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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



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TÍTULO SOLICITADO: "CRISTALES DE SOLVATO NOVEDOSOS.

PUBLICACIÓN: Gaceta 647 de 29 de junio de 2012, N° de publicación 817.

PRIORIDAD: JP 2009-109160 de 28/04/2009

SOLICITANTE: DAIICHI SANKYO COMPANY, LIMITED.

APODERADO: ALICIA LLORED A RICAURTE

TRÁMITE: SUSTENTACIÓN DE OPOSICIÓN

JOSÉ LUIS REYES VILLAMIZAR, mayor de edad, identificado como aparece al pie de mi firma, abogado en ejercicio, titular de la tarjeta profesional número 44655 del Consejo Superior de la Judicatura, obrando en calidad de apoderado de la sociedad **TECNOQUIMICAS S.A.**, en ejercicio de lo dispuesto por el artículo 42, inciso 2° de la Decisión 486 de 2000, por medio del presente escrito, procedo a sustentar y complementar la oposición presentada el 27 de Septiembre de 2012, en los siguientes términos:

I. RATIFICACIÓN

Comedidamente me permito insistir en los argumentos planteados en la oposición respectiva, los cuales, como se dijo en su momento, demuestran que la solicitud de la referencia incumple los requisitos de patentabilidad establecidos por los

artículos 14 y 18 de la Decisión 486 de 2000, y que por ello no merece recibir el beneficio patentario.

La mencionada solicitud colombiana se refiere a cristales de acetona de tritilo-olmesartan-medoxomil y su método de obtención, los cuales al corresponder a una molécula en estado polimórfico, el objeto de la solicitud no puede adjudicársele novedad o nivel inventivo ya que como se mencionó en mi memorial de oposición, el descubrimiento de las condiciones fisicoquímicas de los cristales para llevarlos a este estado no obedece a una invención propiamente dicha. Adicional a lo anterior se observó que las reivindicaciones carecen incluso de claridad porque no ofrece consistencia entre las mismas ni de manera individual ya que para definir no se deben hacer alusiones a figuras.

En este caso, se reclaman cristales de la molécula ya conocida sobre la base de propiedades intrínsecas del compuesto y su estructura sin que estos obedezcan a una abstracción de una idea en un invento, sino a una descripción fenomenológica de una forma cristalina de un compuesto ya conocido.

En ese orden de ideas, cualquier solicitud que pretendiera protección por patente no tendría más que describir patrones bajo condiciones no seleccionadas previamente, dando como resultado datos diferentes en propiedades necesarias para demostrar su estabilidad.

Así, al reclamar los compuestos mediante sus propiedades, no se está definiendo estructuralmente el objeto ya que estas propiedades pueden ser alcanzadas por diferentes configuraciones tanto del mismo como de otros compuestos en una posibilidad indeterminada de procedimientos.

Se tomaron a consideración los siguientes documentos del estado de la técnica:

- La patente americana US 2010/0076200 (equivalente a la patente japonesa JP 2007-509993 publicada el 19 de abril de 2007), revela entonces un proceso para purificar el tritilo olmesartan medoxomil, mencionando en el ejemplo 3 la forma de cristalización del mismo compuesto. En este sentido, el documento de anterioridad mencionado ya divulgaba los cristales de tritilo olmesartan medoxomil por lo que las reivindicaciones 1 – 4 que reclaman los cristales del

compuesto, carecen de plano de novedad.

Las reivindicaciones 5 a 23 implican entonces un método para lograr los cristales reclamados antes. Dicho método como ya se ha mencionado también carece de novedad ya que el mismo documento US 2010/0076200 incluye la purificación del compuesto químico mediante su mezcla con un volumen de solución al 4% de acetona en agua (ver párrafo 0022 y 0061).

[0022] The process can further include the step of heating the solution of olmesartan medoxomil in the C₃₋₆ ketone. In this embodiment, the solution of olmesartan medoxomil in the C₃₋₆ ketone is preferably heated to about 30° C. to about reflux temperature, more preferably about 40° C. to about reflux temperature.

Dicha característica destruye la novedad de las reivindicaciones de método las cuales mencionan el tratamiento con una cantidad de solvente de acetona menor a un 20%, 10% y 5% en volumen de agua¹. Dada la dependencia de las reivindicaciones de método con la reivindicación 13 donde se menciona que el solvente de acetona "opcionalmente" contiene agua, esta característica no es esencial y puede o no estar presente en el proceso por lo que incluso ambas modalidades ya estaban descritas por la anterioridad mencionada.

