

No. 05-112548-00003-0000

Fecha: 2007-05-24 16:45:48 Dep. 2020 NUECREACIONE
Tra. 11 PATENTE Y II Eve: 379 FASE NACIONAL II
Act. 538 PETICION Folios: 4

SEÑORES

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

DIVISIÓN DE NUEVAS CREACIONES

E. _____ S. _____ D. _____

Ref.: Expediente N° 05-112.548

Solicitud de Patente de Invención Titulada: "DERIVADOS DE AMINA CÍCLICA, PROCESOS PARA SU PREPARACIÓN, Y COMPOSICIONES FARMACÉUTICAS QUE CONTIENEN LOS MISMOS"

Solicitante: GLAXO GROUP LIMITED

SOLICITUD DE EXAMEN DE PATENTABILIDAD SEGÚN
EL ARTÍCULO 44 DE LA DECISION 486, GACETA No. 571

J. IAN RAISBECK, mayor de edad y vecino de Bogotá, D.C., identificado tal como aparece al pie de mi firma, en mi condición de apoderado sustituto tal como consta en la sustitución adjunta, respetuosamente me permito solicitar que se examine si la invención reúne los requisitos de patentabilidad previstos en la misma, dando cumplimiento a lo establecido en el artículo 44 de la Decisión 486 de la comisión de la Comunidad Andina de Naciones. Adjunto recibo por el monto de \$404.000 pesos para cubrir la tasa correspondiente, según la Resolución 36155 de 28 de diciembre 2006.

Atentamente,

J. IAN RAISBECK
C.C. 79.376.996 de Bogotá
T.P. 135.799

Anexo: Sustitución
Recibo por \$404.000 pesos

Synthe Zohy Comma

J. Jim Busbeck

75276556DN 757554

Jim Kunkel

22 MAY 2007

COLOMBIA

ROJAS DE URUETA

293

OLARTE RAISBECK

OLARTE RAISBECK & FRIERI LTDA.

Señores

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

DIVISION DE NUEVAS CREACIONES

E. _____ S. _____ D. _____

Ref.:

Expediente N° 05-112.548

**Solicitud de Patente de Invención Titulada: "DERIVADOS DE AMINA
CÍCLICA, PROCESOS PARA SU PREPARACIÓN, Y COMPOSICIONES
FARMACÉUTICAS QUE CONTIENEN LOS MISMOS"**

Solicitante: GLAXO GROUP LIMITED

SUSTITUCIÓN DE PODER

CARLOS R. OLARTE, mayor de edad y vecino de Bogotá D.C., identificado como aparece al pie de mi firma, en mi carácter de apoderado de la sociedad de la referencia, respetuosamente me permito manifestar que **SUSTITUYO** el poder a mi conferido por la mencionada sociedad, en el doctor J. IAN RAISBECK LLINAS, mayor de edad, domiciliado en Bogotá D.C., identificado con la Cédula de Ciudadanía No. 79.376.996 de Bogotá y portador de la Tarjeta Profesional No. 135.799 del Consejo Superior de la Judicatura, para que sea él quien en adelante asuma el trámite de la presente acción.

El apoderado sustituto conserva las mismas facultades del principal.

Atentamente,



CARLOS R. OLARTE

C.C. No. 79.782.747 de Bogotá

T.P. 74.295 del C. S. de la J.

Industria y Comercio

Carlos Ochoa

79782 777 36 de 742950



2 MAY 2017



274
8

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 05-112548- -00003-0000

Fecha: 2007-05-24 16:45:48 Dep. 2020 NUECREACIONE
Tra. 11 PATENTEIYII Eve: 379 FASENACIONALI
Act. 538 PETICION Folios: 4

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

NIT : 800176088-2

RECIBO OFICIAL DE CAJA : 07 - 35,779
FECHA : MAYO 8 DE 2007

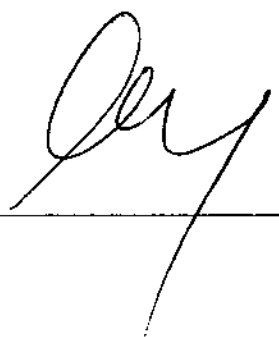
***** CONSIGNACION *****

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PGO	Vr. PAGO
OLARTE RAISBECK	CONSIGNACION	BANCO POPULAR	050-00110-5	52331050	08/05/2007	8,555,000.00

