(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
22 October 2009 (22.10.2009)

PCT

(10) International Publication Number
WO 2009/128088 A2

(51) International Patent Classification:
COIC 209/62 (2006.01) *C07C 311/16* (2006.01)

(21) International Application Number:
PCT/IN2008/000725

(22) International Filing Date:
3 November 2008 (03.1 1.2008)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
923/CHE/2008 15 April 2008 (15.04.2008) IN

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(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, 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, PG, PH, **PL, PT,** RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, **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, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, **FI,** FR, GB, GR, HR, HU, IE, IS, **IT, LT,** LU, LV, MC, MT, NL, NO, PL, **PT,** RO, SE, SI, SK, 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 the applicant's entitlement to claim the priority of the earlier application (Rule 4.1 1(Hi))*

— *of inventorship (Rule 4A l(Iv))*

Published:

— *without international search report and to be republished upon receipt of that report (Rule 48.2(g))*

(54) Title: PREPARATION OF 2-(2-ALKOXY PHENOXY) ETHYLAMINE, AN INTERMEDIATE OF CARVEDILOL AND TAMSULOSIN

(57) Abstract: The present patent application relates to a process for the preparation of 2-(2-Alkoxy phenoxy) ethylamine or a salt thereof, which is a useful intermediate in the preparation of several active pharmaceutical ingredients including Carvedilol and Tamsulosin. It also provides 2-(2-methoxy phenoxy) ethylamine in solid form.

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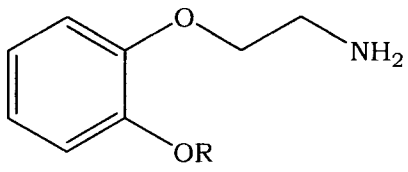
PREPARATION OF 2-(2-ALKOXY PHENOXY) ETHYLAMINE, AN INTERMEDIATE OF CARVEDILOL AND TAMSULOSIN

FIELD

The present patent application relates to a process for the preparation of 2-(2-Alkoxy phenoxy) ethylamine or a salt thereof, which is a useful intermediate in the preparation of several active pharmaceutical ingredients including Carvedilol and Tamsulosin.

BACKGROUND

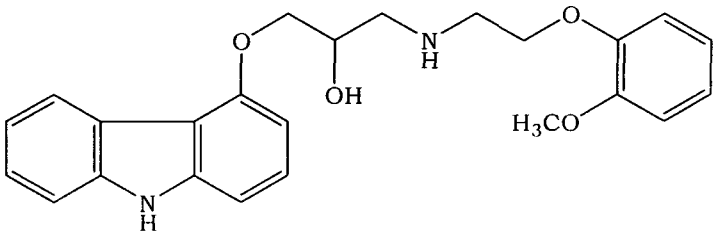
2-(2-Alkoxy phenoxy) ethylamine is chemically represented by the structural Formula I and is a useful intermediate in the preparation of several active pharmaceutical ingredients including Carvedilol and Tamsulosin.



Formula I

wherein R is C1-C4 alkyl.

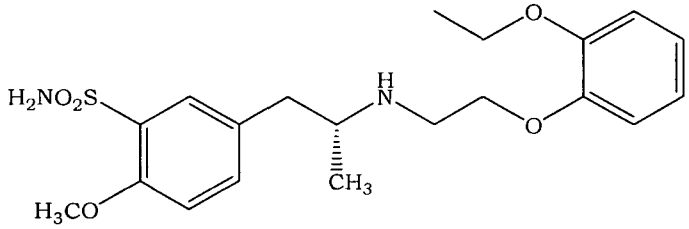
Carvedilol is a non- selective beta blocker indicated in the treatment of mild to moderate congestive heart failure (CHF), hyper tension (high blood pressure), angina and is marketed under various trade names including Coreg (GSK), Dilatrend (Roche) and Eucardic (Roche). Carvedilol is chemically represented by the following structural Formula II



Formula II

U.S. Patent. No. 4,503,067 discloses a process for preparing Carvedilol and its salts by the reaction of 4-(oxiran-2-ylmethoxy)-9H-carbazole with 2-(2-Methoxy phenoxy) ethylamine.

Tamsulosin, an antagonist of alphalA adrenoceptors in the prostate, is chemically described as (-)-(i?)-5-[2-[[2-(o-Ethoxyphenoxy) ethyl]amino]propyl]-2- methoxybenzenesulfonamide and represented by the structural formula III



Formula III

U.S. Patent No. 4,731,478 discloses Tamsulosin, its derivatives and salts along with processes for their preparation using 2-(2-ethoxyphenoxy) ethylamine.

From the abstract of CH 383998 it appears to describe a process for preparation of 2-alkoxyphenoxyethanamines in which liquid ammonia is reacted with 2-Methoxyphenoxyethylbromide in methanol. The mixture is heated for ten hours in an autoclave. This process leads to di & tri substituted amines as side products resulting in less yield. Complicated isolated procedure and the usage of liquid ammonia make the process expensive and not suitable for commercial manufacturing.

U.S. Patent No. 3,412,154 discloses a process for synthesis of 2-(2-Methoxyphenoxy) ethylamine that involves the usage of toxic, corrosive and hazardous substance of chloroacetonitrile and pressurized catalytic hydrogenation in presence of Raney cobalt catalyst. This process results in high manufacturing cost and unsafe reaction procedures.