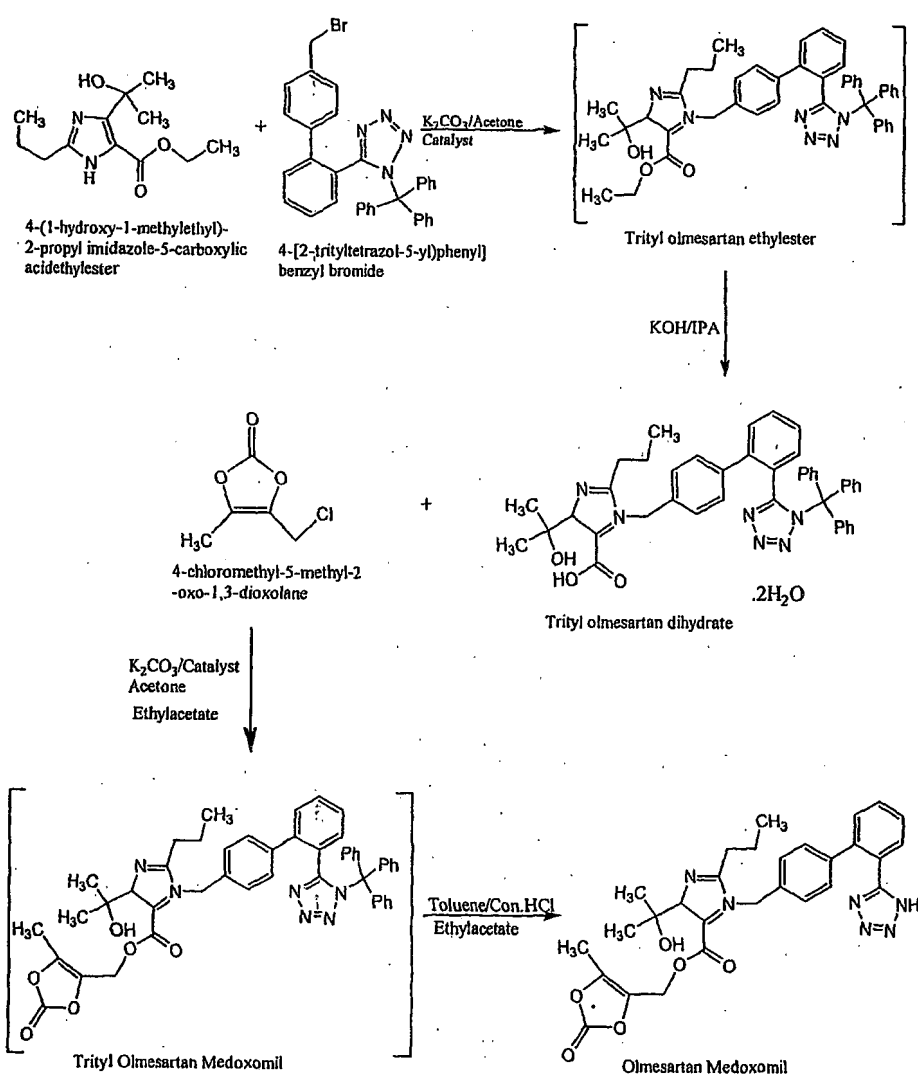
- Por su parte la patente americana US 2006/0069141 (equivalente a la patente Japonesa JP 2007-509992 publicada el 19 de abril de 2007) demuestra que en el estado de la técnica ya se conocía previamente el tritilo-olmesartan-medoxomil, y en segundo lugar, ya se describían procesos de purificación que involucraban dicho compuesto, acetona y agua (inclusive en rangos de porcentajes que incluyen a los mencionados en las reivindicaciones 8 a 10 y 15 a 17).

¹ Las unidades en la solicitud en estudio se dan en porcentaje en peso, mientras que el documento US 2010/0076200 las presenta en volumen, haciendo la conversión a una densidad de 0,78g/ ml y de agua de 1,00 g/ml, el porcentaje en peso corresponde al 3,12%.

II. COMPLEMENTO DE INFORMACION

Adicional a los dos documentos mencionados anteriormente, se pone de presente:

- La publicación internacional WO 2007/148344 del 27 de diciembre de 2007, el cual describe procesos para la preparación de Olmesartan medoxomil en cuyo proceso un producto intermedio de reacción es el tritil Olmesartan medoxomil. La reacción observada en el documento se observa en el siguiente esquema tomado de la página 7:



En el mismo es notable la adición de un catalizador y acetona para la obtención del producto intermedio mencionado por lo que el proceso en sus características esenciales es igual al descrito por la solicitud.

Adicionalmente y con relación a las primeras etapas del proceso en que el paso de tritilación y esterificación del DMDO del omesartan en un solvente de acetona (como se reclama en la reivindicación 13), no solo se observa en el esquema de arriba, sino que se ha divulgado también en la página 9 de la anterioridad citada:

The inventors have further found that the trityl Olmesartan dihydrate form obtained has very good solubility which will facilitate easy dissolution for esterification step.

Se hace notar que el compuesto DMDO hace alusión al 4 -clorometil-5-metil-1,3-dioxol-2 ona igualmente identificable en el esquema bajo la reacción de esterificación que es reclamada por la solicitud. Así mismo y no menos importante, la reacción para obtener tritil Olmesartan medoxomil puede observarse en el ejemplo 4 de del documento analizado WO 2007/148344.

- Por otra parte se pone en consideración la publicación internacional WO 2008/043996 publicado el 17 de abril de 2008, la cual describe metodos para preparar tritil olmesartan medoxomil describiendo los pasos de esterificación del 4 -clorometil-5-metil-1,3-dioxol-2 ona.

Adicional a lo ya mencionado dicha anterioridad permite observar que en la preparación de tritil olmesartan medoxomil, el proceso de purificación admite recoger el producto como sólido en el paso final (ver ejemplo 5), no se especifica qué tipo de sólido es, por lo que para cualquier técnico medio versado en la materia sería normal identificar el polimorfismo reclamado por la solicitud dada su naturaleza cristalina.

