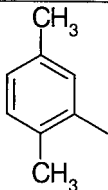
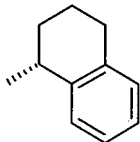
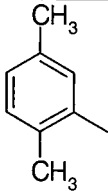
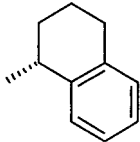
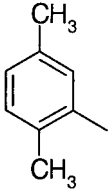
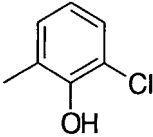
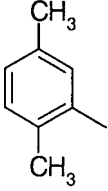
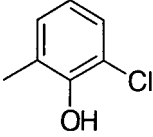
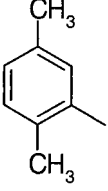
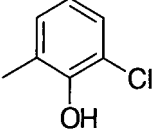
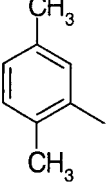
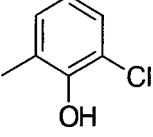
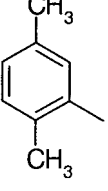
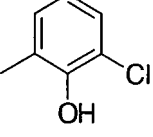
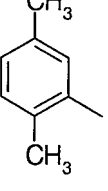
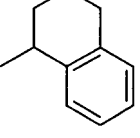
113		-CH ₂ SO ₂ -	-C(=O)O-	
114		-CH ₂ SO ₂ -	-C(=O)NH-	
115		-CH ₂ SO ₂ -	-SO ₂ -	
116		-CH ₂ SO ₂ -	-C(=O)-	
117		-CH ₂ SO ₂ -	-C(=S)-	
118		-CH ₂ SO ₂ -	-C(=O)O-	
119		-CH ₂ SO ₂ -	-C(=O)NH-	
120		-CH ₂ SO ₂ -	-SO ₂ -	
121		-CH ₂ SO ₂ -	-C(=O)-	

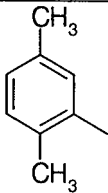
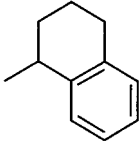
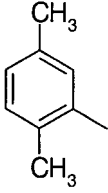
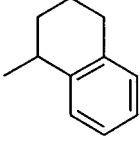
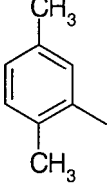
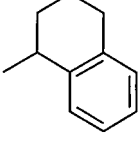
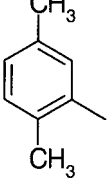
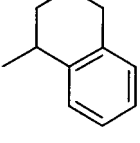
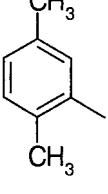
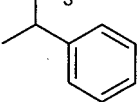
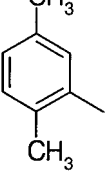
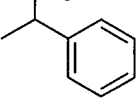
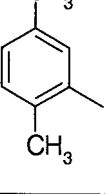
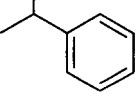
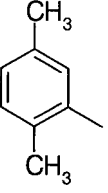
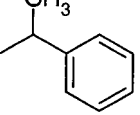
122		-CH ₂ SO ₂ -	-C(=S)-	
123		-CH ₂ SO ₂ -	-C(=O)O-	
124		-CH ₂ SO ₂ -	-C(=O)NH-	
125		-CH ₂ SO ₂ -	-SO ₂ -	
126		-CH ₂ C(=O)-	-C(=O)-	
127		-CH ₂ C(=O)-	-C(=S)-	
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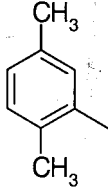
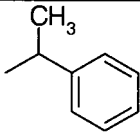
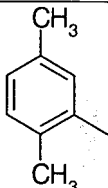
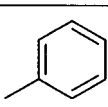
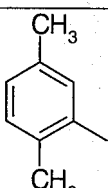
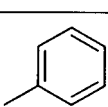
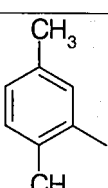
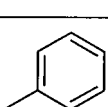
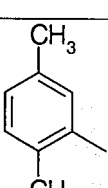
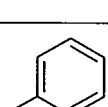
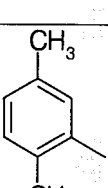
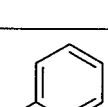
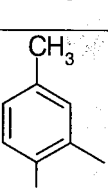
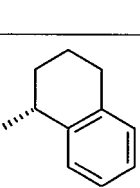
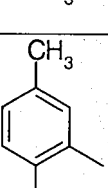
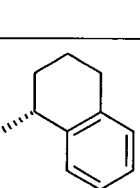
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131		-CH ₂ C(=O)-	-C(=O)-	
132		-CH ₂ C(=O)-	-C(=S)-	
133		-CH ₂ C(=O)-	-C(=O)O-	
134		-CH ₂ C(=O)-	-C(=O)NH-	
135		-CH ₂ C(=O)-	-SO ₂ -	
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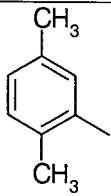
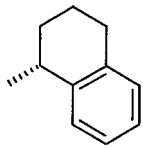
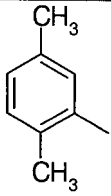
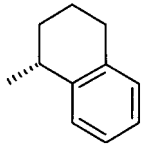
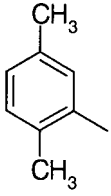
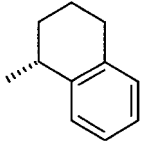
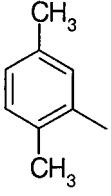
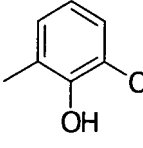
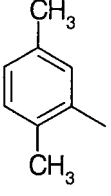
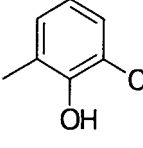
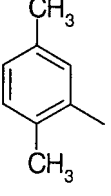
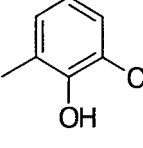
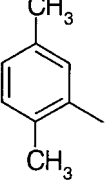
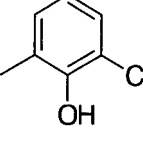
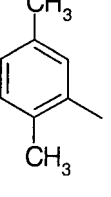
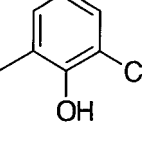
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140		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{SO}_2-$	
141		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{O})-$	
142		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{S})-$	
143		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{O})\text{O}-$	
144		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{O})\text{NH}-$	
145		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{SO}_2-$	

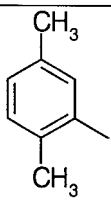
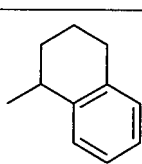
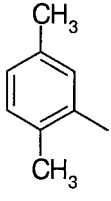
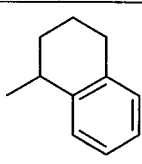
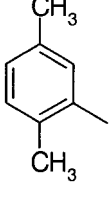
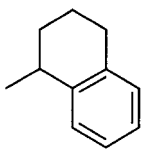
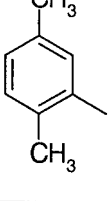
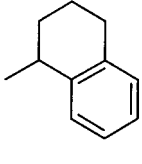
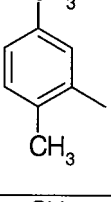
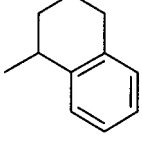
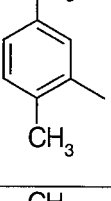
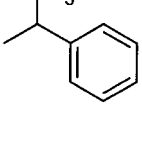
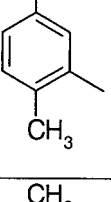
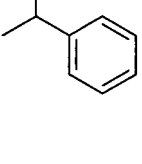
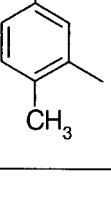
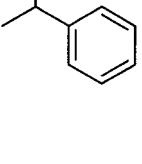
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147		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{S})-$	
148		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{O})\text{O}-$	
149		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{O})\text{NH}-$	
150		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{SO}_2-$	
151		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})-$	
152		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{S})-$	
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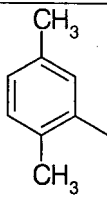
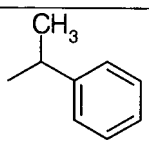
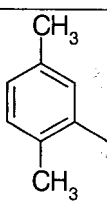
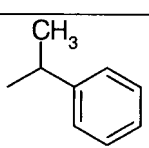
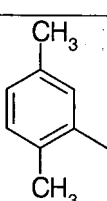
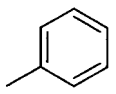
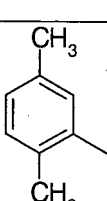
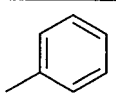
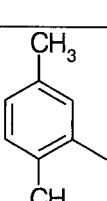
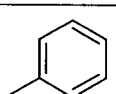
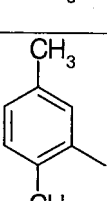
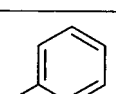
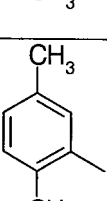
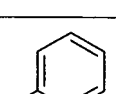
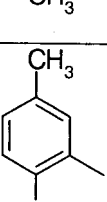
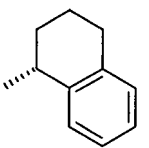
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155		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{SO}_2-$	
156		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})-$	
157		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{S})-$	
158		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})\text{O}-$	
159		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})\text{NH}-$	
160		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{SO}_2-$	
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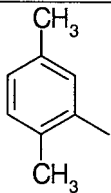
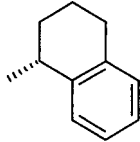
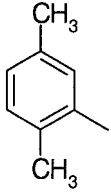
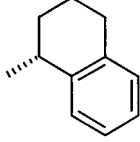
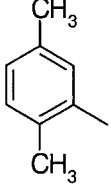
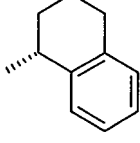
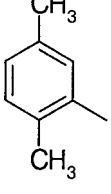
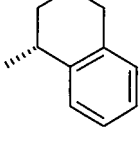
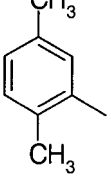
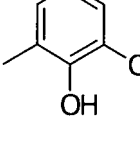
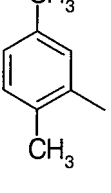
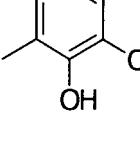
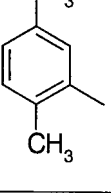
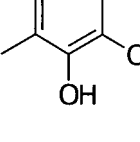
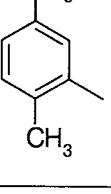
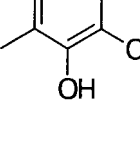
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163		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})\text{O}-$	
164		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})\text{NH}-$	
165		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{SO}_2-$	
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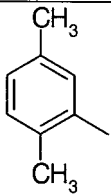
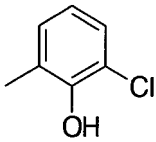
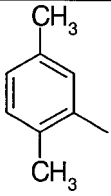
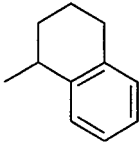
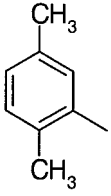
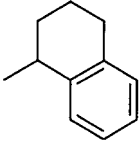
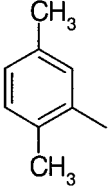
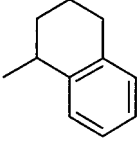
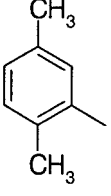
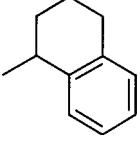
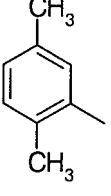
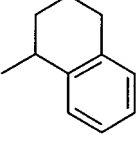
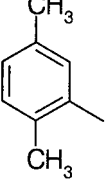
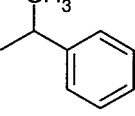
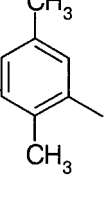
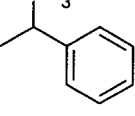
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171		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})-$	
172		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{S})-$	
173		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})\text{O}-$	
174		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})\text{NH}-$	
175		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{SO}_2-$	
176		$-\text{OC}(=\text{O})-$	$-\text{C}(=\text{O})-$	
177		$-\text{OC}(=\text{O})-$	$-\text{C}(=\text{S})-$	

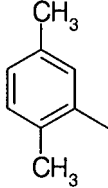
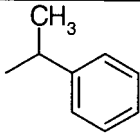
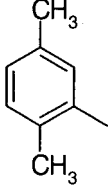
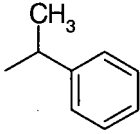
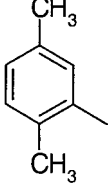
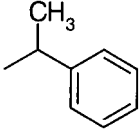
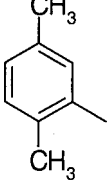
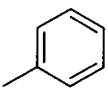
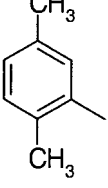
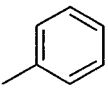
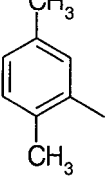
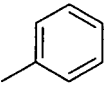
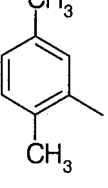
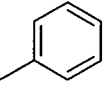
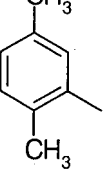
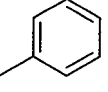
178		-OC(=O)-	-C(=O)O-	
179		-OC(=O)-	-C(=O)NH-	
180		-OC(=O)-	-SO ₂ -	
181		-OC(=O)-	-C(=O)-	
182		-OC(=O)-	-C(=S)-	
183		-OC(=O)-	-C(=O)O-	
184		-OC(=O)-	-C(=O)NH-	
185		-OC(=O)-	-SO ₂ -	

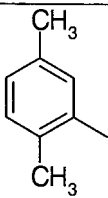
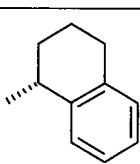
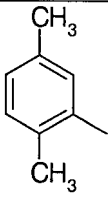
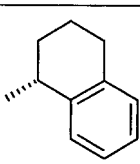
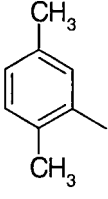
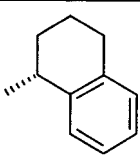
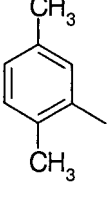
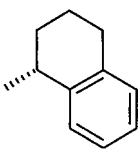
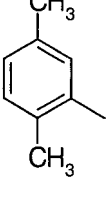
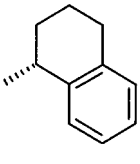
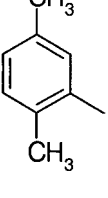
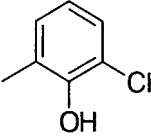
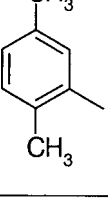
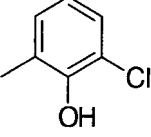
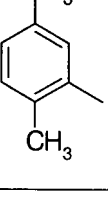
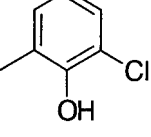
186		-OC(=O)-	-C(=O)-	
187		-OC(=O)-	-C(=S)-	
188		-OC(=O)-	-C(=O)O-	
189		-OC(=O)-	-C(=O)NH-	
190		-OC(=O)-	-SO ₂ -	
191		-OC(=O)-	-C(=O)-	
192		-OC(=O)-	-C(=S)-	
193		-OC(=O)-	-C(=O)O-	

