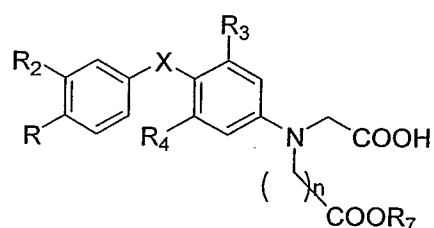


SELECTIVE TR-BETA 1 AGONIST

FIELD OF INVENTION

The present invention relates to novel compounds of general formula (I) which are thyroid receptor (TR) ligands and are preferably selective for the thyroid hormone receptor beta. Further, the present invention relates to processes of preparing such compounds, their tautomeric forms, novel intermediates involved in their synthesis, their pharmaceutically acceptable salts, methods for using such compounds and pharmaceutical compositions containing them.



(1)

BACKGROUND TO THE INVENTION

Thyroid hormone (Triiodothyronine; T₃) is an important endocrine signaling hormone and it is essential for normal development, differentiation and maintenance of metabolic balance in mammals. Natural thyroid hormone, T₃ exhibit its physiological effect by acting on a Thyroid Hormone Receptor (THR), which belongs to the nuclear hormone receptor super family. There are two different isoforms of Thyroid Hormone Receptors, THR- α and THR- β . Further these two isoforms are sub-classified as α 1; α 2 and β 1; β 2 subtypes. THR β 1 is prevalent in liver (85%), while THR α 1 is mainly present in cardiac tissue (Yen P. M., *Physiol. Rev*; 81 (2001) 1097-1142).

At normal levels, T₃ maintains bodyweight, metabolic rate, body temperature, mood and regulate serum cholesterol. Hypothyroidism is associated with weight gain, high levels of low-density lipoproteins (LDL) cholesterol and depression. Hyperthyroidism leads to weight loss, hypermetabolism, lowering of serum LDL levels, cardiac arrhythmia, heart failure, muscle weakness, bone loss and anxiety.

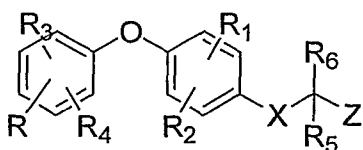
The natural thyroid hormone T₃ does not show any selectivity in binding to both of the THR isoforms (THR α 1 and THR β 1). Thus, administration of T₃ lowers plasma cholesterol, low-density lipoprotein (LDL) and triglyceride levels in animal

models and humans. However, T3 cannot be used therapeutically to treat hypercholesterolemia and obesity due to its cardiac side effects. However, knockout animal studies as well as results with some selective ligands suggest that such cardiac side effects can be attributed to the THR $\alpha 1$ isoform. Thus some effects of T3 may be therapeutically useful in non-thyroid disorders if adverse effects can be minimized or eliminated. These potentially useful influences include weight reduction, lowering of serum LDL levels, amelioration of depression and stimulation of bone formation (Cheng S., Steroids; 70 (2005); 450-454).

Development of specific and selective thyroid hormone receptor ligands, particularly THR $\beta 1$ agonist could lead to specific therapies for disorders such as obesity and hyperlipidemia, while avoiding the cardiovascular and other toxicities of native thyroid hormones. Thus, compounds mimicking only the beneficial effects of the thyroid hormone and lacking their cardiac side effects (tachycardia and arrhythmia) potentially could be used to treat a number of conditions such as obesity and dyslipidemia. In this regard, THR agonists that interact selectively with the $\beta 1$ isoform of the THR offer an especially attractive method for avoiding cardio-toxicity (J. D. Baxter; Trends Endocrinol. Metab., 15 (2004); 154-157).

Various compounds have been disclosed as possible agonists of THR β . Some of the more relevant ones for the present invention includes WO2007039125, WO 0039077, US20040157844 which are incorporated herein as reference.

US20020035153 describes compounds of the following general formula as Thyromimetics.

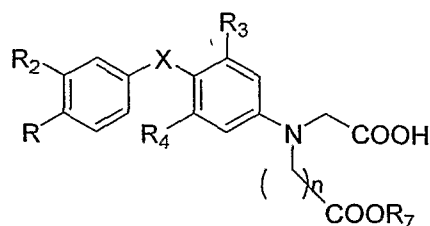


However, none of these compounds have been commercially developed and looking at the beneficial potential and medical need for such compounds, there remains a need for developing further compounds with better therapeutic and/or safety profile. Herein, we disclose novel compounds which shows activity as THR β agonists.

SUMMARY OF THE INVENTION

The present invention describes novel compounds that are thyroid receptor (TR) ligands and are preferably selective for the thyroid hormone receptor beta 1, which are

useful for the treatment of a number of conditions such as obesity and dyslipidemia. The novel compounds are defined by the general formula (I) as given below.



(1)

5 The compounds of the present invention are useful in the treatment of the human or animal body, by regulation of selective thyroid hormone receptor gene expression. The compounds of this invention are therefore suitable for the treatment/mitigation/regulation or prophylaxis of obesity and dyslipidemia.

PREFERRED EMBODIMENTS

10 The main objective of the present invention is to provide novel compounds of general formula (I), their tautomeric forms, novel intermediates involved in their synthesis, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates and pharmaceutical compositions containing them or their mixtures suitable for the treatment of obesity and dyslipidemia.

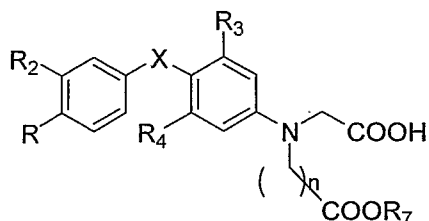
15 In an embodiment is provided a process for the preparation of novel compounds of general formula (I), their tautomeric forms, novel intermediates involved in their synthesis, their pharmaceutically acceptable salts, pharmaceutically acceptable solvates and pharmaceutical compositions containing them.

20 In another embodiment is provided pharmaceutical compositions containing compounds of general formula (I), their tautomeric forms, their pharmaceutically acceptable salts, solvates and their mixtures having pharmaceutically acceptable carriers, solvents, diluents, excipients and other media normally employed in their manufacture.

25 In a further another embodiment is provided the use of the novel compounds of the present invention for the treatment of obesity and dyslipidemia, by administering a therapeutically effective & non-toxic amount of the compound of formula (I), or their pharmaceutically acceptable compositions to the mammals.

DETAILED DESCRIPTION:

30 Accordingly, the present invention relates to compounds of the general formula (I),



(1)

wherein R = OR₁, NHR₁ wherein R₁ may be selected from H, optionally substituted groups selected from (C₁-C₆)alkyl, ar(C₁-C₆)alkyl groups; in a preferred embodiment the alkyl groups is selected from (C₁-C₃)alkyl and the aryl group represents optionally substituted phenyl group;

R₂ represents hydrogen, hydroxyl, halo, acyl, oxo, optionally substituted groups selected from (C₁-C₆)alkyl, (C₃-C₇)cycloalkyl, aryl, heteroaryl, alkoxy, aryloxy, aralkyl, aralkoxy, carboxylic acid and its derivatives selected from (C₁-C₃)alkyl esters and amides, sulphenyl derivatives, sulfonyl derivatives or the groups representing -CONR₅R₆, -SO₂NR₅R₆, wherein

R₅ & R₆ may be same or different and are independently selected from H, optionally substituted groups selected from (C₁-C₆)alkyl, (C₃-C₇)cycloalkyl, bicycloalkyl, aryl or the groups R₅ & R₆ together with the nitrogen atom to which they are attached, form a five to eight membered cyclic ring which may optionally contain one or more hetero atoms selected from N, S, O;

The substituents on R₂ may be selected from hydroxy, halo, optionally substituted groups selected from (C₁-C₆)alkyl, phenyl, heteroaryl groups;

In a preferred embodiment, the various groups representing R₂ may be selected from

- optionally substituted (C₁-C₆)alkyl, acyl, oxo, phenyl, heteroaryl, benzyl, carboxylic acid and its derivatives such as (C₁-C₃)alkyl esters and amides, or the groups representing -CONR₅R₆, -SO₂NR₅R₆, wherein R₅ and R₆ may be same or different and are independently selected from H, optionally substituted groups selected from (C₁-C₆)alkyl, (C₃-C₇)cycloalkyl, bicycloalkyl, phenyl or the groups R₅ & R₆ together with the nitrogen atom to which they are attached, form a five to eight membered cyclic ring which may optionally contain one or more hetero atoms selected from N, O;

R₃, R₄ may be same or different and are independently selected from H, halogen, optionally substituted (C₁-C₆)alkyl groups;

X is selected from O, -CH₂-, CO;

'n' represents 0 or 1;

R₇ represents H, optionally substituted groups selected from (C₁-C₆)alkyl, aryl groups; with the provision that when n = 0, R₇ does not represent 'H'.

5 The substituents on alkyl, aryl, heteroaryl or cycloalkyl groups may be selected from hydroxyl, halo, cyano, optionally substituted groups selected from (C₁-C₆)alkyl, haloalkyl, alkoxy, oxo, aryl, aryloxy, aralkyl, acyl, alkylthio, thioalkyl groups. When any of these groups are further substituted, the substituents on these substitutes may be selected from those described above.

10 In a further preferred embodiment the groups, radicals described above may be selected from:

- the "alkyl" group used either alone or in combination with other radicals, denotes a linear or branched radical containing one to six carbons, selected from methyl, ethyl, *n*-propyl, *iso*-propyl, *n*-butyl, *sec*-butyl, *tert*-butyl, amyl, *t*-amyl, *n*-pentyl, *n*-hexyl, *iso*-hexyl and the like;
- the "cycloalkyl" or "alicyclic" group used either alone or in combination with other radicals, is selected from a cyclic radical containing three to seven carbons, more preferably cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl and the like;
- 20 - the "alkoxy" group used either alone or in combination with other radicals, is selected from groups containing an alkyl radical, as defined above, attached directly to an oxygen atom, more preferably groups selected from methoxy, ethoxy, *n*-propoxy, *iso*-propoxy, *n*-butoxy, *t*-butoxy, *iso*-butoxy, pentyloxy, hexyloxy, and the like;
- 25 - the "haloalkyl" group is selected from an alkyl radical, as defined above, suitably substituted with one or more halogens; such as perhaloalkyl, more preferably, perfluoro(C₁-C₆)alkyl such as fluoromethyl, difluoromethyl, trifluoromethyl, fluoroethyl, difluoroethyl, trifluoroethyl, mono or polyhalo substituted methyl, ethyl, propyl, butyl, pentyl or hexyl groups;
- 30 - the "aryl" or "aromatic" group used either alone or in combination with other radicals, is selected from a suitable aromatic system containing one, two or three rings wherein such rings may be attached together in a pendant manner or may be

fused, more preferably the groups are selected from phenyl, naphthyl, tetrahydronaphthyl, indane, biphenyl, and the like;

- the "heteroaryl" or "heteroaromatic" group used either alone or in combination with other radicals, is selected from suitable single or fused mono, bi or tricyclic aromatic heterocyclic radicals containing one or more hetero atoms selected from O, N or S, more preferably the groups are selected from pyridyl, thienyl, furyl, pyrrolyl, oxazolyl, thiazolyl, isothiazolyl, imidazolyl, isoxazolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, benzofuranyl, benzothienyl, indolinyl, indolyl, azaindolyl, azaindolyl, pyrazolopyrimidinyl, azaquinazolinyl, pyridofuranyl, pyridothienyl, thienopyrimidinyl, quinolinyl, pyrimidinyl, pyrazolyl, quinazolinyl, pyridazinyl, triazinyl, benzimidazolyl, benzotriazolyl, phthalazynil, naphthylidinyl, purinyl, carbazolyl, phenothiazinyl, phenoxazinyl, benzoxazolyl, benzothiazolyl and the like;
- the "acyl" group used either alone or in combination with other radicals, is selected from a radical containing one to eight carbons, more preferably selected from formyl, acetyl, propanoyl, butanoyl, *iso*-butanoyl, pentanoyl, hexanoyl, heptanoyl, benzoyl and the like, which may be substituted;
- the "oxo" or "carbonyl" group used either alone ($-C=O-$) or in combination with other radicals such as alkyl described above, for e.g. "alkylcarbonyl", denotes a carbonyl radical ($-C=O-$) substituted with an alkyl radical described above such as acyl or alkanoyl;
- the "carboxylic acid" group, used alone or in combination with other radicals, denotes a $-COOH$ group, and includes derivatives of carboxylic acid such as esters and amides;
- the "ester" group used alone or in combination with other radicals, denotes $-COO-$ group, and includes carboxylic acid derivatives, more preferably the ester moieties are selected from alkoxycarbonyl, such as methoxycarbonyl, ethoxycarbonyl, and the like, which may optionally be substituted; aryloxycarbonyl group such as phenoxycarbonyl, naphthylloxycarbonyl, and the like, which may optionally be substituted; aralkoxycarbonyl group such as benzyloxycarbonyl, phenethylloxycarbonyl, naphthylmethoxycarbonyl, and the like, which may optionally be substituted; heteroaryloxycarbonyl, heteroaralkoxycarbonyl, wherein the heteroaryl group, is as defined above, which may optionally be substituted;

heterocycloxyoxycarbonyl, where the heterocyclic group, as defined earlier, which may optionally be substituted;

- the “amide” group used alone or in combination with other radicals, represents an aminocarbonyl radical ($\text{H}_2\text{N}-\text{C}=\text{O}-$), wherein the amino group is mono- or di-substituted or unsubstituted, more preferably the groups are selected from methylamide, dimethylamide, ethylamide, diethylamide, and the like;
- the “alkylthio” group used either alone or in combination with other radicals, denotes a straight or branched or cyclic monovalent substituent comprising an alkyl group as defined above, linked through a divalent sulfur atom having a free valence bond from the sulfur atom, more preferably the groups may be selected from methylthio, ethylthio, propylthio, butylthio, pentylthio and the like or cyclic alkylthio selected from cyclopropylthio, cyclobutylthio, cyclopentylthio, cyclohexylthio and the like, which may be optionally substituted;
- the “thioalkyl” group used either alone or in combination with other radicals, denotes an alkyl group, as defined above, attached to a group of formula $-\text{SR}'$, where R' represents hydrogen, alkyl or aryl group, e.g. thiomethyl, methylthiomethyl, phenylthiomethyl and the like, which may be optionally substituted;
- the “sulfenyl” group or “sulfenyl derivatives” used alone or in combination with other radicals, represents a bivalent group, $-\text{SO}-$ or R_xSO , where R_x is an optionally substituted alkyl, aryl, heteroaryl, heterocyclyl, group selected from those described above;
- the “sulfonyl” group or “sulfones derivatives” used either alone or in combination with other radicals, with other terms such as alkylsulfonyl, represents a divalent radical $-\text{SO}_2-$, or R_xSO_2- , where R_x is as defined above. More preferably, the groups may be selected from “alkylsulfonyl” wherein suitable alkyl radicals, selected from those defined above, is attached to a sulfonyl radical, such as methylsulfonyl, ethylsulfonyl, propylsulfonyl and the like, “arylsulfonyl” wherein an aryl radical, as defined above, is attached to a sulfonyl radical, such as phenylsulfonyl and the like.

Preferred compounds according to the present invention include but not limited to:

{[3,5-Dichloro-4-(4-hydroxy-3-isopropyl-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid;

- {[4-(3-sec-Butyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonyl-amino}-acetic acid;
- {[4-(3-Benzyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonyl-amino}-acetic acid;
- 5 ({4-[3-(Bicyclo[2.2.1]hept-2-ylcarbamoyl)-4-hydroxy-phenoxy]-3,5-dichloro-phenyl}-ethoxycarbonyl-amino)-acetic acid;
- ({3,5-Dichloro-4-[4-hydroxy-3-(piperidine-1-carbonyl)-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid;
- {[3,5-Dichloro-4-(3-ethyl-4-hydroxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid;
- 10 acid;
- {[3,5-Dichloro-4-(3-cyclohexylcarbamoyl-4-hydroxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid;
- ({3,5-Dichloro-4-[4-hydroxy-3-(4-methyl-piperazine-1-carbonyl)-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid;
- 15 {[3,5-Dichloro-4-(3-dimethylcarbamoyl-4-hydroxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid;
- {[3,5-Dichloro-4-(3-cyclobutylcarbamoyl-4-hydroxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid;
- {[3,5-Dichloro-4-(4-hydroxy-3-propyl-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid;
- 20 acid;
- {[3,5-Dichloro-4-(4-hydroxy-3-isopropylcarbamoyl-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid;
- {[4-(3-tert-Butyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonyl-amino}-acetic acid;
- 25 {[3,5-Dichloro-4-(6-hydroxy-biphenyl-3-yloxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid;
- ({3,5-Dichloro-4-[3-(4-fluoro-benzoyl)-4-hydroxy-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid;
- {[3,5-Dichloro-4-(3-diethylcarbamoyl-4-hydroxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid;
- 30 amino}-acetic acid;
- ({3,5-Dichloro-4-[3-(5-chloro-thiophene-2-carbonyl)-4-hydroxy-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid;

- {[4-(3-sec-Butyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-ethoxycarbonyl-amino}-acetic acid;
- {[3,5-Dichloro-4-(4-hydroxy-3-phenylcarbamoyl-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid;
- 5 ({3,5-Dichloro-4-[3-(4-chloro-benzoyl)-4-hydroxy-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid;
- {[4-(3-sec-Butyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-carboxymethyl-amino}-acetic acid;
- 10 ({3,5-Dichloro-4-[3-(2,4-dichloro-benzoyl)-4-hydroxy-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid;
- [[4-(3-sec-Butyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- (({4-[3-(4-tert-Butyl-benzoyl)-4-hydroxy-phenoxy]-3,5-dichloro-phenyl}-ethoxycarbonyl-amino)-acetic acid;
- 15 ({3,5-Dichloro-4-[3-(3-chloro-benzoyl)-4-hydroxy-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid;
- {[4-(3-sec-Butyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-carboxymethyl-amino}-acetic acid;
- 20 ({4-[3-(Bicyclo[2.2.1]hept-2-ylcarbamoyl)-4-hydroxy-phenoxy]-3,5-dichloro-phenyl}-carboxymethyl-amino)-acetic acid;
- (Carboxymethyl-{3,5-dichloro-4-[3-(4-chloro-benzoyl)-4-hydroxy-phenoxy]-phenyl}-amino)-acetic acid;
- (Carboxymethyl-{3,5-dichloro-4-[4-hydroxy-3-(piperidine-1-carbonyl)-phenoxy]-phenyl}-amino)-acetic acid;
- 25 ({4-[3-(Bicyclo[2.2.1]hept-2-ylsulfamoyl)-4-hydroxy-phenoxy]-3,5-dichloro-phenyl}-carboxymethyl-amino)-acetic acid;
- {Carboxymethyl-[3,5-dichloro-4-(4-hydroxy-3-isopropyl-phenoxy)-phenyl]-amino}-acetic acid;
- 30 [[3,5-Dichloro-4-(4-hydroxy-3-isopropyl-phenoxy)-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- (Carboxymethyl-{3,5-dichloro-4-[4-hydroxy-3-(piperidine-1-sulfonyl)-phenoxy]-phenyl}-amino)-acetic acid;