20 In examples 4 and 5, filtration steps are involved, but the first and second intermediates in the process are not isolated as solids. The filtration steps are used to remove insoluble by-products and impurities; the intermediates remain in solution as the filtrate. The trityl olmesartan medoxomil is isolated as a solid in the final step. These examples exemplify the embodiment in which neither one of the first or second intermediates is isolated. The
25 isolated trityl olmesartan medoxomil is taken on for purification, as exemplified in example 6.

En conclusión, los documentos observados en el presente escrito mencionan todas las características técnicas esenciales de los cristales de tritil Olmesartan medoxomil, e incluso los procesos reclamados, por lo tanto, la solicitud no cumple

con los criterios de Novedad y en vista de la falta de demostración de un efecto sorprendente, el Nivel inventivo de modalidades particulares no puede ser reconocido.

III. ANEXOS

- La publicación internacional WO 2007/148344 publicado el 27 de diciembre de 2007. Portada, página 7, 15 y reivindicaciones.
- La publicación internacional WO 2008/043996 publicado el 17 de abril de 2008. Portada, página 19.

Señor Superintendente,



JOSÉ LUIS REYES VILLAMIZAR

C.C. 79'152.473 de Usaquén

T.P.A. 44.655 del C.S.J.

(19) World Intellectual Property Organization
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Dharmaraj, Ramachandra [IN/IN]; 4/403, Garden Enclave, Pokharan Road 2, Thane (W) Mumbai-400 601, Maharashtra (IN).

(21) International Application Number:

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(74) Agent: CURTIS, Philip, Anthony; A.A. Thornton & Co., 235 High Holborn, London WC1V 7LE (GB).

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(30) Priority Data:
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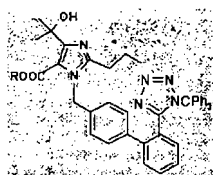
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(75) Inventors/Applicants (for US only): PATHI, Srinivas, Laxminarayan [IN/IN]; 2475/24, 7th B Main RPC Layout, Vijaynagar, Bangalore 560 040, Karnataka (IN). PUPPALA, Ravikumar [IN/IN]; House No.5 A Cross, Vijaya Bank Colony, Banaswadi, Bangalore (IN). KANKAN, Rajendra, Narayanrao [IN/IN]; 1204, Heritage, Hiranandani Gardens, Powai, Mumbai 400 076, Maharashtra (IN). RAO,

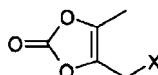
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(54) Title: PROCESS FOR PREPARING TRITYL OLMESARTAN MEDOXOMIL AND OLMESARTAN MEDOXOMIL



(V)



(IV)

(57) Abstract: A process for the preparation of trityl olmesartan comprising (a) condensing 4-(1-hydroxy-1-methylethyl)-2-propyl-imidazol-5-carboxylic acid alkyl ester with trityl biphenyl bromide in the presence of a polar aprotic solvent and a base selected from the group consisting of alkali metal carbonates, alkali metal hydroxides, alkali metal alkoxides, and tertiary amines to obtain a compound of formula (V); b) deesterifying the compound of formula (V) with a base; and c) reacting the product of step (b) with 4-halomethyl-5-methyl-2-oxo-1,3-dioxolene of formula (IV); wherein X is halogen selected from F or Cl or Br or I, to obtain trityl olmesartan medoxomil of formula. The trityl olmesartan medoxomil may be deprotected to produce olmesartan medoxomil.

WO 2008/043996 A2

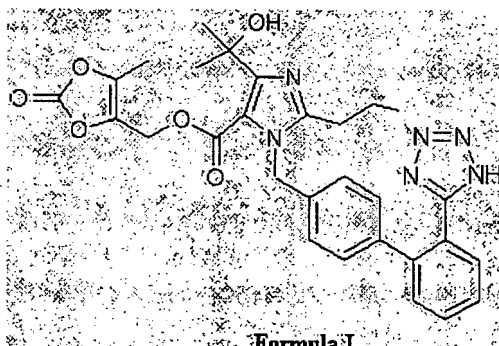
**PROCESS FOR PREPARING TRITYL OLMESARTAN MEDOXOMIL AND
OLMESARTAN MEDOXOMIL**

5 Technical field

The present invention relates to an improved process for the synthesis of trityl olmesartan medoxomil and olmesartan medoxomil.

10 Background and prior art

Olmesartan medoxomil is a prodrug that is hydrolysed to olmesartan during absorption from the gastrointestinal tract. Olmesartan is a selective AT1 type angiotensin II receptor antagonist, which is by virtue of its pharmacological properties, particularly useful in the
15 treatment of hypertension. The chemical name for olmesartan medoxomil is 4-(1-hydroxy-1-methylethyl)-2-propyl-1-[[2-(1H-tetrazol-5-yl)[1,1-biphenyl]-4-yl]methyl]-1H-imidazole-5-carboxylic acid(5-methyl-2-oxo-1,3-dioxol-4-yl)methyl ester, and is represented by the following structure (formula I).



