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ESCOBAR, URIBE ASOCIADOS
Intellectual Property

As. 3051/PCT.

**SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIVISIÓN DE NUEVAS CREACIONES**

E. S. D.

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



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Solicitud de Patente a nombre de
Janssen Pharmaceutica N.V.

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Act 538 PETICION Folios 2

Yo, **JIMENA ESCOBAR URIBE**, identificada como aparece al pie de mi firma, domiciliada en Bogotá, en la Carrera 11 No. 86-53, piso 6, obrando como apoderada de la sociedad **Janssen Pharmaceutica N.V.**, con domicilio en Beerse, Bélgica, solicitante de la patente de la referencia, pido a usted que se proceda a examinar si la invención, cuya patente se tramita en el expediente de la referencia, es patentable.

Adjunto al presente memorial el recibo No. 07 - 87,033 de 23 de octubre de 2007, por la suma de \$404.000.00, con lo cual queda cubierta la tasa oficial correspondiente a dicho estudio.

Señor Superintendente,


JIMENA ESCOBAR URIBE
C.C.39.779.452 de Usaquén
T.P. 68.228

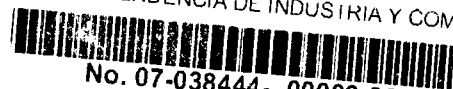
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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

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FECHA : OCTUBRE 23 DE 2007

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***** CONSIGNACION *****

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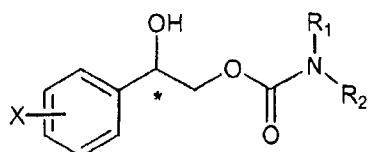
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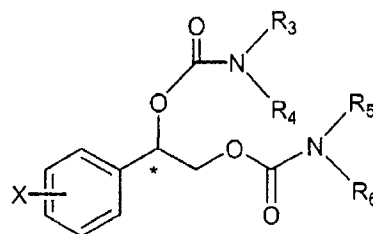
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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: CARBAMATE COMPOUNDS FOR USE IN PREVENTING OR TREATING NEURODEGENERATIVE DISORDERS



(I)



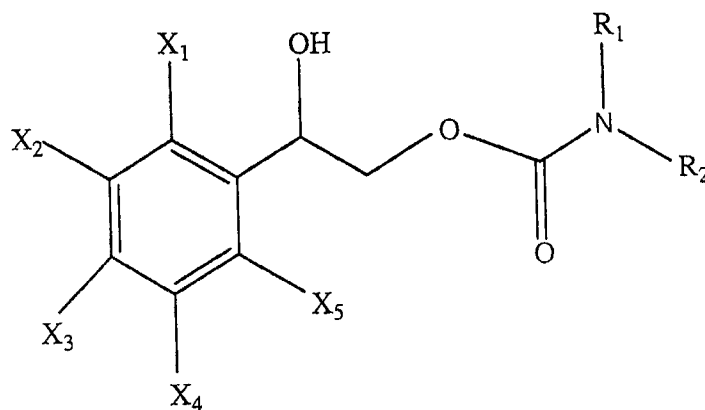
(II)

(57) Abstract: This invention is directed to a method for preventing or treating neurodegenerative disorders comprising administering to a subject in need thereof a therapeutically effective amount of a compound selected from the group consisting of Formula (I) and Formula (II), wherein phenyl is substituted at X with one to five halogen atoms selected from the group consisting of fluorine, chlorine, bromine and iodine; and, R₁, R₂, R₃, R₄, R₅ and R₆ are independently selected from the group consisting of hydrogen and C₁-C₄ alkyl; wherein C₁-C₄ alkyl is optionally substituted with phenyl (wherein phenyl is optionally substituted with substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, amino, nitro and cyano).