- {[4-(3-tert-Butyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-carboxymethyl-amino}-acetic acid;
- [[4-(3-tert-Butyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- 5 {Carboxymethyl-[3,5-dichloro-4-(3-dimethylcarbamoyl-4-hydroxy-phenoxy)-phenyl]-amino}-acetic acid;
- {Carboxymethyl-[4-(4-hydroxy-3-isopropyl-phenoxy)-3,5-dimethyl-phenyl]-amino}-acetic acid;
- 10 [[3,5-Dichloro-4-(3-dimethylsulfamoyl-4-hydroxy-phenoxy)-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- [[3,5-Dichloro-4-(3-dimethylcarbamoyl-4-hydroxy-phenoxy)-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- [{3,5-Dichloro-4-[4-hydroxy-3-(piperidine-1-carbonyl)-phenoxy]-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- 15 [{3,5-Dichloro-4-[4-hydroxy-3-(piperidine-1-sulfonyl)-phenoxy]-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- [[4-(4-Hydroxy-3-isopropyl-phenoxy)-3,5-dimethyl-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- [{4-[3-(4-tert-Butyl-benzoyl)-4-hydroxy-phenoxy]-3,5-dichloro-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- 20 [{3,5-Dichloro-4-[3-(4-chloro-benzoyl)-4-hydroxy-phenoxy]-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- [[3,5-Dichloro-4-(4-hydroxy-3-isopropylsulfamoyl-phenoxy)-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- 25 {Carboxymethyl-[3,5-dichloro-4-(3-ethyl-4-hydroxy-phenoxy)-phenyl]-amino}-acetic acid;
- [{3,5-Dichloro-4-[3-(3-chloro-benzoyl)-4-hydroxy-phenoxy]-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- [[3,5-Dichloro-4-(3-ethyl-4-hydroxy-phenoxy)-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- 30 [[3,5-Dichloro-4-(6-hydroxy-biphenyl-3-yloxy)-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;

- [[4-(3-Benzyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- [[3,5-Dichloro-4-(3-cyclobutylsulfamoyl-4-hydroxy-phenoxy)-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- 5 [[4-[3-(Bicyclo[2.2.1]hept-2-ylsulfamoyl)-4-hydroxy-phenoxy]-3,5-dichloro-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- [[4-[3-(Bicyclo[2.2.1]hept-2-ylsulfamoyl)-4-hydroxy-phenoxy]-3,5-dibromo-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- 10 [[3,5-Dichloro-4-[4-hydroxy-3-(4-hydroxy-benzoyl)-phenoxy]-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- [[3,5-Dichloro-4-[3-(4-fluoro-benzoyl)-4-hydroxy-phenoxy]-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- [(3,5-Dichloro-4-{3-[(4-chloro-phenyl)-hydroxy-methyl]-4-hydroxy-phenoxy}-phenyl)-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- 15 [[4-[3-(Azepane-1-sulfonyl)-4-hydroxy-phenoxy]-3,5-dichloro-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- ((3,5-Dichloro-4-[3-(1-ethyl-propoxy)-4-hydroxy-phenoxy]-phenyl)-ethoxycarbonyl-amino)-acetic acid;
- [[4-(3-sec-Butyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- 20 [[3,5-Dichloro-4-(3-cyclohexylsulfamoyl-4-hydroxy-phenoxy)-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- [[3,5-Dichloro-4-[4-hydroxy-3-(morpholine-4-sulfonyl)-phenoxy]-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- 25 ((3,5-Dichloro-4-[4-hydroxy-3-(3-methyl-benzoyl)-phenoxy]-phenyl)-ethoxycarbonyl-amino)-acetic acid;
- [[3,5-Dichloro-4-[4-hydroxy-3-(pyrrolidine-1-sulfonyl)-phenoxy]-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- {[3,5-Dichloro-4-(4-hydroxy-3-isobutoxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid;
- 30 {[3,5-Dichloro-4-(3-cyclohexylmethoxy-4-hydroxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid;

- [{3,5-Dichloro-4-[4-hydroxy-3-(3-methyl-benzoyl)-phenoxy]-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- [{3,5-Dibromo-4-[3-(4-chloro-benzoyl)-4-hydroxy-phenoxy]-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- 5 ({3,5-Dibromo-4-[3-(4-chloro-benzoyl)-4-hydroxy-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid;
- (({3,5-Dichloro-4-[4-hydroxy-3-(4-methyl-benzoyl)-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid;
- [{3,5-Dichloro-4-[4-hydroxy-3-(4-methyl-benzoyl)-phenoxy]-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- 10 {[3,5-Dichloro-4-(3-isopropyl-4-methoxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester;
- {[4-(4-Benzoyloxy-3-isopropyl-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester;
- 15 {[4-(3-sec-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester;
- {[4-(3-Benzyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester;
- (({4-[3-(Bicyclo[2.2.1]hept-2-ylcarbamoyl)-4-methoxy-phenoxy]-3,5-dichloro-phenyl}-ethoxycarbonyl-amino)-acetic acid ethyl ester;
- 20 ({3,5-Dichloro-4-[4-methoxy-3-(piperidine-1-carbonyl)-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid ethyl ester;
- {[3,5-Dichloro-4-(3-ethyl-4-methoxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester;
- 25 {[3,5-Dichloro-4-(3-cyclohexylcarbamoyl-4-methoxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester;
- (({3,5-Dichloro-4-[4-methoxy-3-(4-methyl-piperazine-1-carbonyl)-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid ethyl ester;
- {[3,5-Dichloro-4-(3-dimethylcarbamoyl-4-methoxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester;
- 30 {[3,5-Dichloro-4-(3-cyclobutylcarbamoyl-4-methoxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester;

- {[3,5-Dichloro-4-(4-methoxy-3-propyl-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester;
- {[3,5-Dichloro-4-(3-isopropylcarbamoyl-4-methoxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester;
- 5 {[4-(3-tert-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester;
- {[3,5-Dichloro-4-(6-methoxy-biphenyl-3-yloxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester;
- 10 ({3,5-Dichloro-4-[3-(4-fluoro-benzoyl)-4-methoxy-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid ethyl ester;
- {[3,5-Dichloro-4-(3-diethylcarbamoyl-4-methoxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester;
- 15 ({3,5-Dichloro-4-[3-(5-chloro-thiophene-2-carbonyl)-4-methoxy-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid ethyl ester;
- {[4-(3-sec-Butyl-4-methoxy-phenoxy)-3,5-dimethyl-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester;
- {[3,5-Dichloro-4-(4-methoxy-3-phenylcarbamoyl-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester;
- 20 ({3,5-Dichloro-4-[3-(4-chloro-benzoyl)-4-methoxy-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid ethyl ester;
- {[4-(3-sec-Butyl-4-methoxy-phenoxy)-3,5-dimethyl-phenyl]-ethoxycarbonylmethyl-amino}-acetic acid ethyl ester;
- 25 ({3,5-Dichloro-4-[3-(2,4-dichloro-benzoyl)-4-methoxy-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid ethyl ester;
- [[4-(3-sec-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- 30 ({4-[3-(4-tert-Butyl-benzoyl)-4-methoxy-phenoxy]-3,5-dichloro-phenyl}-ethoxycarbonyl-amino)-acetic acid ethyl ester;
- (({3,5-Dichloro-4-[3-(3-chloro-benzoyl)-4-methoxy-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid ethyl ester;
- {[4-(3-sec-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonylmethyl-amino}-acetic acid ethyl ester;

- ({4-[3-(Bicyclo[2.2.1]hept-2-ylcarbamoyl)-4-methoxy-phenoxy]-3,5-dichloro-phenyl}-ethoxycarbonylmethyl-amino)-acetic acid ethyl ester;
- ({3,5-Dichloro-4-[3-(4-chloro-benzoyl)-4-methoxy-phenoxy]-phenyl}-ethoxycarbonylmethyl-amino)-acetic acid ethyl ester;
- 5 ({3,5-Dichloro-4-[4-methoxy-3-(piperidine-1-carbonyl)-phenoxy]-phenyl}-ethoxycarbonylmethyl-amino)-acetic acid ethyl ester;
- ({4-[3-(Bicyclo[2.2.1]hept-2-ylsulfamoyl)-4-methoxy-phenoxy]-3,5-dichloro-phenyl}-ethoxycarbonylmethyl-amino)-acetic acid ethyl ester;
- {[3,5-Dichloro-4-(3-isopropyl-4-methoxy-phenoxy)-phenyl]-ethoxycarbonylmethyl-amino}-acetic acid ethyl ester;
- 10 [[3,5-Dichloro-4-(3-isopropyl-4-methoxy-phenoxy)-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- ({3,5-Dichloro-4-[4-methoxy-3-(piperidine-1-sulfonyl)-phenoxy]-phenyl}-ethoxycarbonylmethyl-amino)-acetic acid ethyl ester;
- 15 {[4-(3-tert-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonylmethyl-amino}-acetic acid ethyl ester;
- [[4-(3-tert-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- {[3,5-Dichloro-4-(3-dimethylcarbamoyl-4-methoxy-phenoxy)-phenyl]-ethoxycarbonylmethyl-amino}-acetic acid ethyl ester;
- 20 {Ethoxycarbonylmethyl-[4-(3-isopropyl-4-methoxy-phenoxy)-3,5-dimethyl-phenyl]-amino}-acetic acid ethyl ester;
- [[3,5-Dichloro-4-(3-dimethylsulfamoyl-4-methoxy-phenoxy)-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- 25 [[3,5-Dichloro-4-(3-dimethylcarbamoyl-4-methoxy-phenoxy)-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- [{3,5-Dichloro-4-[4-methoxy-3-(piperidine-1-carbonyl)-phenoxy]-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- [{3,5-Dichloro-4-[4-methoxy-3-(piperidine-1-sulfonyl)-phenoxy]-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- 30 [[4-(3-Isopropyl-4-methoxy-phenoxy)-3,5-dimethyl-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;

- [{4-[3-(4-tert-Butyl-benzoyl)-4-methoxy-phenoxy]-3,5-dichloro-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- [{3,5-Dichloro-4-[3-(4-chloro-benzoyl)-4-methoxy-phenoxy]-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- 5 [[3,5-Dichloro-4-(3-isopropylsulfamoyl-4-methoxy-phenoxy)-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- [{3,5-Dichloro-4-(3-ethyl-4-methoxy-phenoxy)-phenyl]-ethoxycarbonylmethyl-amino}-acetic acid ethyl ester;
- [{3,5-Dichloro-4-[3-(3-chloro-benzoyl)-4-methoxy-phenoxy]-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- 10 [[3,5-Dichloro-4-(3-ethyl-4-methoxy-phenoxy)-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- [[3,5-Dichloro-4-(6-methoxy-biphenyl-3-yloxy)-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- 15 [[4-(3-Benzyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- [[3,5-Dichloro-4-(3-cyclobutylsulfamoyl-4-methoxy-phenoxy)-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- [{4-[3-(Bicyclo[2.2.1]hept-2-ylsulfamoyl)-4-methoxy-phenoxy]-3,5-dichloro-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- 20 [{4-[3-(Bicyclo[2.2.1]hept-2-ylsulfamoyl)-4-methoxy-phenoxy]-3,5-dibromo-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- [{3,5-Dichloro-4-[4-methoxy-3-(4-methoxy-benzoyl)-phenoxy]-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- 25 [{3,5-Dichloro-4-[3-(4-fluoro-benzoyl)-4-methoxy-phenoxy]-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- [{4-[3-(Azepane-1-sulfonyl)-4-methoxy-phenoxy]-3,5-dichloro-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- ({4-[4-Benzoyloxy-3-(1-ethyl-propoxy)-phenoxy]-3,5-dichloro-phenyl}-ethoxycarbonyl-amino)-acetic acid ethyl ester;
- 30 [[4-(3-sec-Butyl-4-methoxy-phenoxy)-3,5-dimethyl-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;

- [[3,5-Dichloro-4-(3-cyclohexylsulfamoyl-4-methoxy-phenoxy)-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- {[3,5-Dichloro-4-[4-methoxy-3-(morpholine-4-sulfonyl)-phenoxy]-phenyl]}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- 5 { [3,5-Dichloro-4-[4-methoxy-3-(3-methyl-benzoyl)-phenoxy]-phenyl]}-ethoxy-carbonyl-amino)-acetic acid ethyl ester;
- { [3,5-Dichloro-4-[4-methoxy-3-(pyrrolidine-1-sulfonyl)-phenoxy]-phenyl]}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- {[4-(4-Benzoyloxy-3-isobutoxy-phenoxy)-3,5-dichloro-phenyl]-ethoxy-carbonyl-amino}-
- 10 acetic acid ethyl ester;
- {[4-(4-Benzoyloxy-3-cyclohexylmethoxy-phenoxy)-3,5-dichloro-phenyl]-ethoxy-carbonyl-amino}-acetic acid ethyl ester;
- { [3,5-Dichloro-4-[4-methoxy-3-(3-methyl-benzoyl)-phenoxy]-phenyl]}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- 15 { [3,5-Dibromo-4-[3-(4-chloro-benzoyl)-4-methoxy-phenoxy]-phenyl]}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- { [3,5-Dibromo-4-[3-(4-chloro-benzoyl)-4-methoxy-phenoxy]-phenyl]}-ethoxy-carbonyl-amino)-acetic acid ethyl ester;
- { [3,5-Dichloro-4-[4-methoxy-3-(4-methyl-benzoyl)-phenoxy]-phenyl]}-
- 20 ethoxy-carbonyl-amino)-acetic acid ethyl ester;
- { [3,5-Dichloro-4-[4-methoxy-3-(4-methyl-benzoyl)-phenoxy]-phenyl]}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;

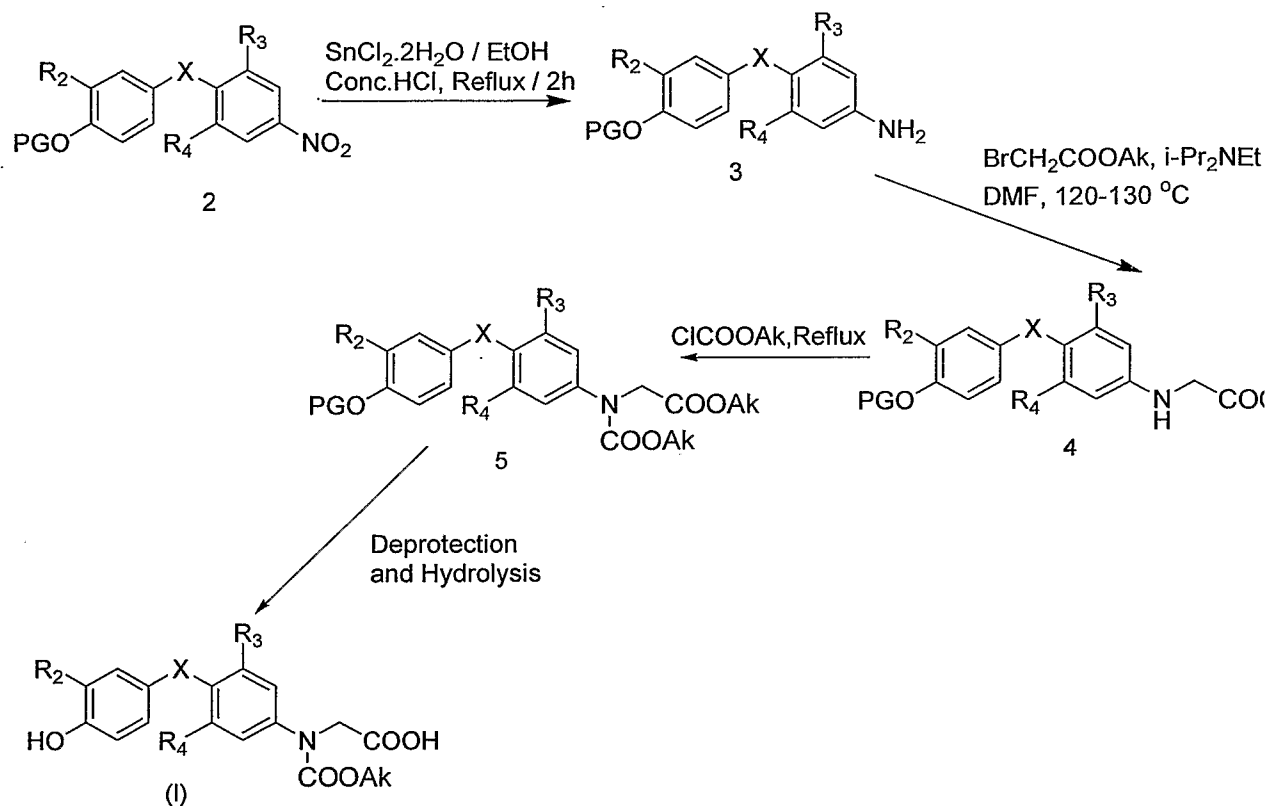
The compounds of this invention may be prepared using the reactions and techniques described in the following section. The reactions are performed in solvents

25 appropriate to the reagents and materials employed and are suitable for the transformations being effected. It is understood by those skilled in the art that the nature and order of the synthetic steps presented may be varied for the purpose of optimizing the formation of the compounds of the present invention. It will also be appreciated that some routine alterations/modifications including requirement of one or

30 more additional steps which may be required for obtaining the compounds of the present invention in preferred yields but are considered to be within the scope of a person skilled in the art, are to be considered to be within the scope of the present invention.

Scheme: 1

$R_7 = \text{Alkyl (Ak)}, n=0$



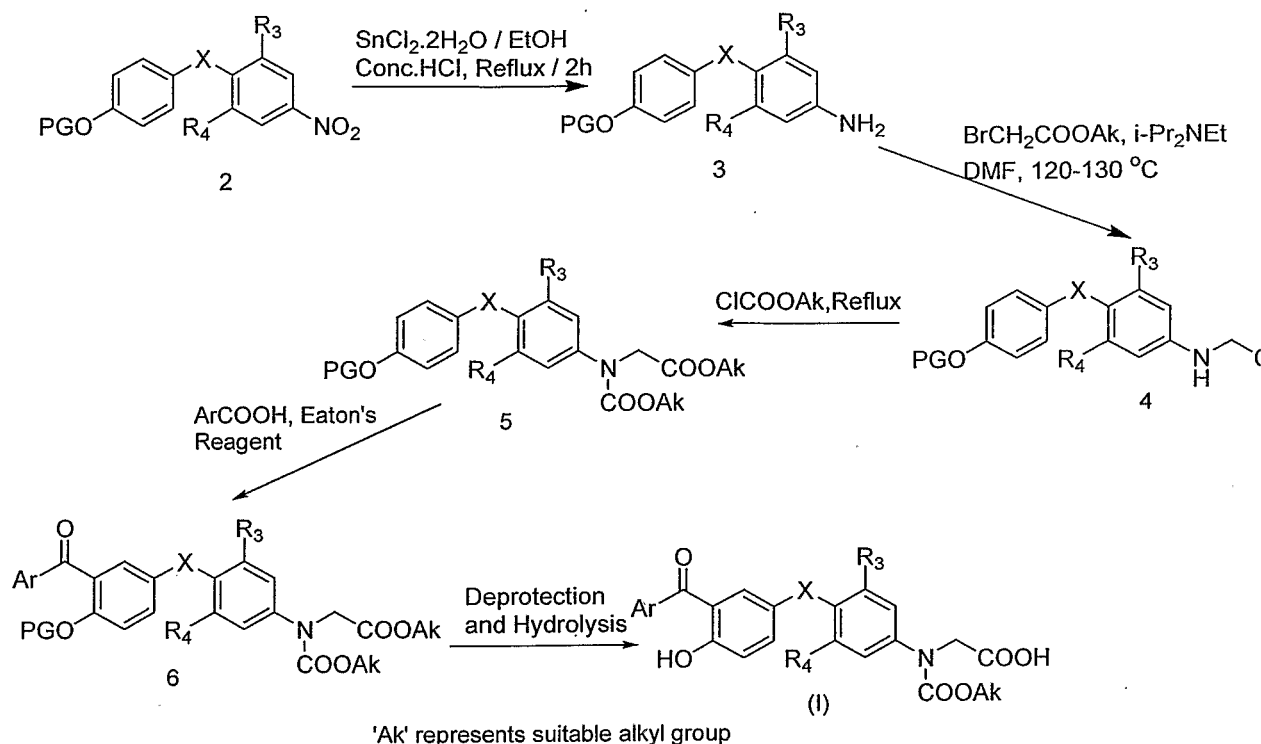
'Ak' represents suitable alkyl group

5

The biaryl ether of formula **2** wherein 'PG' represents suitable protecting groups known to persons skilled in the art (for e.g. those described in T. W. Greene and P. G. M. Wuts "Protective groups in Organic Synthesis", John Wiley & Sons, Inc, 1999, 3rd Ed., 201-245 along with references therein), and all other symbols are as defined elsewhere in the specification, was reduced to give amino compound of formula **3**. Reduction may be carried out using suitable reducing agents such as Raney Ni, Pd/C, $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ and the like. This amine **3** may be reacted with suitable alkyl haloacetate in suitable base(s) such as diisopropyl ethylamine ($i\text{Pr}_2\text{-NEt}$), pyridine, N,N dimethyl aniline or like in solvents selected from DMF, THF and the like or their mixtures to give a compound of formula **4**. Further compound of formula **4** was refluxed in suitable alkyl haloformate to give compound of formula **5**. Suitable deprotection and hydrolysis of compound of formula **5** gives compound of formula (I)