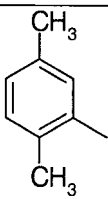
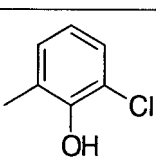
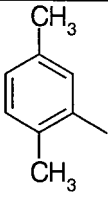
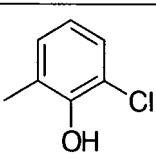
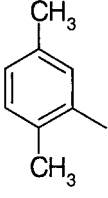
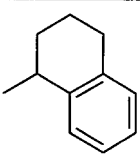
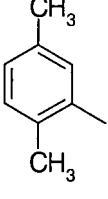
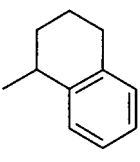
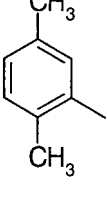
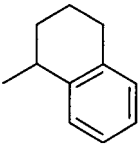
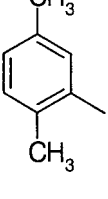
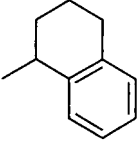
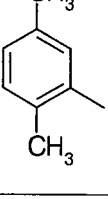
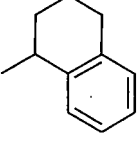
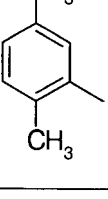
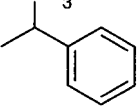
194		-OC(=O)-	-C(=O)NH-	
195		-OC(=O)-	-SO ₂ -	
196		-OC(=O)-	-C(=O)-	
197		-OC(=O)-	-C(=S)-	
198		-OC(=O)-	-C(=O)O-	
199		-OC(=O)-	-C(=O)NH-	
200		-OC(=O)-	-SO ₂ -	
201		-C(=O)-	-C(=O)-	

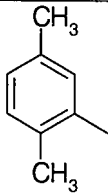
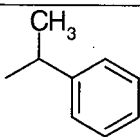
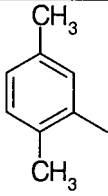
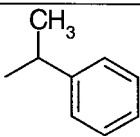
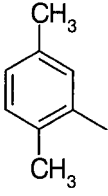
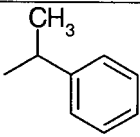
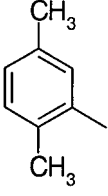
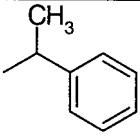
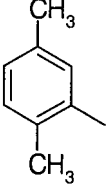
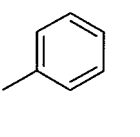
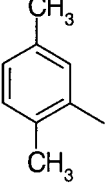
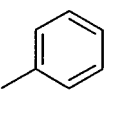
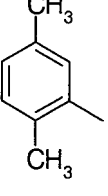
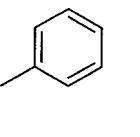
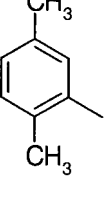
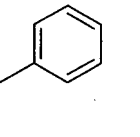
202		-C(=O)-	-C(=S)-	
203		-C(=O)-	-C(=O)O-	
204		-C(=O)-	-C(=O)NH-	
205		-C(=O)-	-SO ₂ -	
206		-C(=O)-	-C(=O)-	
207		-C(=O)-	-C(=S)-	
208		-C(=O)-	-C(=O)O-	
209		-C(=O)-	-C(=O)NH-	

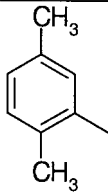
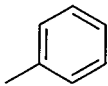
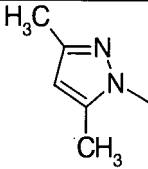
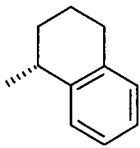
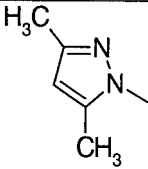
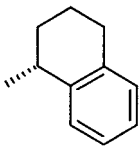
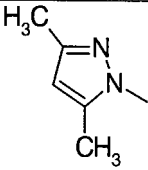
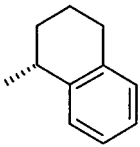
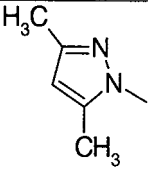
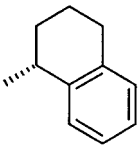
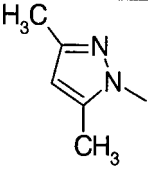
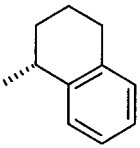
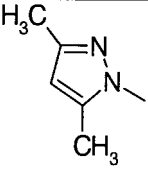
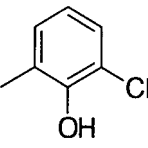
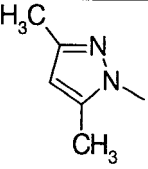
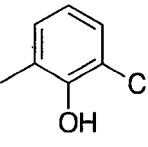
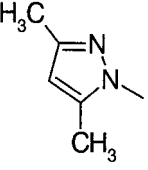
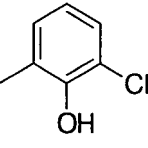
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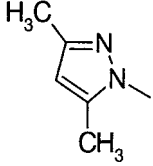
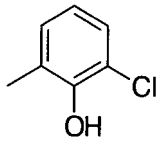
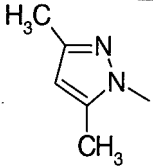
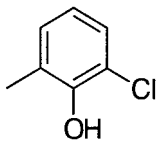
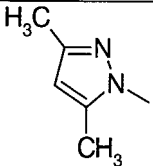
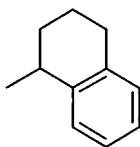
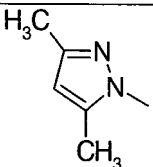
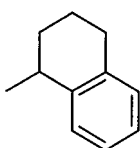
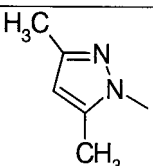
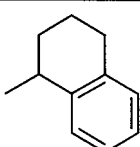
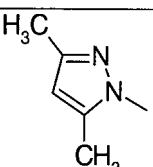
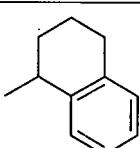
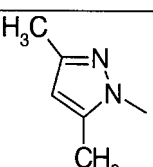
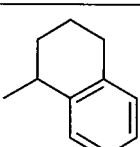
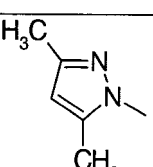
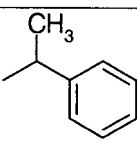
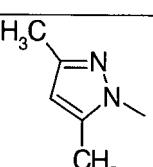
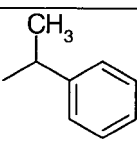
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222		-C(=O)-	-C(=S)-	
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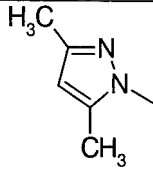
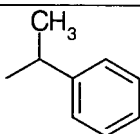
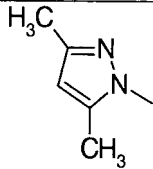
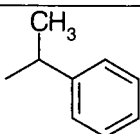
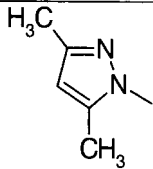
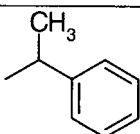
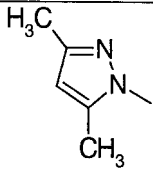
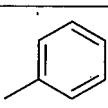
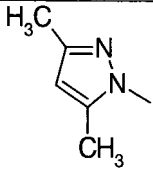
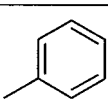
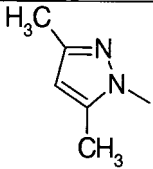
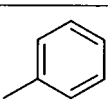
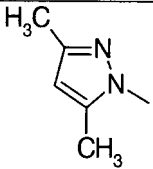
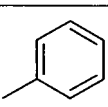
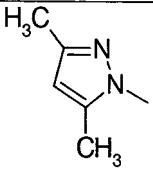
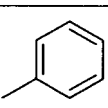
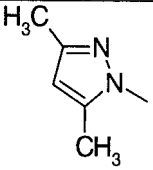
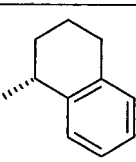
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229		- CH ₂ SO ₂ -	-C(=O)NH-	
230		- CH ₂ SO ₂ -	-SO ₂ -	
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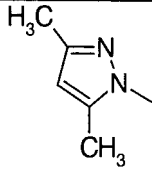
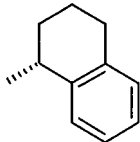
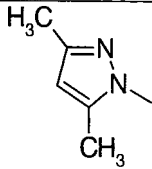
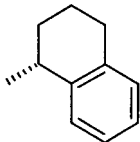
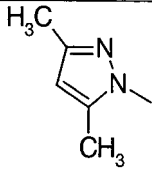
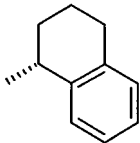
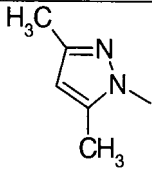
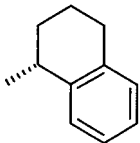
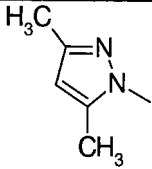
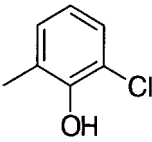
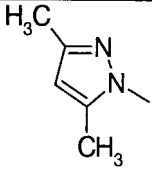
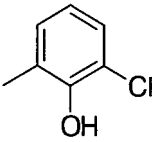
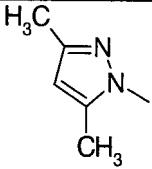
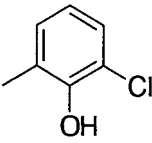
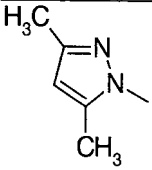
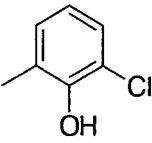
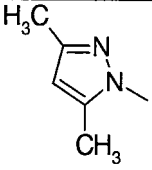
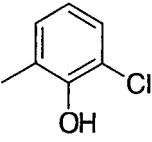
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236		- CH ₂ SO ₂ -	-C(=O)-	
237		- CH ₂ SO ₂ -	-C(=S)-	
238		- CH ₂ SO ₂ -	-C(=O)O-	
239		- CH ₂ SO ₂ -	-C(=O)NH-	
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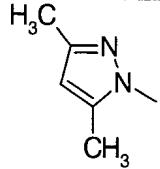
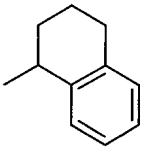
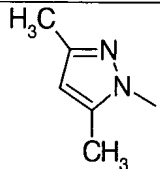
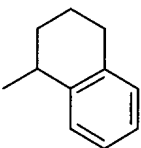
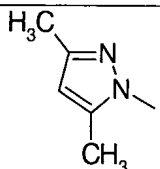
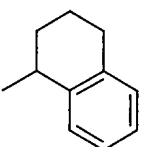
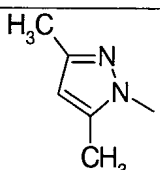
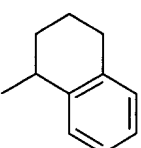
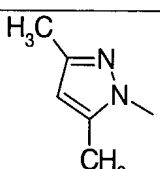
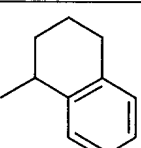
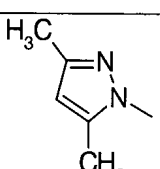
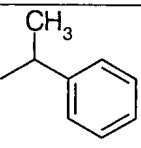
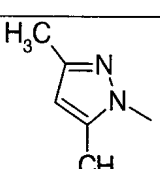
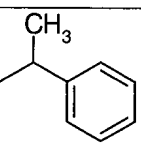
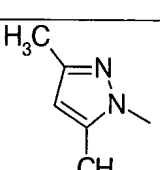
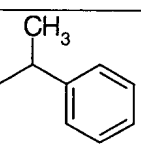
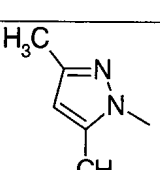
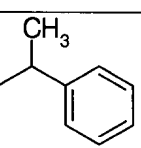
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244		- CH ₂ SO ₂ -	-C(=O)NH-	
245		- CH ₂ SO ₂ -	-SO ₂ -	
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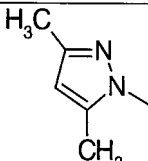
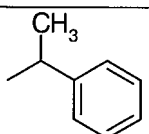
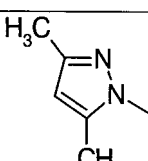
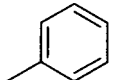
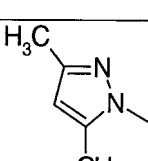
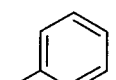
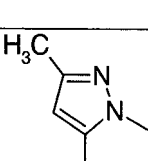
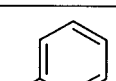
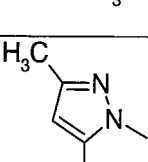
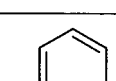
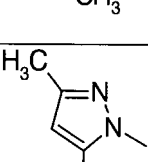
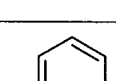
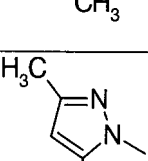
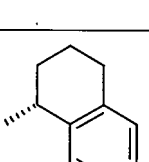
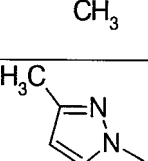
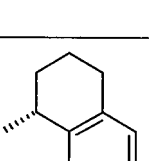
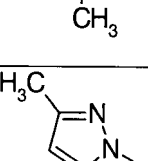
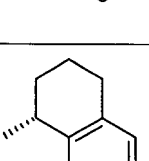
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252		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{S})-$	
253		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{O})\text{O}-$	
254		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{O})\text{NH}-$	
255		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{SO}_2-$	
256		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{O})-$	
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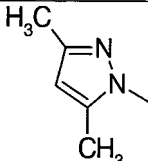
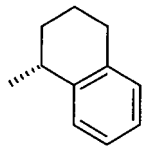
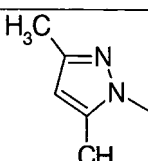
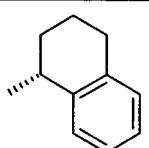
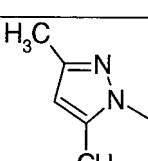
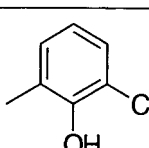
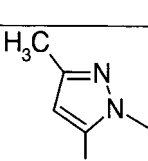
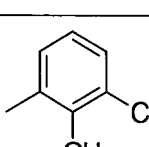
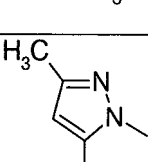
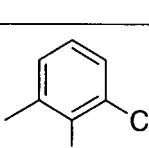
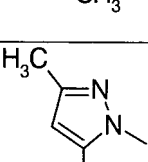
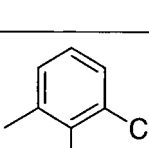
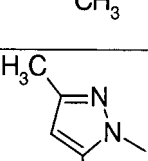
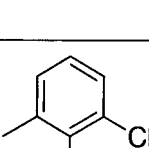
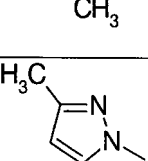
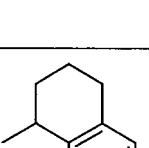
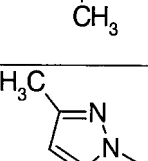
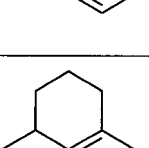
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261		-CH ₂ C(=O)-	-C(=O)-	
262		-CH ₂ C(=O)-	-C(=S)-	
263		-CH ₂ C(=O)-	-C(=O)O-	
264		-CH ₂ C(=O)-	-C(=O)NH-	
265		-CH ₂ C(=O)-	-SO ₂ -	
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267		-CH ₂ C(=O)-	-C(=S)-	