U.S. Patent No. 3,474,134 discloses a process for synthesis of 2-(2-Methoxy phenoxy) ethylamine that involves reaction of l-bromo-2-(2-methoxy phenoxy) ethane with potassium Phthalimide in Dimethyl formamide (DMF) and the Phthalimide derivative was then treated with hydrazine hydrate. Hydrazine hydrate is believed to be toxic, corrosive

and hazardous substance which is not suitable for commercial manufacturing.

International Application publication No. WO 99/51576 discloses a process for synthesis of 2-(2-Methoxy phenoxy) ethylamine that involves reacting Guaiacol with Bromo-acetonitrile in presence of NaH and DMF, which is further reacted with Lithium aluminium hydride ($LiAlH_4$) in presence of ethyl ether. The usage of reagents such as NaH and $LiAlH_4$ are hazardous and not suitable for safe commercial manufacturing.

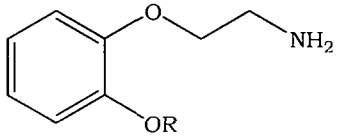
International Application publication No. WO 03/095416 discloses a synthesis of 2-(2-alkoxy phenoxy) ethylamine by the reaction of ortho substituted phenol with a 2-Alkyloxyoxazoline.

2-(2-alkoxy phenoxy) ethylamine prepared according to the above mentioned processes was obtained in the form of liquid which is difficult to store and further more difficult to handle.

Consequently, it would be a contribution to the art to provide a scalable, highly pure and safe process for the preparation of 2-(2-Alkoxy phenoxy) ethylamine and its salts using commercially available raw materials

SUMMARY OF THE INVENTION

In one aspect the present application provides a process for preparation of 2-(2-Alkoxy phenoxy) ethylamine of Formula I

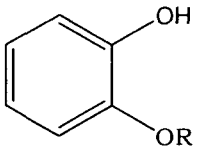


Formula I

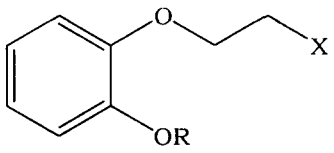
wherein R is C 1-C4 alkyl,

comprising the steps of:

a) reacting 2-alkoxy phenol of Formula IV with 1,2-dihalo ethane to obtain l-halo-2-(2-alkoxy phenoxy) ethane of Formula V;



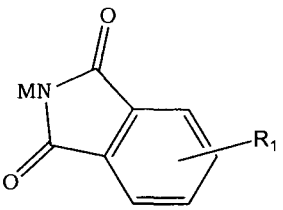
Formula IV



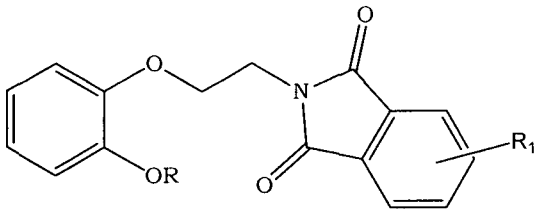
Formula V

Wherein R is C1-C4 alkyl; and X is F, Cl, Br, I;

b) reacting l-halo-2-(2-alkoxy phenoxy) ethane of Formula V with an alkali metal salt of Phthalimide or substituted Phthalimide of Formula VI to form compound of Formula VII; and



Formula VI



Formula VII

wherein R is C1-C4 alkyl; R_1 is H or C1-C4 alkyl, M is Na, K or any alkali metal.

c) reacting compound of Formula VII with a base comprising alkali metal hydroxide.

In this multi step process, each step may be contemplated individually or combination of two steps.

In another aspect, the present invention provides a process for the preparation of 2-(2-methoxyphenoxy)ethylamine of Formula 1 in solid form.

In another aspect the present application relates to use of 2-(2-Alkoxy phenoxy) -ethylamine or salt there of in the synthesis of active pharmaceutical ingredients including Carvedilol and Tamsulosin.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig 1 is an illustrative DSC thermogram of 2-(2-methoxy phenoxy)ethylamine in solid form obtained according to Example 4.

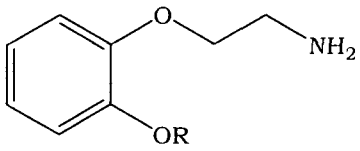
Fig 2 is an illustrative Infrared spectrum (IR) of 2-(2-methoxy phenoxy)ethylamine in solid form obtained according to Example 4.

DETAILED DESCRIPTION OF THE INVENTION

The present patent application relates to a process for the preparation of 2-(2-Alkoxy phenoxy) ethylamine or a salt thereof, which is a useful intermediate in the preparation of several active pharmaceutical

ingredients.