20 **Scheme: 2**

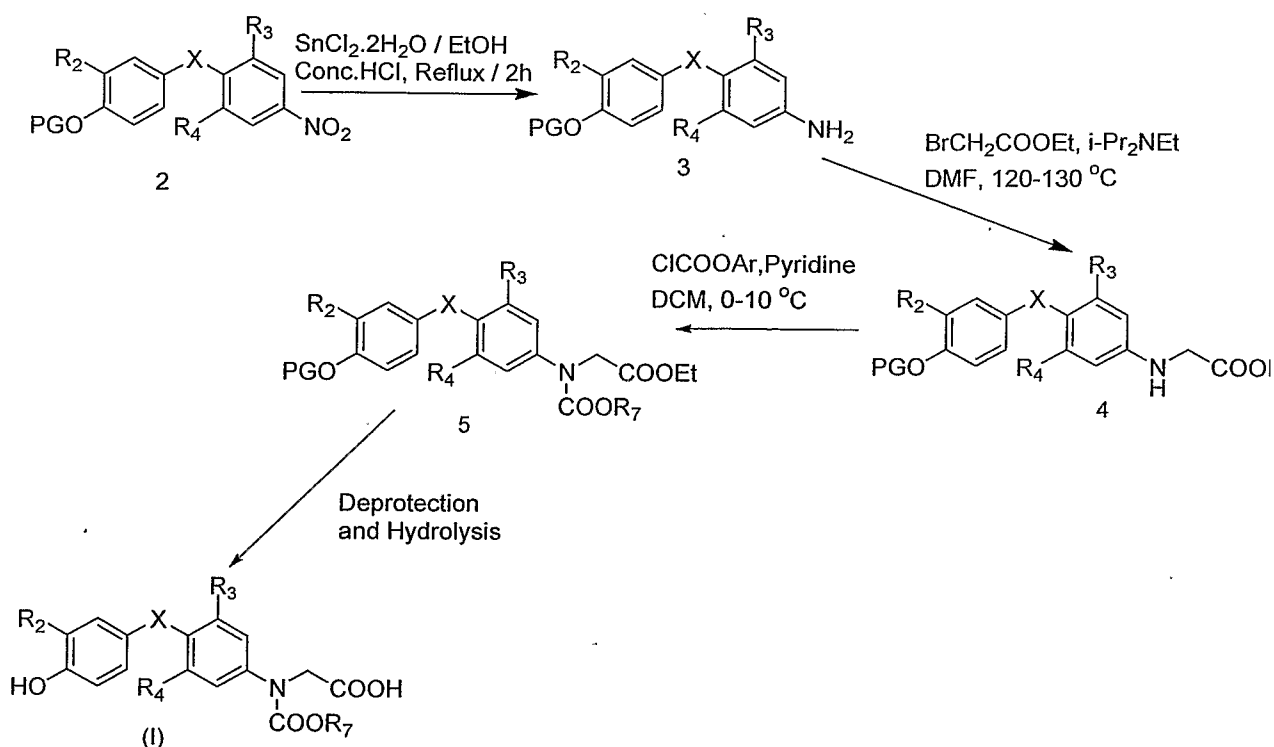
$R_7 = \text{alkyl}$, $R_2 = \text{COAr}$, $n = 0$



- 5 The biaryl ether of formula **2** wherein PG represents suitable protecting groups known to persons skilled in the art (for e.g. those described in T. W. Greene and P. G. M. Wuts "Protective groups in Organic Synthesis", John Wiley & Sons, Inc, 1999, 3rd Ed., 201-245 along with references therein), and all other symbols are as defined elsewhere in the specification, was reduced to give amino compound of formula **3**.
- 10 Reduction may be carried out using reducing agents such as Raney Ni, Pd/C, $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ and the like. This amine **3** may be reacted with suitable alkyl haloacetate in suitable base such as $i\text{Pr}_2\text{NEt}$, pyridine, N,N dimethyl aniline or like in suitable solvent(s) such as DMF, THF and the like or their mixtures to give a compound of formula **4**. Further compound of formula **4** was refluxed in suitable alkyl haloformates to give compound of formula **5**. Compound of Formula **5** was reacted with suitable aromatic acids or suitable aromatic acid chloride and appropriate acylating agents to obtain compound of Formula **6**. Deprotection and hydrolysis of compound of formula **6**, using suitable reagents & techniques as is known in the art, gives compound of formula **(I)**
- 15
- 20

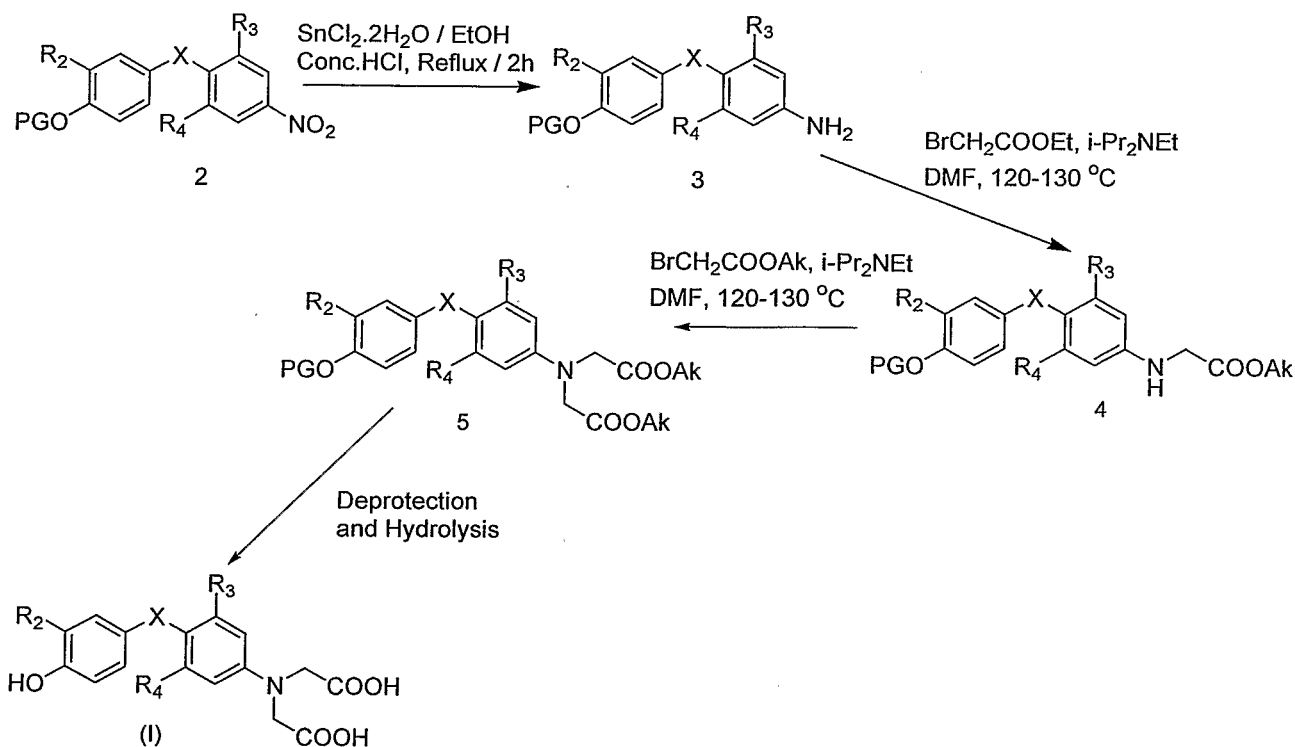
Scheme: 3

$R_7 = \text{Aryl}$, $n = 0$



The biaryl ether of formula 2 wherein 'PG' represents suitable protecting groups known to persons skilled in the art (for e.g. those described in T. W. Greene and P. G. M. Wuts "Protective groups in Organic Synthesis", John Wiley & Sons, Inc, 1999, 3rd Ed., 201-245 along with references therein), and all other symbols are as defined elsewhere in the specification, was reduced to give amino compound of formula 3. Reduction may be carried out using suitable reducing agents such as Raney Ni, Pd/C, SnCl₂·2H₂O and the like. This amine 3 may be reacted with suitable alkyl haloacetates in suitable base(s) such as iPr₂-NEt, pyridine, N,N dimethyl aniline and the like in suitable solvents such as DMF, THF or their suitable mixtures to give a compound of formula 4. Further compound of formula 4 was reacted with ClCOOAr in suitable base such as pyridine, NEt₃ and the like in suitable solvents such as dichloromethane, chloroform and the like or their suitable mixtures to give compound of formula 5. Deprotection and hydrolysis of compound of formula 5 by techniques and reagents known in the art gives compound of formula (I).

5 **Scheme: 4** $R_7=H$, (when 'n' =1)



The biaryl ether of formula **2** wherein PG represents suitable protecting groups known to persons skilled in the art (for e.g. those described in T. W. Greene and P. G. M. Wuts "Protective groups in Organic Synthesis", John Wiley & Sons, Inc, 1999, 3rd Ed., 201-245 along with references therein), and all other symbols are as defined elsewhere in the specification, was reduced to give amino compound of formula **3**. Reduction may be carried out using suitable reducing agents such as Raney Ni, Pd/C, $SnCl_2 \cdot 2H_2O$ and the like. This amine **3** may be reacted with suitable alkyl halo acetates in suitable base such as iPr_2NEt , pyridine, N,N dimethyl aniline and the like in suitable solvents such as DMF, THF and the like to give a compound of formula **4**. Again compound of formula **4** was reacted with suitable alkyl halo acetates in suitable base such as iPr_2NEt , pyridine, N,N dimethyl aniline and the like in suitable solvent(s) such as DMF, THF and the like or their suitable mixtures to give a compound of formula **5**. Deprotection and hydrolysis of compound of formula **5** by techniques and reagents known in the art gives compound of formula (I).

The invention is explained in greater detail by the examples given below, which are provided by way of illustration only and therefore should not be construed to limit the scope of the invention. As will be clear from the specification, few different subclasses of compounds within the single general formula (I) have been described. These
5 different subclasses can be prepared by suitable modifications/alterations of one or two of the general processes described in the schemes. Example 2, Example 23, Example 26 and Example 20 each describe in detail processes of preparing compounds of each of the general sub classes. After describing actual processes for preparing compounds of each sub class, characterization data of all the compounds prepared have been provided
10 in random order. However, all the compounds can be prepared by following one of the three processes described earlier with suitable changes as may be specific to the compounds.

*¹H NMR spectral data given in the examples (vide infra) are recorded using either a 300 MHz spectrometer (Bruker AVANCE-300) or a 400 MHz spectrometer (Bruker
15 Avance2) and reported in δ scale. Until and otherwise mentioned the solvent used for NMR is CDCl₃ using tetramethyl silane as the internal standard.*

EXAMPLE 2

Preparation of {[4-(3-sec-Butyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonyl-amino}-acetic acid

20 Step 1 : Preparation of 4-(3- sec-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenylamine

To a solution of Stannous chloride dihydrate (194.6 g, 0.86 mol) in concentrated HCl (80.0 mL) was added to 3,5-dichloro-4-(4'-methoxy-3-sec-butyl - phenoxy)nitrobenzene (80 g, 0.21 mol) in EtOH (400 mL). The reaction mixture was refluxed for about 2 h. The resulting mixture was brought at 20-30 °C and diluted with
25 ethyl acetate. The mixture was made alkaline with ammonia solution. Resulting solid was filtered through cellite. The organic phase was washed with H₂O, brine & dried over sodium sulphate, filtered and concentrated to give 4-(3-sec-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenylamine (71.8 g; 98 % yield).

Step 2: [4-(3-sec-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenylamino]-acetic acid
30 ethyl ester

To 4-(3- sec-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenylamine (71.8 g, 0.21 mol) was added ethyl bromoacetate (35.26 g, 0.21 mol) and diisopropylethyl amine (27.92 g, 0.21 mol) in DMF (718 mL) were stirred at 120 °C for 18 h. The reaction

mixture was poured in to ice-water . The product was taken up in ethyl acetate, washed with H₂O, brine & dried over sodium sulphate, filtered and concentrated to give the crude product. The crude product was purified by column chromatography over flash silica gel (Hexane : Ethylacetate 90:10) to afford the pure product [4-(3-sec-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenylamino]-acetic acid ethyl ester.(48.0 g, 54 % yield)

Step 3 : {[4-(3-sec-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester

[4-(3-sec-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenylamino]-acetic acid ethyl ester (0.9 g, 2.1 mmol) was stirred with ethyl chloroformate (8 mL) at reflux temperature for 16 hrs. From the reaction mixture ethyl chloroformate was evaporated under reduced pressure and the residue was taken up in ethyl acetate, washed with H₂O, brine and dried over sodium sulphate, filtered and concentrated to give {[4-(3-sec-butyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester.(0.8 g, 76 % yield)

Step 4 : {[4-(3-sec-Butyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonyl-amino}-acetic acid.

A solution of {[4-(3-sec-butyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester (0.8 g, 1.6 mmol) in CH₂Cl₂ (16 mL) was cooled to -60 °C under nitrogen atmosphere. To that 1M BBr₃ solution (4.8 mL) was added dropwise. The reaction mixture was allowed to warm up to 20-25 °C over 5 h. then diluted with more CH₂Cl₂ (25 mL) and quenched with H₂O. After stirring at 20-25 °C for 30 min, organic phase was separated, washed with H₂O, brine & dried over sodium sulphate, filtered and concentrated to give crude product. The crude product was purified by column chromatography over flash silica gel (Hexane : Ethylacetate 90:10) to afford the pure product {[4-(3-sec-Butyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester. (0.77 g, 99 % Yield)

The ester (0.77 g, 1.5 mmol) was dissolved in MeOH (18 mL) and to it a solution of NaOH (0.19g, 4.75 mmol) in H₂O (5.6 mL) was added and it was stirred at 60 °C for 1 hr. Methanol was evaporated from the reaction mixture and H₂O was added, washed with diethyl ether. Aqueous layer was acidified to pH 4 using 10 % HCl solution and extracted with ethyl acetate The organic layer was washed with H₂O, brine & dried over sodium sulphate, filtered and concentrated to give 0.75 g of crude product The

crude product was purified by column chromatography (Silica gel, Chloroform : Methanol) gradient elution from 95:5 to 90:10 to give pure {[4-(3-sec-Butyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonyl-amino}-acetic acid.(0.125 g, 18 % yield)

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EXAMPLE 23

Preparation of [[4-(3-sec-Butyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid

Step 1 : Preparation of [[4-(3-sec-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester

A solution of [4-(3-sec-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenylamino]-acetic acid ethyl ester (Example 2, step2) (5.0 g, 0.01 mol) in CH₂Cl₂ (30 mL) was cooled to 0–5 °C under nitrogen atmosphere. To the solution 4-methoxy phenyl chloroformate (8.75 g, 0.046 mol) in CH₂Cl₂ (20 mL) was added dropwise. The reaction mixture was allowed to warm up to 20-25 °C over 3 h., diluted further with more CH₂Cl₂ (25 mL) and quenched with water. After stirring at 20-25 °C for 30 min, organic phase was separated, washed with water, brine, dried over sodium sulphate, filtered and concentrated to give the crude product. The crude product was purified by column chromatography over flash silica gel (hexane: ethyl acetate 90:10) to afford the pure product [[4-(3-sec-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester (6.4 g, 95 % yield)

Step 2: Preparation of [[4-(3-sec-Butyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid

To a solution of [[4-(3-sec-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester (6.4 g, 0.01 mol) in CH₂Cl₂ (128 mL) was cooled to –60 °C under nitrogen atmosphere. To that 1M BBr₃ (boron tribromide) solution (44.44 mL) was added dropwise. The reaction mixture was allowed to warm up to 20-25 °C over 5 h. then diluted with more CH₂Cl₂ (30 mL) and quenched with H₂O. After stirring at 20-25 °C for 30 min, organic phase was separated, washed with H₂O, brine & dried over sodium sulphate, filtered and concentrated to give crude product. The crude product was purified by column chromatography over flash silica gel (chloroform : methanol) gradient elution from 95:5 to 90:10 to give pure [[4-(3-sec-

Butyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid (3.3 g, 58 % yield)

EXAMPLE 26

Preparation of {[4-(3-sec-Butyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-carboxymethyl-amino}-acetic acid

Step 1: Preparation of {[4-(3-sec-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonylmethyl-amino}-acetic acid ethyl ester

To [4-(3-sec-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenylamino]-acetic acid ethyl ester (Example 2, step2) (48.0 g, 0.11 mol), ethyl bromoacetate (188 g, 1.12 mol) and diisopropylethylamine (145.57 g, 1.12 mol) in DMF (480 mL) were stirred at 120 °C for 18 h. The reaction mixture was poured in to ice-water. The product was taken up in ethyl acetate, washed with water, brine, dried over sodium sulphate, filtered and concentrated to give the crude product, which was purified by column chromatography over flash silica gel (hexane : ethyl acetate 90:10) to give pure {[4-(3-sec-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonylmethyl-amino}-acetic acid ethyl ester (27.1 g, 47 % yield).

Step 2: Preparation of {[4-(3-sec-Butyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-carboxymethyl-amino}-acetic acid

To a solution of {[4-(3-sec-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonylmethyl-amino}-acetic acid ethyl ester (12.5 g, 0.02 mol) in CH₂Cl₂ (250 mL) was cooled to -60 °C under nitrogen atmosphere. To that 1M BBr₃ solution (122 mL) was added dropwise. The reaction mixture was allowed to warm up to 20-25 °C over 5 h. then diluted with more CH₂Cl₂ (250 mL) and quenched with H₂O. After stirring at 20-25 °C for 30 min, organic phase was separated, washed with water, brine, dried over sodium sulphate, filtered and concentrated to give crude product. The crude product was purified by column chromatography over flash silica gel (chloroform : methanol) gradient elution from 95:5 to 90:10 to give pure {[4-(3-sec-Butyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-carboxymethyl-amino}-acetic acid (6.8 g, 63 % yield)

EXAMPLE 20

Preparation of ({3,5-Dichloro-4-[3-(4-chloro-benzoyl)-4-hydroxy-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid

Step 1: 3,5-Dichloro-4-(4-methoxy-phenoxy)-phenylamine

To a solution of stannous chloride dihydrate (32.38 g, 0.14 mol) in concentrated HCl (11 mL) was added 3,5-dichloro-4-(4-methoxy-phenoxy)nitrobenzene (11.3 g, 0.03 mol) in EtOH (56.5 mL). The reaction mixture was refluxed for about 2 h. The resulting mixture was brought at 20-30 °C and diluted with ethyl acetate. The mixture was made alkaline with ammonia solution. Resulting solid was filtered through cellite. The organic phase was washed with water, brine, dried over sodium sulphate, filtered and concentrated to give 3,5-Dichloro-4-(4-methoxy-phenoxy)-phenylamine (10.2 g; % Yield: 99 %).