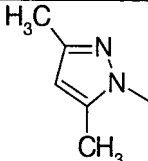
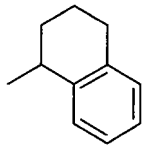
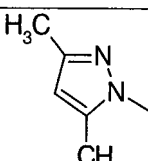
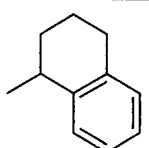
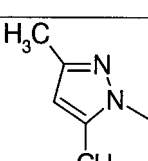
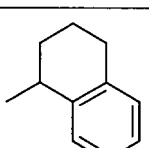
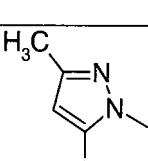
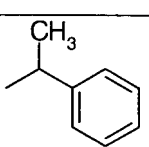
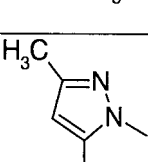
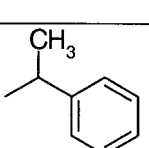
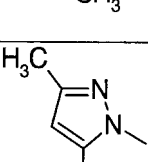
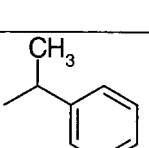
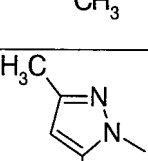
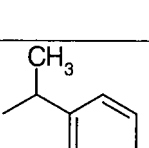
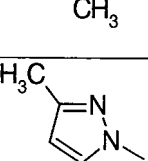
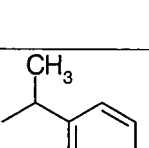
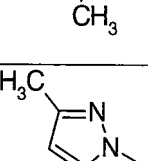
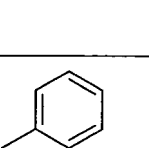
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269		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{O})\text{NH}-$	
270		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{SO}_2-$	
271		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{O})-$	
272		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{S})-$	
273		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{O})\text{O}-$	
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275		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{SO}_2-$	
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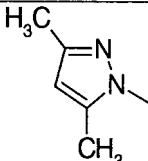
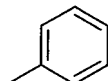
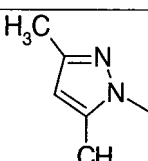
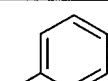
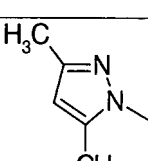
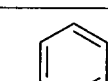
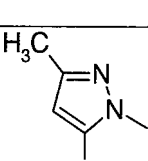
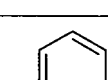
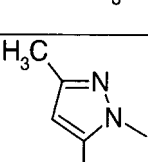
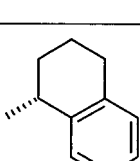
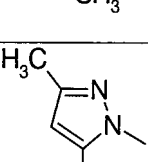
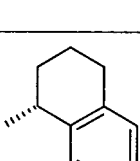
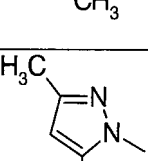
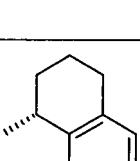
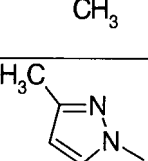
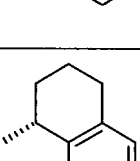
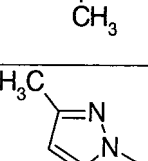
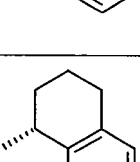
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279		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})\text{NH}-$	
280		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{SO}_2-$	
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282		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{S})-$	
283		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})\text{O}-$	
284		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})\text{NH}-$	
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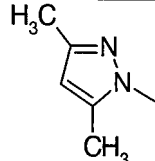
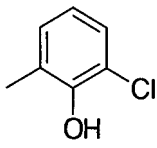
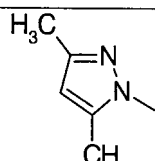
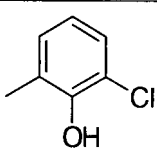
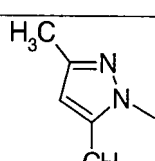
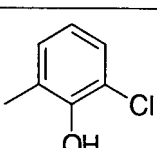
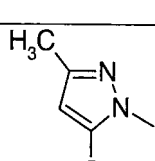
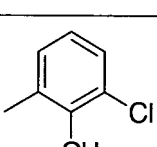
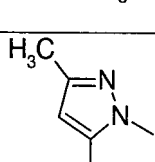
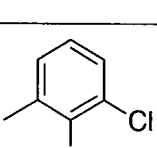
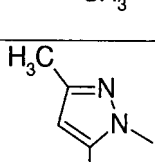
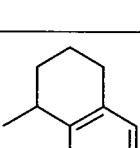
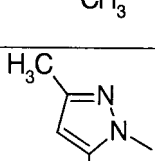
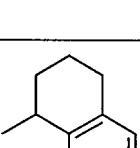
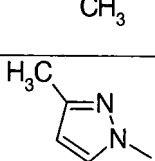
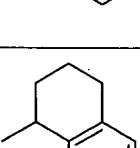
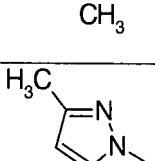
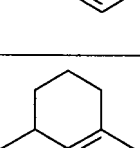
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288		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})\text{O}-$	
289		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})\text{NH}-$	
290		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{SO}_2-$	
291		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})-$	
292		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{S})-$	
293		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})\text{O}-$	
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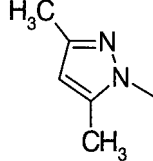
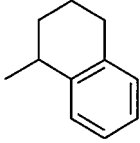
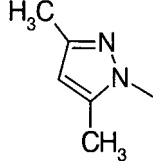
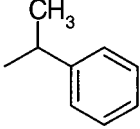
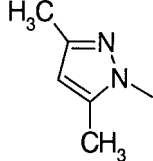
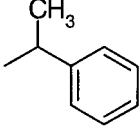
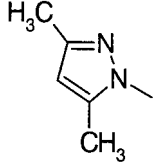
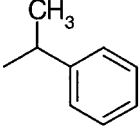
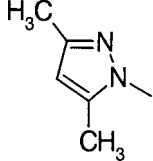
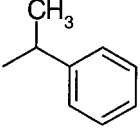
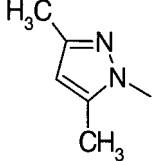
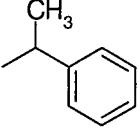
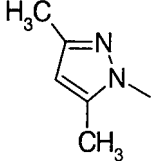
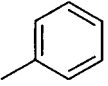
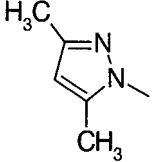
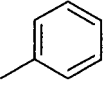
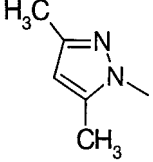
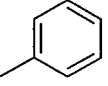
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297		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{S})-$	
298		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})\text{O}-$	
299		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})\text{NH}-$	
300		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{SO}_2-$	
301		$-\text{OC}(=\text{O})-$	$-\text{C}(=\text{O})-$	
302		$-\text{OC}(=\text{O})-$	$-\text{C}(=\text{S})-$	
303		$-\text{OC}(=\text{O})-$	$-\text{C}(=\text{O})\text{O}-$	

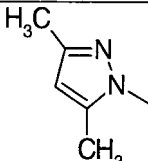
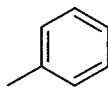
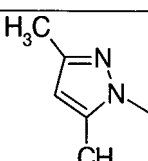
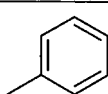
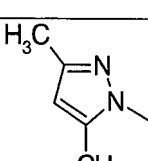
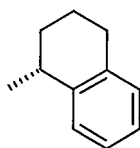
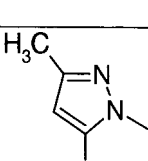
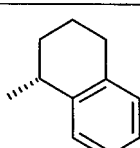
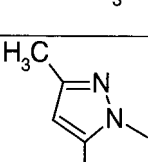
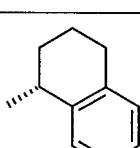
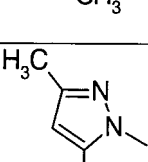
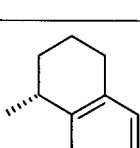
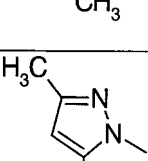
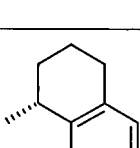
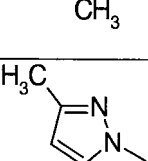
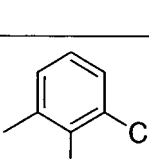
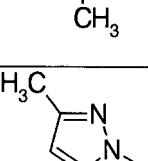
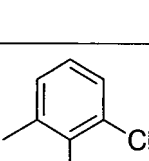
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305		-OC(=O)-	-SO ₂ -	
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308		-OC(=O)-	-C(=O)O-	
309		-OC(=O)-	-C(=O)NH-	
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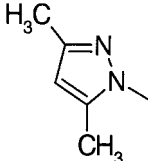
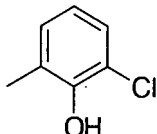
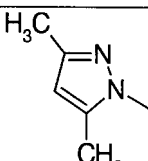
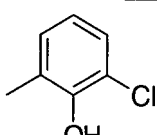
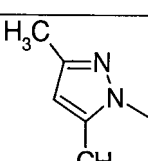
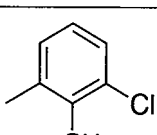
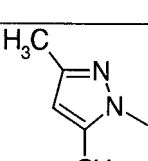
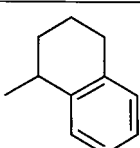
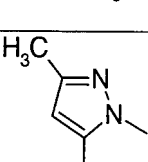
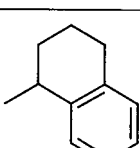
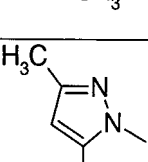
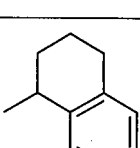
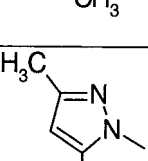
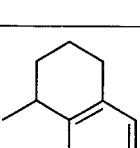
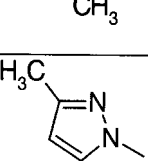
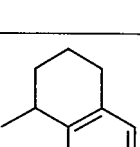
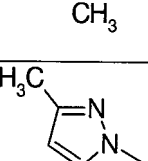
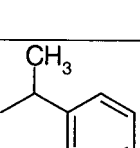
313		-OC(=O)-	-C(=O)O-	
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315		-OC(=O)-	-SO ₂ -	
316		-OC(=O)-	-C(=O)-	
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318		-OC(=O)-	-C(=O)O-	
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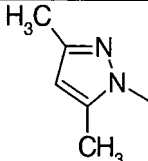
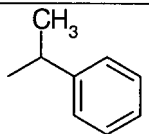
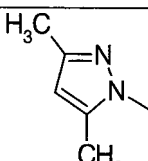
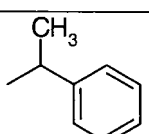
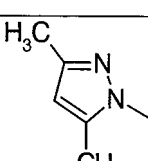
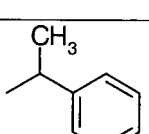
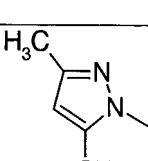
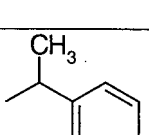
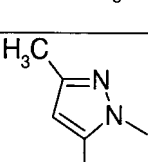
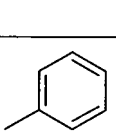
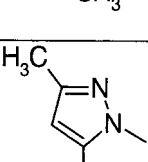
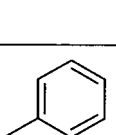
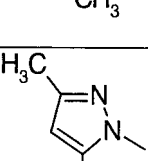
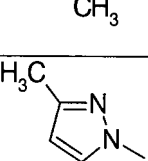
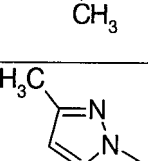
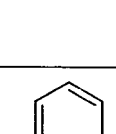
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323		-OC(=O)-	-C(=O)O-	
324		-OC(=O)-	-C(=O)NH-	
325		-OC(=O)-	-SO ₂ -	
326		-C(=O)-	-C(=O)-	
327		-C(=O)-	-C(=S)-	
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329		-C(=O)-	-C(=O)NH-	
330		-C(=O)-	-SO ₂ -	