In one aspect the present application provides a process for preparation of 2-(2-Alkoxy phenoxy) ethylamine of Formula I

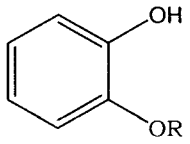


Formula 1

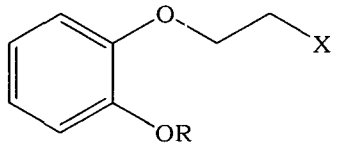
wherein R is C1-C4 alkyl,

comprising the steps of:

a) reacting 2-alkoxy phenol of Formula IV with 1,2-dihalo ethane to obtain l-halo-2-(2-alkoxy phenoxy) ethane of Formula V;



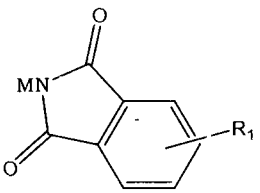
Formula IV



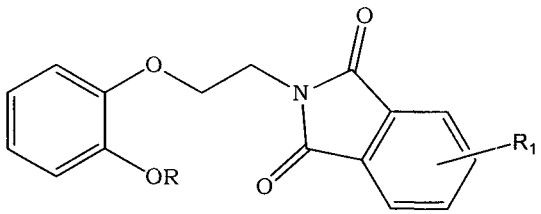
Formula V

wherein R is C1-C4 alkyl; and X is F, Cl, Br, I;

b) reacting l-halo-2-(2-methoxy phenoxy) ethane of Formula V with an alkali metal salt of Phthalimide or substituted Phthalimide of Formula VI to form compound of Formula VII; and



Formula VI



Formula VII

wherein R is C1-C4 alkyl; Ri is H or C1-C4 alkyl, M is Na, K or any alkali metal

c) reacting compound of Formula VII with a base comprising alkali metal hydroxide.

Step a) involves 2-alkoxy phenol of Formula IV with 1,2-dihalo ethane.

2-alkoxy phenol includes C1-C4 alkoxy phenols, preferably 2-methoxy phenol and 2-ethoxy phenol.

1,2-Dihaloethane is selected form 1,2-dichloroethane, 1,2-dibromoethae and the like. 1,2-dichloroethane is preferred. The reaction may be carried out with or without an external solvent. Suitably the 1, 2-dihaloethane acts both as reagent and solvent.

Suitably the reaction is carried out in the presence of a base. Suitable base that can be used include alkali metal hydroxides such as sodium hydroxide, potassium hydroxide and the like.

In one variant, the reaction of step a) may be carried out in the presence of a phase transfer catalyst. Suitable phase transfer catalyst includes but is not limited to tetra butyl ammonium bromide(TBAB), methyltrioctylammonium chloride, potassium bromide, and the like. Tetra butyl ammonium bromide is preferred.

Suitable temperatures for conducting the reaction can range from about 25°C to about reflux temperature of the solvent used, preferably reflux temperature of the solvent used. The reaction can be conducted till the completion of the reaction. Typically the reaction time varies from about 1 hour to about 15 hours.

After completion of the reaction, the organic layer containing the product may be separated, washed with water and proceeds to next step directly or it can be distilled to obtain the product as residue.

In one embodiment the l-halo-2-(2-alkoxy phenoxy) ethane obtained as residue may be purified by using suitable techniques including high vacuum distillation.

Step b) involves reacting l-halo-2-(2-alkoxy phenoxy) ethane of Formula V with an alkali metal salt of Phthalimide or substituted Phthalimide of Formula VI to form the compound of Formula VII.

Phthalimide derivative or an alkali metal salt that can be used include alkali metal salt of Phthalimide or a substituted Phthalimide such as sodium phthalimide, potassium phthalimide, sodium or potassium salt of methyl or ethyl phthalimide, preferably potassium phthalimide.

In one embodiment, the reaction of step b) may also be carried out in the presence of phase transfer catalyst. Suitable phase transfer

catalyst includes but is not limited to tetra butyl ammonium bromide, methyltrioctylammonium chloride, potassium bromide, and the like. Tetra bµtyl ammonium bromide is preferred.

The reaction can be carried out with or without an external solvent. Preferably the reaction is carried out with out an external solvent.

Suitable temperatures for conducting the reaction can range from about 50°C to about 250 °C, preferably from about 180°C to about 190 °C. The reaction can be conducted till the completion of the reaction. Typically the reaction time varies from about 30 minutes to about 5 hours.

The molar ratio of l-halo-2-(2-alkoxy phenoxy) ethane to Phthalimide derivative can range from about 1:0.5 to about 1:5.

After completion of the reaction, the reaction mixture is quenched with water and processed using suitable techniques for precipitation of the solid.

The solid product thus obtained may be further purified by methods such as precipitation, crystallization or slurrying in a solvent. Solvents that may be used for such purposes include, but are not limited to alcohols such as methanol, ethanol, isopropanol and the like; esters such as ethyl acetate, n-propylacetate, isopropyl acetate and the like; ketones such as acetone, ethyl methyl ketone and the like; acetonitrile, water or mixtures thereof.

The solid product is recovered by suitable techniques such as decantation, filtration by gravity or by suction, centrifugation, and the like. Other techniques for separating the solids from the reaction mixtures are also within the scope of this invention. The process may include further drying of the product obtained with or without vacuum and in presence or absence of inert atmosphere.

Step c) involves reacting compound of Formula VII with a base comprising alkali metal hydroxide.

Suitable bases that can be used include alkali metal hydroxide such as sodium hydroxide, potassium hydroxide and the like

Alkali metal hydroxide may be used in the form of solid or as a solution obtained by dissolving alkali metal hydroxide in water.