10 Step 2: [3,5-Dichloro-4-(4-methoxy-phenoxy)-phenylamino]-acetic acid ethyl ester

3,5-Dichloro-4-(4-methoxy-phenoxy)-phenylamine (10.2 g, 0.03 mol), ethyl bromoacetate (5.39 g, 0.03 mol) and diisopropylethylamine (5.1 g, 0.03 mol) in 50 mL of DMF were stirred at 120 °C for 18 h. The reaction mixture was poured in to ice-water. The product was taken up in ethyl acetate, washed with water, brine, dried over sodium sulphate, filtered and concentrated to give the crude product, which was purified by column chromatography over flash silica gel, (hexane : ethyl acetate 90:10) to afford pure [3,5-Dichloro-4-(4-methoxy-phenoxy)-phenylamino]-acetic acid ethyl ester. (10.0 g, 76 % yield)

20 Step 3 : {[3,5-Dichloro-4-(4-methoxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester

[3,5-Dichloro-4-(4-methoxy-phenoxy)-phenylamino]-acetic acid ethyl ester (10.0 g, 0.02 mol) was stirred with ethyl chloroformate (95 mL) at reflux temperature for 16 hrs. From the reaction mixture ethyl chloroformate was evaporated under reduced pressure and the residue was taken up in ethyl acetate, washed with water, brine, dried over sodium sulphate, filtered and concentrated to give {[3,5-Dichloro-4-(4-methoxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester (7.25 g, 61 % Yield)

Step 4: ({[3,5-Dichloro-4-[3-(4-chloro-benzoyl)-4-methoxy-phenoxy]-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester

30 A mixture of {[3,5-Dichloro-4-(4-methoxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester (7.25 g, 0.016mol) and 4-chlorobenzoic acid (5.13 g, 0.03 mol) in Eaton's reagent (25 mL) was heated at 60 °C for 16 h. The reaction mixture was poured over ice. The product was taken up in ethyl acetate, washed with water, brine,

dried over sodium sulphate, filtered and concentrated to give the crude product, which was purified by column chromatography over flash silica gel (hexane : ethylacetate 90:10) to afford pure ({3,5-Dichloro-4-[3-(4-chloro-benzoyl)-4-methoxy-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid ethyl ester. (3.36 g, 36 % yield)

5 Step 5 : Preparation of ({3,5-Dichloro-4-[3-(4-chloro-benzoyl)-4-hydroxy-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid

A solution of {[4-(3-sec-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonylmethyl-amino}-acetic acid ethyl ester (3.36 g, 5.7 mmol) in CH₂Cl₂ (67 mL) was cooled to -60 °C under nitrogen atmosphere. To that 1M BBr₃ solution (11.57 mL) was added dropwise. The reaction mixture was stirred at -40 to -60 °C over 0.5 to 1 h. then diluted with more CH₂Cl₂ (50 mL) and quenched with H₂O. After stirring at 10 20-25 °C for 30 min, organic phase was separated, washed with water, brine, dried over sodium sulphate, filtered and concentrated. The residue was purified by column chromatography silica gel (hexane : ethyl acetate 90:10) to afford the pure product 15 ({3,5-Dichloro-4-[3-(4-chloro-benzoyl)-4-hydroxy-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid ethyl ester. (2.27 g, 70 % Yield)

The ester (2.27 g, 4.0 mmol) was dissolved in MeOH (14 mL) and to that solution of NaOH (0.48g, 12 mmol) in H₂O (7 mL) was added and it was stirred at 60 °C for 1hr. Methanol was evaporated from the reaction mixture and H₂O was added, 20 washed with diethyl ether. The aqueous layer was acidified to pH 4 using 10 % HCl solution and extracted with ethyl acetate The organic layer was washed with water, brine, dried over sodium sulphate, filtered and concentrated to give pure product ({3,5-Dichloro-4-[3-(4-chloro-benzoyl)-4-hydroxy-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid. (1.7 g, 79 % yield)

25 Using appropriate starting materials and suitable modifications of one or more of the processes described above, either alone or in suitable combination of the steps disclosed therein, including suitable addition and/or deletion of steps as may be necessary, well within the scope of a person skilled in the art, the following compounds were prepared in an analogous manner.

30 EXAMPLE 1

{[3,5-Dichloro-4-(4-hydroxy-3-isopropyl-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid

¹H NMR : (CDCl₃, 300MHz) : 1.22-1.25(9H, m), 3.18(1H, m), 4.22-4.24(2H, m), 4.37(2H, s) 6.39(1H, m), 6.61-6.64(1H, d, J=8.7Hz), 6.85(1H, s), 7.39(2H, s)

% Yield: 18 %

EXAMPLE 2

- 5 { [4-(3-sec-Butyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonyl-amino }-acetic acid

¹H NMR : (CDCl₃, 300MHz) : 0.86(3H, t, J=7.35Hz), 1.21(3H, d, J=6.9Hz), 1.22-1.26(2H, m), 1.55-1.57(3H, m), 2.89-2.94(1H, m), 4.22-4.24(2H, m), 4.38(2H, s), 6.40-6.41(1H, m), 6.64(1H, d, J=9Hz), 6.78(1H, d, J=2.88Hz), 7.38(2H, s)

- 10 % Yield: 18 %

EXAMPLE 3

{ [4-(3-Benzyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonyl-amino }-acetic acid

- 15 ¹H NMR : (DMSO-D₆, 300MHz) : 1.15(3H, t, J=7.05Hz), 3.82(2H, s), 4.11(4H, m), 6.61(1H, m), 6.70(1H, m), 6.73(1H, m), 7.18-7.25(5H, m), 7.54(2H, s)

% Yield : 25 %

EXAMPLE 4

(({4-[3-(Bicyclo[2.2.1]hept-2-ylcarbamoyl)-4-hydroxy-phenoxy]-3,5-dichloro-phenyl}-ethoxycarbonyl-amino)-acetic acid

- 20 ¹H NMR : (DMSO-D₆, 300MHz) : 1.15-1.19(7H, m), 1.47-1.71(4H, m), 2.21-2.26(2H, m), 3.72(1H, bs), 4.09-4.16(2H, q, J=6.96Hz & 7.02Hz), 4.34(2H, s), 6.68-6.72(1H, dd, J=2.94Hz & 8.94 Hz), 6.85(1H, d, J=8.94Hz), 7.58(2H, s), 7.66(1H, d, J=2.85Hz)

% Yield : 86 %

EXAMPLE 5

- 25 ({3,5-Dichloro-4-[4-hydroxy-3-(piperidine-1-carbonyl)-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid

¹H NMR : (DMSO-D₆, 300MHz) : 1.15(3H, t, J=7Hz), 1.43(4H, m), 1.54(2H, m), 3.14(4H, m), 4.06-4.14(2H, m), 4.34(2H, s), 6.46(1H, d, J=2.94Hz), 6.72-6.83(2H, m), 7.55(2H, s)

- 30 % Yield : 80 %

EXAMPLE 6

{ [3,5-Dichloro-4-(3-ethyl-4-hydroxy-phenoxy)-phenyl]-ethoxycarbonyl-amino }-acetic acid

¹H NMR: (DMSO-D₆, 300MHz): 1.07(3H, t, J=7.47Hz), 1.15(3H, t, J=7.02Hz), 2.48-2.52(2H, m), 4.06-4.13(2H, q, J=6.87Hz & 7.02Hz), 4.31(2H, s), 6.32-6.36(1H, dd, J=3.15Hz & 8.79Hz), 6.62(1H, d, J=3Hz), 6.67(1H, d, J=8.7Hz), 7.54(2H, s)

% Yield : 38 %

5 **EXAMPLE 7**

{[3,5-Dichloro-4-(3-cyclohexylcarbamoyl-4-hydroxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid

¹H NMR : (DMSO-D₆, 300MHz) : 1.16(3H, t, J=6.9Hz), 1.2-1.3(6H, m), 1.5-1.6(4H, m), 3.78(1H, m), 4.07-4.14(2H, q, J=6.93Hz & 6.99Hz), 4.30(2H, s), 6.69-6.73(1H, dd, J=3.03Hz & 9.06Hz), 6.85(1H, d, J=9Hz), 7.57(3H, s)

% Yield : 39 %

EXAMPLE 8

({3,5-Dichloro-4-[4-hydroxy-3-(4-methyl-piperazine-1-carbonyl)-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid

15 ¹H NMR : (CD₃OD, 300MHz) : 1.23(3H, t, J=7.67Hz), 2.92(3H, s), 3.29(4H, m), 3.71(4H, m), 4.16-4.23(2H, q, J=6.78Hz & 7.02Hz), 4.35(2H, s), 6.71(1H, m), 6.85(2H, m), 7.52(2H, s)

% Yield: 59 %

EXAMPLE 9

20 {[3,5-Dichloro-4-(3-dimethylcarbamoyl-4-hydroxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid

¹H NMR : (CD₃OD, 300MHz) : 1.25(3H, m), 2.97(6H, s), 4.18-4.20(2H, m), 4.35(2H, s),

6.6(1H, m), 6.8(2H, m), 7.51(2H, s)

25 % Yield : 77 %

EXAMPLE 10

{[3,5-Dichloro-4-(3-cyclobutylcarbamoyl-4-hydroxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid

30 ¹H NMR : (DMSO-D₆, 300MHz) : 1.16(3H, t, J=7Hz), 1.67-1.69(2H, m), 2.03-2.09(2H, m), 2.20(2H, m), 3.14(1H, m), 4.07-4.14(2H, q, J=6.7Hz & 6.7Hz), 4.33(2H, s), 6.72-6.75(1H, m), 6.85(1H, d, J=9Hz), 7.57(3H, m)

% Yield : 72 %

EXAMPLE 11

{[3,5-Dichloro-4-(4-hydroxy-3-propyl-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid

¹H NMR : (DMSO-D₆, 300MHz) : 0.85(3H, t, J=7.33Hz), 1.15(3H, t, J=7.02Hz), 1.47-1.49(2H, m), 2.48-2.49(2H, m), 4.07-4.09(2H, m), 4.17(2H, s), 6.37-6.40(1H, m), 6.56(1H, d, J=3Hz), 6.68(1H, d, J=8.79Hz), 7.55(2H, s)

% Yield : 10 %

EXAMPLE 12

{[3,5-Dichloro-4-(4-hydroxy-3-isopropylcarbamoyl-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid

¹H NMR : (DMSO-D₆, 300 MHz) : 1.14-1.22(9H, m), 2.52(1H, m), 4.07-4.14(2H, m), 4.34(2H, s), 6.69-6.73(1H, dd, J=3Hz & 8.94Hz), 6.84(1H, d, J=9Hz), 7.57(2H, s), 7.60(1H, d, J=3.06Hz)

% Yield : 74 %

EXAMPLE 13

{[4-(3-tert-Butyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonyl-amino}-acetic acid

¹H NMR: (DMSO-D₆, 300MHz): 1.15(3H, t, J=6.90Hz), 1.29(9H, s), 4.06-4.13(2H, q, J=6.87Hz & 6.99Hz), 4.28(2H, s), 6.29(1H, d, J=5.99Hz), 6.66(1H, d, J=8.71Hz), 6.73(1H, m), 7.54(2H, s)

% Yield : 25 %

EXAMPLE 14

{[3,5-Dichloro-4-(6-hydroxy-biphenyl-3-yloxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid

¹H NMR : (DMSO-D₆, 300MHz) : 1.14(3H, t, J=7Hz), 4.05-4.12(2H, q, J=6.93Hz & 7.14Hz), 4.22(2H, s), 6.60-6.64(1H, dd, J=3.3Hz & 8.7Hz), 6.70(1H, d, J=2.8Hz), 6.89(1H, d, J=8.7Hz), 7.28-7.30(1H, m), 7.34-7.39(2H, m), 7.46-7.48(2H, m), 7.56(2H, s)

% Yield : 20 %

EXAMPLE 15

({3,5-Dichloro-4-[3-(4-fluoro-benzoyl)-4-hydroxy-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid

¹H NMR : (DMSO-D₆, 300MHz) : 1.11(3H, t, J=6.04Hz), 4.05-4.12(2H, q, J=7.11Hz & 7.11Hz), 4.23(2H, s), 6.72(1H, m), 6.94(2H, m), 7.30-7.35(2H, m), 7.56(2H, s), 7.73-7.78(2H, m)

% Yield : 81 %

5 **EXAMPLE 16**

{[3,5-Dichloro-4-(3-diethylcarbamoyl-4-hydroxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid

¹H NMR : (CDCl₃, 300MHz) : 1.15(6H, t, J=6.99Hz), 1.26(3H, m), 3.40-3.49(4H, m), 4.21-4.24(2H, q, J=7.14Hz & 7.14Hz), 4.37(2H, s), 6.60(1H, m), 6.95-6.98(2H, m), 7.40(2H, s)

% Yield: 87 %

EXAMPLE 17

((3,5-Dichloro-4-[3-(5-chloro-thiophene-2-carbonyl)-4-hydroxy-phenoxy]-phenyl)-ethoxycarbonyl-amino)-acetic acid

15 ¹H NMR : (DMSO-D₆, 300MHz) : 1.13(3H, t, J=6.7Hz), 4.03-4.10(2H, q, J=6.96Hz & 7.23Hz), 4.13(2H, s), 6.76(1H, d, J=2.4Hz), 6.89-6.97(2H, m), 7.25(1H, d, J=3.9Hz), 7.38(1H, d, J=4.2Hz), 7.57(2H, s)

% Yield: 81 %

EXAMPLE 18

20 {[4-(3-sec-Butyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-ethoxycarbonyl-amino}-acetic acid

¹H NMR: (DMSO-D₆, 300MHz) : 0.74(3H, t, J=7.2Hz), 1.06(3H, d, J=6.8Hz), 1.13-1.18(3H, m), 1.41-1.49(2H, m), 2.00(6H, s), 2.71-2.95(1H, m), 4.00-4.05(2H, m), 4.18(2H, s), 6.22(1H, d, J=6.3Hz), 6.54(1H, m), 6.64(1H, d, J=8.7Hz), 7.04(2H, s)

25 % Yield : 90 %

EXAMPLE 19

{[3,5-Dichloro-4-(4-hydroxy-3-phenylcarbamoyl-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid

30 ¹H NMR : (CDCl₃, 300MHz) : 1.28(3H, t, J=7.17Hz), 4.21-4.25(2H, m), 4.39(2H, s), 6.91-6.98(1H, m), 7.13(1H, m), 7.21-7.26(2H, m), 7.37-7.42(4H, m), 7.55-7.57(2H, d, J=7.8Hz)

% Yield : 91 %

EXAMPLE 20

((3,5-Dichloro-4-[3-(4-chloro-benzoyl)-4-hydroxy-phenoxy]-phenyl)-ethoxycarbonyl-amino)-acetic acid

¹H NMR : (CDCl₃, 300MHz) : 1.25-1.33(3H, m), 4.21-4.24(2H, m), 4.36(2H, s), 7.01-7.08(3H, m), 7.38(2H, m), 7.46(2H, d, J=8.43Hz), 7.63(2H, d, J=8.43Hz)

5 % Yield : 79 %

EXAMPLE 21

{[4-(3-sec-Butyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-carboxymethyl-amino}-acetic acid

¹H NMR : (DMSO-D₆, 300MHz) : 0.75(3H, t, J=7.2Hz), 1.06(3H, d, J=6.6Hz), 1.13-1.44(2H, m), 1.96(6H, d, J=8.7Hz), 2.84-2.91(1H, m), 4.01(4H, s), 6.15-6.21(3H, m), 6.45-6.62(2H, m)

% Yield : 75 %

EXAMPLE 22

15 ((3,5-Dichloro-4-[3-(2,4-dichloro-benzoyl)-4-hydroxy-phenoxy]-phenyl)-ethoxycarbonyl-amino)-acetic acid

¹H NMR : (CDCl₃, 300MHz) : 1.25-1.28(3H, m), 4.22-4.25(2H, m), 4.36(2H, s), 6.78(1H, m), 7.00(2H, m), 7.32-7.36(3H, m), 7.49(2H, s)

% Yield : 15 %

EXAMPLE 23

20 [[4-(3-sec-Butyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid

¹H NMR : (DMSO-D₆, 300MHz) : 0.75(3H, t, J=7.2Hz), 1.07(3H, d, J=6.9Hz), 1.40-1.53(2H, m), 2.89-2.96(1H, m), 4.44(2H, s), 6.29-6.32(1H, dd, J=3.3Hz & 8.7Hz), 6.57(2H, d, J=8.7Hz), 6.65(2H, d, J=3.3Hz), 6.92(2H, d, J=9Hz), 7.82(2H, s)

25 % Yield : 58 %

EXAMPLE 24

((4-[3-(4-tert-Butyl-benzoyl)-4-hydroxy-phenoxy]-3,5-dichloro-phenyl)-ethoxycarbonyl-amino)-acetic acid

¹H NMR : (CDCl₃, 300MHz) : 1.25(3H, m), 1.36(9H, s), 4.21-4.24(2H, m), 4.35(2H, s), 6.97-7.02(3H, m), 7.37(2H, s), 7.51(2H, d, J=8.31Hz), 7.66(2H, d, J=8.28Hz)

% Yield : 64 %

EXAMPLE 25

({3,5-Dichloro-4-[3-(3-chloro-benzoyl)-4-hydroxy-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid

¹H NMR: (DMSO-D6, 300MHz): 1.14(3H, t, J=7.02Hz), 4.06-4.13(2H, q, J=6.87Hz & 6.99Hz), 4.32(2H, s), 6.75(1H, m), 6.94-7.02(2H, m), 7.53(3H, m), 7.61(2H, d, J=7.17Hz), 7.69(1H, d, J=7.59Hz)

% Yield: 43 %

EXAMPLE 26

{[4-(3-sec-Butyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-carboxymethyl-amino}-acetic acid

¹H NMR : (DMSO-D6, 300MHz) : 0.76(3H, t, J=7.23Hz), 1.07(3H, d, J=6.9Hz), 1.45-1.52(2H, m), 2.90-2.92(1H, m), 3.98(4H, bs), 6.22(1H, m), 6.45(2H, s), 6.62-6.65(2H, m)

% Yield : 63 %

EXAMPLE 27

({4-[3-(Bicyclo[2.2.1]hept-2-ylcarbamoyl)-4-hydroxy-phenoxy]-3,5-dichloro-phenyl}-carboxymethyl-amino)-acetic acid

¹H NMR : (DMSO-D6, 300MHz) : 1.10-1.21(4H, m), 1.46(4H, d, J=7.5Hz), 2.21(2H, d), 3.70(1H, m), 4.11(4H, s), 6.62(2H, d, J=4Hz), 6.81(1H, d, J=9Hz), 7.60(1H, d, J=2.7Hz), 8.43(1H, d, J=8.8Hz)

% Yield : 43 %

EXAMPLE 28

(Carboxymethyl-{3,5-dichloro-4-[3-(4-chloro-benzoyl)-4-hydroxy-phenoxy]-phenyl}-amino)-acetic acid

¹H NMR : (DMSO-D6, 300MHz) : 4.12(4H, s), 6.66-6.70(3H, m), 6.90(2H, s), 7.57(2H, d, J=8.55Hz), 7.68(2H, d, J=8.58Hz)

% Yield : 81 %

EXAMPLE 29

(Carboxymethyl-{3,5-dichloro-4-[4-hydroxy-3-(piperidine-1-carbonyl)-phenoxy]-phenyl}-amino)-acetic acid

¹H NMR : (DMSO-D6, 300MHz) : 1.43(4H, bs), 1.54(2H, bs), 3.15(4H, m), 3.97(4H, s), 6.40(1H, m), 6.47(2H, s), 6.67(1H, m), 6.78(1H, d, J=8.82Hz)