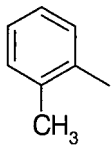
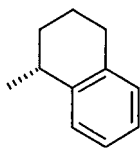
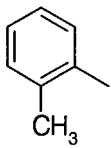
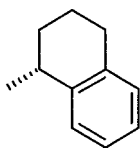
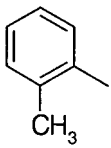
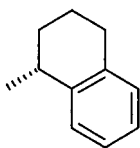
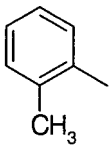
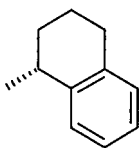
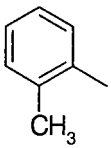
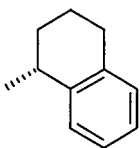
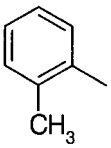
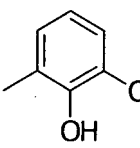
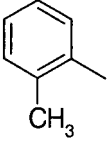
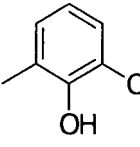
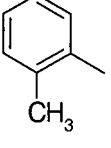
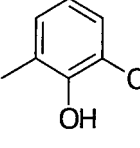
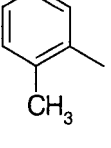
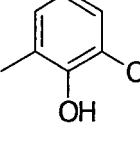
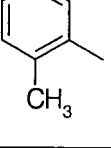
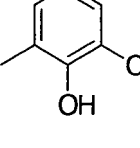
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335		-C(=O)-	-SO ₂ -	
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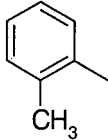
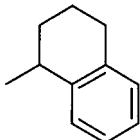
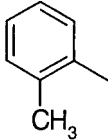
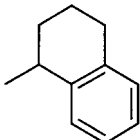
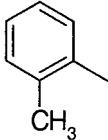
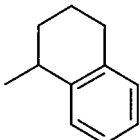
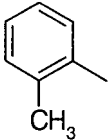
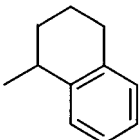
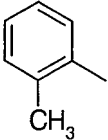
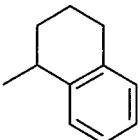
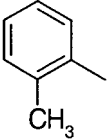
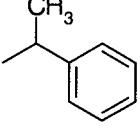
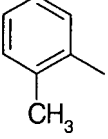
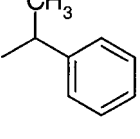
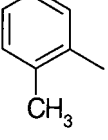
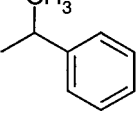
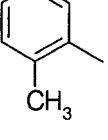
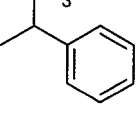
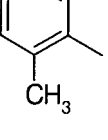
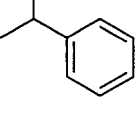
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344		-C(=O)-	-C(=O)NH-	
345		-C(=O)-	-SO ₂ -	
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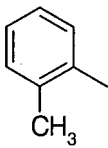
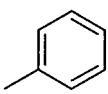
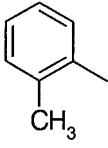
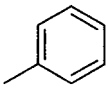
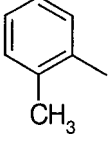
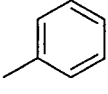
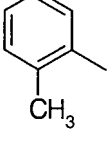
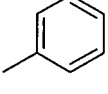
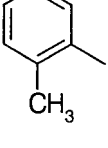
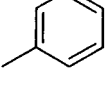
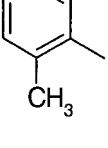
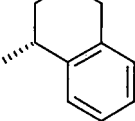
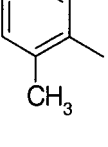
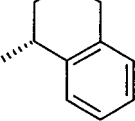
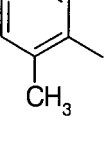
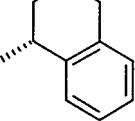
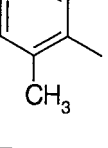
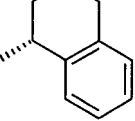
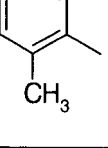
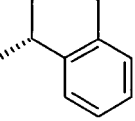
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352		-CH ₂ SO ₂ -	-C(=S)-	
353		-CH ₂ SO ₂ -	-C(=O)O-	
354		-CH ₂ SO ₂ -	-C(=O)NH-	
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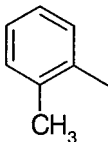
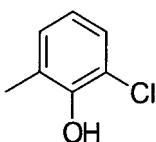
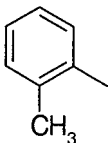
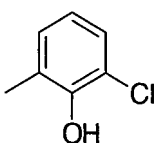
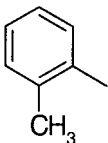
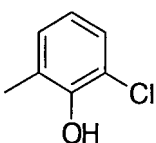
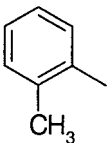
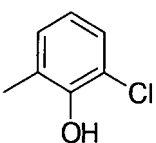
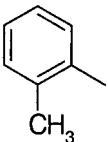
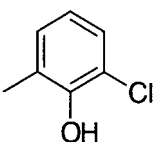
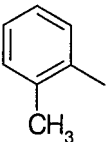
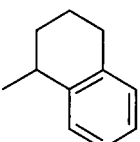
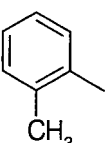
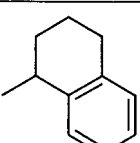
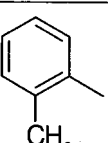
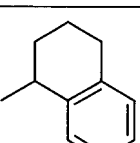
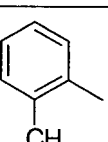
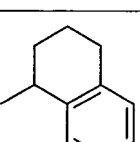
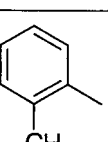
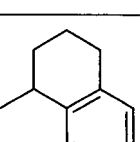
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361		-CH ₂ SO ₂ -	-C(=O)-	
362		-CH ₂ SO ₂ -	-C(=S)-	
363		-CH ₂ SO ₂ -	-C(=O)O-	
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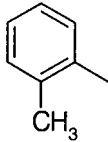
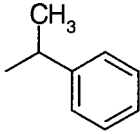
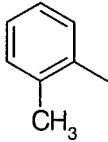
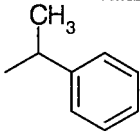
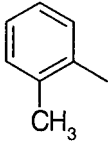
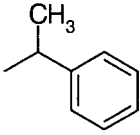
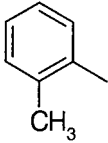
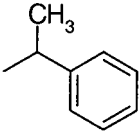
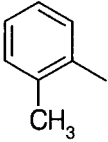
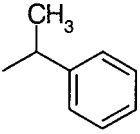
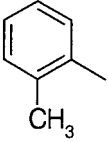
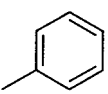
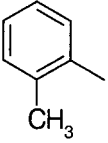
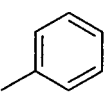
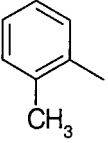
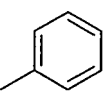
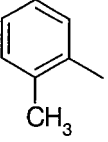
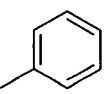
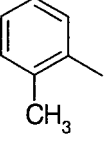
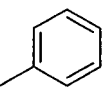
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369		- CH ₂ SO ₂ -	-C(=O)NH-	
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372		- CH ₂ SO ₂ -	-C(=S)-	
373		- CH ₂ SO ₂ -	-C(=O)O-	
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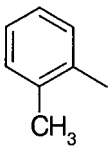
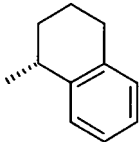
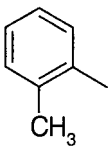
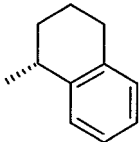
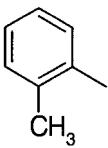
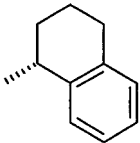
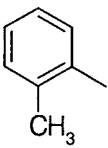
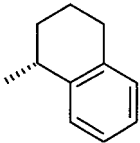
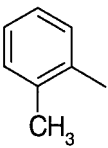
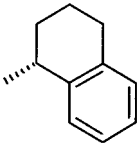
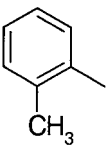
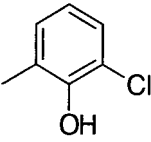
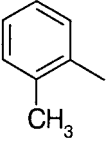
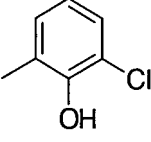
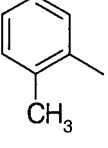
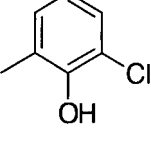
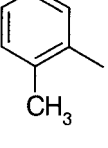
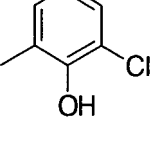
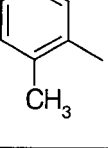
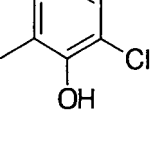
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378		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{O})\text{O}-$	
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380		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{SO}_2-$	
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383		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{O})\text{O}-$	
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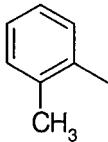
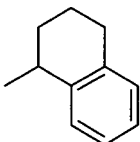
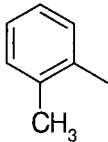
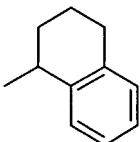
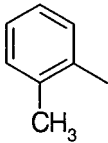
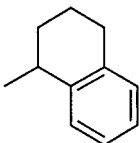
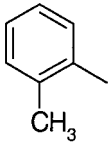
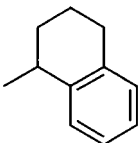
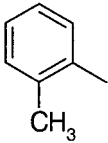
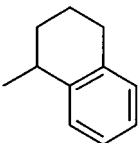
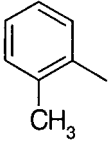
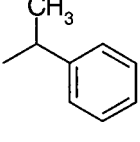
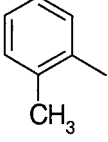
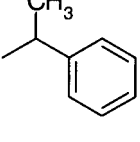
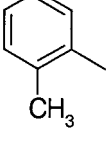
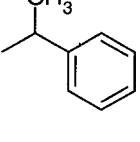
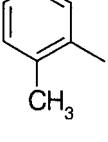
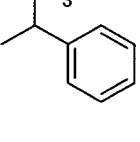
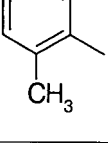
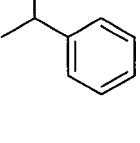
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388		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{O})\text{O}-$	
389		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{O})\text{NH}-$	
390		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{SO}_2-$	
391		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{O})-$	
392		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{S})-$	
393		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{C}(=\text{O})\text{O}-$	
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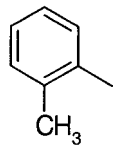
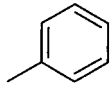
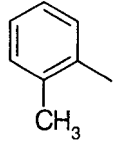
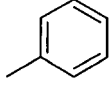
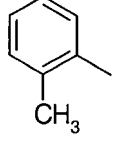
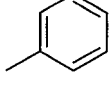
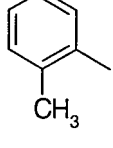
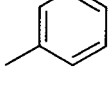
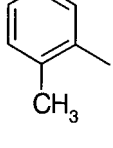
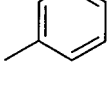
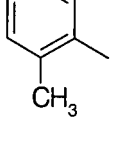
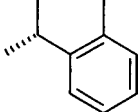
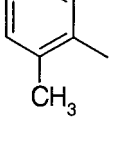
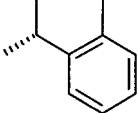
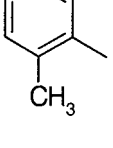
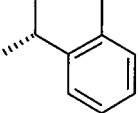
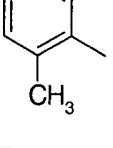
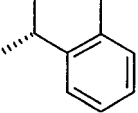
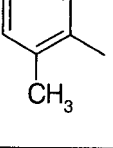
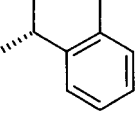
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400		$-\text{CH}_2\text{C}(=\text{O})-$	$-\text{SO}_2-$	
401		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})-$	
402		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{S})-$	
403		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})\text{O}-$	
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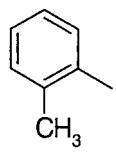
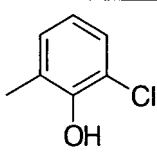
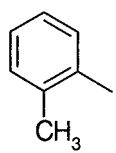
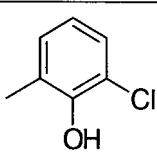
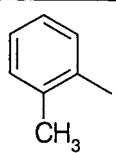
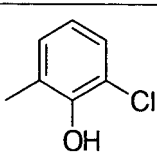
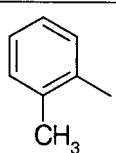
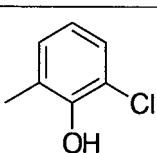
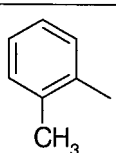
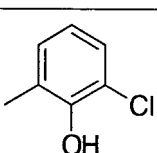
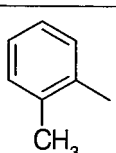
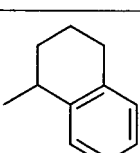
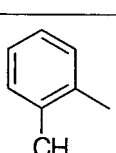
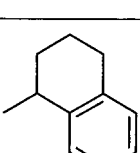
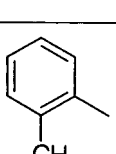
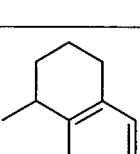
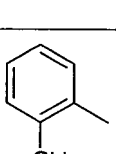
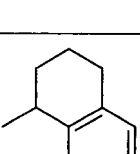
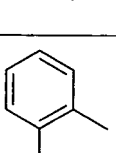
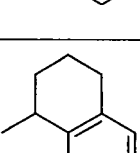
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410		-CH ₂ C(=S)-	-SO ₂ -	
411		-CH ₂ C(=S)-	-C(=O)-	
412		-CH ₂ C(=S)-	-C(=S)-	
413		-CH ₂ C(=S)-	-C(=O)O-	
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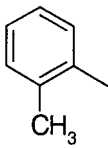
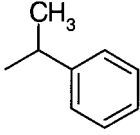
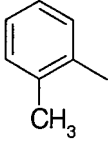
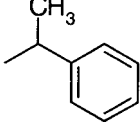
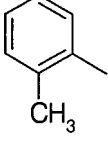
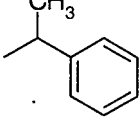
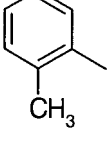
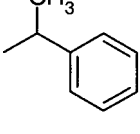
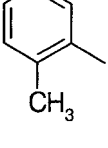
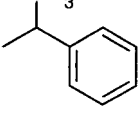
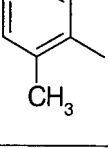
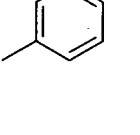
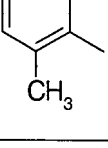
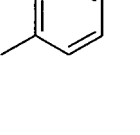
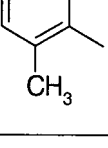
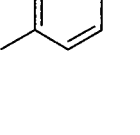
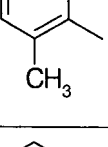
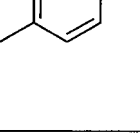
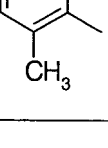
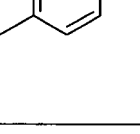
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419		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})\text{NH}-$	
420		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{SO}_2-$	
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422		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{S})-$	
423		$-\text{CH}_2\text{C}(=\text{S})-$	$-\text{C}(=\text{O})\text{O}-$	
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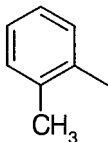
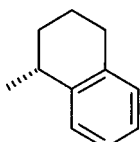
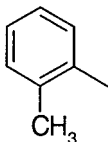
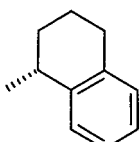
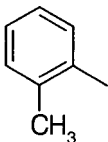
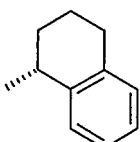
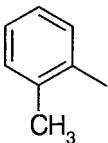
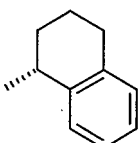
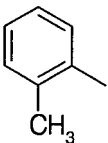
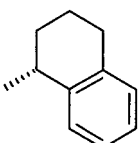
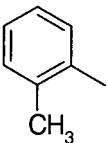
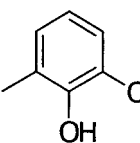
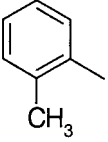
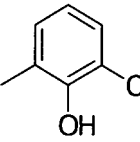
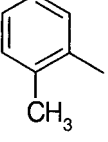
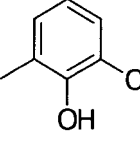
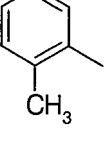
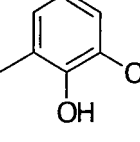
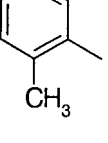
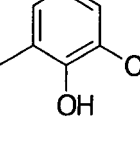
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430		-OC(=O)-	-SO ₂ -	
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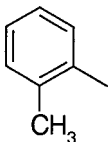
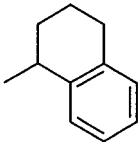
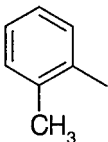
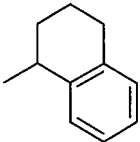
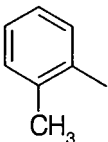
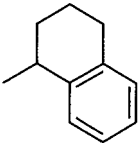
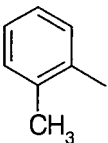
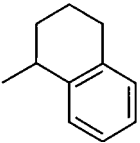
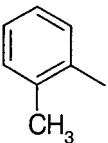
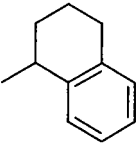
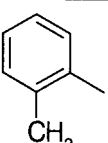
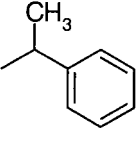
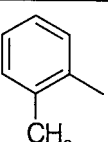
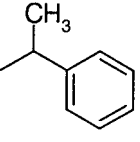
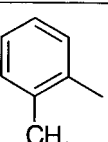
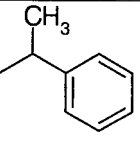
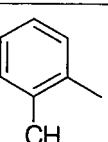
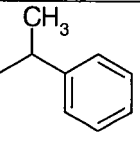
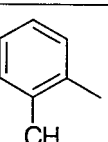
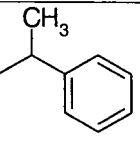
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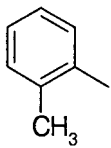
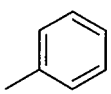
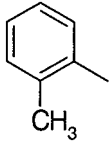
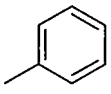
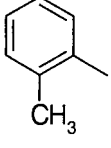
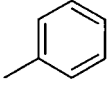
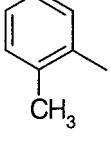
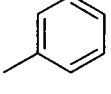
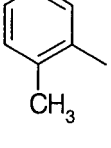
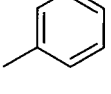
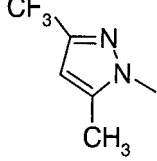
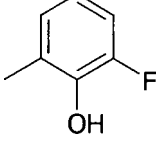
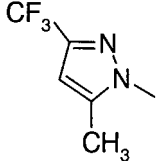
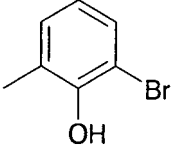
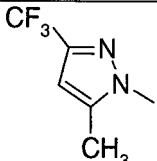
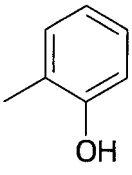
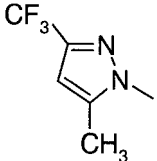
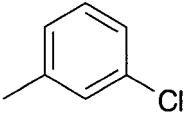
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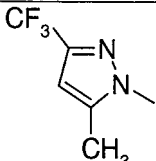
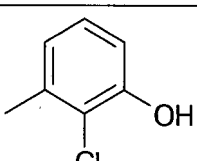
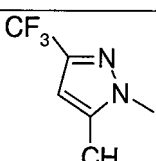
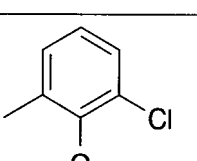
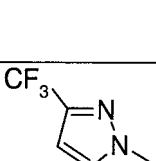
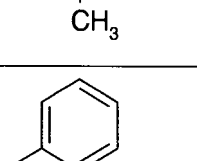
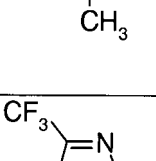
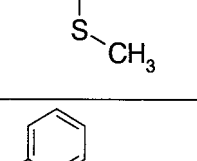
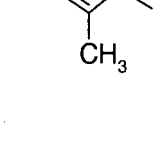
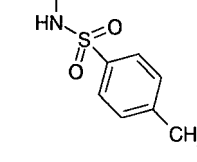
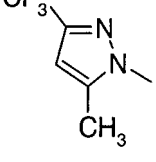
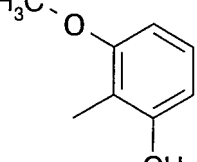
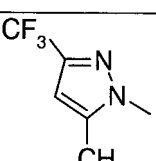
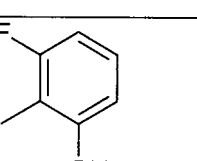
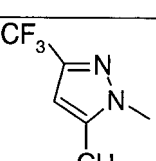
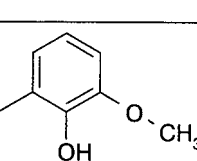
456		-C(=O)-	-C(=O)-	
457		-C(=O)-	-C(=S)-	
458		-C(=O)-	-C(=O)O-	
459		-C(=O)-	-C(=O)NH-	
460		-C(=O)-	-SO ₂ -	
461		-C(=O)-	-C(=O)-	
462		-C(=O)-	-C(=S)-	
463		-C(=O)-	-C(=O)O-	
464		-C(=O)-	-C(=O)NH-	
465		-C(=O)-	-SO ₂ -	