***** CONCEPTO *****

CANT.	RENTISTICO	CONCEPTO	TOTAL CONCEPTO
1	50005-01-01	SOLICITUDES	
		114 PTO CAP-11 EXAMEN DE PATENTIBILID	202,000.00
		TOTAL :	202,000.00

SON: OCHOCIENTOS DOS MIL PESOS

RESPONSABLE : 

RECIBO DE CAJA APLICADO AL EXPEDIENTE No. _____

295
4

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 05-112548- -00003-0000

Fecha: 2007-05-24 16:45:48 Dep. 2020 NUECREACION
Tra. 11 PATENTEIYII Eve: 379 FASENACIONALI
Act. 538 PETICION Folios: 4

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

NIT : 806176089-2

RECIBO OFICIAL DE CASH : 07 - 38,780
FECHA : MAYO 8 DE 2007

***** CONSIGNACION *****

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PGO	Vr. PAGO
CLARTE RAISBECK	CONSIGNACION	BANCO POPULAR	050-00110-6	52331050	08/05/2007	8,595,000.00

***** D O N D E P E T O *****

CONCEPTO	TOTAL CONCEPTO
114 PTC CAP-11 EXAMEN DE PATENTIBILIDAD	282,000.00
1 50005-01-01 SOLICITUDES	282,000.00
TOTAL :	\$ 282,000.00

SON: OCHOCIENTOS DOS MIL PESOS

RESPONSABLE :

RECIBO DE CASH APLICADO AL EXPEDIENTE No. _____

206
296

DIVISIÓN DE NUEVAS CREACIONES

RADICACIÓN EXPEDIENTE No. 05-112548

EL EXTRACTO DE LA PRESENTE SOLICITUD DE **PATENTE DE INVENCION**

FUE PUBLICADO EN LA GACETA DE PROPIEDAD INDUSTRIAL No **571** DE

FECHA **29 DE DICIEMBRE DE 2006** EL TÉRMINO HÁBIL SEÑALADO POR LA

LEY EXPIRA EL **28 DE MARZO DE 2007**

NOTA: Dentro del plazo de los seis (6) meses siguientes a partir de la fecha de publicación en la gaceta de Propiedad Industrial, deberá solicitar y cancelar el examen de patentabilidad so pena de que la solicitud caiga en abandono, de acuerdo con lo establecido en el Artículo 44 de la Decisión 486/2000.

SE PRESENTARON OPOSICIONES POR PARTE DE TERCEROS.

SI _____

NO X

297

302

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIVISIÓN DE NUEVAS CREACIONES

2020
Bogotá, D.C.

Abogado
Carlos R. Olarte

ASUNTO	Radicación	05-112548
	Trámite	011
	Evento	379
	Actuación	430
	Oficio	
	Folios	009

Patente de Invención ☒ Patente de Modelo de Utilidad ☐

Vía Nacional ☐

Vía PCT (fase nacional) ☒ Cap. I ☐ Cap. II ☒

No. Sol. Internacional PCT/EP2004/005005
Fecha de Presentación Internal. Mayo 7 de 2005

Como resultado del examen de fondo, realizado con fundamento en el artículo 45 de la Decisión 486 de la Comisión de la Comunidad Andina, se le comunica:

1. Documentos estudiados

- 1.1. Descripción: Folios: 133 a 262 (como se radicó inicialmente)
- 1.2. Reivindicaciones: Folios: 263 a 267 (como se radicó inicialmente)
- 1.3. Prioridad: GB 0310724.0 de Mayo 9 de 2003.

2. Objeto de la invención

- Título de la solicitud: "DERIVADOS DE AMINA CLICLICA, PROCESOS PARA SU PREPARACIÓN Y COMPOSICIONES FARMACEUTICAS QUE CONTIENEN LOS MISMOS", folio 1, campo 54.
- El objeto de la presente solicitud de patente de invención consiste en:

Reivindicaciones 1-10 y 12: Compuesto derivados de la fórmula (I).

Reivindicación 11: Un procedimiento para preparación de dichos compuestos.

Reivindicaciones 13-14: Uso de los compuestos en medicamentos y tratamientos.

Reivindicación 15: Una composición farmacéutica que los contiene.

El problema planteado en esta solicitud es la necesidad de nuevos compuestos útiles para el tratamiento de trastornos del SNC y trastornos sicóticos (folio 133).