% Yield : 32 %

EXAMPLE 30

((4-[3-(Bicyclo[2.2.1]hept-2-ylsulfamoyl)-4-hydroxy-phenoxy]-3,5-dichloro-phenyl}-carboxymethyl-amino)-acetic acid

¹H NMR : (DMSO-D₆, 300MHz) : 1.22-1.28(6H, m), 1.42-1.45(2H, m), 2.07(2H, m), 3.49(1H, s), 3.98(4H, s), 6.48(2H, m), 6.91(3H, m)

5 % Yield : 26 %

EXAMPLE 31

{Carboxymethyl-[3,5-dichloro-4-(4-hydroxy-3-isopropyl-phenoxy)-phenyl]-amino}-acetic acid

¹H NMR : (DMSO-D₆, 300MHz) : 1.10(6H, d, J=8.8Hz), 3.08-3.17(1H, m), 4.14(4H, s), 6.19-6.23(1H, dd, J=3Hz & 8.7Hz), 6.62-6.67(4H, m)

% Yield : 41 %

EXAMPLE 32

[[3,5-Dichloro-4-(4-hydroxy-3-isopropyl-phenoxy)-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid

¹H NMR : (CDCl₃, 300MHz) : 1.22-1.28(6H, m), 3.14-3.19(1H, m), 4.46(2H, s), 6.35-6.38(1H, m), 6.59-6.62(1H, m), 6.76-6.79(2H, m), 6.87(1H, m), 6.98(2H, d, J=8.7Hz), 7.49(2H, s)

% Yield: 16 %

EXAMPLE 33

(Carboxymethyl-{3,5-dichloro-4-[4-hydroxy-3-(piperidine-1-sulfonyl)-phenoxy]-phenyl}-amino)-acetic acid

¹H NMR : (CDCl₃, 300MHz) : 1.25(2H, m), 1.62(4H, m), 3.01(4H, m), 4.23(4H, s), 6.60(2H, s), 6.83(1H, m), 7.00(1H, m), 7.05(1H, m)

% Yield: 10 %

EXAMPLE 34

{[4-(3-tert-Butyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-carboxymethyl-amino}-acetic acid

¹H NMR : (DMSO-D₆, 300MHz) : 1.29(9H, s), 4.14 (4H, s), 6.20-6.24(1H, dd, J=2.87Hz & 8.65Hz), 6.63 (1H, d, J=8.73Hz), 6.67(2H, s), 6.73(1H, d, J=2.87Hz)

30 % Yield: 12 %

EXAMPLE 35

[[4-(3-tert-Butyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid

¹H NMR: (CDCl₃, 300MHz) : 1.38(9H, s), 4.45(2H, s), 6.30-6.32(1H, m), 6.49-6.52(1H, m), 6.71-6.77(2H, m), 6.95-6.99(3H, m), 7.60(2H, s)

% Yield : 98 %

EXAMPLE 36

- 5 {Carboxymethyl-[3,5-dichloro-4-(3-dimethylcarbamoyl-4-hydroxy-phenoxy)-phenyl]-amino}-acetic acid

¹H NMR : (DMSO-D₆, 300MHz) : 2.81(6H, s), 4.00(4H, s), 6.42(1H, d, J=3Hz), 6.48(2H, s), 6.64-6.68(1H, dd, J=3Hz & 8.7Hz), 6.79(1H, d, J=9Hz)

% Yield: 82 %

10 EXAMPLE 37

{Carboxymethyl-[4-(4-hydroxy-3-isopropyl-phenoxy)-3,5-dimethyl-phenyl]-amino}-acetic acid

¹H NMR : (DMSO-D₆, 400MHz) : 0.93(6H, d, J=6.8Hz), 1.90(6H, s), 3.09-3.14(1H, m), 4.02(4H, s), 6.12-6.15(1H, dd, J=2.8 & 8.4Hz), 6.24(2H, s), 6.58-6.63(2H, m)

- 15 % Yield: 50 %

EXAMPLE 38

[[3,5-Dichloro-4-(3-dimethylsulfamoyl-4-hydroxy-phenoxy)-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid

- 20 ¹H NMR : (CDCl₃, 400MHz) : 2.71(6H, s), 4.45(2H, s), 6.76(2H, d, J=8Hz), 6.94(3H, d, J=7.2Hz), 7.02(1H, d, J=8.8Hz), 7.08(1H, d, J=8Hz), 7.51(2H, s)

% Yield : 71 %

EXAMPLE 39

[[3,5-Dichloro-4-(3-dimethylcarbamoyl-4-hydroxy-phenoxy)-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid

- 25 ¹H NMR: (DMSO-D₆, 400MHz): 2.87(6H, bs), 4.5(2H, s), 6.49(1H, d, J=2.4Hz), 6.73(3H, d, J=8.4Hz), 6.82(1H, d, J=9.2Hz), 6.92(2H, d, J=8.8Hz), 7.8(2H, s)

% Yield: 56 %

EXAMPLE 40

- 30 [{3,5-Dichloro-4-[4-hydroxy-3-(piperidine-1-carbonyl)-phenoxy]-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid

¹H NMR : (DMSO-D₆, 400 MHz) : 1.41-1.52(6H, m), 3.16-3.19(4H, m), 4.45(2H, s), 6.47(1H, d, J=2.8Hz), 6.72-6.76(3H, m), 6.81(1H, d, J=8.8Hz), 6.93(2H, d, J=8.8Hz), 7.84(2H, s)

% Yield : 23 %

EXAMPLE 41

[{3,5-Dichloro-4-[4-hydroxy-3-(piperidine-1-sulfonyl)-phenoxy]-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid

5 ¹H NMR : (CDCl₃, 400 MHz) : 1.44(2H, m), 1.59(4H, m), 3.02(4H, m), 4.46(2H, s), 6.77(2H, m), 6.92-7.00(4H, m), 7.05(1H, m), 7.51(2H, s)

% Yield: 77 %

EXAMPLE 42

10 [[4-(4-Hydroxy-3-isopropyl-phenoxy)-3,5-dimethyl-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid

¹H NMR : (DMSO-D₆, 400MHz) : 1.09(6H, d, J=6.8Hz), 2.03(6H, s), 3.09-3.16(1H, m), 4.26(2H, bs), 6.15-6.18 (1H, dd, J=2.8Hz & 8.8Hz), 6.62(1H, d, J=8.8Hz), 6.66(1H, d, J=3.2Hz), 6.71(2H, d, J=8.4Hz), 6.88(2H, d, J=8.4Hz), 7.19(2H, s)

% Yield: 14 %

15 EXAMPLE 43

[{4-[3-(4-tert-Butyl-benzoyl)-4-hydroxy-phenoxy]-3,5-dichloro-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid

¹H NMR: (CDCl₃, 400MHz): 1.33(9H, s), 4.39(2H, s), 6.69-6.72(2H, m), 6.92(2H, d, J=8.4Hz), 6.98(2H, d, J=8.8Hz), 7.26-7.32(1H, m), 7.47-7.50(4H, m), 7.65(2H, d, J=6.4Hz)

% Yield : 66 %

EXAMPLE 44

[{3,5-Dichloro-4-[3-(4-chloro-benzoyl)-4-hydroxy-phenoxy]-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid

25 ¹H NMR: (CDCl₃, 400MHz): 4.51(2H, s), 6.79(2H, d, J=8.4Hz), 6.99-7.04(4H, m), 7.07(1H, d, J=2.8Hz), 7.43(2H, d, J=7.6Hz), 7.49 (2H, s), 7.61(2H, d, J=8Hz)

% Yield : 68 %

EXAMPLE 45

30 [[3,5-Dichloro-4-(4-hydroxy-3-isopropylsulfamoyl-phenoxy)-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid

¹H NMR : (DMSO-D₆, 400MHz) : 0.93(6H, d, J=6.8Hz), 3.20-3.25(1H, m), 4.24(2H, d, J=6.4Hz), 6.53(2H, m), 6.65(1H, m), 6.75(2H, d, J=8.8Hz), 6.84(2H, m), 6.90-6.98(2H, m)

% Yield : 42 %

EXAMPLE 46

{Carboxymethyl-[3,5-dichloro-4-(3-ethyl-4-hydroxy-phenoxy)-phenyl]-amino}-acetic acid

5 ¹H NMR: (DMSO-D₆, 400MHz): 1.06(3H, t, J=7.4Hz), 2.43-2.48(2H, m), 4.10(4H, s), 6.28-6.31(1H, dd, J=3.2Hz & 8.8Hz), 6.57(1H, d, J=3.2Hz), 6.63-6.66(3H, m)

% Yield: 55%

EXAMPLE 47

10 [{3,5-Dichloro-4-[3-(3-chloro-benzoyl)-4-hydroxy-phenoxy]-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid

¹H NMR : (CDCl₃, 400MHz) : 4.36(2H, bs), 6.71(2H, d, J=6.8Hz), 6.89(4H, m), 6.99-7.04(1H, m), 7.15(1H, m), 7.47-7.51(4H, m), 7.58(1H, m)

% Yield : 68%

EXAMPLE 48

15 [[3,5-Dichloro-4-(3-ethyl-4-hydroxy-phenoxy)-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid

¹H NMR : (DMSO-D₆, 400MHz) : 1.07(3H, t, J=7.4Hz), 2.44-2.48(2H, m), 4.44(2H, s), 6.33-6.36(1H, dd, J=2.8Hz & 8.4Hz), 6.64-6.68(2H, m), 6.73(2H, d, J=8.8Hz), 6.92(2H, d, J=8.8Hz), 7.67(2H, s)

20 % Yield : 16%

EXAMPLE 49

[[3,5-Dichloro-4-(6-hydroxy-biphenyl-3-yloxy)-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid

25 ¹H NMR: (CD₃OD, 400MHz): 4.24(2H, s), 6.61-6.64(1H, m), 6.71-6.82(4H, m), 6.96(2H, d, J=8Hz), 7.27(1H, d, J=7.2Hz), 7.35(2H, d, J=7.2Hz), 7.48(2H, d, J=7.2Hz), 7.64(2H, s)

% Yield: 35%

EXAMPLE 50

30 [[4-(3-Benzyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid

¹H NMR : (CD₃OD, 400MHz) : 3.86(2H, s), 4.5(2H, s), 6.46-6.49(2H, dd, J=2.8Hz & 8.8Hz), 6.69(1H, d, J=8.4Hz), 6.76(2H, d, J=8.8Hz), 6.95(2H, d, J=7.6Hz), 7.15-7.17(5H, m), 7.57 (2H, s)

% Yield : 18%

EXAMPLE 51

[[3,5-Dichloro-4-(3-cyclobutylsulfamoyl-4-hydroxy-phenoxy)-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid

5 ¹H NMR : (CD₃OD, 400MHz) : 1.47-1.59(2H, m), 1.79-1.86(2H, m), 1.95-1.97(2H, m), 3.63-3.69(1H, m), 4.45(2H, s), 6.77(2H, d, J=8.8Hz), 6.92-6.96(3H, m), 7.01(1H, d, J=3.2Hz), 7.04(1H, d, J=3.2Hz), 7.68(2H, s)

% Yield : 39%

EXAMPLE 52

10 [{4-[3-(Bicyclo[2.2.1]hept-2-ylsulfamoyl)-4-hydroxy-phenoxy]-3,5-dichloro-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid

¹H NMR : (CD₃OD, 400MHz) : 0.95-0.99(2H, m), 1.06(1H, m), 1.29-1.34(2H, m), 1.37-1.42(2H, m), 2.00(2H, m), 2.14(1H, m), 3.01-3.02(1H, m), 4.41(2H, s), 6.76(2H, d, J=8.8Hz), 6.94-6.98(3H, m), 7.07(2H, d, J=6.8Hz), 7.69(2H, s)

15 % Yield : 16%

EXAMPLE 53

[{4-[3-(Bicyclo[2.2.1]hept-2-ylsulfamoyl)-4-hydroxy-phenoxy]-3,5-dibromo-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid

20 ¹H NMR : (DMSO-D₆, 400MHz) : 0.85-0.93(3H, m), 1.22-1.28(3H, m), 1.35-1.45(2H, m), 1.89(1H, m), 2.06(1H, m), 2.92-2.93(1H, m), 4.23(2H, s), 6.53(1H, s), 6.62(1H, d, J=5.6Hz), 6.75(2H, d, J=8.8Hz), 6.83-6.93(3H, m), 6.99(2H, d, J=2.4Hz),

% Yield : 14%

EXAMPLE 54

25 [{3,5-Dichloro-4-[4-hydroxy-3-(4-hydroxy-benzoyl)-phenoxy]-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid

¹H NMR : (CD₃OD, 400MHz) : 4.34(2H, s), 6.76(2H, d, J=8.8Hz), 6.79-6.85(3H, m), 6.98(3H, d, J=8.8Hz), 7.11-7.14(1H, dd, J=3.2Hz & 9.2Hz), 7.56-7.58(2H, m), 7.65(2H, s)

% Yield : 34%

30 **EXAMPLE 55**

[{3,5-Dichloro-4-[3-(4-fluoro-benzoyl)-4-hydroxy-phenoxy]-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid

¹H NMR: (DMSO-D₆, 400MHz): 4.35(2H, s), 6.53(1H, m), 6.71-6.76(3H, m), 6.89-6.94(4H, m), 7.30-7.34(2H, m), 7.74-7.77(3H, m)

% Yield: 48%

EXAMPLE 56

5 [(3,5-Dichloro-4-{3-[(4-chloro-phenyl)-hydroxy-methyl]-4-hydroxy-phenoxy}-phenyl)-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid

¹H NMR : (CD₃OD, 400MHz) : 4.4(2H, s), 6.01(1H, s), 6.55-6.58(1H, dd, J=2.8Hz & 8.8Hz), 6.68(1H, d, J=8.8Hz), 6.76(2H, d, J=8.8Hz), 6.85(1H, m), 6.96(2H, d, J=8Hz), 7.25-7.31(4H, m), 7.61(2H, s)

10 % Yield : 90%

EXAMPLE 57

[[4-[3-(Azepane-1-sulfonyl)-4-hydroxy-phenoxy]-3,5-dichloro-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid

¹H NMR: (CDCl₃, 400MHz): 1.52(4H, bs), 1.64(4H, bs), 3.27(4H, bs), 4.46(2H, s),
15 6.76(2H, d, J=8.4Hz), 6.96-7.02(5H, m), 7.51(2H, s)

% Yield : 95%

EXAMPLE 58

((3,5-Dichloro-4-[3-(1-ethyl-propoxy)-4-hydroxy-phenoxy]-phenyl)-ethoxycarbonyl-amino)-acetic acid

20 ¹H NMR : (DMSO-D₆, 400MHz) : 0.82(6H, t, J=7.4Hz), 1.15(3H, t, J=7Hz), 1.55-1.6(4H, m), 4.06 (1H, t, J=5Hz), 4.08-4.12 (2H, m), 4.29(2H, s), 6.04-6.07(1H, dd, J=2Hz & 8.8Hz), 6.47(1H, m), 6.67(1H, d, J=8.4Hz), 7.55(2H, s)

% Yield : 89%

EXAMPLE 59

25 [[4-(3-sec-Butyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid

¹H NMR: (DMSO-D₆, 400MHz): 0.7(3H, t, J=7.2Hz), 1.23(3H, d, J=7.2Hz), 1.38-1.51(2H, m), 2.07(6H, s), 2.86-3.0(1H, m), 4.27(2H, s), 6.20-6.22(1H, dd, J=2.4Hz & 8.4Hz), 6.57(1H, d, J=2.8Hz), 6.63(1H, d, J=8.8Hz), 6.71(2H, d, J=7.6Hz), 6.88(2H, d, J=8.8Hz), 7.17-7.20(2H, m)

30

% Yield: 24%

EXAMPLE 60

[[3,5-Dichloro-4-(3-cyclohexylsulfamoyl-4-hydroxy-phenoxy)-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid

¹H NMR: (DMSO-D₆, 400MHz) : 0.94-1.16(6H, m), 1.54(4H, d, J=8.8Hz), 2.89(1H, m), 4.48(2H, s), 6.73(2H, d, J=8.8Hz), 6.92-6.98(4H, m), 7.19(1H, d, J=7.2Hz),
5 7.72(2H, s)

% Yield: 99%

EXAMPLE 61

{[3,5-Dichloro-4-[4-hydroxy-3-(morpholine-4-sulfonyl)-phenoxy]-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid

10 ¹H NMR: (DMSO-D₆, 400MHz): 3.04(4H, bs), 3.55(4H, bs), 4.44(2H, s), 6.73(2H, d, J=8.4Hz), 6.92(2H, d, J=8.4Hz), 7.01-7.08(3H, m), 7.72(2H, s)

% Yield: 10%

EXAMPLE 62

15 ({3,5-Dichloro-4-[4-hydroxy-3-(3-methyl-benzoyl)-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid

¹H NMR: (CDCl₃, 400MHz): 1.36(3H, m), 2.40(3H, s), 4.19(2H, m), 4.29(2H, s), 6.99-7.09(3H, m), 7.28-7.35(4H, m), 7.44-7.51(2H, m)

% Yield: 83%

EXAMPLE 63

20 {[3,5-Dichloro-4-[4-hydroxy-3-(pyrrolidine-1-sulfonyl)-phenoxy]-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid

¹H NMR: (DMSO-D₆, 400MHz): 1.71(4H, t, J=6.4Hz), 3.22(4H, t, J=6.0Hz), 4.46(2H, s), 6.73(2H, d, J=8.4Hz), 6.93(2H, d, J=8.4Hz), 6.99-7.07(3H, m), 7.72(2H, s)

% Yield : 52%

25 EXAMPLE 64

{[3,5-Dichloro-4-(4-hydroxy-3-isobutoxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid

¹H NMR: (CDCl₃, 400MHz): 1.04(6H, d, J=6.8Hz), 1.25(3H, t, J=6.6Hz), 2.08-2.17(1H, m), 3.79(2H, d, J=6.8Hz), 4.19-4.25(2H, q, J=6.8Hz & 6.8Hz), 4.36(2H, s),
30 6.09-6.12(1H, dd, J=2.8Hz & 8.8Hz), 6.61(1H, d, J=2.8Hz), 6.76(1H, d, J=8.8Hz), 7.38(2H, s)

% Yield: 80%

EXAMPLE 65

{[3,5-Dichloro-4-(3-cyclohexylmethoxy-4-hydroxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid

¹H NMR: (CDCl₃, 400MHz): 1.05(3H, m), 1.26-1.32(6H, m), 1.6-1.86(5H, m), 3.81(2H, d, J=6Hz), 4.21- 4.26(2H, q, J=6.8Hz & 7.2Hz), 4.38(2H, s), 6.09-6.12(1H, dd, J=2.4Hz & 8.8Hz), 6.6(1H, d, J=2.4Hz), 6.76(1H, d, J=8.4Hz), 7.38(2H, s)
% Yield: 53 %

EXAMPLE 66

{[3,5-Dichloro-4-[4-hydroxy-3-(3-methyl-benzoyl)-phenoxy]-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid

¹H NMR : (DMSO-D₆, 400MHz) : 2.32(3H, s), 4.21(2H, bs), 6.53(2H, m), 6.62(2H, m), 6.75(2H, d, J=8.8Hz), 6.82(1H, m), 6.89(2H, d, J=8.8Hz), 7.36-7.46(4H, m)
% Yield: 32 %

EXAMPLE 67

{[3,5-Dibromo-4-[3-(4-chloro-benzoyl)-4-hydroxy-phenoxy]-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid

¹H NMR: (DMSO-D₆, 400MHz): 4.43(2H, s), 6.73(3H, d, J=8.8Hz), 6.90-6.95(4H, m), 7.57(2H, d, J=8.4Hz), 7.68(2H, d, J=8.4Hz), 7.83(2H, s)
% Yield: 42 %