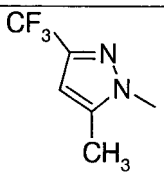
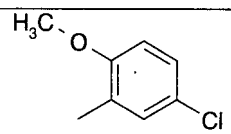
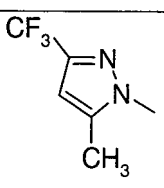
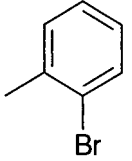
466		-C(=O)-	-C(=O)-	
467		-C(=O)-	-C(=S)-	
468		-C(=O)-	-C(=O)O-	
469		-C(=O)-	-C(=O)NH-	
470		-C(=O)-	-SO ₂ -	
471		-C(=O)-	-C(=O)-	
472		-C(=O)-	-C(=S)-	
473		-C(=O)-	-C(=O)O-	
474		-C(=O)-	-C(=O)NH-	
475		-C(=O)-	-SO ₂ -	

476		-CH ₂ SO ₂ -	-C(=O)-	
477		-CH ₂ SO ₂ -	-C(=S)-	
478		-CH ₂ SO ₂ -	-C(=O)O-	
479		-CH ₂ SO ₂ -	-C(=O)NH-	
480		-CH ₂ SO ₂ -	-SO ₂ -	
481		-CH ₂ SO ₂ -	-C(=O)-	
482		-CH ₂ SO ₂ -	-C(=S)-	
483		-CH ₂ SO ₂ -	-C(=O)O-	
484		-CH ₂ SO ₂ -	-C(=O)NH-	
485		-CH ₂ SO ₂ -	-SO ₂ -	

486		-CH ₂ SO ₂ -	-C(=O)-	
487		-CH ₂ SO ₂ -	-C(=S)-	
488		-CH ₂ SO ₂ -	-C(=O)O-	
489		-CH ₂ SO ₂ -	-C(=O)NH-	
490		-CH ₂ SO ₂ -	-SO ₂ -	
491		-CH ₂ SO ₂ -	-C(=O)-	
492		-CH ₂ SO ₂ -	-C(=S)-	
493		-CH ₂ SO ₂ -	-C(=O)O-	
494		-CH ₂ SO ₂ -	-C(=O)NH-	
495		-CH ₂ SO ₂ -	-SO ₂ -	

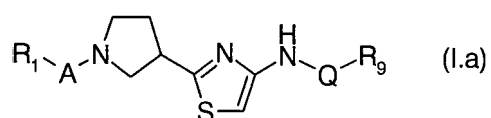
496		-CH ₂ SO ₂ -	-C(=O)-	
497		-CH ₂ SO ₂ -	-C(=S)-	
498		-CH ₂ SO ₂ -	-C(=O)O-	
499		-CH ₂ SO ₂ -	-C(=O)NH-	
500		-CH ₂ SO ₂ -	-SO ₂ -	
501		-CH ₂ C(=O)-	-C(=O)-	
502		-CH ₂ C(=O)-	-C(=O)-	
503		-CH ₂ C(=O)-	-C(=O)-	
504		-CH ₂ C(=O)-	-C(=O)-	

505		-CH ₂ C(=O)-	-C(=O)-	
506		-CH ₂ C(=O)-	-C(=O)-	
507		-CH ₂ C(=O)-	-C(=O)-	
508		-CH ₂ C(=O)-	-C(=O)-	
509		-CH ₂ C(=O)-	-C(=O)-	
510		-CH ₂ C(=O)-	-C(=O)-	
511		-CH ₂ C(=O)-	-C(=O)-	
512		-CH ₂ C(=O)-	-C(=O)-	

513		-CH ₂ C(=O)-	-C(=O)-	
514		-CH ₂ C(=O)-	-C(=O)-	

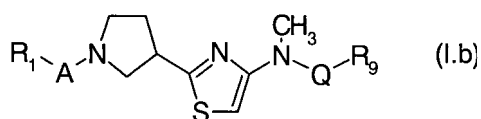
donde

a) 514 compuestos de fórmula (I.a):



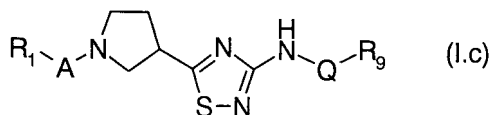
5 en donde A, Q, R¹ y R⁹ son tales como fueron definidos en la Tabla 1.

b) 514 compuestos de fórmula (I.b):



10 en donde A, Q, R¹ y R⁹ son tales como fueron definidos en la Tabla 1.

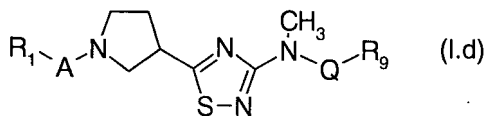
c) 514 compuestos de fórmula (I.c):



en donde A, Q, R¹ y R⁹ son tales como fueron definidos en la Tabla 1.

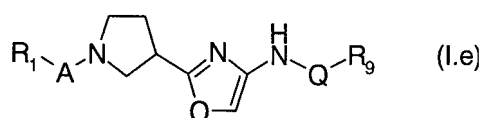
15

d) 514 compuestos de fórmula (I.d):



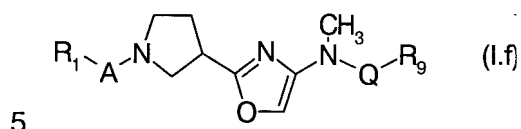
en donde A, Q, R¹ y R⁹ son tales como fueron definidos en la Tabla 1.

20 e) 514 compuestos de fórmula (I.e):



en donde A, Q, R¹ y R⁹ son tales como fueron definidos en la Tabla 1.

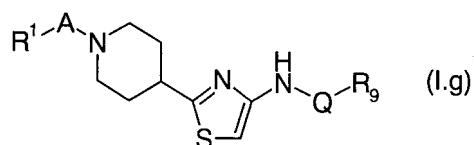
f) 514 compuestos de fórmula (l.f):



5

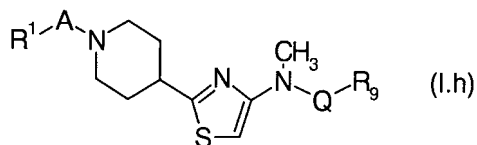
en donde A, Q, R¹ y R⁹ son tales como fueron definidos en la Tabla 1.

g) 514 compuestos de fórmula (l.g):



10 en donde A, Q, R¹ y R⁹ son tales como fueron definidos en la Tabla 1.

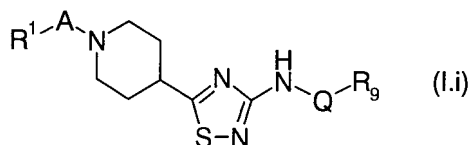
h) 514 compuestos de fórmula (l.h):



en donde A, Q, R¹ y R⁹ son tales como fueron definidos en la Tabla 1.

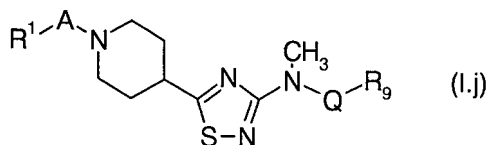
15

i) 514 compuestos de fórmula (l.i):



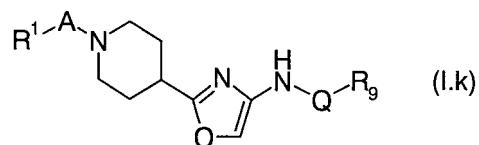
en donde A, Q, R¹ y R⁹ son tales como fueron definidos en la Tabla 1.