Para solucionar este problema técnico la solicitud en estudio proporciona derivados de amina cíclica de fórmula (I), composiciones que los contienen, procesos para obtenerlos, métodos de tratamiento y usos en medicamentos y tratamientos.

- La invención se catalogó en la categoría C07D211/34, según la Clasificación Internacional de Patentes (IPC).

3. Excepción a la patentabilidad (artículo 20 D486 literal a)-d))

- La reivindicación 16 presenta un método de tratamiento. Según la decisión 486 los métodos de tratamiento no son patentables.
- Por lo anterior la reivindicación 16 no pueden ser patentada.

4. Reivindicaciones relativas a un uso o a un segundo uso (artículos 14 y 21 D 486)

- En las reivindicaciones 13 y 14 se presenta el uso de los compuestos en medicamentos y tratamientos, respectivamente. De acuerdo con la decisión 486 el uso no se considera invención y por lo tanto no se le puede otorgar patente.
- Por lo tanto las reivindicaciones 13 y 14 no pueden obtener patente.

5. Determinación del Estado de la Técnica

La fecha que se ha tenido en cuenta para determinar el Estado de la Técnica es la fecha de presentación de la solicitud prioritaria Mayo 9 de 2003.

Teniendo en cuenta la fecha indicada se realizó la búsqueda en el estado de la técnica de documentos relacionados con la solicitud encontrándose los siguientes documentos más relevantes:

Nº	Documento	Título	Fecha de publicación
D1	WO9925685	4-SUBSTITUTED-4-PIPERIDINE CARBOXAMIDE DERIVATIVES	1999-05-27
D2	WO02083134	ARYL AND BIARYL PIPERIDINES USED AS MCH ANTAGONISTS	2002-10-24

6. Análisis de patentabilidad (artículo 14 D486)

6.1. Nivel inventivo (artículo 18 D486)

- En la primera reivindicación se presentan compuestos derivados de la amina cíclica (I) como se observa en la tabla a continuación.

7. Conclusión:

Los requisitos de patentabilidad de la presente solicitud se encuentran afectados así:

N°	Documento N°	Reivindicaciones afectadas	Requisito que afecta
D1	WO9925685	Reivindicaciones 1 y dependientes (2-10; 12;15)	Nivel inventivo
D2	WO02083134	Reivindicaciones 1 y dependientes (2-10; 12;15)	Nivel inventivo

En cumplimiento del artículo 45 de la Decisión 486 de la Comisión de la Comunidad Andina, se le indica que debe dar respuesta dentro del término de sesenta días contados a partir de la fecha de notificación de la presente comunicación. En caso de no dar respuesta al presente requerimiento, o si a pesar de la respuesta subsistieran los impedimentos para la concesión, se denegará la patente.

Notifíquese el presente oficio conforme a lo dispuesto en el numeral 5.2, literal e), del capítulo quinto del título primero de la Circular Única N° 10 de 2001.

ALIX CARMENZA CÉSPEDES DE VERGEL

Jefe de División de Nuevas Creaciones

El anterior requerimiento fue notificado por fijación en lista, de fecha 14

CONCEPTO TÉCNICO
No.3081

EXAMINADOR TÉCNICO
Código No.202074

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau



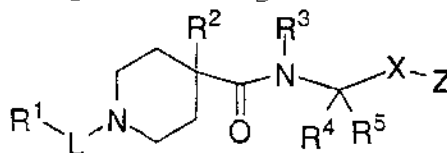
257
301
D7

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C07D 211/30, 211/06, 211/60, A01N 43/40		A1	(11) International Publication Number: WO 99/25685
			(43) International Publication Date: 27 May 1999 (27.05.99)
(21) International Application Number: PCT/US98/24513			(81) Designated States: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SC, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
(22) International Filing Date: 16 November 1998 (16.11.98)			
(30) Priority Data: 60/065,917 18 November 1997 (18.11.97) US 9727214.0 23 December 1997 (23.12.97) GB			
(71) Applicant (for all designated States except US): MERCK & CO., INC. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US).			
(72) Inventors; and (75) Inventors/Applicants (for US only): DELASZLO, Stephen, E. [GB/US]; (US). HAGMANN, William, K. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US).			
(74) Common Representative: MERCK & CO., INC. ; 126 East Lincoln Avenue, Rahway, NJ 07065 (US).			Published With international search report.
(54) Title: 4-SUBSTITUTED-4-PIPERIDINE CARBOXAMIDE DERIVATIVES			
(57) Abstract 4-substituted-4-piperidine carboxamides of Formula (I) are antagonists of VLA-4 and/or $\alpha 4\beta 7$, and as such are useful in the inhibition or prevention of cell adhesion and cell-adhesion mediated pathologies. These compounds may be formulated into pharmaceutical compositions and are suitable for use in the treatment of asthma, allergies, inflammation, multiple sclerosis, and other inflammatory and autoimmune disorders.			