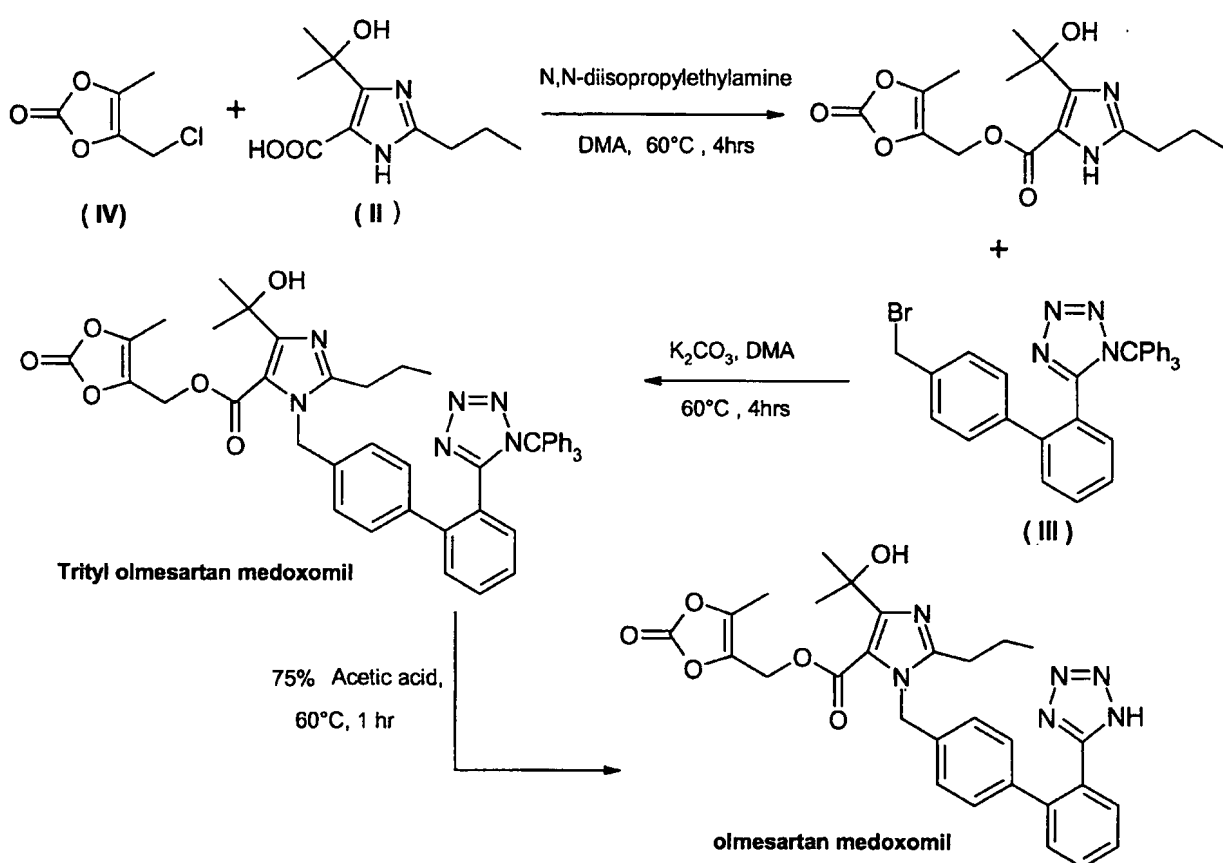
20 Olmesartan medoxomil was first disclosed in US patent 5,616,599. The synthetic method employed is depicted in the following reaction Scheme 1, where an imidazole derivative is condensed with a dioxolyl compound, then reacted with a substituted biphenyl methyl

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halide to obtain trityl olmesartan medoxomil which is then deprotected to obtain crude olmesartan medoxomil.

Scheme 1

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The '599 patent also discloses a process for preparing olmesartan medoxomil in examples 10 18(a) and 78. The process focuses on the coupling reaction between the imidazole derivative and the substituted biphenyl methyl halide, the condensation with the dioxolyl compound and the subsequent deprotection to isolate crude olmesartan medoxomil. Example 18(a) describes the coupling reaction which involves the use of a strong base (sodium hydride). Such strong bases are hazardous and difficult to handle on an industrial 15 scale. The coupling reaction is conducted at a temperature of 60°C . The reaction

Preparation of trityl olmesartan medoxomil

To dimethyl sulphoxide (800 ml), sodium hydroxide powder (50 gms) was added under nitrogen atmosphere and stirred at 20-25°C for 10 minutes. To this, 4-(1-hydroxy-1-methylethyl)-2-propyl-imidazole-5-ethyl carboxylate (100 gms) was added at 20-25°C. 5-(4'-bromomethyl-biphenyl)-2-yl-1-trityl tetrazole (270 gms) was added slowly at 20-25°C, and the reaction mass was stirred at 20-25°C for 12 hours. Further 10% sodium hydroxide solution (100 ml) was added to the reaction mass at 20-25°C. The temperature of the reaction mass was raised to 40-45°C, the contents stirred at 40-45°C for 2 hours and 5-methyl-2-oxo-1,3-dioxane-4-yl)methyl chloride (160 gms) was added slowly at 45-50°C over a period of 45 minutes. The contents were stirred at 45-50°C for 2 hours. The reaction mass was then cooled to 0-5°C, stirred for 1 hour at 0-5°C, filtered and slurried in water (1.0 lt) at 40-45°C for 1 hour, filtered at 40°C and dried at 40°C. To the dried material, ethyl acetate (2.5 lt) was added, heated to 50-55°C for complete dissolution, ethyl acetate was distilled off to 1.0 lt stage under vacuum at 45-50°C. The contents were cooled to 0-5°C, stirred at 0-5°C for 3 hours, filtered, washed with chilled methanol (100 ml) and dried under vacuum at 40-45°C to give 250 gms of the title compound.