20 j) 514 compuestos de fórmula (l.j):



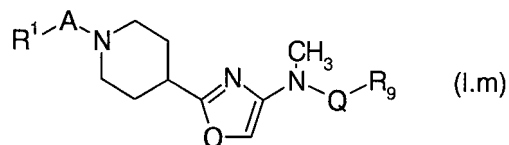
en donde A, Q, R¹ y R⁹ son tales como fueron definidos en la Tabla 1.

k) 514 compuestos de fórmula (l.k):



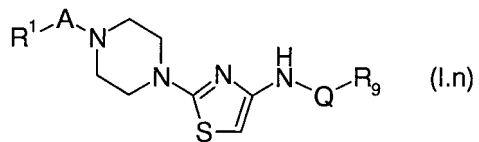
en donde A, Q, R¹ y R⁹ son tales como fueron definidos en la Tabla 1.

5 m) 514 compuestos de fórmula (l.m):



en donde A, Q, R¹ y R⁹ son tales como fueron definidos en la Tabla 1.

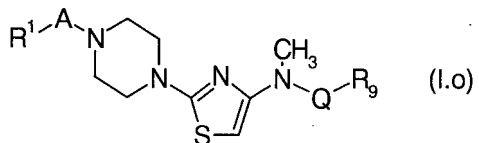
n) 514 compuestos de fórmula (l.n):



10

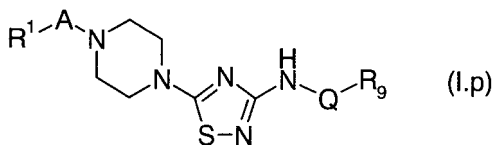
en donde A, Q, R¹ y R⁹ son tales como fueron definidos en la Tabla 1.

o) 514 compuestos de fórmula (l.o):



15 en donde A, Q, R¹ y R⁹ son tales como fueron definidos en la Tabla 1.

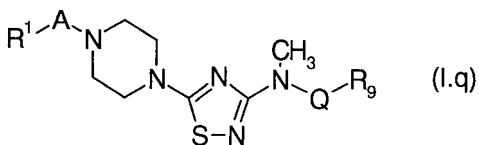
p) 514 compuestos de fórmula (l.p):



en donde A, Q, R¹ y R⁹ son tales como fueron definidos en la Tabla 1.

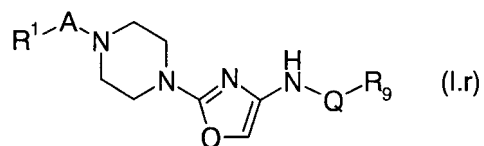
20

q) 514 compuestos de fórmula (l.q):



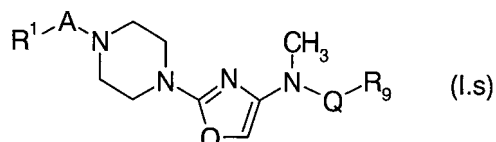
en donde A, Q, R¹ y R⁹ son tales como fueron definidos en la Tabla 1.

r) 514 compuestos de fórmula (l.r):



5 en donde A, Q, R¹ y R⁹ son tales como fueron definidos en la Tabla 1.

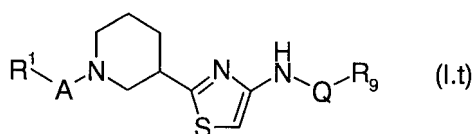
s) 514 compuestos de fórmula (l.s):



en donde A, Q, R¹ y R⁹ son tales como fueron definidos en la Tabla 1.

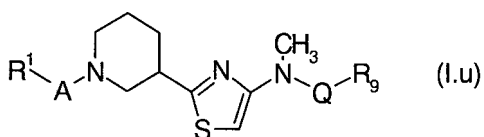
10

t) 514 compuestos de fórmula (l.t):



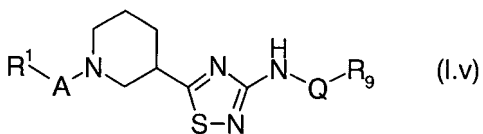
en donde A, Q, R¹ y R⁹ son tales como fueron definidos en la Tabla 1.

15 u) 514 compuestos de fórmula (l.u):



en donde A, Q, R¹ y R⁹ son tales como fueron definidos en la Tabla 1.

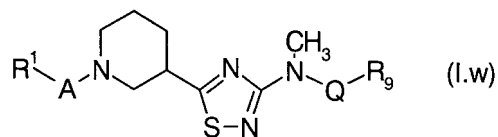
v) 514 compuestos de fórmula (l.v):



20

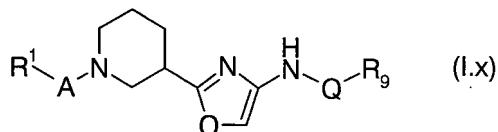
en donde A, Q, R¹ y R⁹ son tales como fueron definidos en la Tabla 1.

w) 514 compuestos de fórmula (I.w):



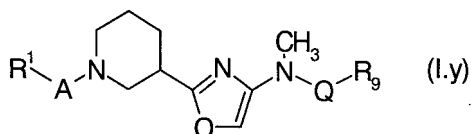
en donde A, Q, R¹ y R⁹ son tales como fueron definidos en la Tabla 1.

5 x) 514 compuestos de fórmula (I.x):



en donde A, Q, R¹ y R⁹ son tales como fueron definidos en la Tabla 1.

y) 514 compuestos de fórmula (I.y):



10

en donde A, Q, R¹ y R⁹ son tales como fueron definidos en la Tabla 1.

A lo largo de esta descripción, las temperaturas se dan en grados Celsius y "p.f." significa punto de fusión. CL/EM significa cromatografía líquida/espectrometría de masas y la descripción del aparato y el método es la siguiente: (HPLC HP 1100 de Agilent,
 15 columna Phenomenex Gemini C18, tamaño de partícula 3 μ m, 110 Angström, 30 x 3 mm, 1.7mL/min., 60 °C, H₂O + HCOOH al 0.05% (95%) / CH₃CN/MeOH 4:1 + HCOOH al 0.04% (5%) – 2 min. – CH₃CN/MeOH 4:1 + HCOOH al 0.04% (5%) – 0.8 min.,
 espectrómetro de masas ZQ de Waters, método de ionización: electroaspersión (ESI), polaridad: iones positivos, capilar (kV) 3.00, cono (V) 30.00, extractor (V) 2.00,
 20 temperatura de la fuente (°C) 100, temperatura de desolvatación (°C) 250, flujo de gas del cono (L/h) 50, flujo de gas de desolvatación (L/h) 400).

La Tabla 2 muestra datos seleccionados de p.f y datos seleccionados de CL/EM para los compuestos de la Tabla 1.

Tabla 2: Datos de punto de fusión y CL/EM para los compuestos de la Tabla 1

Compuesto No.	Punto de fusión (°C)	CL/EM
I.g.001	175	
I.g.006		Tr = 3.27 min. ; EM: m/z = 527 (M+1)
I.g.011	179 - 181	
I.g.013		Tr = 2.02 min. ; EM: m/z = 570 (M+23)
I.g.016		Tr = 1.9 min. ; EM: m/z = 506 (M+1)
I.g.018		Tr = 1.91 min. ; EM: m/z = 522 (M+23)
I.g.021 ¹		Tr = 2.77 min ; EM: m/z = 478 (M+1)
I.g.023	154 - 156	Tr = 1.94 min ; EM: m/z = 508 (M+1)
I.g.024		Tr = 1.85 min ; EM: m/z = 494 (M+1)
I.g.025 ¹		Tr = 2.75 min ; EM: m/z = 514 (M+1)
I.g.136		Tr = 2.01 min ; EM: m/z = 488 (M+1)
I.g.141		Tr = 1.98 min ; EM: m/z = 462 (M+1)
I.g.196		Tr = 2.17 min ; EM: m/z = 490 (M+1)
I.g.211	233-234	
I.g.246	173-175	
I.g.386	174-175	
I.g.501		Tr = 1.88 min ; EM: m/z = 512 (M+1)
I.g.502	193-195	
I.g.503		Tr = 1.85 min ; EM: m/z = 494 (M+1)
I.g.504		Tr = 1.95 min ; EM: m/z = 512 (M+1)
I.g.505		Tr = 1.70 min ; EM: m/z = 528(M+1)
I.g.506		Tr = 1.97 min ; EM: m/z = 542 (M+1)
I.g.507		Tr = 1.85 min ; EM: m/z = 524 (M+1)
I.g.508		Tr = 1.98 min ; EM: m/z = 647 (M+1)
I.g.509		Tr = 2.03 min ; EM: m/z = 524 (M+1)
I.g.510		Tr = 1.94 min ; EM: m/z = 512 (M+1)
I.g.511		Tr = 1.85 min ; EM: m/z = 524 (M+1)
I.g.512		Tr = 1.96 min ; EM: m/z = 530 (M+1)
I.g.513		Tr = 2.03 min ; EM: m/z = 542 (M+1)
I.g.514		Tr = 1.86 min ; EM: m/z = 558 (M+2)

I.h.011		Tr = 1.90 min ; EM: m/z = 546 (M+1)
I.n.011	207-209	
I.n.021		Tr = 1.78 min ; EM: m/z = 479 (M+1)
I.n. 023		Tr = 1.83 min ; EM: m/z = 495 (M+1)
I.n. 024	175-178	

Los compuestos de conformidad con la presente invención pueden ser preparados de conformidad con los esquemas de reacción mencionados anteriormente, en los cuales, a menos de que se indique algo diferente, la definición de cada variable es tal y como se
5 definió anteriormente para un compuesto de fórmula (I).

Ejemplos biológicos

Phytophthora infestans / tomate / disco de hoja, preventivo (tizón tardío del tomate)

- 10 Los discos de hoja de tomate son colocados en agar agua en placas de hoyos múltiples (formato de 24 hoyos) y atomizados con el compuesto de prueba formulado, diluido en agua. Los discos de hoja son inoculados con una suspensión de esporas del hongo, 1 día después de la aplicación. Los discos de hoja inoculados son incubados a 16°C y 75% HR, bajo un régimen de luz de 24 h de oscuridad, seguidas por 12 h luz / 12 h de oscuridad,
15 en una vitrina de clima controlado y la actividad de un compuesto es evaluada como el porcentaje de control de la enfermedad, en comparación con las muestras sin tratar, cuando un nivel apropiado de daño por la enfermedad aparece en los discos de hoja sin tratar (5 – 7 días después de la aplicación).

Los compuestos I.g.001, I.g.006, I.g.011, I.g.013, I.g.016, I.g.018, I.g.021, I.g.023,
20 I.g.024, I.g.136, I.g.386, I.g.501, I.g.503, I.g.506, I.g.508, I.g.509, I.g.510, I.g.511, I.h.011, I.n.011 y I.n.021, a 200 ppm, dan al menos un 80% de control de la enfermedad en esta prueba, cuando son comparados con los discos de hoja de control, sin tratar, bajo las mismas condiciones, los cuales muestran un desarrollo muy significativo de la enfermedad.

25

Phytophthora infestans / papa o patata / preventivo (tizón tardío de la papa o patata)

- Las plantas de papa o patata (variedad Bintje) de 2 semanas son rociadas en una cámara de rociado con el compuesto de prueba formulado, diluido en agua. Las plantas de prueba son inoculadas al rociarlas con una suspensión de los esporangios, 2 días después de la
30 aplicación. Las plantas de prueba inoculadas son incubadas a 18° C con 14h de luz/día y

100 % HR en una cámara de crecimiento y el porcentaje del área de la hoja cubierto por la enfermedad es evaluado cuando un nivel apropiado de la enfermedad aparece en las plantas de control, sin tratar (5 – 7 días después de la aplicación).

Los compuestos I.g.001, I.g.006, I.g.011, I.g.016, I.g.023, I.g.024, I.g.136, I.g.501, 5 I.g.502 y I.g.511, a 200 ppm, dan al menos un 80% de control de la enfermedad en esta prueba, cuando son comparados con los discos de hoja de control, sin tratar, bajo las mismas condiciones, los cuales muestran un desarrollo muy significativo de la enfermedad.

10 *Phytophthora infestans* / papa o patata/ duración prolongada (tizón tardío de la papa o patata)

Las plantas de papa o patata (variedad Bintje) de 2 semanas son rociadas en una cámara de rociado con el compuesto de prueba formulado, diluido en agua. Las plantas de prueba son inoculadas al rociarlas con una suspensión de los esporangios, 6 días después de la 15 aplicación. Las plantas de prueba inoculadas son incubadas a 18° C con 14h de luz/día y 100 % HR en una cámara de crecimiento y el porcentaje del área de la hoja cubierto por la enfermedad es evaluado cuando un nivel apropiado de la enfermedad aparece en las plantas de control, sin tratar (9 – 11 días después de la aplicación).

Los compuestos I.g.001, I.g.006, I.g.011, I.g.016, I.g.023, I.g.024, I.g.501 y I.g.502, 20 a 200 ppm, dan al menos un 80% de control de la enfermedad en esta prueba, cuando son comparados con los discos de hoja de control, sin tratar, bajo las mismas condiciones, los cuales muestran un desarrollo muy significativo de la enfermedad.

Phytophthora infestans / papa o patata / curativo (tizón tardío de la papa o patata)

25 Las plantas de papa o patata (variedad Bintje) de 2 semanas, son inoculadas al rociarlas con una suspensión de esporangios un día antes de la aplicación. Las plantas inoculadas son rociadas en una cámara de rociado con el compuesto de prueba formulado, diluido en agua. Las plantas de prueba inoculadas son incubadas a 18° C con 14h de luz/día y 100 % HR en una cámara de crecimiento y el porcentaje del área de la hoja cubierto por la 30 enfermedad es evaluado cuando un nivel apropiado de la enfermedad aparece en las plantas de control, sin tratar (3 – 4 días después de la aplicación).

Los compuestos I.g.001, I.g.011 y I.g.023, a 200 ppm, dan al menos un 80% de control de la enfermedad en esta prueba, cuando son comparados con los discos de hoja de control, sin tratar, bajo las mismas condiciones, los cuales muestran un desarrollo muy 35 significativo de la enfermedad.