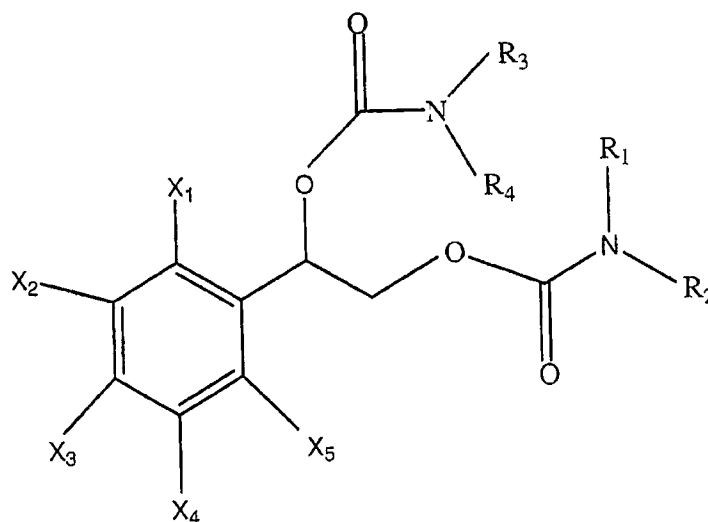
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Accordingly, the present invention provides methods for providing neuroprotection comprising administering to a subject in need thereof a therapeutically effective amount of a composition that comprises at least one compound having Formula 1 or Formula 2:

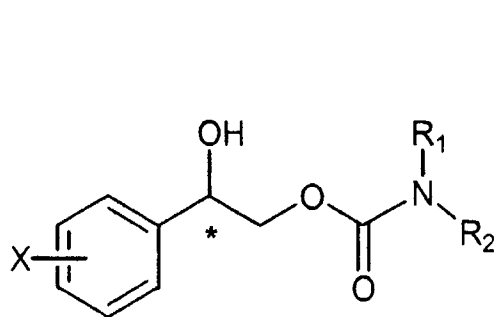


Formula 1

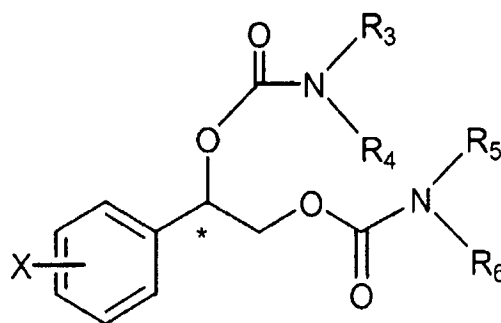


Formula 2

- wherein R_1 , R_2 , R_3 , and R_4 are, independently, hydrogen or $\text{C}_1\text{-C}_4$ alkyl; and X_1 , X_2 , X_3 , X_4 , and X_5 are, independently, hydrogen, fluorine, chlorine, bromine or iodine. The said $\text{C}_1\text{-C}_4$ alkyl group of Formula 1 or Formula 2 can be substituted or unsubstituted. In one aspect of the present invention, the $\text{C}_1\text{-C}_4$ alkyl group is substituted with a phenyl group. The phenyl group can be unsubstituted or substituted. In certain embodiments, the phenyl group is



Formula (I)



Formula (II)

wherein

phenyl is substituted at X with one to five halogen atoms selected from the group consisting of fluorine, chlorine, bromine and iodine; and,

- 5 R_1 , R_2 , R_3 , R_4 , R_5 and R_6 are independently selected from the group consisting of hydrogen and C_1 - C_4 alkyl; wherein C_1 - C_4 alkyl is optionally substituted with phenyl (wherein phenyl is optionally substituted with substituents independently selected from the group consisting of halogen, C_1 - C_4 alkyl, C_1 - C_4 alkoxy, amino, nitro and cyano).

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Embodiments of the invention include a method for preventing or treating neurodegenerative disorders comprising administering to a subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound
15 selected from the group consisting of Formula (I) and Formula (II).

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Embodiments of the invention include the use of a compound selected from the group consisting of Formula (I) and Formula (II) for the preparation of a medicament for preventing or treating neurodegenerative disorders in a
20 subject in need thereof.