EXAMPLE 68

{[3,5-Dibromo-4-[3-(4-chloro-benzoyl)-4-hydroxy-phenoxy]-phenyl] ethoxycarbonyl-amino)-acetic acid

¹H NMR: (DMSO-D₆, 400MHz): 1.14(3H, t, J=6.8Hz), 4.05-4.11(2H, q, J=6.8Hz & 6.8Hz), 4.22(2H, s), 6.71(1H, d, J=2.4Hz), 6.92-6.96(2H, m), 7.57(2H, d, J=8.4Hz), 7.68-7.71(4H, m)
% Yield: 98 %

EXAMPLE 69

{[3,5-Dichloro-4-[4-hydroxy-3-(4-methyl-benzoyl)-phenoxy]-phenyl]-ethoxycarbonyl-amino)-acetic acid

¹H NMR : (DMSO-D₆, 400MHz) : 1.14(3H, t, J=7Hz), 2.36(3H, s), 4.06-4.12(2H, q, J=6.8Hz & 6.8Hz), 4.32(2H, s), 6.68(1H, d, J=2.4Hz), 6.92-6.98(2H, m), 7.30(2H, d, J=8Hz), 7.55-7.59(4H, m)
% Yield : 95 %

EXAMPLE 70

[{3,5-Dichloro-4-[4-hydroxy-3-(4-methyl-benzoyl)-phenoxy]-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid

¹H NMR: (DMSO-D₆, 400MHz): 2.34(3H, s), 4.22(2H, s), 6.53(1H, s), 6.60-6.65(2H, m), 6.71-6.76 (1H, m), 6.82-6.85(1H, m), 6.89-6.96(3H, m), 7.31(2H, d, J=4.8Hz),
5 7.57(2H, d, J=8.0Hz), 7.83(1H, s)

% Yield : 55 %

Example 71

{[3,5-Dichloro-4-(3-isopropyl-4-methoxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester

10 ¹H NMR: (CDCl₃, 300MHz): 1.19(6H, d, J=6.4Hz), 1.29-1.35(6H, m), 3.24-3.31(1H, m), 3.76(3H, s), 4.19-4.28(4H, m), 4.31(2H, s), 6.43-6.46(1H, dd, J=2.8Hz & 8.8Hz), 6.69(1H, d, J=8.8Hz), 6.87(1H, d, J=2.8Hz), 7.38(2H, s)

Example 72

{[4-(4-Benzyloxy-3-isopropyl-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonyl-amino}-
15 acetic acid ethyl ester

¹H NMR : (CDCl₃, 300 MHz): 1.24(6H, d, J=6.9 Hz), 1.31(6H, t, J=7.2Hz), 3.35-3.40(1H, m), 4.21-4.24(4H, m), 4.31(2H, s), 5.01(2H, s), 6.41-6.45(1H, dd, J=2.9Hz & 8.7Hz), 6.77(1H, d, J=8.9Hz), 6.90(1H, d, J=2.4Hz), 7.34-7.44(7H, m)

Example 73

20 {[4-(3-sec-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester

¹H NMR : (CDCl₃, 300MHz) : 0.83(3H, t, J=7.35Hz), 1.16(3H, d, J=6.93Hz), 1.23-1.26(2H, m), 1.28-1.33(4H, m), 1.33-1.53(2H, m), 3.03-3.10(1H, m), 3.77(3H, s), 4.18-4.27(4H, m), 4.31(2H, s), 6.45-6.49(1H, dd, J=3.0Hz & 8.79Hz), 6.74(1H, d, J=8.6Hz),
25 6.8(1H, d, J=2.91Hz), 7.47(2H, s)

Example 74

{[4-(3-Benzyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester

¹H NMR: (CDCl₃, 300MHz): 1.25-1.38(6H, m), 3.7(3H, s), 3.93(2H, s), 4.12-4.30(6H, m),
30 6.54-6.57(1H, dd, J=3.09Hz & 8.7Hz), 6.69-6.75(2H, m), 7.17-7.36(5H, m), 7.45(2H, s)

Example 75

{4-[3-(Bicyclo[2.2.1]hept-2-ylcarbamoyl)-4-methoxy-phenoxy]-3,5-dichloro-phenyl}-ethoxycarbonyl-amino}-acetic acid ethyl ester

¹H NMR: (CDCl₃, 300MHz): 1.13-1.19(2H, m), 1.26-1.31(7H, m), 1.50(2H, m),
 5 1.54(3H, m), 1.82-1.88(1H, m), 2.30(2H, s), 3.93(3H, s), 4.18-4.27(4H, q, J=7.02Hz &
 7.14Hz), 4.30(2H, s), 6.93(1H, d, J=8.88Hz), 7.02(1H, m), 7.37(2H, s), 7.61(1H, d,
 J=2.6Hz)

Example 76

{[3,5-Dichloro-4-(3-ethyl-4-methoxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic
 10 acid ethyl ester

¹H NMR: (CDCl₃, 300MHz): 1.17(3H, t, J=7.5Hz), 1.24-1.26(3H, m), 1.28-1.33(3H, m)
 2.56-2.64(2H, q, J=7.44Hz & 7.47Hz), 3.78(3H, s), 4.22-4.29(4H, m), 4.31(2H, s) 6.50-
 6.54(1H, dd, J=3.03Hz & 8.79Hz), 6.71(1H, d, J=8.8Hz), 6.77(1H, d, J=3Hz),
 7.39(2H,s)

Example 77

{[3,5-Dichloro-4-(3-dimethylcarbamoyl-4-methoxy-phenoxy)-phenyl]-ethoxycarbonyl-
 amino}-acetic acid ethyl ester

¹H NMR: (CDCl₃, 300MHz): 1.24-1.33(6H, m), 2.84(3H, s), 3.08(3H, s), 3.79(3H, s),
 4.19-4.29(4H, m), 4.31(2H, s), 6.70 (1H, d, J=2.7Hz), 6.81-6.90(2H, m), 7.38(2H, s)

Example 78

{[3,5-Dichloro-4-(3-cyclobutylcarbamoyl-4-methoxy-phenoxy)-phenyl]-
 ethoxycarbonyl-amino}-acetic acid ethyl ester

¹H NMR: (CDCl₃, 300MHz): 1.23-1.34(6H, m), 1.77-1.80(2H, m), 1.91-1.97(2H, m),
 2.41(2H, bs), 3.95(3H, s), 4.20-4.27(4H, q, J=6.93Hz & 7.08Hz), 4.30(2H, s), 4.47-
 25 4.55(1H, m), 6.94(1H, d, J=8.9Hz), 7.03(1H, m), 7.37(2H, s), 7.60(1H, s)

Example 79

{[3,5-Dichloro-4-(4-methoxy-3-propyl-phenoxy)-phenyl]-ethoxycarbonyl-amino}-
 acetic acid ethyl ester

¹H NMR : (DMSO-D₆, 300MHz) : 0.85(3H, t, J=7.32Hz), 1.13-1.22(6H, m), 1.44-
 30 1.52(2H, m), 2.44-2.48(2H, m), 3.71(3H, s), 4.07-4.19(4H, m), 4.43(2H, s), 6.48-
 6.52(1H, dd, J=3.09Hz & 8.85Hz), 6.68(1H, d, J=3Hz), 6.86(1H, d, J=8.9Hz), 7.56(2H,
 s)

Example 80

{[3,5-Dichloro-4-(3-isopropylcarbamoyl-4-methoxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester

¹H NMR : (CDCl₃, 300MHz) : 1.22 -1.34(12H, m), 3.95(3H, s), 4.20-4.27(5H, m), 4.31(2H, s), 6.92(1H, d, J=9Hz), 7.38(2H, m), 7.62(1H, m), 7.78(1H, d, J=6.9Hz)

5 **Example 81**

{[3,5-Dichloro-4-(6-methoxy-biphenyl-3-yloxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester

¹H NMR: (CDCl₃, 300MHz): 1.23-1.33(6H, m), 3.76(3H, s), 4.20-4.28(4H, m), 4.30(2H, s), 6.80(1H, d, J=3Hz), 6.85(1H, d, J=2.7Hz), 6.91(1H, m), 7.26(1H, m), 7.29-
10 7.41(4H, m), 7.50(2H, d, J=7Hz)

Example 82

({3,5-Dichloro-4-[3-(4-fluoro-benzoyl)-4-methoxy-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid ethyl ester

¹H NMR: (CDCl₃, 300MHz) : 1.23-1.30(6H, m), 3.69(3H, s), 4.20-4.28(4H, m),
15 4.30(2H, s), 6.85(1H, d, J=3Hz), 6.90-7.0(2H, m), 7.07-7.13(2H, m), 7.38(2H, s), 7.81-7.86(2H, m)

Example 83

{[3,5-Dichloro-4-(3-diethylcarbamoyl-4-methoxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester

¹H NMR : (DMSO-D₆, 300MHz) : 0.91(3H, t, J=6.9Hz), 1.07(3H, t, J=7.0Hz), 1.12-1.22(6H, m), 3.01-3.03(4H, m), 3.72(3H, s), 4.02-4.18(4H, m), 4.43(2H, s), 6.51(1H, d, J=3Hz), 6.84-6.88(1H, dd, J=3Hz & 9Hz), 7.04(1H, d, J=9Hz), 7.58(2H, s)

Example 84

({3,5-Dichloro-4-[3-(5-chloro-thiophene-2-carbonyl)-4-methoxy-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid ethyl ester

¹H NMR : (CDCl₃, 300MHz) : 1.23-1.32(6H, m), 3.77(3H, s), 4.22-4.28(4H, m), 4.30(2H, s), 6.84(2H, s), 6.92-6.97(3H, m), 7.38(2H, s)

Example 85

{[4-(3-sec-Butyl-4-methoxy-phenoxy)-3,5-dimethyl-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester

¹H NMR: (CDCl₃, 300MHz): 0.83(6H, t, J=6.2Hz), 1.03-1.32(6H, m), 1.49-1.60(2H, m), 2.10(6H, s), 3.11-3.18(1H, m), 4.20-4.27(4H, m), 4.31(2H, s), 4.99(2H, s), 6.37(1H, d, J=6 Hz), 6.74(2H, d, J=8.7Hz), 7.02(2H, s), 7.31-7.43(5H, m)

Example 86

{[3,5-Dichloro-4-(4-methoxy-3-phenylcarbamoyl-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester

¹H NMR: (CDCl₃, 300MHz): 1.26-1.29(6H, m), 4.04(3H, s), 4.19-4.28(4H, m),
 5 4.32(2H, s) 7.01(1H, d, J=9Hz), 7.09-7.14(2H, m), 7.32-7.39(4H, m), 7.62-7.70(3H, m)

Example 87

((3,5-Dichloro-4-[3-(4-chloro-benzoyl)-4-methoxy-phenoxy]-phenyl)-ethoxycarbonyl-amino)-acetic acid ethyl ester

¹H NMR : (CDCl₃, 300MHz) : 1.28-1.32(6H, m), 3.68(3H, s), 4.18-4.30(4H, m),
 10 4.31(2H, s), 6.82-6.86(1H, m), 6.92(1H, d, J=8.8Hz), 6.97-7.01(1H, m), 7.38-7.42(4H, m), 7.72-7.75(2H, m)

Example 88

((3,5-Dichloro-4-[3-(2,4-dichloro-benzoyl)-4-methoxy-phenoxy]-phenyl)-ethoxycarbonyl-amino)-acetic acid ethyl ester

¹H NMR : (CDCl₃, 300MHz) : 1.26-1.31(6H, m), 3.58(3H, s), 4.19-4.29(4H, m),
 15 4.32(2H, s), 6.86(1H, d, J=9Hz), 7.05-7.15(2H, m), 7.30-7.40(3H, m), 7.51(2H, s)

Example 89

[[4-(3-sec-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-(4-methoxy-phenoxy)-amino]-acetic acid ethyl ester

¹H NMR : (CDCl₃, 300MHz) : 0.83(3H, t, J=7.5Hz), 1.16(3H, d, J=7.2Hz), 1.23-1.34(3H, m), 1.48-1.62(2H, m), 3.02-3.09(1H, m), 3.76(3H, s), 3.79(3H, s), 4.27-4.29(2H, m), 4.39(2H, bs), 6.44-6.48(1H, dd, J=3Hz & 8.7Hz), 6.70(1H, d, J=8.7Hz),
 20 6.82(1H, d, J=3Hz), 6.88(2H, d, J=8.7Hz), 7.05(2H, d, J=8.7Hz), 7.49(2H, s)

Example 90

((4-[3-(4-tert-Butyl-benzoyl)-4-methoxy-phenoxy]-3,5-dichloro-phenyl)-ethoxycarbonyl-amino)-acetic acid ethyl ester

¹H NMR: (CDCl₃, 300MHz): 1.28-1.32(6H, m), 1.35(9H, s), 3.7(3H, s), 4.15-4.28(4H, m), 4.29(2H, s), 6.82(1H, m), 6.91-6.94(2H, m), 7.37(2H, m), 7.43-7.50(2H, m), 7.75-7.78(2H, m)

Example 91

{[4-(3-sec-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonylmethyl-amino}-acetic acid ethyl ester

¹H NMR : (CDCl₃, 400MHz) : 0.83(3H, t, J=7.4Hz), 1.15(3H, d, J=6.8Hz), 1.24-1.28(6H, m), 1.5-1.6(2H, m), 3.04-3.05(1H, m), 3.76(3H, s), 4.10(4H, s), 4.22-4.28(4H, m), 6.44-6.47(1H, dd, J=2.8Hz & 8.8Hz), 6.59(2H, s), 6.69(1H, d, J=9.2Hz), 6.78(1H, d, J=3.2Hz)

5 **Example 92**

{3,5-Dichloro-4-[3-(4-chloro-benzoyl)-4-methoxy-phenoxy]-phenyl}-ethoxycarbonylmethyl-amino)-acetic acid ethyl ester

¹H NMR: (CDCl₃, 300MHz) : 1.24-1.29(6H, m), 3.68(3H, s), 4.09(4H, s), 4.14-4.31(4H, m), 6.57(2H, m), 6.84-6.94(3H, m), 7.40(2H, d, J=8.43Hz), 7.75(2H, d, J=8.43Hz)

Example 93

[[3,5-Dichloro-4-(3-isopropyl-4-methoxy-phenoxy)-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester

¹H NMR: (CDCl₃, 300MHz): 1.19(6H, d, J=6.84Hz), 1.28-1.34(3H, m), 3.25-3.30(1H, m), 3.77(3H, s), 3.79(3H, s), 4.26-4.29(2H, m), 4.40(2H, bs), 6.41-6.45(1H, dd, J=3.03Hz & 8.79Hz), 6.69(1H, d, J=8.88Hz), 6.86-6.89(3H, m), 7.05(2H, d, J=8.79Hz), 7.50(2H, s)

Example 94

[[4-(3-tert-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester

¹H NMR : (CDCl₃, 300MHz) : 1.26-1.29(3H, m), 1.35(9H, s), 3.78(3H, s), 3.79(3H, s), 4.29(2H, m), 4.39(2H, bs), 6.40-6.44(1H, dd, J=3Hz & 8.79Hz), 6.7(1H, d, J=8.85Hz), 6.88(2H, d, J=8.67Hz), 6.99-7.06(3H, m), 7.50(2H, s)

Example 95

[[3,5-Dichloro-4-(3-dimethylsulfamoyl-4-methoxy-phenoxy)-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester

¹H NMR : (CDCl₃, 400MHz) : 1.14(3H, t, J=11.2Hz), 2.83(6H, s), 3.79(3H, s), 3.89(3H, s), 4.29(2H, m), 4.40(2H, bs), 6.59-6.86(2H, m), 6.95(2H, d, J=9.2Hz), 7.04(2H, d, J=8.8Hz), 7.41(1H, s), 7.51(2H, s)

30 **Example 96**

[[3,5-Dichloro-4-(3-dimethylcarbamoyl-4-methoxy-phenoxy)-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester

¹H NMR : (CDCl₃, 300MHz) : 1.29-1.34(3H, m), 2.84(3H, s), 3.08(3H, s), 3.8(6H, s), 4.20-4.29(2H, m), 4.40 (2H, s), 6.71(1H, d, J=2.64Hz), 6.82-6.89(4H, m), 7.05(2H, d, J=8.8Hz), 7.69(2H, s)

Example 97

- 5 [{3,5-Dichloro-4-[4-methoxy-3-(piperidine-1-sulfonyl)-phenoxy]-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester

¹H NMR: (CDCl₃, 400MHz): 1.30-1.34(6H, m), 1.50-1.52(3H, m), 3.17-3.2(4H, m), 3.79(3H, s), 3.88(3H, s), 4.28-4.29(2H, m), 4.40(2H, bs), 6.87(2H, d, J=8.4Hz), 6.93(1H, d, J=8.8Hz), 6.99-7.05(3H, m), 7.40(1H, d, J=3.2Hz), 7.51(2H, s)

10 Example 98

[{4-(3-Isopropyl-4-methoxy-phenoxy)-3,5-dimethyl-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester

¹H NMR: (CDCl₃, 400MHz): 1.17(6H, d, J=6.8Hz), 1.27-1.32(3H, m), 2.12(6H, s), 3.23-3.30(1H, m), 3.76(6H, s), 4.24-4.27(2H, m), 4.38(2H, s), 6.32-6.35(1H, dd, J=3Hz & 8.7Hz), 6.65(1H, d, J=8.8Hz), 6.80(1H, d, J=2.8Hz), 6.84-6.86(2H, m), 7.03-7.05(2H, m), 7.14(2H, s)

Example 99

[{4-[3-(4-tert-Butyl-benzoyl)-4-methoxy-phenoxy]-3,5-dichloro-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester

20 ¹H NMR : (CDCl₃, 400MHz) : 1.24-1.33(12H, m), 3.70(3H, s), 3.79(3H, s), 4.27(2H, s), 4.37 (2H, s), 6.83-6.94(5H, m), 7.03(2H, d, J=8.4Hz), 7.44(2H, d, J=8.4Hz), 7.49(2H, s), 7.76(2H, d, J=8.4Hz)

Example 100

25 [{3,5-Dichloro-4-[3-(4-chloro-benzoyl)-4-methoxy-phenoxy]-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester

¹H NMR: (CDCl₃, 400MHz): 1.24(3H, t, J=7.2Hz), 3.66(3H, s), 3.85(3H, s), 4.27(2H, m), 4.38(2H, s), 6.86-6.9(4H, m), 6.98-7.04(3H, m), 7.38(2H, d, J=2.4Hz), 7.5(2H, s), 7.72(2H, d, J=6.8Hz)

Example 101

30 [[3,5-Dichloro-4-(3-isopropylsulfamoyl-4-methoxy-phenoxy)-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester

¹H NMR: (CDCl₃, 400MHz): 1.05(6H, d, J=6.8Hz), 1.32(3H, t, J=6.8Hz), 3.4-3.45(1H, m), 3.79(3H, s), 3.95(3H, s), 4.28(2H, bs), 4.41(2H, s), 6.87(2H, d, J=8.8Hz), 6.96(1H, d, J=8.8Hz), 7.04(3H, d, J=8.8Hz), 7.41(1H, d, J=2.8Hz), 7.52(2H, s)

Example 102

- 5 {{[3,5-Dichloro-4-(3-ethyl-4-methoxy-phenoxy)-phenyl]-ethoxycarbonylmethyl-amino}-acetic acid ethyl ester

¹H NMR : (CDCl₃, 400MHz) : 1.16(3H, t, J=7.6 Hz), 1.26-1.32(6H, m), 2.58-2.60(2H, m), 3.77(3H, s), 4.11(4H, s), 4.23-4.28(4H, q, J=6.8Hz & 7.2Hz), 6.52-6.53(1H, m), 6.60(2H, s), 6.6(1H, d, J=8.8Hz), 6.74(1h, d, J=3.4Hz)