WHAT IS CLAIMED IS:

1. A compound having the formula I:



I

or a pharmaceutically acceptable salt thereof wherein:

- | | | |
|-------------------|----|---|
| L is | 1) | -C(O)-, |
| | 2) | -O-C(O)-, |
| | 3) | -NRe-C(O)-, |
| | 4) | -S(O) ₂ -, |
| | 5) | -P(O)(OR ⁴)-, |
| | 6) | -C(O)C(O)-; |
| X is | 1) | a bond or |
| | 2) | C(R ⁶)(R ⁷); |
| Z is | 1) | -C(O)OR ^d , |
| | 2) | -P(O)(OR ^d)(OR ^e) |
| | 3) | -P(O)(R ^d)(OR ^e) |
| | 4) | -S(O) _m OR ^d , |
| | 5) | -C(O)NR ^d R ^h , or |
| | 6) | -5-tetrazolyl; |
| R ¹ is | 1) | C ₁ -10alkyl, |
| | 2) | C ₂ -10alkenyl, |
| | 3) | C ₂ -10alkynyl, |
| | 4) | Cy, |
| | 5) | Cy-C ₁ -10alkyl, |
| | 6) | Cy-C ₂ -10alkenyl, |
| | 7) | Cy-C ₂ -10alkynyl, |

wherein alkyl, alkenyl, and alkynyl are optionally substituted with one to four substituents independently selected from R^a; and Cy is optionally substituted with one to four substituents independently selected from R^b;

- R² is 1) a group selected from R¹;

299
303

R³ is

- 1) hydrogen,
- 2) C₁₋₁₀alkyl optionally substituted with one to four substituents independently selected from R^a, or
- 3) Cy optionally substituted with one to four substituents independently selected from R^b,

R⁴ is

- 1) hydrogen,
- 2) C₁₋₁₀alkyl,
- 3) C₂₋₁₀alkenyl,
- 4) C₂₋₁₀alkynyl,
- 5) Cy, or
- 6) Cy-C₁₋₁₀alkyl,

wherein alkyl, alkenyl and alkynyl are optionally substituted with one to four substituents independently selected from R^a, and Cy is optionally substituted with one to four substituents independently selected from R^b;

R⁵ is

- 1) hydrogen,
- 2) C₁₋₁₀alkyl,
- 3) C₂₋₁₀alkenyl,
- 4) C₂₋₁₀alkynyl,
- 5) Cy-(Cy¹)_p,
- 6) Cy-(Cy¹)_p-C₁₋₁₀alkyl,
- 7) Cy-(Cy¹)_p-C₂₋₁₀alkenyl,
- 8) Cy-(Cy¹)_p-C₂₋₁₀alkynyl,

alkyl, alkenyl and alkynyl are optionally substituted with one to four substituents independently selected from R^a; and Cy and Cy¹ are optionally substituted with one to four substituents independently selected from R^b;

R⁶ is

- 1) hydrogen,
- 2) a group selected from R^a, or
- 3) a group selected from R¹;

R⁷ is

- 1) hydrogen,
- 2) C₁₋₁₀alkyl,
- 3) C₂₋₁₀alkenyl,
- 4) C₂₋₁₀alkynyl,
- 5) Cy, or

United States Patent Office

3,097,209

Patented July 9, 1963

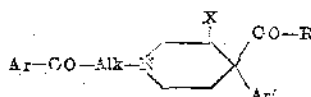
1

3,097,209

1-AROYLALKYL-4-ARYLPIPERIDINE-CARBOXAMIDES

Paul A. J. Janssen, Vosselaar, near Turnhout, Belgium, assignor to Research Laboratorium Dr. C. Janssen, N.V., Beerse, Belgium, a company of Belgium
No Drawing. Filed Mar. 14, 1960, Ser. No. 14,570
16 Claims. (Cl. 260-293.4)

The present invention relates to a novel group of 1-4-arylpiperidinecarboxamides of the structural formula



wherein Ar is a member of the class consisting of phenyl, lower alkylphenyl, xylyl, halophenyl, methoxyphenyl, and thienyl radicals; Ar' is a member of the class consisting of phenyl, lower alkylphenyl, xylyl, halophenyl, methoxyphenyl, and trifluoromethylphenyl radicals; Alk is a lower alkylene radical of at least 3 carbon atoms; X is a member of the class consisting of hydrogen and the methyl radical; and R is a member of the class consisting of a primary, secondary, or tertiary amino radical.