Plasmopara viticola / uva / disco de hoja, preventivo (moho o mildiú de la uva)

Los discos de hoja de vid son colocados en agar agua en placas de hoyos múltiples (formato de 24 hoyos) y atomizados con el compuesto de prueba formulado, diluido en agua. Los discos de hoja son inoculados con una suspensión de esporas del hongo, 1 día
5 después de la aplicación. Los discos de hoja inoculados son incubados a 9°C y 80% HR bajo un régimen de luz de 12 h luz / 12 h de oscuridad, en una vitrina de clima controlado y la actividad de un compuesto es evaluada como el porcentaje de control de la enfermedad, en comparación con las muestras sin tratar, cuando un nivel apropiado de daño por la enfermedad aparece en los discos de hoja de control, sin tratar (6 – 8 días
10 después de la aplicación).

Los compuestos l.g.001, l.g.011, l.g.013, l.g.016, l.g.018, l.g.021, l.g.023, l.g.024, l.g.246 l.g.386, l.g.501, l.g.503, l.g.506, l.g.508, l.g.509, l.g.510, l.n.011 y l.n.021, a 200 ppm, dan al menos un 80% de control de la enfermedad en esta prueba, cuando son comparados con los discos de hoja de control, sin tratar, bajo las mismas condiciones, los
15 cuales muestran un desarrollo muy significativo de la enfermedad.

Plasmopara viticola / uva / preventivo (moho o mildiú de la uva)

Las plántulas de 5 semanas de vid (variedad Gutedel) son rociadas en una cámara de rociado con el compuesto de prueba formulado, diluido en agua. Las plantas de prueba
20 son inoculadas al rociarles una suspensión de esporangios en la superficie inferior de las hojas, un día después de la aplicación. Las plantas de prueba inoculadas son incubadas a 22° C y 100% HR en un invernadero y el porcentaje del área de la hoja cubierto por la enfermedad es evaluado cuando un nivel apropiado de la enfermedad aparece en las plantas de control, sin tratar (6 – 8 días después de la aplicación).

25 Los compuestos l.g.001, l.g.006, l.g.011, l.g.016, l.g.023 y l.g.024, l.g.501, l.g.502 y l.g.503, a 200 ppm, dan al menos un 80% de control de la enfermedad en esta prueba, cuando son comparados con los discos de hoja de control, sin tratar, bajo las mismas condiciones, los cuales muestran un desarrollo muy significativo de la enfermedad.

30 Plasmopara viticola / uva / duración prolongada (moho o mildiú de la uva)

Las plántulas de 5 semanas de vid (variedad Gutedel) son rociadas en una cámara de rociado con el compuesto de prueba formulado, diluido en agua. Las plantas de prueba son inoculadas al rociarles una suspensión de esporangios en la superficie inferior de las hojas, 6 días después de la aplicación. Las plantas de prueba inoculadas son incubadas a
35 22° C y 100% HR en un invernadero y el porcentaje del área de la hoja cubierto por la

enfermedad es evaluado cuando un nivel apropiado de la enfermedad aparece en las plantas de control, sin tratar (11 – 13 días después de la aplicación).

Los compuestos l.g.001, l.g.006, l.g.011, l.g.023 y l.g.024, l.g.501 y l.g.502, a 200 ppm, dan al menos un 80% de control de la enfermedad en esta prueba, cuando son comparados con los discos de hoja de control, sin tratar, bajo las mismas condiciones, los cuales muestran un desarrollo muy significativo de la enfermedad.

Plasmopara viticola / uva / curativo (moho o mildiú de la uva)

Las plántulas de 5 semanas de vid (variedad Gutedel) son inoculadas al rociarles una suspensión de esporangios en la superficie inferior de las hojas, un día antes de la aplicación. Las plantas de vid inoculadas son rociadas en una cámara de rociado con el compuesto de prueba formulado, diluido en agua. Las plantas de prueba inoculadas son incubadas a 22° C y 100% HR en un invernadero y el porcentaje del área de la hoja cubierto por la enfermedad es evaluado cuando un nivel apropiado de la enfermedad aparece en las plantas de control, sin tratar (4 – 6 días después de la aplicación).

Los compuestos l.g.001, l.g.006, l.g.011 y l.g.023, a 200 ppm, dan al menos un 80% de control de la enfermedad en esta prueba, cuando son comparados con los discos de hoja de control, sin tratar, bajo las mismas condiciones, los cuales muestran un desarrollo muy significativo de la enfermedad.

Pythium ultimum / cultivo líquido (marchitamiento de plántulas)

Los fragmentos de micelio y oosporas de un cultivo líquido recién preparado del hongo son mezclados directamente con caldo nutritivo (caldo papa-dextrosa, CPD). Después de colocar una disolución (DMSO) del compuesto de prueba en una placa de microtítulo (formato de 96 hoyos), se añade el caldo nutritivo que contiene la mezcla de micelio/esporas fúngicos. Las placas de prueba son incubadas a 24°C y la inhibición del crecimiento es determinada fotométricamente, 2-3 días después de la aplicación.

Los compuestos l.g.006, l.g.501, l.g.502, l.g.503 y l.g.511, a 200 ppm, dan al menos un 80% de control de la enfermedad en esta prueba, cuando son comparados con los discos de hoja de control, sin tratar, bajo las mismas condiciones, los cuales muestran un desarrollo muy significativo de la enfermedad.

Pythium ultimum / algodón / impregnación del suelo (marchitamiento de plántulas)

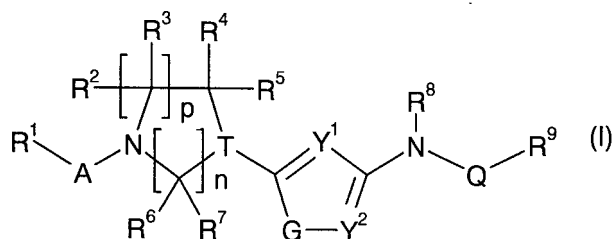
La prueba es realizada en recipientes de plástico (650 mL de volumen) utilizando una mezcla de (50% de vermiculita + 50% tierra Cugy estéril) + 10% v/v de agua. En cada recipiente, se siembran 10 semillas (algodón, variedad Sure Grow 747), en 2 filas de 5

semillas (3 repeticiones para la evaluación de la actividad, 3 repeticiones para la evaluación de la fitotoxicidad). La aplicación se realiza directamente después de la siembra al verter 10 mL del compuesto diluido en agua por fila, sobre las semillas. Inmediatamente después de que las semillas son cubiertas con una capa delgada de la
5 misma tierra y la inoculación está sucediendo. El *Pythium ultimum* es cultivado por 14 días en rebanadas de zanahoria, en botellas de Roux. Para la inoculación, el contenido de las botellas de Roux es mezclado y aplicado homogéneamente sobre los recipientes de plástico, sin filtración adicional (70ml de suspensión por recipiente). Condiciones de incubación: 20°C, periodos de 12h/12h día/noche, en el invernadero. La actividad de un
10 compuesto es evaluada como el porcentaje de control de la enfermedad, con respecto a las plantas de control, sin tratar cuando un nivel apropiado de daño por la enfermedad aparece en las plantas de control, sin tratar (13 – 16 días después de la aplicación).

Los compuestos I.g.006, I.g.501, I.g.502 y I.g.511, a 200 ppm, dan al menos un 80% de control de la enfermedad en esta prueba, cuando son comparados con los discos de
15 hoja de control, sin tratar, bajo las mismas condiciones, los cuales muestran un desarrollo muy significativo de la enfermedad.

REIVINDICACIONES

1. Un compuesto de fórmula I:



5

en donde

A es $x-C(=O)-$, $x-C(=S)-$, $x-C(R^{10}R^{11})-C(=O)-$, $x-C(R^{12}R^{13})-C(=S)-$, $x-O-C(=O)-$, $x-O-C(=S)-$, $x-N(R^{14})-C(=O)-$, $x-N(R^{15})-C(=S)-$, $x-C(R^{16}R^{17})-SO_2-$ o $x-N=C(R^{26})-$, en cada caso x representa el enlace que está conectado a R^1 ;

10 T es CR^{18} o N;

G es O o S;

Y^1 y Y^2 son independientemente CR^{19} o N;

Q es $-C(=O)-z$, $-C(=S)-z$, $-C(=O)-O-z$, $-C(=S)-O-z$, $-C(=O)-N(R^{20})-z$, $-C(=S)-N(R^{21})-z$ o $-SO_2-z$, en cada caso z representa el enlace que está conectado a R^9 ;

15 n es 1 o 2;

p es 1 o 2, con la condición de que cuando n es 2, p es 1;

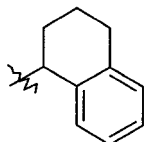
R^1 es fenilo, piridilo, imidazolilo, o pirazolilo; en donde cada uno de los fenilo, piridilo, imidazolilo y pirazolilo están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre alquilo C_1-C_4 , haloalquilo C_1-C_4 , halógeno, ciano,

20 hidroxilo y amino;

R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^{10} , R^{11} , R^{12} , R^{13} , R^{16} , R^{17} , R^{18} , R^{19} y R^{26} son, cada uno independientemente, hidrógeno, halógeno, ciano, C_1-C_4 alquilo o C_1-C_4 haloalquilo;

R^8 , R^{14} , R^{15} , R^{20} y R^{21} son, cada uno independientemente, hidrógeno, alquilo C_1-C_4 o alcoxi C_1-C_4 ; y

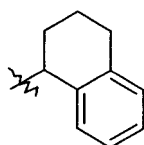
25 R^9 es fenilo, bencilo o el grupo (a):



(a)

en donde cada uno de fenilo, bencilo y el grupo (a) están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre alquilo C_1-C_4 , haloalquilo

- C₁-C₄, alcoxi C₁-C₄, haloalcoxi C₁-C₄, halógeno, ciano, hidroxilo, N(R²⁷)₂, SH, alquiltio C₁-C₄, nitro, fenilsulfonilo y fenilsulfinilo, en donde el fenilsulfonilo y el fenilsulfinilo están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre alquilo C₁-C₄, haloalquilo C₁-C₄, alcoxi C₁-C₄, haloalcoxi C₁-C₄, halógeno y ciano;
- 5 cada R²⁷ es independientemente hidrógeno, alquilo C₁-C₄, fenilsulfonilo o fenilsulfinilo, en donde el fenilsulfonilo y el fenilsulfinilo están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre alquilo C₁-C₄, haloalquilo C₁-C₄, alcoxi C₁-C₄, haloalcoxi C₁-C₄, halógeno y ciano;
- o una sal o un N-óxido del mismo.
- 10
2. El compuesto de conformidad con la reivindicación 1, en donde
A es x-C(=O)-, x-C(=S)-, x-C(R¹⁰R¹¹)-C(=O)-, x-C(R¹²R¹³)-C(=S)-, x-O-C(=O)-, x-O-C(=S)-, x-N(R¹⁴)-C(=O)-, x-N(R¹⁵)-C(=S)- o x-C(R¹⁶R¹⁷)-SO₂-, en cada caso x representa el enlace que está conectado a R¹;
- 15 T es CR¹⁸ o N;
- G es O o S;
- Y¹ y Y² son independientemente CR¹⁹ o N;
- Q es -C(=O)-z, -C(=S)-z, -C(=O)-O-z, -C(=S)-O-z, -C(=O)-N(R²⁰)-z, -C(=S)-N(R²¹)-z o -SO₂-z-, en cada caso z representa el enlace que está conectado a R⁹;
- 20 n es 1 o 2;
- p es 1 o 2, con la condición de que cuando n es 2, p es 1;
- R¹ es fenilo, piridilo, imidazolilo o pirazolilo; en donde cada uno de los fenilo, piridilo, imidazolilo y pirazolilo están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre alquilo C₁-C₄, haloalquilo C₁-C₄, halógeno, ciano,
- 25 hidroxilo y amino;
- R², R³, R⁴, R⁵, R⁶, R⁷, R¹⁰, R¹¹, R¹², R¹³, R¹⁶, R¹⁷, R¹⁸ y R¹⁹ son, cada uno independientemente, hidrógeno, halógeno, ciano, alquilo C₁-C₄ o haloalquilo C₁-C₄;
- R⁸, R¹⁴, R¹⁵, R²⁰, y R²¹ son, cada uno independientemente, hidrógeno o alquilo C₁-C₄; y
- R⁹ es fenilo, bencilo o el grupo (a):



30

(a)

en donde cada uno de fenilo, bencilo y el grupo (a) están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre alquilo C₁-C₄, haloalquilo C₁-C₄, halógeno, ciano, hidroxí y amino.

5 3. El compuesto de conformidad con la reivindicación 1, en donde

A es x-C(=O)-, x-C(=S)-, x-C(R¹⁰R¹¹)-C(=O)-, x-C(R¹²R¹³)-C(=S)-, x-O-C(=O)-, x-O-C(=S)- o x-C(R¹⁶R¹⁷)-SO₂-, en cada caso x representa el enlace que está conectado a R¹;

T es CR¹⁸ o N;

G es O o S;

10 Y¹ es N;

Y² es CR¹⁹ o N;

Q es -C(=O)-z, -C(=S)-z, -C(=O)-O-z, -C(=S)-O-z, -C(=O)-N(R²⁰)-z, -C(=S)-N(R²¹)-z o -SO₂-z-, en cada caso z representa el enlace que está conectado a R⁹;

n es 1 o 2;

15 p es 1;

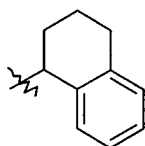
R¹ es fenilo o pirazolilo; en donde cada uno de los fenilo y pirazolilo están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre alquilo C₁-C₄, haloalquilo C₁-C₄, halógeno, ciano, hidroxí, y amino;

R², R³, R⁴, R⁵, R⁶, R⁷, R¹⁰, R¹¹, R¹², R¹³, R¹⁶, R¹⁷, R¹⁸ y R¹⁹ son, cada uno

20 independientemente, hidrógeno, halógeno, alquilo C₁-C₄ o haloalquilo C₁-C₄;

R⁸, R²⁰ y R²¹ son, cada uno independientemente, hidrógeno o alquilo C₁-C₄; y

R⁹ es fenilo, bencilo o el grupo (a):



(a)

25 en donde cada uno de fenilo, bencilo y el grupo (a) están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre alquilo C₁-C₄, haloalquilo C₁-C₄, halógeno, ciano, hidroxí y amino.