10 Example 103

[{3,5-Dichloro-4-[3-(3-chloro-benzoyl)-4-methoxy-phenoxy]-phenyl}-(4-methoxy-phoxycarbonyl)-amino]-acetic acid ethyl ester

- ¹H NMR: (CDCl₃, 400MHz) : 1.24-1.32(3H, m), 3.68(3H, s), 3.79(3H, s), 4.27(2H, bs), 4.37-4.45(2H, m), 6.86-6.88(3H, m), 6.93(1H, d, J=8.4Hz), 6.99-7.04(3H, m), 7.34-
15 7.38(1H, m), 7.50-7.53(3H, m), 7.64-7.66(1H, m), 7.77(1H, s)

Example 104

[[3,5-Dichloro-4-(3-ethyl-4-methoxy-phenoxy)-phenyl]-(4-methoxy-phoxycarbonyl)-amino]-acetic acid ethyl ester

- ¹H NMR : (CDCl₃, 400MHz) : 1.17(3H, t, J=7.4Hz), 1.3(2H, t, J=7.2Hz), 2.57-
20 2.63(2H, q, J=7.6Hz & 7.6 Hz), 3.78(6H, s), 4.28(2H, m), 4.39(2H, s), 6.50-6.53(1H, dd, J=3.2Hz & 8.8Hz), 6.7(1H, d, J=8.8Hz), 6.77(1H, s), 6.88(2H, d, J=8.8Hz), 7.05(2H, d, J=8.8Hz), 7.50(2H, s)

Example 105

- [[3,5-Dichloro-4-(6-methoxy-biphenyl-3-yloxy)-phenyl]-(4-methoxy-phoxycarbonyl)-amino]-acetic acid ethyl ester

¹H NMR: (CDCl₃, 400MHz): 1.24-1.32(3H, t, J=7.0Hz), 3.76(3H, s), 3.79(3H, s), 4.27-4.38(2H, m), 4.45(2H, bs), 6.76-6.79(1H, dd, J=3.2Hz & 8.8Hz), 6.86-6.89(4H, m), 7.04(2H, d, J=8.4Hz), 7.25-7.33(1H, m), 7.36-7.40(2H, m), 7.49-7.51(4H, m)

Example 106

- 30 [[4-(3-Benzyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-(4-methoxy-phoxycarbonyl)-amino]-acetic acid ethyl ester

¹H NMR : (CDCl₃, 400MHz) : 1.24-1.33(3H, m), 3.75(3H, s), 3.79(3H, s), 3.93(2H, s), 4.28-4.39(2H, m), 4.42(2H, s), 6.54-6.57(1H, dd, J=2.8Hz & 8.8Hz), 6.69-6.74(2H, m),

6.87(2H, d, J=8.8Hz), 7.04(2H, d, J=8.4Hz), 7.13-7.18(3H, m), 7.22-7.25(2H, m), 7.47(2H, s)

Example 107

5 [[3,5-Dichloro-4-(3-cyclobutylsulfamoyl-4-methoxy-phenoxy)-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester

¹H NMR: (CDCl₃, 400MHz): 1.32(3H, t, J=7.2Hz), 1.51-1.56(2H, m), 1.69-1.75(2H, m), 1.98-2.03(2H, m), 3.74(1H, m), 3.79(3H, s), 3.96(3H, s), 4.29(2H, m), 4.41(2H, s), 6.87(2H, d, J=8.4Hz), 6.96(1H, d, J=9.2Hz), 7.04(3H, d, J=8.8Hz), 7.37(1H, d, J=2.8Hz), 7.52(2H, s)

10 **Example 108**

[{4-[3-(Bicyclo[2.2.1]hept-2-ylsulfamoyl)-4-methoxy-phenoxy]-3,5-dichloro-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester

¹H NMR : (CDCl₃, 400MHz) : 0.98-1.01(2H, m), 1.10-1.19(2H, m), 1.26-1.27(2H, m), 1.30-1.34(4H, m), 1.37-1.40(3H, m), 3.09-3.11(1H, m), 3.79(3H, s), 3.94(3H, s), 15 4.29(2H, m), 4.41(2H, bs), 6.87(2H, d, J=8.8Hz), 6.97(1H, d, J=9.2Hz), 7.03-7.06(3H, m), 7.41(1H, s), 7.52(2H, s)

Example 109

[{4-[3-(Bicyclo[2.2.1]hept-2-ylsulfamoyl)-4-methoxy-phenoxy]-3,5-dibromo-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester

20 ¹H NMR: (CDCl₃, 400MHz): 0.98-1.00(2H, m), 1.10-1.19(2H, m), 1.30-1.39(5H, m), 2.03-2.04(2H, m), 2.17-2.20(2H, m), 3.09-3.14(1H, m), 3.79(3H, s), 3.94(3H, s), 4.29(2H, m), 4.48(2H, s), 6.87(2H, d, J=8.4Hz), 6.96-6.99(1H, m), 7.05(3H, d, J=8.8Hz), 7.39(1H, d, J=2.8Hz), 7.72(2H, s)

Example 110

25 [{3,5-Dichloro-4-[4-methoxy-3-(4-methoxy-benzoyl)-phenoxy]-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester

¹H NMR : (CDCl₃, 400MHz) : 1.28-1.32(3H, m), 3.70(3H, s), 3.81(3H, s), 3.86(3H, s), 4.26(2H, s), 4.37-4.45(2H, m), 6.83(1H, d, J=3.2Hz), 6.85-6.94(6H, m), 7.03(2H, d, J=8.4Hz), 7.49(2H, s), 7.78-7.81(2H, m)

30 **Example 111**

[{3,5-Dichloro-4-[3-(4-fluoro-benzoyl)-4-methoxy-phenoxy]-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester

¹H NMR: (CDCl₃, 400MHz): 1.31(3H, t, J=7.2Hz), 3.68(3H, s), 3.79(3H, s), 4.27(2H, bs), 4.45(2H, bs), 6.86-6.92(2H, m), 7.02-7.11(3H, m), 7.49(2H, s), 7.81-7.84(2H, m)

Example 112

5 [{4-[3-(Azepane-1-sulfonyl)-4-methoxy-phenoxy]-3,5-dichloro-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester

¹H NMR: (CDCl₃, 400MHz): 1.32(3H, t, J=7.0Hz), 1.60-1.61(4H, m), 1.71(4H, bs), 3.31-3.34(4H, m), 3.79(3H, s), 3.88(3H, s), 4.29(2H, m), 4.47(2H, s), 6.86-6.92(3H, m), 6.97-6.99(1H, m), 7.04(2H, d, J=8.8Hz), 7.44(1H, d, J=3.2Hz), 7.51(2H, s)

Example 113

10 ({4-[4-Benzoyloxy-3-(1-ethyl-propoxy)-phenoxy]-3,5-dichloro-phenyl}-ethoxy-carbonyl-amino)-acetic acid ethyl ester

¹H NMR: (CDCl₃, 400MHz): 0.95(6H, t, J=7.2Hz), 1.3 (6H, t, J=7.2Hz), 1.64-1.74 (4H, m), 4.09-4.13(1H, m), 4.19-4.28(4H, m), 4.3(2H, s), 5.04(2H, s), 6.15-6.18(1H, dd, J=2.4Hz & 8.8Hz), 6.57(1H, d, J=2Hz), 6.78(2H, d, J=8.8Hz), 7.30-7.43(7H, m)

15 Example 114

[[4-(3-sec-Butyl-4-methoxy-phenoxy)-3,5-dimethyl-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester

¹H NMR: (CDCl₃, 400MHz) : 0.82(3H, t, J=7.2Hz), 1.14(3H, d, J=6.8Hz), 1.30(3H, t, J=6.8Hz), 1.45-1.60(2H, m), 2.12(6H, s), 3.01-3.06(1H, m), 3.74(3H, s), 3.78(3H, s),
20 4.24-4.27(2H, m), 4.38-4.48(2H, m), 6.35-6.38(1H, dd, J=2.8Hz & 8.8Hz), 6.66(1H, d, J=8.8Hz), 6.72(1H, d, J=2.8Hz), 6.85(2H, d, J=8.4Hz), 7.04(2H, d, J=8.8Hz), 7.14(2H, s)

Example 115

25 [[3,5-Dichloro-4-(3-cyclohexylsulfamoyl-4-methoxy-phenoxy)-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester

¹H NMR: (CDCl₃, 400MHz): 1.11-1.27(8H, m), 1.29-1.34(3H, m), 1.68-1.72(2H, m), 3.11-3.13(1H, m), 3.79(3H, s), 3.94(3H, s), 4.25-4.28(2H, m), 4.41(2H, bs), 4.83(1H, d, J=7.6Hz), 6.87(2H, d, J=8.0Hz), 6.94-6.97(1H, m), 7.05(3H, d, J=8.4Hz), 7.40-7.41(1H, m), 7.52(2H, s)

30 Example 116

[{3,5-Dichloro-4-[4-methoxy-3-(morpholine-4-sulfonyl)-phenoxy]-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester

¹H NMR: (CDCl₃, 400MHz): 1.32(3H, t, J=7.2Hz), 3.23(4H, t, J=4.8Hz), 3.71(4H, t, J=4.8Hz), 3.79(3H, s), 3.89(3H, s), 4.41(2H, m), 4.46(2H, s), 6.87(2H, d, J=8.8Hz), 6.92(1H, d, J=4.8Hz), 6.95 -7.03(3H, m), 7.4(1H, d, J=2.8Hz), 7.52(2H, s)

Example 117

5 [{3,5-Dichloro-4-[4-methoxy-3-(pyrrolidine-1-sulfonyl)-phenoxy]-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester

¹H NMR : (DMSO-D₆, 400MHz) : 1.32(3H, t, J=7.2Hz), 1.81-1.84(4H, m), 3.36-3.39(4H, m), 3.79(3H, s), 3.90(3H, s), 4.29(2H, m), 4.40-4.47(2H, bs), 6.87(2H, d, J=8.8Hz), 6.94(1H, d, J=8.8Hz), 7.04(3H, d, J=8.8Hz), 7.44(1H, d, J=2.8Hz), 7.51(2H, s)

Example 118

{[4-(4-Benzoyloxy-3-isobutoxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonyl-amino}-acetic acid ethyl ester

¹H NMR: (CDCl₃, 400MHz): 1.05(6H, d, J=6.8Hz), 1.26-1.32(6H, m), 2.12-2.19(1H, m), 3.77(2H, d, J=6.4Hz), 4.19-4.28(4H, m), 4.31(2H, s), 5.05(2H, s), 6.08-6.11(1H, dd, J=2.4Hz & 8.4Hz), 6.64(1H, d, J=2.8Hz), 6.77(1H, d, J=8.8Hz), 7.29-7.30(1H, m), 7.33-7.38(4H, m), 7.42-7.44(2H, m)

Example 119

20 [{3,5-Dichloro-4-[4-methoxy-3-(3-methyl-benzoyl)-phenoxy]-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester

¹H NMR: (CDCl₃, 400MHz) : 1.30(3H, t, J=7.2Hz), 2.37(3H, s), 3.68(3H, s), 3.78(3H, s), 4.27(2H, s), 4.37-4.45(2H, bs), 6.84-6.87(3H, m), 6.92(1H, d, J=9.2Hz), 7.02(3H, d, J=8Hz), 7.30(1H, d, J=7.6Hz), 7.35(1H, d, J=7.2Hz), 7.49(2H, s), 7.56(1H, d, J=7.6Hz), 7.64(1H, s)

25 **Example 120**

[{3,5-Dibromo-4-[3-(4-chloro-benzoyl)-4-methoxy-phenoxy]-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester

¹H NMR: (DMSO-D₆, 400MHz): 4.43(2H, s), 6.73(3H, d, J=8.8Hz), 6.90-6.95(4H, m), 7.57(2H, d, J=8.4Hz), 7.68(2H, d, J=8.4Hz), 7.83(2H, s)

30 **Example 121**

[{3,5-Dichloro-4-[4-methoxy-3-(4-methyl-benzoyl)-phenoxy]-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester

¹H NMR: (CDCl₃, 400MHz) : 1.3(3H, t, J=7.2Hz), 2.36(3H, s), 3.68(3H, s), 4.27(2H, s), 4.37-4.45(2H, bs), 6.83-6.99(5H, m), 7.03(2H, d, J=8.0Hz), 7.22(2H, d, J=8.0Hz), 7.49(2H, s), 7.71(2H, d, J=8.0Hz)

Activity data:

- 5 Invitro **TR-α** & **TR-β** activities were determined as per in-house protocols and the results of representative compounds are provided in tables 1 & 2 below as a proof of the efficacies of the novel class of compounds disclosed above.

Table 1 :

Example No	EC ₅₀ TR-α (nM)	EC ₅₀ TR-β (nM)	EC ₅₀ TR α/β
1	440	146	3
2	118.9	161.90	0.73
3	274	89	3
23	9.26	2.6	3.56
26	176.3	28.1	6.27
44	84.83	14.83	5.72
47	16.4	11.3	1.45
49	38	10.3	3.68
50	23.3	6.2	3.76
55	106.78	64.3	1.66
56	13.4	20.4	0.65
63	337	254	1.33
67	49	12.8	3.82

10

Table 2:

Example	Conc. nM	TR-α *	TR-β *
13	10	49.80	44.16
	100	96.60	80.60
	1000	72.90	75.00
14	10	11.10	16.40
	100	36.30	58.50
	1000	45.90	77.30
15	10	11.34	23.47
	100	39.66	70.50
	1000	33.74	66.77
17	10	21.19	27.69
	100	51.82	72.82
	1000	53.12	77.89
18	1	6.62	09.44
	10	8.90	18.57
	100	12.97	22.99
	1000	16.87	42.59
20	1	10.42	19.94
	10	15.74	40.69
	100	21.47	87.72
	1000	18.49	81.20
21	1	17.17	33.41
	10	56.81	152.99

	100	110.66	201.73
	1000	93.53	147.91
24	1	10.00	20.00
	10	20.00	40.00
	100	50.00	100.0
	1000	70.00	75.00
25	1	4.22	10.93
	10	8.55	26.29
	100	12.70	70.11
	1000	7.15	51.67
28	1	8.97	10.36
	10	14.71	20.94
	100	25.77	45.43
	1000	33.47	46.14
31	1	8.17	12.05
	10	17.06	27.80
	100	50.99	64.35
	1000	46.21	75.23
32	1	23.36	24.67
	10	74.20	73.68
	100	87.50	118.67
	1000	72.37	94.91
33	1	9.66	8.63
	10	13.90	11.87
	100	25.46	25.96
	1000	46.33	46.76
34	1	12.66	08.37
	10	26.23	21.27
	100	62.95	51.14
	1000	53.76	55.67
35	1	25.40	22.44
	10	106.00	80.46
	100	130.68	124.98
	1000	72.06	81.27
37	1	14.93	21.20
	10	40.84	66.73
	100	71.78	124.67
	1000	63.71	95.64
38	1	09.36	12.28
	10	13.61	16.85
	100	25.32	43.53
	1000	41.59	81.37
41	1	20.78	23.34
	10	56.19	73.45
	100	99.00	89.96
	1000	78.50	66.97
42	1	11.05	12.86
	10	26.63	41.39
	100	72.96	91.91
	1000	80.89	86.01
45	1	10.48	13.47
	10	12.02	18.73
	100	23.05	47.09
	1000	50.62	88.93
48	1	08.16	09.02
	10	17.51	19.36
	100	34.61	47.69
	1000	45.08	37.61

51	1	08.05	08.68
	10	14.43	16.98
	100	32.52	54.59
	1000	83.34	101.51
53	1	11.19	11.00
	10	12.00	12.91
	100	17.15	26.99
	1000	50.30	91.71
57	1	21.61	12.61
	10	24.62	14.81
	100	35.93	23.62
	1000	60.40	62.50
61	1	11.55	10.24
	10	12.50	12.16
	100	12.30	28.87
	1000	28.11	85.19
66	1	20.56	36.67
	10	15.36	25.90
	100	18.11	40.67
	1000	25.75	55.21

*** Fold Induction w.r.t T3(100 nm)**

The data above clearly indicates that several of the novel compounds of the present invention are selective to TR-beta receptor and therefore have potential therapeutically beneficial properties.

In-vivo studies:

Dose-response effects of T3 and selected compounds disclosed in the present invention on cholesterol lowering and change in heart rate in cholesterol-fed rats (treated for 7 days) was determined according to the general protocol described in PNAS, August 19, 2003, vol. 100 (17) 10067-10072. Many of the compounds were found to be reducing cholesterol and having very little effect on the heart rate. Therefore, these compounds have the potential to be further developed as selective TR-beta agonists for the treatment of human and other animals in need of such treatment.

The novel compounds of the present invention may be formulated into suitable pharmaceutically acceptable compositions by combining with suitable excipients by techniques and processes and concentrations as are well known.

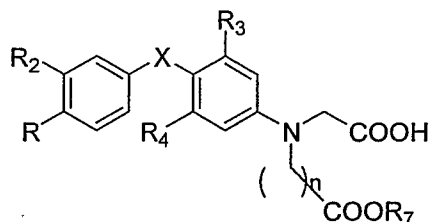
The compounds of formula (I) or pharmaceutical compositions containing them are useful as Thyroid hormone receptor ligands suitable for humans and other warm blooded animals, and may be administered either by oral, topical or parenteral administration for the treatment of various disease conditions associated with dyslipidemia, obesity etc.

The pharmaceutical composition is provided by employing conventional techniques. Preferably the composition is in unit dosage form containing an effective amount of the active component, that is, the compounds of formula (I) according to this invention.

5 The quantity of active component, that is, the compounds of formula (I) according to this invention, in the pharmaceutical composition and unit dosage form thereof may be varied or adjusted widely depending upon the particular application method, the potency of the particular compound and the desired concentration. Generally, the quantity of active component will range between 0.5% to 90% by weight
10 of the composition.

We claim

1. A compound of formula (I) including its tautomers and pharmaceutically acceptable salts



Formula (1)

wherein, $R = OR_1, NHR_1$, wherein further R_1 is selected from H, optionally substituted groups selected from (C_1-C_6) alkyl, ar (C_1-C_6) alkyl groups; R_2 represents hydrogen, hydroxyl, halo, optionally substituted groups selected from (C_1-C_6) alkyl, acyl, oxo, (C_3-C_7) cycloalkyl, aryl, heteroaryl, alkoxy, aryloxy, aralkyl, aralkoxy, carboxylic acid and its derivatives selected from (C_1-C_3) alkyl esters and amides, sulfenyl derivatives, sulfonyl derivatives or the groups representing $-CONR_5R_6$, $-SO_2NR_5R_6$, wherein R_5 & R_6 may be same or different and are independently selected from H, optionally substituted groups selected from (C_1-C_6) alkyl, (C_3-C_7) cycloalkyl, bicycloalkyl, aryl or the groups R_5 & R_6 together with the nitrogen atom to which they are attached, form a five to eight membered cyclic ring which may optionally contain one or more hetero atoms selected from N, S, O; R_3, R_4 are same or different and independently selected from H, halogen, optionally substituted (C_1-C_6) alkyl groups; X is selected from O, $-CH_2-$, CO; 'n' represents the integers 0 or 1; R_7 represents H, optionally substituted groups selected from (C_1-C_6) alkyl, aryl groups; with the provision that when $n = 0$, R_7 does not represent 'H'.