Typical examples of the lower alkylphenyl groups which Ar and Ar' can represent are tolyl, ethylphenyl, cumyl, and the like.

The radical Alk represents a lower alkylene radical of at least 3 carbon atoms including trimethylene, propylene, butylene, methylpropylene, tetramethylene, and pentamethylene. An especially preferred embodiment of this invention is represented by the compounds in which Alk is a trimethylene radical.

The primary, secondary, and tertiary amino radicals which R can represent are members of the class consisting of $-NH_2$, $-N(CH_3)$ -phenyl, anilino, benzylamino, pyrrolidino, piperidino, morpholino, methylmorpholino, dimethylmorpholino, piperazino, and phenylpiperazino radicals. R can also represent radicals of the formula NH (lower alkyl) and N (lower alkyl)₂, wherein the lower alkyl radical represents methyl, ethyl, straight-chain or branched propyl, butyl, amyl, or hexyl.

The compounds described herein have potent biological effects as apomorphine inhibitors and barbiturate potentiators. At therapeutic levels they produce little or no Parkinson-like side effects, hypnosis, and cortical inhibition. They are thus highly useful as selective anti-vomiting agents.

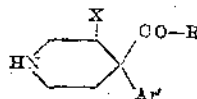
The organic bases of this invention form pharmaceutically acceptable salts with a variety of inorganic and strong organic acids including sulfuric, phosphoric, hydrochloric, hydrobromic, hydriodic, sulfamic, citric, lactic, maleic, malic, succinic, tartaric, cinnamic, acetic, benzoic, gluconic, ascorbic, and related acids. They also form quaternary ammonium salts with a variety of organic esters of sulfuric, hydrohalic and aromatic sulfonic acids. Among such esters are methyl chloride and bromide, ethyl chloride, propyl chloride, butyl chloride, isobutyl chloride, benzyl chloride and bromide, phenethyl bromide, naphthylmethyl chloride, dimethylsulfate, diethylsulfate, methyl benzenesulfonate, ethyl toluenesulfonate, ethylene chlorohydrin, propylene chlorohydrin, allyl bromide, methallyl bromide and crotyl bromide.

The compounds of this invention are prepared by the condensation of an aroylalkyl halide of the formula

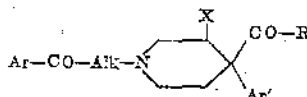


2

with an appropriately selected 4-arylpiperidine carboxamide



to produce a compound of the formula

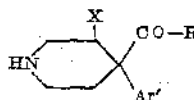


where Alk, Ar, Ar', R, and X are defined as above. The reaction can be carried out in an inert solvent such as an aromatic hydrocarbon e.g. benzene, toluene, xylene, a lower alkanol e.g. ethanol, propanol, butanol, or an aprotic solvent e.g. acetone, butanone, pentanone, or hexanone. A particularly useful solvent for the preparation is the 4-methyl-2-pentanone. The reaction carried out can be accelerated by use of elevated temperatures.

The aroylalkyl halides used as intermediates can be prepared conveniently by the Friedel-Crafts reaction including its milder variation employing, for example, γ -chlorobutyl chloride and benzene or an appropriately substituted benzene such as toluene and xylene, a halogenated benzene such as chlorobenzene, bromobenzene, and fluorobenzene, or an alkoxybenzene such as anisole and phenetole.

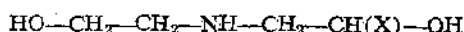
These intermediates can also be prepared by treating an α -haloalkanonitrile with the appropriate arylmagnesium bromide followed by acid hydrolysis of the adduct.

The compounds of the formula

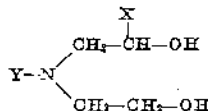


wherein Ar', R, and X are defined as above, which are used as intermediates in the process described above, are prepared by the following reaction schemes.