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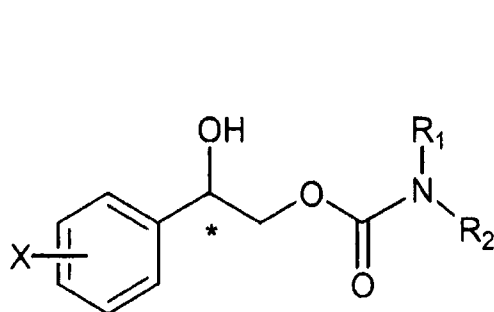
Embodiments of the method include the use of an enantiomer selected from the group consisting of Formula (I) and Formula (II) or enantiomeric mixture wherein one enantiomer selected from the group consisting of Formula
25 (I) and Formula (II) predominates. For enantiomeric mixtures wherein one

Enantiomer

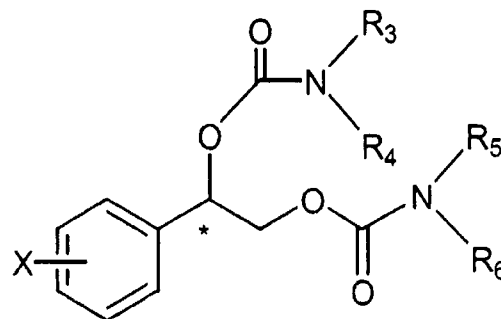
enantiomer selected from the group consisting of Formula (I) and Formula (II) predominates, preferably, one enantiomer selected from the group consisting of Formula (I) and Formula (II) predominates to the extent of about 90% or greater. More preferably, one enantiomer selected from the group consisting of Formula (I) and Formula (II) predominates to the extent of about 98% or greater.

Detailed Description of the Invention

The present invention is directed to a method for preventing or treating neurodegenerative disorders comprising administering to a subject in need thereof a therapeutically effective amount of a compound selected from the group consisting of Formula (I) and Formula (II):



Formula (I)



Formula (II)

wherein

phenyl is substituted at X with one to five halogen atoms selected from the group consisting of fluorine, chlorine, bromine and iodine; and,

R₁, R₂, R₃, R₄, R₅ and R₆ are independently selected from the group consisting of hydrogen and C₁-C₄ alkyl; wherein C₁-C₄ alkyl is optionally substituted with phenyl (wherein phenyl is optionally substituted with substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, amino, nitro and cyano).

The present method includes the use of a compound selected from the group consisting of Formula (I) and Formula (II) wherein X is chlorine;

preferably, X is substituted at the ortho position of the phenyl ring.

The present method also includes the use of a compound selected from the group consisting of Formula (I) and Formula (II) wherein R₁, R₂, R₃, R₄, R₅ and R₆ are preferably selected from hydrogen.

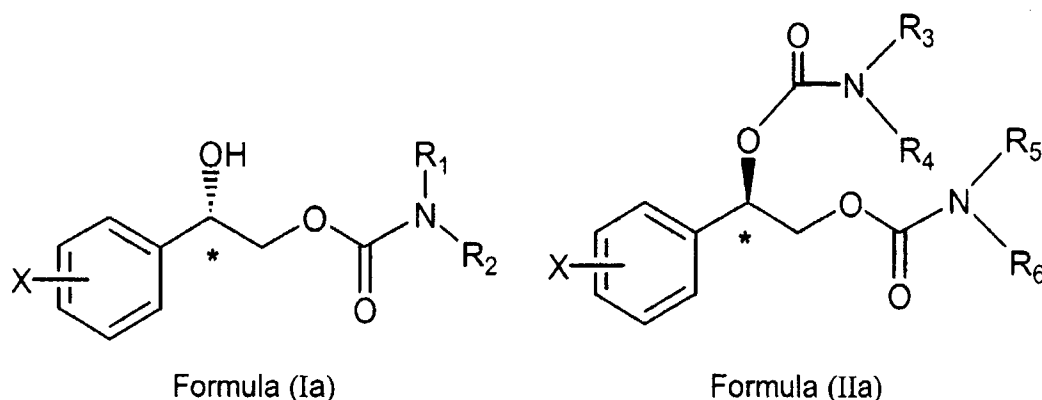
An embodiment of the present method includes the use of an enantiomer selected from the group consisting of Formula (I) and Formula (II) or enantiomeric mixture wherein one enantiomer selected from the group consisting of Formula (I) and Formula (II) predominates wherein X is chlorine; preferably, X is substituted at the ortho position of the phenyl ring.