Reaction may be conducted without an additional solvent, when alkali metal hydroxide solution is used or solvents such as water may be used.

Suitable temperatures for conducting the reaction can range from about 50°C to about 250 °C, preferably from about 100°C to about 120 °C. The reaction can be conducted till the completion of the reaction. Typically the reaction time varies from about 1 hour to about 15 hours.

The molar ratio of compound of Formula VII to alkali metal hydroxide can range from about 1:1 to about 1:10.

After completion of the reaction, the reaction mixture is quenched with water and processed using suitable techniques for precipitation of the solid.

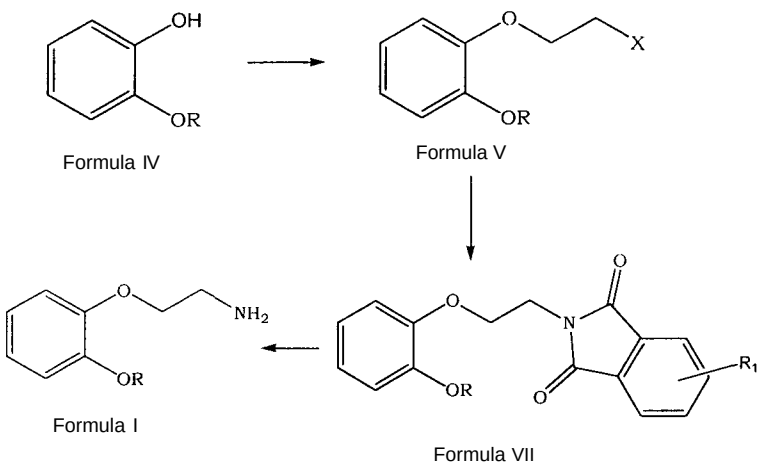
The solid product is recovered by suitable techniques such as decantation, filtration by gravity or by suction, ccntπfugation, and he like. The product may be further dried. Drying can be carried out in a tray dryer, vacuum oven, air oven, fluidized bed drier, spin flash dryer at temperatures of about 35°C to about 70°C with or without vacuum.

In a more specific embodiment of the present invention, the 2-(2-alkoxy-phenoxy) ethylamine of Formula 1 is prepared in solid form having melting range from about 80°C to 90°C.

Differential scanning calorimetric analysis reported herein was carried out on TAQlOOO. The thermogram was recorded from 40°C to 150°C under the nitrogen flow of 50mL/min at a heating rate of 2°C/min

In a specific embodiment of the present invention, 2-(2-Methoxy-phenoxy) ethylamine is prepared from 2-methoxy phenol and 2-(2-ethoxy-phenoxy) ethylamine is prepared from 2-ethoxy phenol.

The process of the present application is described in Scheme I.



Scheme I

In this multi step process, each step may be contemplated individually or combination of two steps.

In another aspect the present application relates to use of 2-(2-Alkoxy phenoxy)-ethylamine or a salt there of in the synthesis of active pharmaceutical ingredients including Carvedilol and Tamsulosin.

This process of the present application involves the usage of inexpensive, less hazardous and easily available raw materials and makes the process suitable for commercial manufacturing.

Certain specific aspects and embodiments of the present application will be explained in more detail with reference to the following examples, which are provided by way of illustration only and should not be construed as limiting the scope of the invention in any manner.

Examples

Example 1: Preparation of l-(2-Chloro ethoxy)-2-methoxy benzene

2-Methoxy phenol (200 kg) in 1000 L of 1,2-dichloroethane, 300 L of caustic lye and 14 kg of tetrabutyl ammonium bromide were heated to reflux and stirred for about for 16 hours. Cooled the reaction mixture to ambient temperature and separated the layers. Aqueous layer was extracted with dichloroethane (2 X 200 L). Total organic layer was washed with water and distilled off the solvent completely under the vacuum to get the residue (310 kg). The residue was further purified by

high vacuum distillation to obtain 210 kg of pure l-(2-Chloro ethoxy)-2-methoxy benzene.

Example 2: Preparation of Phthalimide derivative of l-(2-Chloro-ethoxy)-2-methoxy-benzene

150 kg of pure l-(2-Chloro ethoxy)-2-methoxy benzene obtained according to the procedure described in Example 1, 195 kg of Potassium Phthalimide and 7.5 kg of tetrabutyl ammonium bromide were charged in a reactor and heated to about 180 °C and stirred for about 3 hours at about 180 °C to 185 °C. The reaction mixture was transferred in to a container having 1650 L of water and the precipitated solid was filtered. The wet material (300 kg) was charged into a reactor containing 300 L of methanol and heated to reflux. The contents were stirred at reflux for about 1 hour. The reaction mixture was cooled to ambient temperature and filtered the solid .The wet solid was dried at 60-80 °C to obtain 2-10 kg of the title compound.