Purity by HPLC : > 99%

- 20 In examples 4 and 5, filtration steps are involved, but the first and second intermediates in the process are not isolated as solids. The filtration steps are used to remove insoluble by-products and impurities; the intermediates remain in solution as the filtrate. The trityl olmesartan medoxomil is isolated as a solid in the final step. These examples exemplify the embodiment in which neither one of the first or second intermediates is isolated.
- 25 isolated trityl olmesartan medoxomil is taken on for purification, as exemplified in example 6.

Example 6**Purification**

Crude trityl olmesartan medoxomil (140 gms) was dissolved in 1120 ml of ethyl acetate, distilled up to 560 ml and chilled to 0-5°C. Isopropyl acetate (70 ml) and methanol (35 ml) were charged to the reaction mass. The contents were stirred at 0-5°C for 30 minutes. Pure trityl olmesartan medoxomil was isolated by filtration and was dried under reduced pressure at 45-50°C to give 110 gms of the title compound. Purity by HPLC - > 99%.

Example 7

Preparation of olmesartan medoxomil

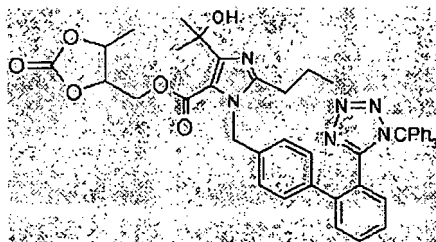
- 10 To 75 % aqueous acetic acid (1000 ml) was slowly added trityl olmesartan medoxomil (110 gms)[prepared as described in example 5] at 25-30°C. The contents were stirred at 60°C for 1 hour. The reaction mass was chilled to 0-5°C and filtered to remove tritanol. The reaction mass was concentrated under reduced pressure. The residue was quenched with water (500 ml), neutralized with a base and extracted in dichloromethane (500 ml).
- 15 The clear dichloromethane extract was then concentrated under reduced pressure and stripped off with acetone. The residue thus obtained was isolated from the acetone (250 ml) to give 55 gms of the title compound. Chromatographic purity - > 99%

It will be appreciated that the invention may be modified within the scope of the appended
20 claims.

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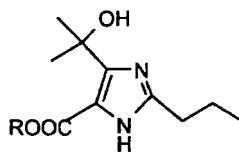
CLAIMS

1. A process for the preparation of trityl olmesartan medoxomil of formula (VI)



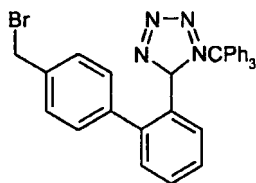
(VI)

comprising (a) condensing 4-(1-hydroxy-1-methylethyl)-2-propyl-imidazol-5-carboxylic acid alkyl ester of formula (II)



(II)

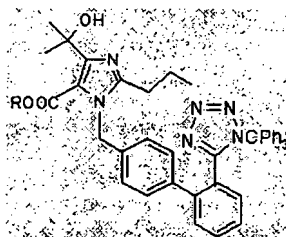
wherein R is C₁-C₆ alkyl with trityl biphenyl bromide of formula (III)



(III)

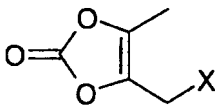
in the presence of a polar aprotic solvent and a base selected from the group consisting of alkali metal carbonates, alkali metal hydroxides, alkali metal alkoxides, and tertiary amines to obtain a compound of formula V,

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(V)

- b) deesterifying the compound of formula (V) with a base; and c) reacting the product of step (b) with 4-halomethyl-5-methyl-2-oxo-1,3-dioxolene of formula (IV),



(IV)

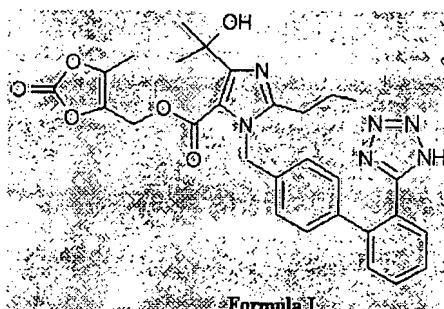
- 10 wherein X is halogen selected from F or Cl or Br or I, to obtain trityl olmesartan medoxomil of formula (VI).
2. A process according to claim 1, wherein R is C₁-C₆ alkyl.
- 15 3. A process according to claim 1 or 2, wherein R is ethyl.
4. A process according to claim 1, 2 or 3, wherein said polar aprotic solvent in step (a) is selected from the group consisting of acetone, tetrahydrofuran, methyl ethyl ketone, acetonitrile, ethyl acetate, dimethyl formamide, dimethyl acetamide, dimethyl sulfoxide and
- 20 mixtures thereof.
5. A process according to claim 4, wherein the polar aprotic solvent is dimethyl acetamide.