First a mixture of one mole of a compound of the formula



and 0.5 mole of sodium carbonate in 2-N aqueous solution is heated at about 70-95° C. At that temperature is added one mole of a compound of the formula $Y-Cl$, wherein X is defined as above and Y is a radical capable of blocking the nitrogen atom such as p-toluenesulfonyl or benzyl. This mixture is then heated to about 95° C. for one hour. After extraction with ether, the solvent is evaporated and the residue is dissolved in 2-propanol. Ether is added and the mixture is chilled. The solid which precipitates is collected on a filter and dried to yield a compound of the formula



wherein X and Y are defined as above.

When X is defined as a methyl radical and Y is a 4-toluenesulfonyl radical, the compound can be purified by chilling in a 1:3 by volume mixture of ethanol and acetone. N-(β -hydroxyethyl) - N-(β -hydroxypropyl)-4-toluenesulfamide thus obtained melts at about 66.2-68.2° C.

A mixture of 1.73 moles of the foregoing product and 6 moles of thionyl chloride is heated to about 125° C. for one hour and then cooled. The excess thionyl chloride is evaporated and the residue is dissolved in toluene,

33

is dissolved in methanol. To this solution is added a methanolic solution of oxalic acid. After chilling the solution at -20°C , the solid which precipitates is collected on a filter and then recrystallized from a 4:1 mixture of acetone and methanol to yield 1-(3-benzoylbutyl)-4-phenyl-4-carboxypiperidine pyrrolidide oxalate melting at about $187-188^{\circ}\text{C}$.

By substituting the appropriate starting materials in the above procedure, 1-(γ -benzoylpropyl)-4-(3-chlorophenyl)-4-carboxypiperidine pyrrolidide oxalate melting at about $203-209.3^{\circ}\text{C}$ is obtained.

Example 100

By substituting 2-xylene and 4-xylene in the procedure of Example 1, γ -chloro-2,4-dimethylbutyrophenone boiling at about $140-146^{\circ}\text{C}$ at 5 mm. pressure and γ -chloro-2,5-butyrophenone boiling at about $142-148^{\circ}\text{C}$ at 7 mm. pressure are obtained.

A mixture of 4.2 parts of γ -chloro-2,5-dimethylbutyrophenone, 6 parts of 4-phenyl-4-carboxypiperidine pyrrolidide, 12 parts of sodium carbonate, 0.1 part of potassium iodide in 280 parts of 4-methyl-2-pentanone is refluxed for 59 hours and then filtered. The filtrate is evaporated and the residue dissolved in 2-propanol. To this solution is added oxalic acid in 2-propanol. The precipitate is collected on a filter, washed with acetone, and then recrystallized from methanol to yield 1-[γ -(2,5-dimethylbenzoyl)propyl]-4-phenyl-4-carboxypiperidine pyrrolidide oxalate melting at about $183.6-184^{\circ}\text{C}$.

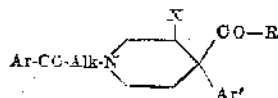
By substituting appropriate starting materials in the above procedure, 1-[γ -(2,4-dimethylbenzoyl)propyl]-4-phenyl-4-carboxypiperidine pyrrolidide oxalate melting at about $186.5-187.5^{\circ}\text{C}$ is obtained. In a similar manner 1-[γ -(2,4-dimethylbenzoyl)propyl]-4-(4-tolyl)-4-carboxypiperidine pyrrolidide oxalate is obtained.

Example 101

A mixture of 5 parts of γ ,4-dichlorobutyrophenone, 6 parts of 4-phenyl-4-carboxypiperidine pyrrolidide, 12 parts of sodium carbonate, 0.1 part of potassium iodide, and 280 parts of 4-methyl-2-pentanone is refluxed for 69 hours and then filtered. The filtrate is evaporated and the residue dissolved in 2-propanol. To this solution is added oxalic acid in 2-propanol. The solid which precipitates is collected on a filter and then triturated with acetone to yield 1-[γ -(4-chlorobenzoyl)propyl]-4-phenyl-4-carboxypiperidine pyrrolidide oxalate melting at about $202.5-203.5^{\circ}\text{C}$.