Example 3: Preparation of 2-(2-Methoxy phenoxy) ethylamine

50 gm of potassium hydroxide was dissolved in 50 ml of water and 50 gm of Phthalimide derivative of l-(2-Chloroethoxy)-2-methoxy benzene was added to the solution. The contents were heated to about 130 °C and stirred for about 13 hours. The reaction mixture was cooled and ambient temperature and extracted with 2 X 200 ml of dichloromethane (DCM). 20 ml of 36% aqueous hydrochloric acid was added to the organic layer and stirred the contents for 15 minutes and separated the layers. The aqueous layer was washed with DCM (2 X 25 ml) and then pH was adjusted to about 8 using aqueous sodium hydroxide solution. The aqueous layer was extracted with toluene (2 XlOO ml) and distilled off the solvent completely to obtain 20 gm of the title compound as residue.

Purity by HPLC: 98.05 %

Example 4: Preparation of 2-(2-methoxyphenoxy) ethylamine in solid form:

Add 10 ml of water to 100 gm of crude 2-(2-methoxyphenoxy) ethylamine (obtained from the procedure of Example 3) and allowed the crude to dry for 36 hours to get the wet solid (100 gm). The wet solid (100 gm) was taken into round bottom flask and added (200 ml) of ethyl acetate and maintained for half an hour at room temperature. The solid was filtered, washed with 50 ml of ethyl acetate and dried to get 73.5 gm of the title compound in the form of solid.

M.R: 84 °C - 87 °C

Purity by HPLC: 99.71%

Example 5: Preparation of Carvedilol using 2-(2-methoxyphenoxy) ethylamine solid:

In a dry reaction flask, 4-(2,3-epoxy propoxy) carbazole (50 gm), 2-(2-methoxy phenoxy) ethyl amine solid (75.5 gm) and 500 ml of ethyl acetate were charged and heated to reflux for about 24 hours. After completion of the reaction, solvent was distilled off from the reaction mixture to obtain 117 gm of the residue. Ethyl acetate (175 ml) was added to the residue and stirred for about 12 hours at room temperature. The suspension was cooled to 0 °C, filtered and dried to get 65 gm of the title compound.

M.R: 115 °C-117°C

Purity by HPLC: 99.74%

Example 6: Preparation of 2-(2-Methoxy phenoxy) ethylamine using NaOH

50 gm of Phthalimide derivative of l-(2-Chloroethoxy)-2-methoxy benzene was added to 50 ml 48 % aqueous sodium hydroxide solution (Caustic lye) in 50 ml of water. The contents were heated to about 130 °C and stirred for about 13 hours. The reaction mixture was cooled and ambient temperature and charged 100 ml of toluene. The aqueous layer was separated and extracted with toluene (1 XlOO ml; 1 X50 ml) and dried the total organic layer with 20 gm of sodium chloride. The organic

layer was distilled completely to obtain 21.5 gm of the title compound as residue.

Purity by HPLC: 98.74 %

Example 7: Preparation of l-(2-chloroethoxy)-2-ethoxy benzene

100 gm of 2-ethoxy phenol was added to 150ml of caustic lye dissolved in 450 ml of water at 25-35°C. 500 ml of 1,2-dichloroethane and 7 gm of TBAB was added to the above reaction mixture at 25-35°C and heated to reflux for about 16 hours. After completion, the reaction mixture was cooled to 25-35°C and separated the layers. Aqueous layer was extracted with dichloroethane (2XlOOmI). Total organic layer was washed with 5% caustic lye and distilled off the solvent completely to get residue (140 gm). The residue was further purified by high vacuum distillation to get 112 gm of pure title compound.

Example 8: Preparation of phthalimide derivative of l-l-(2-chloroethoxy)-2-ethoxy benzene:

About 70 gm of l-(2-chloroethoxy)-2-ethoxy benzene obtained from Example 5, 91 gm of potassium phthalimide and 3.5 gm of TBAB were charged in a reactor and heated to 175-185°C and stirred for about 4 hours. The reaction mixture was cooled to about 80°C, 800 ml of water was added and cooled further to 25-35°C. The contents were stirred for about 2 hours, filtered the reaction mixture and washed with 200 ml of water to get 136 gm of wet solid. The wet material was dissolved in 200 ml of methanol, heated to reflux and maintained for about 30 minutes at 60-70°C. Cooled the reaction mixture to 25-35°C and stirred for about 2 hours. The reaction mixture was filtered and washed with methanol. The wet solid was dried to get 98.5 gm of title compound.

Example 9: Preparation of 2-(2-ethoxy phenoxy) ethylamine:

About 50 gms of phthalimide derivative of l-l-(2-chloroethoxy)-2-ethoxy benzene obtained from Example 6, 50 gm of potassium hydroxide and 50 ml of water were charged in a flask. The contents were heated to

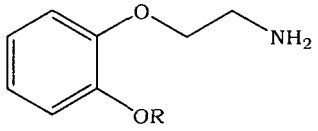
reflux and maintained for about 6 hours. After completion of the reaction, the reaction mixture was cooled to room temperature and extracted with 200 ml of toluene. The organic layer was acidified with aqueous HCl and 250 ml of water was added to the organic layer. Separated the layers, the aqueous layer was basified with caustic lye and extracted into dichloromethane (300, 100, 100 ml.). The total organic layer was washed with water, dried with sodium sulfate and distilled off to remove the solvent completely to get 23 grams of the title compound as residue.

Example 10: Preparation of Phthalimide derivative of l-(2-Chloro-ethoxy)-2-methoxy -benzene.