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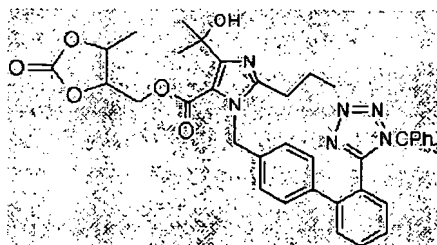
6. A process according to any preceding claim, wherein the alkali metal carbonate is potassium carbonate.
7. A process according to any one of claims 1 to 5, wherein the alkali metal hydroxide is sodium hydroxide or potassium hydroxide.
8. A process according to any preceding claim, wherein step (a) is carried out at a temperature ranging from 40°C to 55°C .
9. A process according to claim 8, wherein step (a) is carried out at a temperature ranging from 40°C to 50°C.
10. A process according to claim 9, wherein step (a) is carried out at a temperature ranging from 45°C to 50°C.
11. A process according to any preceding claim, wherein the base used in step (b) is selected from the group consisting of inorganic bases and organic bases.
12. A process according to claim 11, wherein the inorganic base is selected from the group consisting of alkali metal hydroxides, alkali metal carbonates and alkali metal alkoxides.
13. A process according to claim 11, wherein the organic base is a tertiary amine.
14. A process according to any preceding claim, further comprising neutralizing the reaction mass of step (c) with an acid selected from the group consisting of carboxylic acids and inorganic acids.
15. A process according to claim 14, wherein the carboxylic acid is formic acid or acetic acid.

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16. A process according to claim 14, wherein the inorganic acid is hydrochloric acid, hydrobromic acid or sulfuric acid.
17. A process according to any preceding claim, wherein steps (a), (b) and (c) are carried out in a single reaction vessel.
18. A process according to any preceding claim, wherein neither one of the products of steps (a) or (b) is isolated.
19. A process for the preparation of olmesartan medoxomil of formula I



- comprising preparing trityl olmesartan medoxomil of formula (VI) according to any preceding claim;



- and d) deprotecting the trityl olmesartan medoxomil (VI) to yield olmesartan medoxomil.

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20. A process according to claim 19, wherein steps (a), (b), (c), and (d) are carried out in a single reaction vessel.

21. A process according to any one of claims 19, wherein steps (a), (b) and (c) are
5 carried out in a single reaction vessel.

22. A process according to claim 21, wherein the trityl olmesartan medoxomil of formula (VI) is isolated prior to deprotection in step (d).

10 23. A process according to claim 22, wherein the trityl olmesartan medoxomil of formula (VI) is purified prior to deprotection in step (d).

24. A process according to any preceding claim, wherein neither one of the products of steps (a) or (b) is isolated as a solid.

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25. A process according to any one of claims 19 to 20, wherein none of the products of steps (a), (b) or (c) is isolated as a solid.

26. A process according to any one of claims 19 to 25, wherein the deprotection is
20 carried out in the presence of an acid selected from the group consisting of organic carboxylic acids, sulfonic acids, and inorganic acids.

27. A process according to claim 26, wherein the organic carboxylic acid is formic acid, oxalic acid, acetic acid, trimethyl acetic acid or trifluoroacetic acid.

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28. A process according to claim 27, wherein the organic carboxylic acid is acetic acid.

29. A process according to claim 26, wherein the sulfonic acid is methanesulfonic acid or p-toluene sulfonic acid.

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30. A process according to claim 26, wherein the inorganic acid is hydrochloric acid, hydrobromic acid, sulfuric acid, pivalic acid or phosphoric acid.

31. A process according to claim 30, wherein the inorganic acid is hydrochloric acid.

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32. A process for the preparation of olmesartan medoxomil substantially as described herein with reference to the foregoing examples 1 to 3 and 7.

33. A process for the preparation of trityl olmesartan medoxomil substantially as
10 described herein with reference to the foregoing examples 4 and 5.

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International Bureau



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[IN/IN]; Plot N°34A, Anrich Industrial Estate, Bollaram, Jinnaram Mandal, Medak Dist., Hyderabad, Andhrapradesh 500 055 (IN).

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(74) Agents: **KAUSHIK, Geetesh et al.**; Plot N°34A, Anrich Industrial Estate, Bollaram, Jinnaram Mnadal, Medak Dist., Hyderabad 500 055, Andhrapradesh (IN).