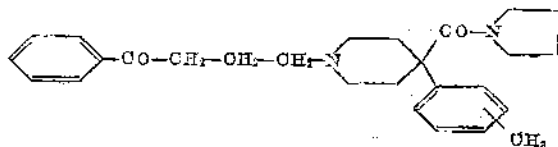
What is claimed is:

1. A compound of the formula



wherein Alk is a lower alkylene radical of at least 3 carbon atoms; Ar is a member of the class consisting of phenyl, lower alkylphenyl, xylyl, halophenyl, methoxyphenyl, and thienyl; Ar' is a member of the class consisting of phenyl, lower alkylphenyl, xylyl, halophenyl, methoxyphenyl, and trifluoromethylphenyl; R is a member of the class consisting of NH_2 , NH -(lower alkyl), N -(lower alkyl), anilino, $\text{N}(\text{CH}_3)$ -phenyl, benzylamino, pyrrolidino, piperidino, morpholino, methylmorpholino, dimethylmorpholino, piperazino, and phenylpiperazino; and X is a member of the class consisting of hydrogen and methyl radicals.

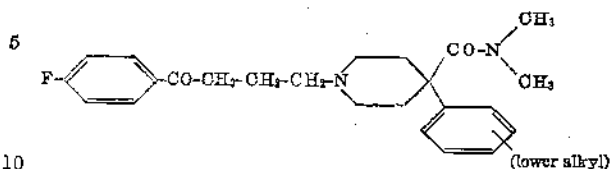
2. A compound of the formula



34

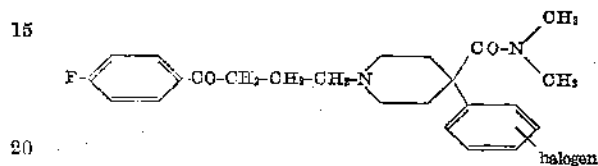
3. 1-(γ -benzoylpropyl)-4-(4-tolyl)-4-carboxypiperidine pyrrolidide.

4. A compound of the formula



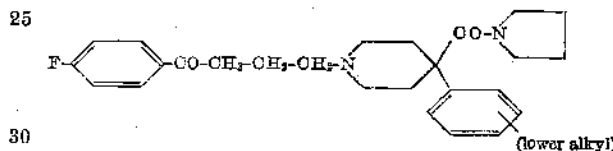
5. 1-[γ -(4-fluorobenzoyl)propyl]-4-(3-tolyl)piperidine-4-(N,N-dimethyl)carboxamide.

6. A compound of the formula



7. 1-[γ -(4-fluorobenzoyl)propyl]-4-(4-chlorophenyl)piperidine-4-(N,N-dimethyl)carboxamide.

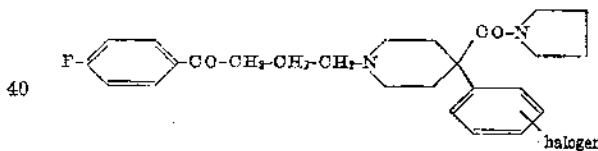
8. A compound of the formula



9. 1-[γ -(4-fluorobenzoyl)propyl]-4-(4-tolyl)-4-carboxypiperidine pyrrolidide.

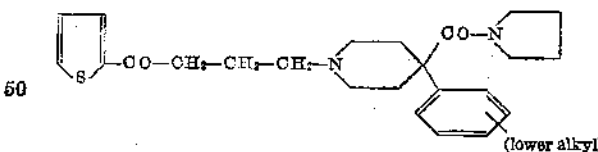
10. 1-[γ -(4-fluorobenzoyl)propyl]-4-(3-tolyl)-4-carboxypiperidine pyrrolidide.

11. A compound of the formula



12. 1-[γ -(4-fluorobenzoyl)propyl]-4-(3-methoxyphenyl)-4-carboxypiperidine pyrrolidide.

13. A compound of the formula



14. 1-[γ -(2-thienyl)propyl]-4-(3-tolyl)-4-carboxypiperidine pyrrolidide.

15. 1-[γ -(4-fluorobenzoyl)propyl]-4-(2,4-xylyl)piperidine-4-(N,N-dimethyl)carboxamide.

16. 1-[γ -(4-fluorobenzoyl)propyl]-4-(3-chlorophenyl)-4-carboxypiperidine pyrrolidide.

References Cited in the file of this patent

UNITED STATES PATENTS

2,167,351	Eisleb	July 25, 1939
2,703,324	Binkley et al.	Mar. 1, 1955
2,833,776	Ruddy	May 6, 1958
2,846,437	Elpern	Aug. 5, 1958
2,951,080	Pohland	Aug. 30, 1960