50 gm of pure l-(2-Chloro ethoxy)-2-methoxy benzene obtained according to the procedure described in Example 1, 65 gm of Potassium Phthalimide and 2.5gm of tetra butyl ammonium bromide were charged in a flask and heated to about 180°C and stirred for about 3 hours at about 180°C to 185°C. The reaction mixture was cooled to below 100^0C, added 25 ml of methanol, maintained at reflux. Cool to room temperature and filtered the solid to obtain 63 gm of the title compound

Claims:

1. A process for preparation of 2-(2-Alkoxyoxy phenoxy) ethylamine of Formula I

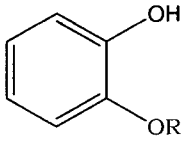


Formula J

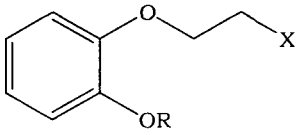
wherein R is C1-C4 alkyl,

comprising the steps of:

a) reacting 2-alkoxy phenol of Formula IV with 1,2-dihalo ethane to obtain l-halo-2-(2-alkoxy phenoxy) ethane of Formula V;



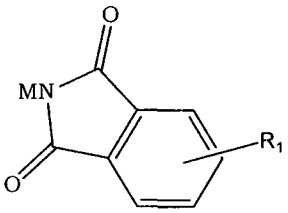
Formula IV



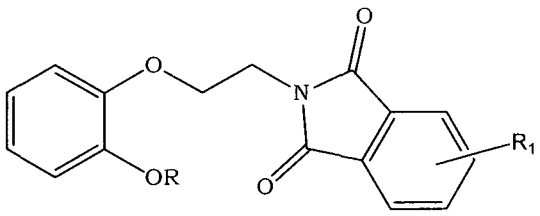
Formula V

wherein R is C1-C4 alkyl; and X is F, Cl, Br, I;

b) reacting l-halo-2-(2-methoxy phenoxy) ethane of Formula V with an alkali metal salt of Phthalimide or substituted Phthalimide of Formula VI to form compound of Formula VII; and



Formula VI



Formula VII

wherein R is C1-C4 alkyl; Ri is H or C1-C4 alkyl, M is Na, K or any alkali metal

c) reacting compound of Formula VII with a base comprising alkali metal hydroxide.

2. The process of Claim 1 wherein 2-alkoxy phenol used in step a) includes 2-methoxy phenol and 2-ethoxy phenol.

3. The process of Claim 1 wherein 1,2-Dihaloethane used in step a) is selected form 1,2-dichloroethane and 1,2-dibromoethane.

4. The process of Claim 1 wherein the process of step a) is carried out in the presence of a base selected from alkali metal hydroxides such as sodium hydroxide, potassium hydroxide.

5. The process of Claim I wherein the process of step a) is carried out in the presence of a phase transfer catalyst selected from tetra butyl ammonium bromide and methyltrioctylammonium chloride

6. The process of Claim 1 wherein Phthalimide derivative or an alkali metal salt used in step b) is selected from sodium phthalimide, potassium phthalimide, sodium or potassium salt of methyl or ethyl phthalimide.

7. The process of Claim 1 wherein the process of step b) is carried out in the presence of a phase transfer catalyst selected from tetra butyl ammonium bromide and methyltrioctylammonium chloride,

8. The process of Claim 1 wherein the process of step b) is carried put with out any solvent.

9. The process of Claim 1 wherein the process of step b) is carried out at temperatures from about 50°C to about 250 °C.

10. The process of Claim 1 wherein the molar ratio of l-halo-2-(2-methoxy phenoxy) ethane to Phthalimide derivative used in step b) range from about 1:0.5 to about 1:5.

11. The process of Claim 1 wherein the process of step c) is carried out in the presence of a base selected from alkali metal hydroxide such as sodium hydroxide, potassium hydroxide.

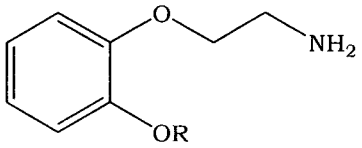
12. The process of Claim 1 wherein the process of step c) is carried out without any additional organic solvent, when alkali metal hydroxide solution is used.

13. The process of Claim 1 wherein the process of step c) is carried out at temperatures from about 50°C to about 250 °C.

14. The process of Claim 1 wherein the molar ratio of compound of Formula VII to alkali metal hydroxide in step c) can range from about 1:1 to about 1:10.

15. The process of Claim 1 wherein the compound of formula I is obtained in the form of solid powder or oily residue.

16. A process for preparation of 2-(2-Alkoxy phenoxy) ethylamine of Formula I

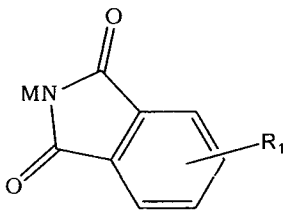


Formula I

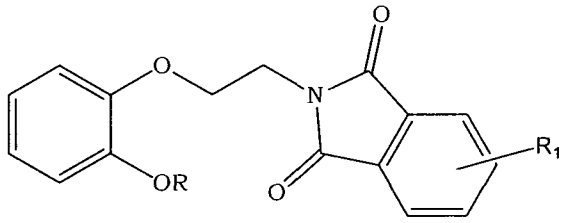
wherein R is C1-C4 alkyl,

comprising the steps of:

a) reacting l-halo-2-(2-alkoxy phenoxy) ethane of Formula V with an alkali metal salt of Phthalimide or substituted Phthalimide of Formula VI to form compound of Formula VII; and



Formula VI

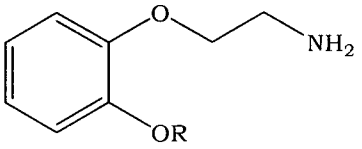


Formula VII

wherein R is C1-C4 alkyl; R_1 is H or C1-C4 alkyl, M is Na, K or any alkali metal

b) reacting compound of Formula VII with a base comprising alkali metal hydroxide.