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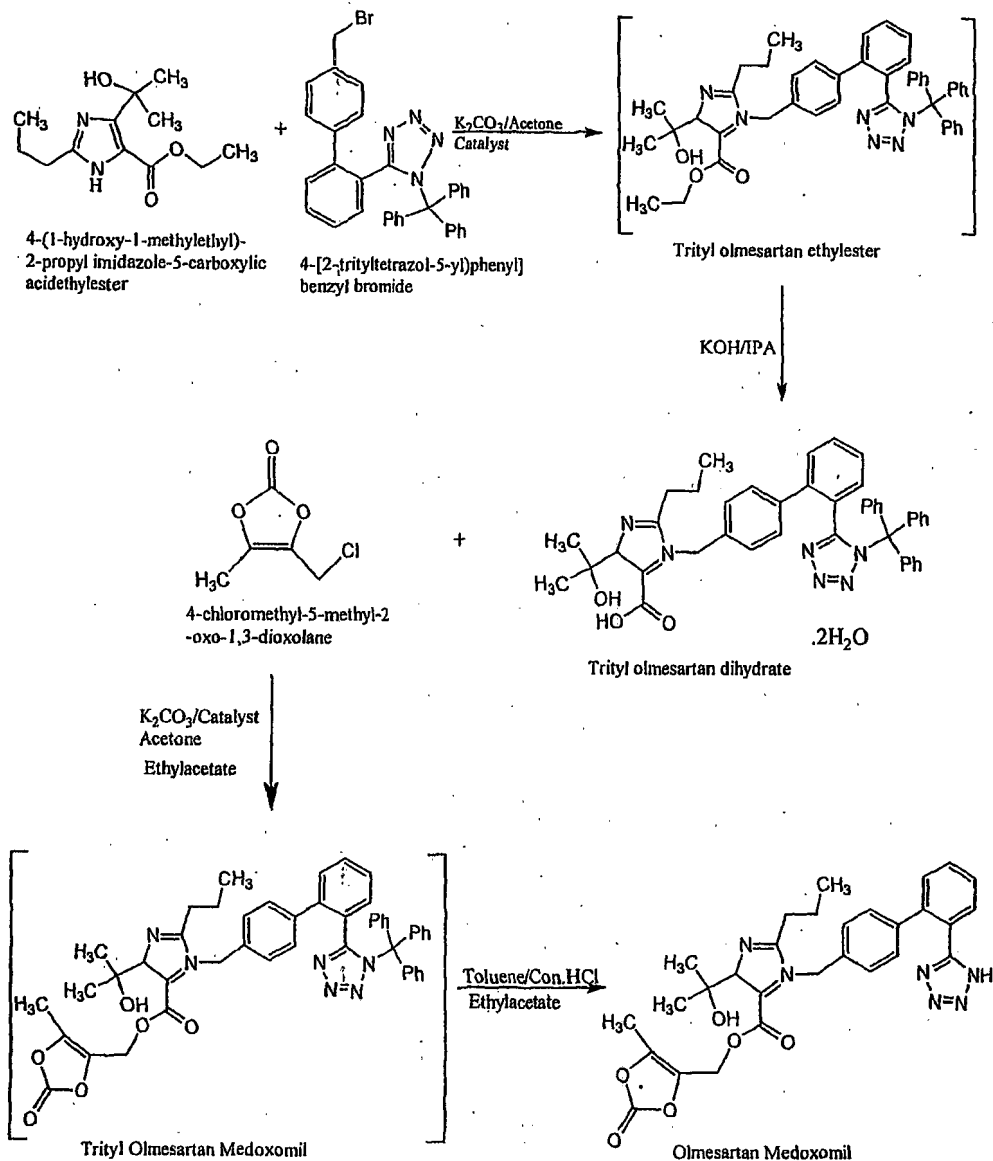
(54) Title: PROCESS FOR THE PREPARATION OF OLMESARTAN MEDOXOMIL

(57) Abstract: The present invention provides a process for the preparation of Olmesartan medoxomil by condensing the ethyl 4-(1-hydroxy-1-methylethyl)-2-propylimidazole-5-carboxylate with 4-[2-(trityl tetrazol-5-yl) phenyl] benzyl bromide to obtain ethyl 4-(1-hydroxy-1-methyl ethyl)-2-propyl-1-[4-[2-(trityl tetrazol-5-yl)phenyl]phenyl] methylimidazole-5-carboxylate and then hydrolyzing ethyl 4-(1-hydroxy-1-methyl ethyl)-2-propyl-1-[4-[2-(trityl tetrazol-5-yl) phenyl] phenyl] methyl imidazole-5-carboxylate to obtain trityl Olmesartan dihydrate followed by reacting trityl Olmesartan dihydrate with 4-chloromethyl-5-methyl-2-oxo-1,3-dioxolene to obtain trityl Olmesartan medoxomil and then deprotecting trityl Olmesartan medoxomil to obtain Olmesartan medoxomil.

WO 2007/148344 A2

DETAILED DESCRIPTION OF THE INVENTION

Thus in accordance with the present invention preparation of Olmesartan medoxomil comprises the following steps: :



In a specific embodiment, the present invention provides a process for the preparation of Olmesartan medoxomil, which involves condensing the ethyl 4-(1-hydroxy-1-methylethyl)-2-propylimidazole-5-carboxylate with 4-[2-(trityltetrazol-5-yl)phenyl]

Example 4**Preparation of Trityl Olmesartan Medoxomil (*insitu*)**

4-(1-Hydroxy-1-methylethyl)-2-Propyl-1H-imidazole-5-carboxylic acid ethyl ester (100g), N-(triphenylmethyl)-5-(4'-bromomethylbiphenyl-2-yl)tetrazole (250g), potassium carbonate (170 g) & tetra butyl ammonium bromide (15 g) in acetone (2.5 L) were refluxed for 15 hours. The reaction mass was cooled & filtered to remove the salts. Salts were washed with acetone (300ml). Acetone from combine the filtrate & washings was distilled. The residue obtained was refluxed with acetonitrile (500ml). The reaction mass was cooled, filtered & solid after filtration was dissolved in Isopropyl alcohol (1500 ml). Separately prepared solution of potassium hydroxide (180g) in IPA (2.0L) was added to above solution at room temperature. Reaction was stirred for 3 hrs at 30 -40°C. Isopropyl alcohol was distilled under reduced pressure. Brine (1.0 L) & ethyl acetate (2.0L) was added to the residue. After layer separation aqueous layer was extracted with ethyl acetate (3 x 1000 ml). Combined ethyl acetate layer was washed with sodium bicarbonate solution (2 x 2.0 L) & dried (Na₂SO₄). Ethyl acetate was distilled completely under reduced pressure. Acetone (4.0 L) was added to the residue & heated to reflux; the solution obtained was added to suspension of potassium carbonate (50 g), potassium iodide (15 g) & 4-chloromethyl-5-methyl-1, 3-dioxol-2-one (75 g) in acetone (1500ml) at reflux temperature. Reaction mass was refluxed for 2 - 6 hrs. After completion of reaction, the reaction mass was filtered & the acetone was distilled from combined mother liquor. The residue obtained was dissolved in toluene (2.5 L) toluene layer was washed with brine (3 x 750 ml) Toluene was removed under reduced pressure. Methanol (1.5 L) was added to the residue and stirred at 35°C for 2 hr. Reaction mass was cooled to 0°C, filtered, washed with (2 x 500 ml) chilled methanol & dried to get pure Trityl Olmesartan Medoxomil (200g).