4. El compuesto de conformidad con la reivindicación 1, en donde

30 A es x-C(=O)-, -x-CR¹⁰R¹¹-C(=O)-, x-O-C(=O)- o x-C(R¹⁶R¹⁷)-SO₂-, en cada caso x representa el enlace que está conectado a R¹;

T es CR¹⁸ o N;

G es S;

Y^1 es N;

Y^2 es CR^{19} o N;

Q es $-C(=O)-z$, $-C(=O)-O-z$, $-C(=O)-N(R^{20})-z$ o $-SO_2-z$, en cada caso z es el enlace con R^9 ;

5 n es 1 o 2;

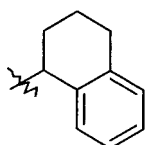
p es 1;

R^1 es fenilo o pirazolilo, en donde cada uno de los fenilo y pirazolilo están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre alquilo C_1-C_4 , haloalquilo C_1-C_4 y halógeno;

10 R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^{10} , R^{11} , R^{16} , R^{17} , R^{18} , y R^{19} son, cada uno independientemente, hidrógeno, fluoro o metilo;

R^8 y R^{20} son, cada uno independientemente, hidrógeno o metilo; y

R^9 es fenilo, bencilo o el grupo (a):



15 (a)

en donde cada uno de fenilo, bencilo y el grupo (a) están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre alquilo C_1-C_4 , haloalquilo C_1-C_4 , hidroxilo y halógeno.

20 5. El compuesto de conformidad con la reivindicación 1, en donde

A es $x-C(=O)-$, $x-CH_2-C(=O)-$, $x-O-C(=O)-$ o $x-CH_2-SO_2-$, en cada caso x representa el enlace que está conectado a R^1 ;

T es CH o N;

G es S;

25 Y^1 es N;

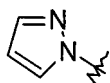
Y^2 es CH o N;

Q es $-C(=O)-z$, $-C(=O)-O-z$, $-C(=O)-NH-z$ o $-SO_2-z$, en cada caso z representa el enlace que está conectado a R^9 ;

n es 1 o 2;

30 p es 1;

R^1 es fenilo o el grupo (b):



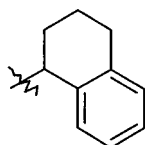
(b)

en donde el fenilo y el grupo (b) están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre halógeno, alquilo C₁-C₄ y haloalquilo C₁-C₄;

5 R², R³, R⁴, R⁵, R⁶ y R⁷ son, cada uno, hidrógeno;

R⁸ es hidrógeno; y

R⁹ es fenilo, bencilo o el grupo (a):



(a)

10 en donde cada uno de fenilo, bencilo y el grupo (a) están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre C₁-C₄ alquilo, C₁-C₄ haloalquilo, hidroxi y halógeno.

6. El compuesto de conformidad con la reivindicación 1, en donde

15 A es x-CH₂-C(=O)- en donde x representa el enlace que está conectado a R¹;

T es CH;

G es S;

Y¹ es N;

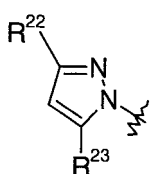
Y² es CH;

20 Q es -C(=O)-z, -C(=O)-O-z o C(=O)-N(R²⁰)-z, en cada caso z representa el enlace que está conectado a R⁹;

n es 2;

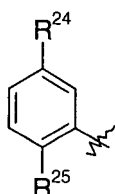
p es 1;

R¹ es escogido entre los grupos (c) o (d):



25

(c)



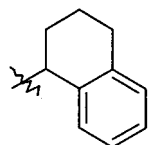
(d)

en donde R²², R²³, R²⁴ y R²⁵ son escogidos independientemente entre hidrógeno, halógeno, metilo y halometilo;

R₂, R₃, R₄, R₅, R₆, y R₇ son, cada uno, hidrógeno;

30 R₈, es hidrógeno;

R^9 es fenilo, bencilo o el grupo (a):



(a)

en donde el fenilo, bencilo y el grupo(a) están sustituidos opcionalmente con entre 1 y 3
5 sustituyentes escogidos independientemente entre halógeno, hidroxilo, metilo y halometilo.

7. El compuesto de conformidad con cualesquiera de las reivindicaciones 1 a 6, en
donde G es S, Y^1 es N y Y^2 es CH.

10 8. El compuesto de conformidad con cualesquiera de las reivindicaciones 1 a 7, en
donde p es 1 y n es 2.

9. El compuesto de conformidad con cualesquiera de las reivindicaciones 1 a 8, en
donde R^2 , R^3 , R^4 , R^5 , R^6 y R^7 son H

15

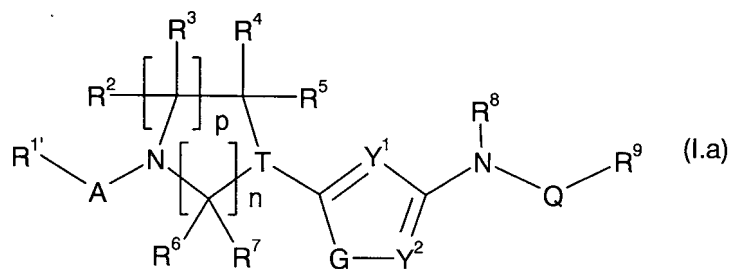
10. El compuesto de conformidad con cualesquiera de las reivindicaciones 1 a 9, en
donde Q es $-C(=O)-z$, en donde z representa el enlace que está conectado a R^9 .

11. El compuesto de conformidad con cualesquiera de las reivindicaciones 1 a 10, en
20 donde R^9 es fenilo sustituido con hidroxilo y sustituido opcionalmente con uno o dos
sustituyentes adicionales.

12. El compuesto de conformidad con la reivindicación 11, en donde el hidroxilo está en
la posición orto.

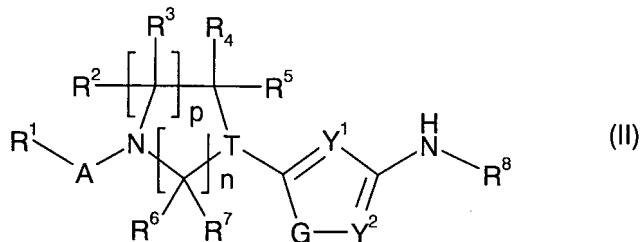
25

13 Un compuesto de fórmula I.a:



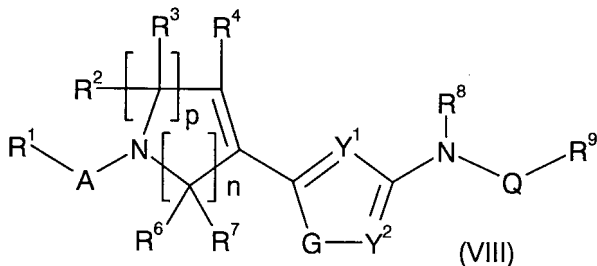
en la cual R^1 es alquilo C_1-C_8 y A, T, G, Y^1 , Y^2 , Q, n, p, R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 y R^9 tienen las definiciones tales como las definidas para fórmula I en cualesquiera de las reivindicaciones 1 a 12;

5 o un compuesto de fórmula II:



en donde R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , A, T, G, Y^1 , Y^2 , n y p son tales como los definidos para la fórmula I en cualesquiera de las reivindicaciones 1 a 12;

10 o un compuesto de fórmula VIII:



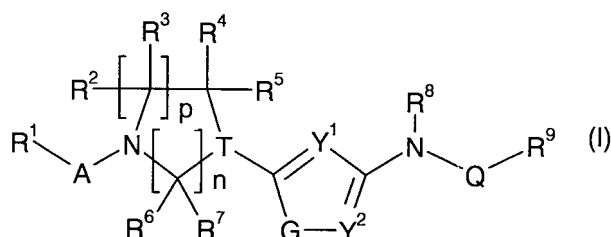
en donde R^1 , R^2 , R^3 , R^4 , R^6 , R^7 , R^8 , A, T, G, Y^1 , Y^2 , p y n son tales como los definidos para la fórmula I en cualesquiera de las reivindicaciones 1 a 12.

15 14. Una composición fungicida que comprende al menos un compuesto tal y como los definidos en cualesquiera de las reivindicaciones 1 a 12 y un vehículo aceptable para ser utilizado en agricultura, la cual comprende opcionalmente un adyuvante y comprende opcionalmente al menos un compuesto adicional con actividad fungicida.

20 15. Un método para controlar o evitar una infestación de plantas, material de propagación de las mismas, cultivos cosechados o materiales no vivientes, por parte de microorganismos fitopatógenos o causantes de deterioro o de organismos potencialmente dañinos para el hombre, el cual incluye la aplicación de un compuesto tal y como los definidos en cualesquiera de las reivindicaciones 1 a 12, a la planta, a partes de las
25 plantas o al locus de las mismas, al material de propagación de las mismas o a cualquier parte de los materiales no vivientes; en donde los microorganismos fitopatógenos son preferiblemente organismos fúngicos.

RESUMEN

La presente invención trata acerca de compuestos heterocíclicos de fórmula (I) los cuales tienen actividad microbici da, en particular actividad fungici da, así como acerca de 5 métodos de utilización de los compuestos de fórmula (I) para controlar microbios.



en donde

A es $x\text{-C(=O)-}$, $x\text{-C(=S)-}$, $x\text{-C(R}^{10}\text{R}^{11}\text{)-C(=O)-}$, $x\text{-C(R}^{12}\text{R}^{13}\text{)-C(=S)-}$, $x\text{-O-C(=O)-}$, $x\text{-O-C(=S)-}$, $x\text{-N(R}^{14}\text{)-C(=O)-}$, $x\text{-N(R}^{15}\text{)-C(=S)-}$, $x\text{-C(R}^{16}\text{R}^{17}\text{)-SO}_2\text{-}$ o $x\text{-N=C(R}^{26}\text{)-}$, en cada caso x

10 representa el enlace que está conectado a R^1 ;

T es CR¹⁸ o N:

Ges O o S:

Y^1 y Y^2 son independientemente CR^{19} o N :

Q es -C(=O)-z, -C(=S)-z, -C(=O)-O-z, -C(=S)-O-z, -C(=O)-N(R²⁰)-z, -C(=S)-N(R²¹)-z o -

15 SO₂-z-, en cada caso z representa el enlace que está conectado a R⁹;

nes 1 o 2:

p es 1 o 2, con la condición de que cuando n es 2, p es 1;

R¹ es fenilo, piridilo, imidazolilo, o pirazolilo; en donde cada uno de los fenilo, piridilo, imidazolilo y pirazolilo están sustituidos opcionalmente con entre 1 y 3 sustituyentes

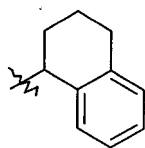
20 escogidos independientemente entre alquilo C₁-C₄, haloalquilo C₁-C₄, halógeno, ciano, hidroxí y amino;

R², R³, R⁴, R⁵, R⁶, R⁷, R¹⁰, R¹¹, R¹², R¹³, R¹⁶, R¹⁷, R¹⁸, R¹⁹ y R²⁶ son, cada uno independientemente, hidrógeno, halógeno, ciano, alquilo C₁-C₄ o haloalquilo C₁-C₄;

R⁸, R¹⁴, R¹⁵, R²⁰ y R²¹ son, cada uno independientemente, hidrógeno, alquilo C₁-C₄ o

25 alcoxî C₁-C₄; y

R⁹ es fenilo, bencilo o el grupo (a):



(a)

en donde cada uno de fenilo, bencilo y el grupo (a) están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre alquilo C₁-C₄, haloalquilo C₁-C₄, alcoxi C₁-C₄, haloalcoxi C₁-C₄, halógeno, ciano, hidroxilo, N(R²⁷)₂, SH, alquiltio C₁-C₄, nitro, fenilsulfonilo y fenilsulfinilo, en donde el fenilsulfonilo y el fenilsulfinilo están
5 sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre alquilo C₁-C₄, haloalquilo C₁-C₄, alcoxi C₁-C₄, haloalcoxi C₁-C₄, halógeno y ciano; cada R²⁷ es independientemente hidrógeno, alquilo C₁-C₄, fenilsulfonilo o fenilsulfinilo, en donde el fenilsulfonilo y el fenilsulfinilo están sustituidos opcionalmente con entre 1 y 3 sustituyentes escogidos independientemente entre alquilo C₁-C₄, haloalquilo C₁-C₄, alcoxi
10 C₁-C₄, haloalcoxi C₁-C₄, halógeno y ciano; o una sal o un N-óxido de los mismos.

 Industria y Comercio SUPERINTENDENCIA		SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO DIVISION DE NUEVAS CREACIONES TARJETA ARCHIVO PROPIETARIOS				
		PATENTE DE INVENCION ____ PCT <u>X</u> MODELO DE UTILIDAD ____ DISEÑO INDUSTRIAL ____				
(21) N° de solicitud:		(22) Fecha de solicitud:				
(51) Clasificación Internacional :						
(71) Solicitante(s) SYNGENTA PARTICIPATIONS AG						
(72) Inventor(es) SARA SULZER-MOSSE, CLEMENS LAMBERTH, MATHIAS STEPHAN RESPONDEK, LAURA QUARANTA						
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(30) Prioridad	(31)	No. Prioridad	32)	Fecha	(33)	País
		09167736.9		12/08/2009		EP
(85) Fecha inicio fase nacional:					(87) Publicación internacional	
(86) Datos relativos a la presentación de la solicitud PCT					Fecha: 17/02/2011	
Fecha de presentación de la solicitud: 05/08/2010					Nº publicación: WO 2011/018401 A1	
No. de solicitud PCT/EP2010/061381						
(54) Título: HETEROCICLOS MICROBICIDAS						



No. 12-022024- -00000-0000

Fecha: 2012-02-08 15:51:36 Dep. 2020 DIR.NUEVASCR
Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI
Act. 411 PRESENTACION Folios: 245



LISTA DE CHEQUEO
ADMISION A TRAMITE - NUEVAS CREACIONES

PATENTE DE INVENCION ☐ MODELO DE UTILIDAD ☐ Art. 33 Decisión 486/00

- ☐ Indicación que se solicita una patente
- ☐ Datos de identificación del solicitante o de la persona que presenta la solicitud
- ☐ Descripción de la invención
- ☐ Dibujos de ser estos pertinentes
- ☐ Comprobante de pago de las tasas establecidas (de ser el caso formato de descuento)
- Completa ☐ Incompleta ☐

PATENTE DE INVENCION PCT ☒ MODELO DE UTILIDAD PCT ☐ Art. 33 Decisión 486/00
Circular Única

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- ☐ Indicación que se solicita un esquema de trazado
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- ☐ Representación gráfica de un esquema de trazado
- ☐ Comprobante de pago de las tasas establecidas
- Completa ☐ Incompleta ☐