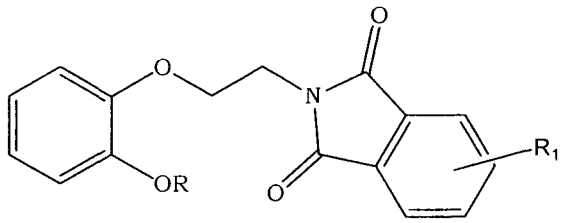
16. A process for preparation of 2-(2-Alkoxy phenoxy) ethylamine of Formula I



Formula I

wherein R is C1-C4 alkyl,

comprises of reacting compound of Formula VII



Formula VII

with a base comprising alkali metal hydroxide.

18. A process for preparation of 2-(2-methoxy phenoxy) ethylamme comprising the steps of:

a) reacting l-chloro-2-(2-methoxy phenoxy) ethane with potassium phthalimide; and

b) reacting the product obtained in step a) with potassium hydroxide.

19. 2-(2-methoxy phenoxy) ethylamine in solid form.

20. A process for the preparation of Carvedilol or a salt there of using 2-(2-methoxy phenoxy) ethylamine in solid form

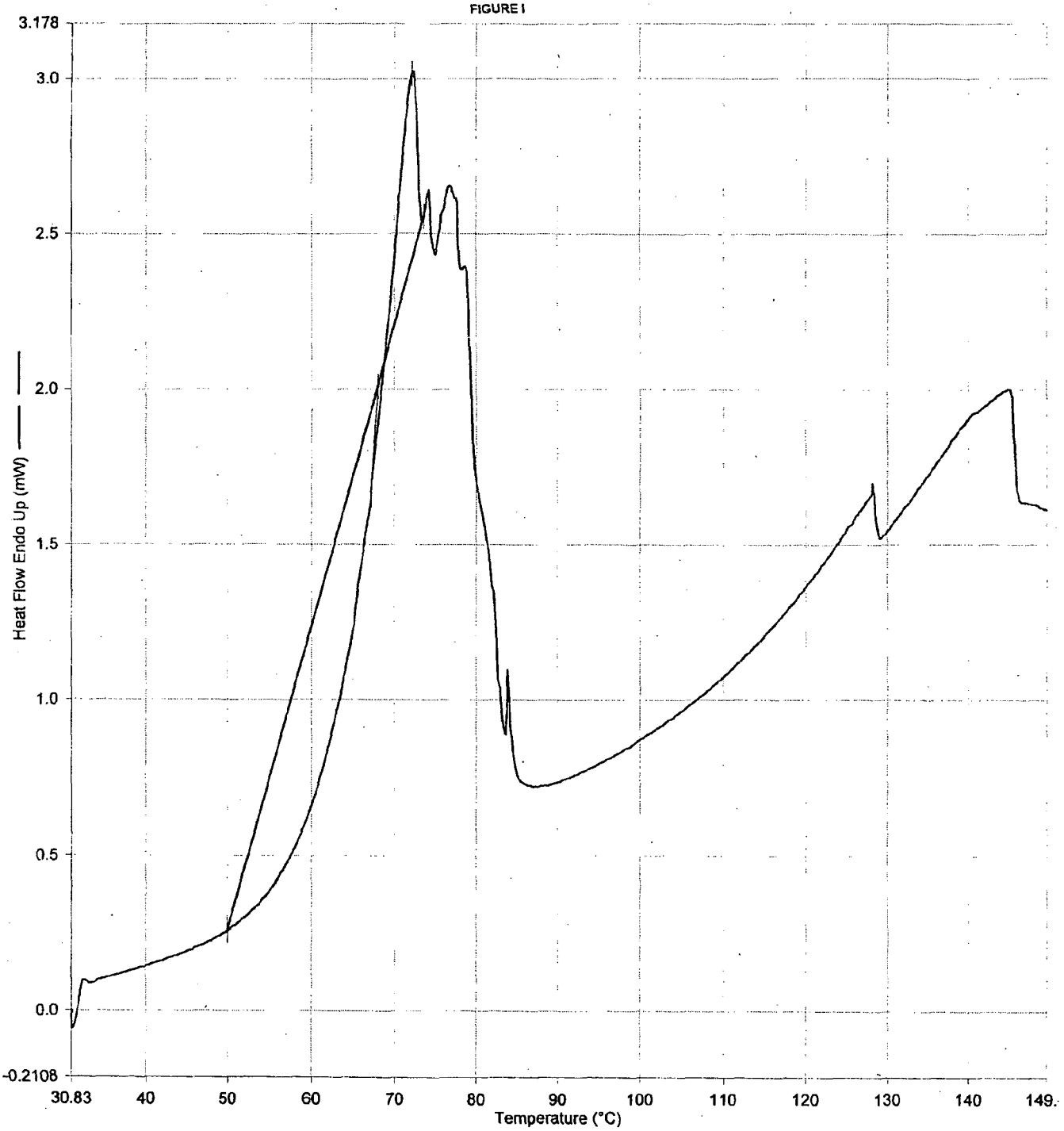
21. A process for preparation of 2-(2-ethoxy phenoxy) ethylamine comprising the steps of:

a) reacting l-chloro-2-(2-ethoxy phenoxy) ethane with potassium phthalimide; and

b) reacting the product obtained in step a) with potassium hydroxide.

22. A method of using of 2-(2-Alkoxy phenoxy)-ethylamine or s salt there of in the synthesis of active pharmaceutical ingredients including Carvedilol and Tamsulosin.

FIGURE I


3.178
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.2108
Heat Flow Endo Up (mW)
30.83
40
50
60
70
80
90
100
110
120
130
140
149.
Temperature (°C)

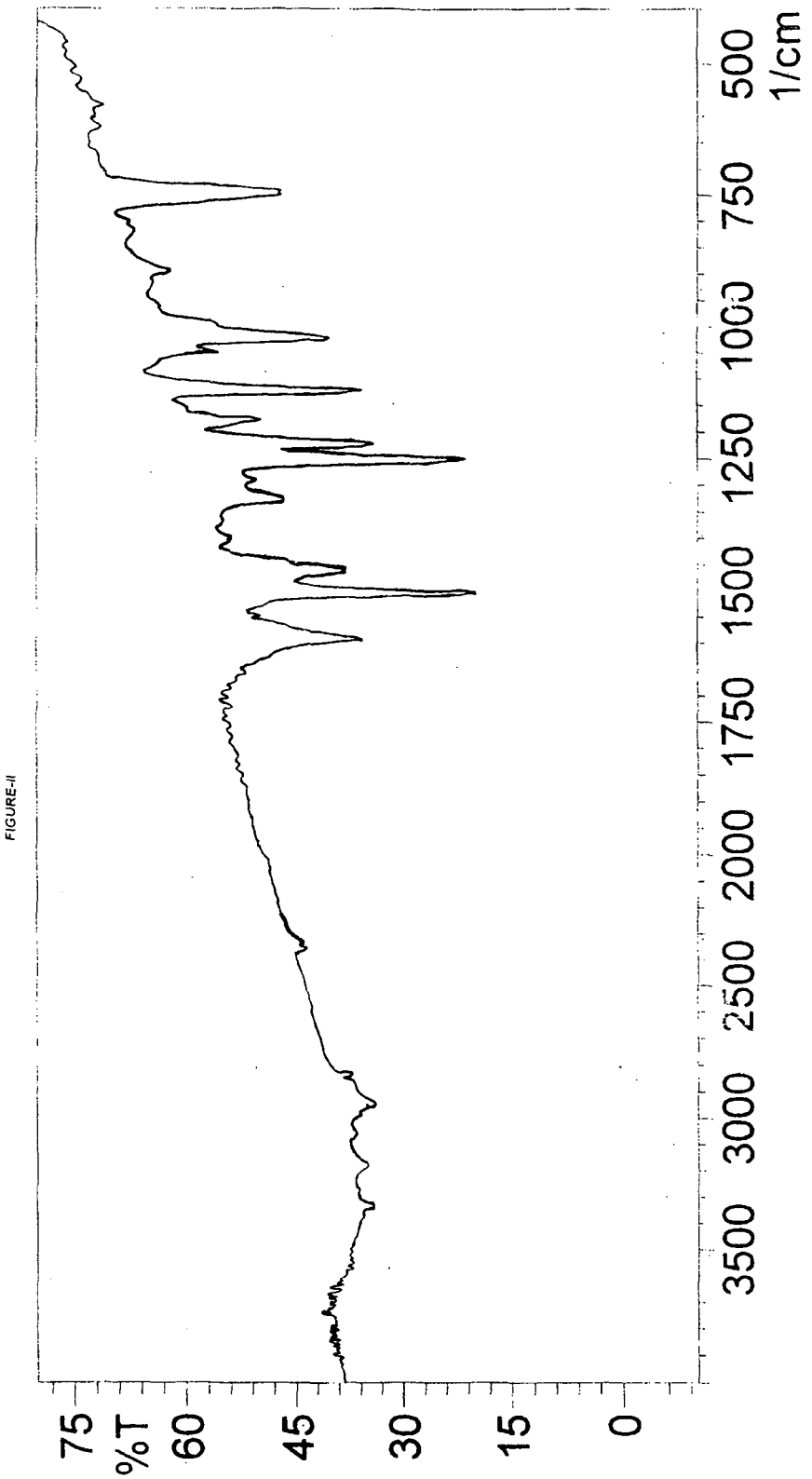

75
%T
60
45
30
15
0
3500
3000
2500
2000
1750
1500
1250
1000
750
500
1/cm

FIGURE-II