The present method also includes the use of an enantiomer selected from the group consisting of Formula (I) and Formula (II) or enantiomeric mixture wherein one enantiomer selected from the group consisting of Formula (I) and Formula (II) predominates wherein R₁, R₂, R₃, R₄, R₅ and R₆ are preferably selected from hydrogen.

For enantiomeric mixtures wherein one enantiomer selected from the group consisting of Formula (I) and Formula (II) predominates, preferably, an enantiomer selected from the group consisting of Formula (I) and Formula (II) predominates to the extent of about 90% or greater. More preferably, an enantiomer selected from the group consisting of Formula (I) and Formula (II) predominates to the extent of about 98% or greater.

25

An embodiment of the present method includes the use of an enantiomer selected from the group consisting of Formula (Ia) and Formula (IIa) or enantiomeric mixture wherein one enantiomer selected from the group consisting of Formula (Ia) and Formula (IIa) predominates:



wherein

phenyl is substituted at X with one to five halogen atoms selected from the group consisting of fluorine, chlorine, bromine and iodine; and,

- 5 R_1 , R_2 , R_3 , R_4 , R_5 and R_6 are independently selected from the group consisting of hydrogen and C_1 - C_4 alkyl; wherein C_1 - C_4 alkyl is optionally substituted with phenyl (wherein phenyl is optionally substituted with substituents independently selected from the group consisting of halogen, C_1 - C_4 alkyl, C_1 - C_4 alkoxy, amino, nitro and cyano).

10

The present method includes the use of an enantiomer selected from the group consisting of Formula (Ia) and Formula (IIa) or enantiomeric mixture wherein one enantiomer selected from the group consisting of Formula (Ia) and Formula (IIa) predominates wherein X is chlorine; preferably, X is substituted
15 at the ortho position of the phenyl ring.

The present method also includes the use of an enantiomer selected from the group consisting of Formula (Ia) and Formula (IIa) or enantiomeric mixture wherein one enantiomer selected from the group consisting of Formula
20 (Ia) and Formula (IIa) predominates wherein R_1 , R_2 , R_3 , R_4 , R_5 and R_6 are preferably selected from hydrogen.

For enantiomeric mixtures wherein one enantiomer selected from the group consisting of Formula (Ia) and Formula (IIa) predominates, preferably,
25 an enantiomer selected from the group consisting of Formula (Ia) and Formula

As used herein, the term "composition" is intended to encompass a product comprising the specified ingredients in the specified amounts, as well as any product which results, directly or indirectly, from combinations of the specified ingredients in the specified amounts.

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To prepare a pharmaceutical composition of the present invention, a compound of Formula (I) or Formula (II) as the active ingredient is intimately admixed with a pharmaceutical carrier according to conventional pharmaceutical compounding techniques, which carrier may take a wide variety of forms depending of the form of preparation desired for administration (e.g. oral or parenteral). Suitable pharmaceutically acceptable carriers are well known in the art. Descriptions of some of these pharmaceutically acceptable carriers may be found in The Handbook of Pharmaceutical Excipients, published by the American Pharmaceutical Association and the Pharmaceutical Society of Great Britain.

Methods of formulating pharmaceutical compositions have been described in numerous publications such as Pharmaceutical Dosage Forms: Tablets, Second Edition, Revised and Expanded, Volumes 1-3, edited by Lieberman et al; Pharmaceutical Dosage Forms: Parenteral Medications, Volumes 1-2, edited by Avis et al; and Pharmaceutical Dosage Forms: Disperse Systems, Volumes 1-2, edited by Lieberman et al; published by Marcel Dekker, Inc.

Preferably, a pharmaceutical composition is in a unit dosage form such as a tablet, pill, capsule, caplet, gelcap, lozenge, granule, powder, sterile parenteral solution or suspension, metered aerosol or liquid spray, drop, ampoule, autoinjector device or suppository for administration by oral, intranasal, sublingual, intraocular, transdermal, parenteral, rectal, vaginal, inhalation or insufflation means. Alternatively, the composition may be presented in a form suitable for once-weekly or once-monthly administration or may be adapted to provide a preparation for intramuscular injection.