WE CLAIM :

- 1) An improved process for the preparation of Olmesartan medoxomil which comprises
 - i) alkylating the ethyl 4-(1-hydroxy-1-methylethyl)-2-propylimidazole-5-carboxylate with 4-[2-(trityltetrazol-5-yl) phenyl]benzyl bromide in presence of catalyst and base in the organic solvent to obtain ethyl 4-(1-hydroxy-1-methylethyl)-2-propyl-1-{4-[2-(trityl tetrazol-5-yl)phenyl] phenyl} methylimidazole-5-carboxylate,
 - i) hydrolyzing ethyl 4-(1-hydroxy-1-methylethyl)-2-propyl-1-{4-[2-(trityl tetrazol-5-yl) phenyl] phenyl} methyl imidazole-5-carboxylate to obtain trityl Olmesartan dihydrate,
 - ii) esterifying trityl Olmesartan dihydrate with 4-chloromethyl-5-methyl-2-oxo-1,3-dioxolene in the organic solvent in presence of base and catalyst to obtain trityl Olmesartan medoxomil,
 - iii) deprotecting the trityl Olmesartan medoxomil to obtain Olmesartan medoxomil
- 2) The process according to claim 1, wherein the catalyst employed is selected from phase transfer catalyst like tetrabutyl ammonium bromide, tetrabutyl ammonium iodide, tetrapropyl ammonium bromide, tri butyl benzyl ammonium bromide, tetraoctyl ammonium bromide, tetra butyl ammonium hydrogen sulphate, benzyl trimethyl ammonium chloride, benzyl triethyl ammonium chloride, tetrabutyl ammonium acetate, ethyl triphenyl phosphonium bromide, alkyl iodides selected from potassium iodide, sodium iodide and lithium iodide
- 3) The process according to claim 1, wherein the base employed is selected from

alkali metal carbonates such as sodium carbonate, potassium carbonate, alkali metal hydrogen carbonates such as sodium hydrogen carbonate or potassium hydrogen carbonate, alkali metal hydrides such as sodium hydride, potassium hydride or lithium hydride, alkali metal alkoxides such as sodium methoxide, sodium ethoxide, potassium t-butoxide or lithium methoxide, organic amines such as triethylamine, pyridine, *N*-methyl morpholine

- 4) The process according to claim 1, wherein the organic solvent used is selected from aromatic hydrocarbons such as benzene, toluene or xylene, ethers such as tetrahydrofuran or dioxane, alcohols such as methanol, ethanol, or t-butanols, amides such as *N,N*-dimethylacetamide, *N,N*-dimethylformamide or *N*-methyl-2-pyrrolidinone, ketones such as acetone or methyl ethyl ketone, nitriles such as acetonitrile, sulfoxides such as dimethyl sulfoxide, halogenated aliphatic hydrocarbons such as methylene chloride,
- 5) An improved process for preparing Olmesartan medoxomil comprising :
 - i) contacting trityl Olmesartan medoxomil with an acid in water and water-immiscible organic solvent
 - ii) separating aqueous and organic layers
 - iii) adjusting the pH of aqueous layer with base
 - iv) extracting the resulting solution of step (iii) with water miscible organic solvents and
 - v) isolating Olmesartan medoxomil
- 6) The process according to claim 5 step (i), wherein the acid is selected from organic acids such as formic acid, acetic acid, benzoic acid, and oxalic acid, oxoacids such as sulfuric acid, sulfurous acid, *p*-toluene sulfonic acid, nitric acid, nitrous acid, phosphoric acid, and carbonic acid; and binary acids such as hydrofluoric acid, hydrochloric acid, hydrobromic acid, hydrocyanic acid, and hydrosulfuric acid.

- 7) The process according to claim 5 step (i), wherein the water-immiscible organic solvent is selected from hydrocarbons such as benzene, cyclohexane, toluene, xylene, aliphatic solvents which includes halocarbons such as methylene chloride, chloroform, ketones such as methyl isobutyl ketone, and carboxylic esters such as ethyl acetate
- 8) The process according to claim 5 step (iii) wherein the pH is adjusted with a base selected from sodium hydroxide, potassium hydroxide, calcium hydroxide, magnesium hydroxide, sodium carbonate, potassium carbonate, sodium bicarbonate, potassium bicarbonate, and calcium carbonate more preferably potassium carbonate or sodium bicarbonate.
- 9) The process according to claim 5 step (iv) wherein the extraction is performed using water-immiscible organic solvent selected from ethyl ether, isopropyl ether, ethyl acetate, *n*-propyl acetate, methyl isobutyl ketone, cyclohexanone, tert.amyl alcohol, 2-ethyl-1-hexanol
- 10) Trityl Olmesartan dihydrate
- 11) Trityl Olmesartan dihydrate as claimed in claim 11, wherein the moisture content is in the range of 4.0-6.0 % w/w
- 12) Use of Trityl Olmesartan dihydrate in the preparation of Olmesartan modoxomil.