2. A compound of formula (I) as claimed in claim 1, wherein R_1 is selected from H, optionally substituted groups selected from (C_1-C_3) alkyl, phenyl (C_1-C_3) alkyl groups; R_2 is selected from acyl, oxo groups or optionally substituted groups selected from (C_1-C_6) alkyl, phenyl, heteroaryl, benzyl, carboxylic acid and its derivatives selected from (C_1-C_3) alkyl esters and amides, or the groups representing $-CONR_5R_6$, $-SO_2NR_5R_6$, wherein R_5 & R_6 may be same or different and are independently selected from H, optionally substituted groups selected from (C_1-C_6) alkyl, (C_3-C_7) cycloalkyl, bicycloalkyl, phenyl or the groups R_5 & R_6 together with the nitrogen atom to which they are attached, form a five to eight membered

cyclic ring which may optionally contain one or more hetero atoms selected from N, O; R₃, R₄ are same or different and independently selected from H, halogen, optionally substituted (C₁-C₆)alkyl groups; X is selected from O, -CH₂-, CO; 'n' represents 0 or 1; R₇ represents H, optionally substituted groups selected from (C₁-C₆)alkyl, aryl groups; with the provision that when n=0, R₇ does not represent 'H'.

3. The compound as claimed in claim 1 or 2 wherein the substituents on R₂ are selected from hydroxy, halo, or optionally substituted groups selected from (C₁-C₆)alkyl, phenyl, heteroaryl groups.

4. The compound as claimed in claim 1 or 2 wherein the substituents on alkyl, aryl, heteroaryl or cycloalkyl groups may be selected from hydroxyl, halo, cyano, optionally substituted groups selected from (C₁-C₆)alkyl, haloalkyl, alkoxy, oxo, aryl, aryloxy, aralkyl, acyl, alkylthio, thioalkyl groups.

5. The compound as claimed in any one of claims 1 to 4 selected from

{[3,5-Dichloro-4-(4-hydroxy-3-isopropyl-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid;

{[4-(3-sec-Butyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonyl-amino}-acetic acid;

{[4-(3-Benzyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonyl-amino}-acetic acid;

{[4-{3-(Bicyclo[2.2.1]hept-2-ylcarbamoyl)-4-hydroxy-phenoxy}-3,5-dichloro-phenyl]-ethoxycarbonyl-amino}-acetic acid;

{[3,5-Dichloro-4-[4-hydroxy-3-(piperidine-1-carbonyl)-phenoxy]-phenyl]-ethoxycarbonyl-amino}-acetic acid;

{[3,5-Dichloro-4-(3-ethyl-4-hydroxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid;

{[3,5-Dichloro-4-(3-cyclohexylcarbamoyl-4-hydroxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid;

{[3,5-Dichloro-4-[4-hydroxy-3-(4-methyl-piperazine-1-carbonyl)-phenoxy]-phenyl]-ethoxycarbonyl-amino}-acetic acid;

{[3,5-Dichloro-4-(3-dimethylcarbamoyl-4-hydroxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid;

{[3,5-Dichloro-4-(3-cyclobutylcarbamoyl-4-hydroxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid;

- {[3,5-Dichloro-4-(4-hydroxy-3-propyl-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid;
- {[3,5-Dichloro-4-(4-hydroxy-3-isopropylcarbamoyl-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid;
- 5 { [4-(3-tert-Butyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonyl-amino}-acetic acid;
- {[3,5-Dichloro-4-(6-hydroxy-biphenyl-3-yloxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid;
- ({3,5-Dichloro-4-[3-(4-fluoro-benzoyl)-4-hydroxy-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid;
- 10 { [3,5-Dichloro-4-(3-diethylcarbamoyl-4-hydroxy-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid;
- ({3,5-Dichloro-4-[3-(5-chloro-thiophene-2-carbonyl)-4-hydroxy-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid;
- 15 { [4-(3-sec-Butyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-ethoxycarbonyl-amino}-acetic acid;
- { [3,5-Dichloro-4-(4-hydroxy-3-phenylcarbamoyl-phenoxy)-phenyl]-ethoxycarbonyl-amino}-acetic acid;
- ({3,5-Dichloro-4-[3-(4-chloro-benzoyl)-4-hydroxy-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid;
- 20 { [4-(3-sec-Butyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-carboxymethyl-amino}-acetic acid;
- ({3,5-Dichloro-4-[3-(2,4-dichloro-benzoyl)-4-hydroxy-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid;
- 25 [[4-(3-sec-Butyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- ({4-[3-(4-tert-Butyl-benzoyl)-4-hydroxy-phenoxy]-3,5-dichloro-phenyl}-ethoxycarbonyl-amino)-acetic acid;
- ({3,5-Dichloro-4-[3-(3-chloro-benzoyl)-4-hydroxy-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid;
- 30 { [4-(3-sec-Butyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-carboxymethyl-amino}-acetic acid;

- ({4-[3-(Bicyclo[2.2.1]hept-2-ylcarbamoyl)-4-hydroxy-phenoxy]-3,5-dichloro-phenyl}-carboxymethyl-amino)-acetic acid;
- (Carboxymethyl-{3,5-dichloro-4-[3-(4-chloro-benzoyl)-4-hydroxy-phenoxy]-phenyl}-amino)-acetic acid;
- 5 (Carboxymethyl-{3,5-dichloro-4-[4-hydroxy-3-(piperidine-1-carbonyl)-phenoxy]-phenyl}-amino)-acetic acid;
- ({4-[3-(Bicyclo[2.2.1]hept-2-ylsulfamoyl)-4-hydroxy-phenoxy]-3,5-dichloro-phenyl}-carboxymethyl-amino)-acetic acid;
- {Carboxymethyl-[3,5-dichloro-4-(4-hydroxy-3-isopropyl-phenoxy)-phenyl]-amino}-acetic acid;
- 10 [[3,5-Dichloro-4-(4-hydroxy-3-isopropyl-phenoxy)-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- (Carboxymethyl-{3,5-dichloro-4-[4-hydroxy-3-(piperidine-1-sulfonyl)-phenoxy]-phenyl}-amino)-acetic acid;
- 15 {[4-(3-tert-Butyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-carboxymethyl-amino}-acetic acid;
- [[4-(3-tert-Butyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- {Carboxymethyl-[3,5-dichloro-4-(3-dimethylcarbamoyl-4-hydroxy-phenoxy)-phenyl]-amino}-acetic acid;
- 20 {Carboxymethyl-[4-(4-hydroxy-3-isopropyl-phenoxy)-3,5-dimethyl-phenyl]-amino}-acetic acid;
- [[3,5-Dichloro-4-(3-dimethylsulfamoyl-4-hydroxy-phenoxy)-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- 25 [[3,5-Dichloro-4-(3-dimethylcarbamoyl-4-hydroxy-phenoxy)-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- [{3,5-Dichloro-4-[4-hydroxy-3-(piperidine-1-carbonyl)-phenoxy]-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- [{3,5-Dichloro-4-[4-hydroxy-3-(piperidine-1-sulfonyl)-phenoxy]-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- 30 [[4-(4-Hydroxy-3-isopropyl-phenoxy)-3,5-dimethyl-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;

- [{4-[3-(4-tert-Butyl-benzoyl)-4-hydroxy-phenoxy]-3,5-dichloro-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- [{3,5-Dichloro-4-[3-(4-chloro-benzoyl)-4-hydroxy-phenoxy]-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- 5 [[3,5-Dichloro-4-(4-hydroxy-3-isopropylsulfamoyl-phenoxy)-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- {Carboxymethyl-[3,5-dichloro-4-(3-ethyl-4-hydroxy-phenoxy)-phenyl]-amino}-acetic acid;
- [{3,5-Dichloro-4-[3-(3-chloro-benzoyl)-4-hydroxy-phenoxy]-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- 10 [[3,5-Dichloro-4-(3-ethyl-4-hydroxy-phenoxy)-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- [[3,5-Dichloro-4-(6-hydroxy-biphenyl-3-yloxy)-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- 15 [[4-(3-Benzyl-4-hydroxy-phenoxy)-3,5-dichloro-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- [[3,5-Dichloro-4-(3-cyclobutylsulfamoyl-4-hydroxy-phenoxy)-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- [{4-[3-(Bicyclo[2.2.1]hept-2-ylsulfamoyl)-4-hydroxy-phenoxy]-3,5-dichloro-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- 20 [{4-[3-(Bicyclo[2.2.1]hept-2-ylsulfamoyl)-4-hydroxy-phenoxy]-3,5-dibromo-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- [{3,5-Dichloro-4-[4-hydroxy-3-(4-hydroxy-benzoyl)-phenoxy]-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- 25 [{3,5-Dichloro-4-[3-(4-fluoro-benzoyl)-4-hydroxy-phenoxy]-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- [(3,5-Dichloro-4-{3-[(4-chloro-phenyl)-hydroxy-methyl]-4-hydroxy-phenoxy}-phenyl)-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- [{4-[3-(Azepane-1-sulfonyl)-4-hydroxy-phenoxy]-3,5-dichloro-phenyl}-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- 30 ({3,5-Dichloro-4-[3-(1-ethyl-propoxy)-4-hydroxy-phenoxy]-phenyl}-ethoxy-carbonyl-amino)-acetic acid;

- [[4-(3-sec-Butyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- [[3,5-Dichloro-4-(3-cyclohexylsulfamoyl-4-hydroxy-phenoxy)-phenyl]-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- 5 [{3,5-Dichloro-4-[4-hydroxy-3-(morpholine-4-sulfonyl)-phenoxy]-phenyl }-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- ({3,5-Dichloro-4-[4-hydroxy-3-(3-methyl-benzoyl)-phenoxy]-phenyl }-ethoxycarbonyl-amino)-acetic acid;
- [{3,5-Dichloro-4-[4-hydroxy-3-(pyrrolidine-1-sulfonyl)-phenoxy]-phenyl }-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- 10 { [3,5-Dichloro-4-(4-hydroxy-3-isobutoxy-phenoxy)-phenyl]-ethoxycarbonyl-amino }-acetic acid;
- { [3,5-Dichloro-4-(3-cyclohexylmethoxy-4-hydroxy-phenoxy)-phenyl]-ethoxycarbonyl-amino }-acetic acid;
- 15 [{3,5-Dichloro-4-[4-hydroxy-3-(3-methyl-benzoyl)-phenoxy]-phenyl }-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- [{3,5-Dibromo-4-[3-(4-chloro-benzoyl)-4-hydroxy-phenoxy]-phenyl }-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- ({3,5-Dibromo-4-[3-(4-chloro-benzoyl)-4-hydroxy-phenoxy]-phenyl }-ethoxycarbonyl-amino)-acetic acid;
- 20 ({3,5-Dichloro-4-[4-hydroxy-3-(4-methyl-benzoyl)-phenoxy]-phenyl }-ethoxycarbonyl-amino)-acetic acid;
- [{3,5-Dichloro-4-[4-hydroxy-3-(4-methyl-benzoyl)-phenoxy]-phenyl }-(4-hydroxy-phenoxy-carbonyl)-amino]-acetic acid;
- 25 { [3,5-Dichloro-4-(3-isopropyl-4-methoxy-phenoxy)-phenyl]-ethoxycarbonyl-amino }-acetic acid ethyl ester;
- { [4-(4-Benzoyloxy-3-isopropyl-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonyl-amino }-acetic acid ethyl ester;
- { [4-(3-sec-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonyl-amino }-acetic acid ethyl ester;
- 30 { [4-(3-Benzyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonyl-amino }-acetic acid ethyl ester;

- ({4-[3-(Bicyclo[2.2.1]hept-2-ylcarbamoyl)-4-methoxy-phenoxy]-3,5-dichloro-phenyl}-ethoxycarbonyl-amino)-acetic acid ethyl ester;
 ({3,5-Dichloro-4-[4-methoxy-3-(piperidine-1-carbonyl)-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid ethyl ester;
 5 { [3,5-Dichloro-4-(3-ethyl-4-methoxy-phenoxy)-phenyl]-ethoxycarbonyl-amino }-acetic acid ethyl ester;
 { [3,5-Dichloro-4-(3-cyclohexylcarbamoyl-4-methoxy-phenoxy)-phenyl]-ethoxycarbonyl-amino }-acetic acid ethyl ester;
 ({3,5-Dichloro-4-[4-methoxy-3-(4-methyl-piperazine-1-carbonyl)-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid ethyl ester;
 10 { [3,5-Dichloro-4-(3-dimethylcarbamoyl-4-methoxy-phenoxy)-phenyl]-ethoxycarbonyl-amino }-acetic acid ethyl ester;
 { [3,5-Dichloro-4-(3-cyclobutylcarbamoyl-4-methoxy-phenoxy)-phenyl]-ethoxycarbonyl-amino }-acetic acid ethyl ester;
 15 { [3,5-Dichloro-4-(4-methoxy-3-propyl-phenoxy)-phenyl]-ethoxycarbonyl-amino }-acetic acid ethyl ester;
 { [3,5-Dichloro-4-(3-isopropylcarbamoyl-4-methoxy-phenoxy)-phenyl]-ethoxycarbonyl-amino }-acetic acid ethyl ester;
 { [4-(3-~~tert~~-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonyl-amino }-acetic acid ethyl ester;
 20 { [3,5-Dichloro-4-(6-methoxy-biphenyl-3-yloxy)-phenyl]-ethoxycarbonyl-amino }-acetic acid ethyl ester;
 ({3,5-Dichloro-4-[3-(4-fluoro-benzoyl)-4-methoxy-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid ethyl ester;
 25 { [3,5-Dichloro-4-(3-diethylcarbamoyl-4-methoxy-phenoxy)-phenyl]-ethoxycarbonyl-amino }-acetic acid ethyl ester;
 ({3,5-Dichloro-4-[3-(5-chloro-thiophene-2-carbonyl)-4-methoxy-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid ethyl ester;
 { [4-(3-sec-Butyl-4-methoxy-phenoxy)-3,5-dimethyl-phenyl]-ethoxycarbonyl-amino }-acetic acid ethyl ester;
 30 { [3,5-Dichloro-4-(4-methoxy-3-phenylcarbamoyl-phenoxy)-phenyl]-ethoxycarbonyl-amino }-acetic acid ethyl ester;

- ({3,5-Dichloro-4-[3-(4-chloro-benzoyl)-4-methoxy-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid ethyl ester;
 {[4-(3-sec-Butyl-4-methoxy-phenoxy)-3,5-dimethyl-phenyl]-ethoxycarbonylmethyl-amino}-acetic acid ethyl ester;
- 5 ({3,5-Dichloro-4-[3-(2,4-dichloro-benzoyl)-4-methoxy-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid ethyl ester;
 [[4-(3-sec-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
 ({4-[3-(4-tert-Butyl-benzoyl)-4-methoxy-phenoxy]-3,5-dichloro-phenyl}-ethoxycarbonyl-amino)-acetic acid ethyl ester;
- 10 ({3,5-Dichloro-4-[3-(3-chloro-benzoyl)-4-methoxy-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid ethyl ester;
 {[4-(3-sec-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonylmethyl-amino}-acetic acid ethyl ester;
- 15 ({4-[3-(Bicyclo[2.2.1]hept-2-ylcarbonyl)-4-methoxy-phenoxy]-3,5-dichloro-phenyl}-ethoxycarbonylmethyl-amino)-acetic acid ethyl ester;
 ({3,5-Dichloro-4-[3-(4-chloro-benzoyl)-4-methoxy-phenoxy]-phenyl}-ethoxycarbonylmethyl-amino)-acetic acid ethyl ester;
 ({3,5-Dichloro-4-[4-methoxy-3-(piperidine-1-carbonyl)-phenoxy]-phenyl}-ethoxycarbonylmethyl-amino)-acetic acid ethyl ester;
- 20 ({4-[3-(Bicyclo[2.2.1]hept-2-ylsulfonyl)-4-methoxy-phenoxy]-3,5-dichloro-phenyl}-ethoxycarbonylmethyl-amino)-acetic acid ethyl ester;
 {[3,5-Dichloro-4-(3-isopropyl-4-methoxy-phenoxy)-phenyl]-ethoxycarbonylmethyl-amino}-acetic acid ethyl ester;
- 25 [[3,5-Dichloro-4-(3-isopropyl-4-methoxy-phenoxy)-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
 ({3,5-Dichloro-4-[4-methoxy-3-(piperidine-1-sulfonyl)-phenoxy]-phenyl}-ethoxycarbonylmethyl-amino)-acetic acid ethyl ester;
- 30 {[4-(3-tert-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-ethoxycarbonylmethyl-amino}-acetic acid ethyl ester;
 [[4-(3-tert-Butyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;

- {[3,5-Dichloro-4-(3-dimethylcarbamoyl-4-methoxy-phenoxy)-phenyl]-ethoxycarbonylmethyl-amino}-acetic acid ethyl ester;
- {Ethoxycarbonylmethyl-[4-(3-isopropyl-4-methoxy-phenoxy)-3,5-dimethyl-phenyl]-amino}-acetic acid ethyl ester;
- 5 [[3,5-Dichloro-4-(3-dimethylsulfamoyl-4-methoxy-phenoxy)-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- [[3,5-Dichloro-4-(3-dimethylcarbamoyl-4-methoxy-phenoxy)-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- 10 [{3,5-Dichloro-4-[4-methoxy-3-(piperidine-1-carbonyl)-phenoxy]-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- [[3,5-Dichloro-4-[4-methoxy-3-(piperidine-1-sulfonyl)-phenoxy]-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- [[4-(3-Isopropyl-4-methoxy-phenoxy)-3,5-dimethyl-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- 15 [{4-[3-(4-tert-Butyl-benzoyl)-4-methoxy-phenoxy]-3,5-dichloro-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- [[3,5-Dichloro-4-[3-(4-chloro-benzoyl)-4-methoxy-phenoxy]-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- [[3,5-Dichloro-4-(3-isopropylsulfamoyl-4-methoxy-phenoxy)-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- 20 { [3,5-Dichloro-4-(3-ethyl-4-methoxy-phenoxy)-phenyl]-ethoxycarbonylmethyl-amino}-acetic acid ethyl ester;
- [[3,5-Dichloro-4-[3-(3-chloro-benzoyl)-4-methoxy-phenoxy]-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- 25 [[3,5-Dichloro-4-(3-ethyl-4-methoxy-phenoxy)-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- [[3,5-Dichloro-4-(6-methoxy-biphenyl-3-yloxy)-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- [[4-(3-Benzyl-4-methoxy-phenoxy)-3,5-dichloro-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;
- 30 [[3,5-Dichloro-4-(3-cyclobutylsulfamoyl-4-methoxy-phenoxy)-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;

[{4-[3-(Bicyclo[2.2.1]hept-2-ylsulfamoyl)-4-methoxy-phenoxy]-3,5-dichloro-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;

[{4-[3-(Bicyclo[2.2.1]hept-2-ylsulfamoyl)-4-methoxy-phenoxy]-3,5-dibromo-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;

5 [3,5-Dichloro-4-[4-methoxy-3-(4-methoxy-benzoyl)-phenoxy]-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;

[3,5-Dichloro-4-[3-(4-fluoro-benzoyl)-4-methoxy-phenoxy]-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;

10 [4-[3-(Azepane-1-sulfonyl)-4-methoxy-phenoxy]-3,5-dichloro-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;

{{4-[4-Benzyloxy-3-(1-ethyl-propoxy)-phenoxy]-3,5-dichloro-phenyl}-ethoxycarbonyl-amino)-acetic acid ethyl ester;

[[4-(3-sec-Butyl-4-methoxy-phenoxy)-3,5-dimethyl-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;

15 [[3,5-Dichloro-4-(3-cyclohexylsulfamoyl-4-methoxy-phenoxy)-phenyl]-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;

[{3,5-Dichloro-4-[4-methoxy-3-(morpholine-4-sulfonyl)-phenoxy]-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;

20 [{3,5-Dichloro-4-[4-methoxy-3-(3-methyl-benzoyl)-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid ethyl ester;

[{3,5-Dichloro-4-[4-methoxy-3-(pyrrolidine-1-sulfonyl)-phenoxy]-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;

{{4-(4-Benzyloxy-3-isobutoxy-phenoxy)-3,5-dichloro-phenyl}-ethoxycarbonyl-amino}-acetic acid ethyl ester;

25 {{4-(4-Benzyloxy-3-cyclohexylmethoxy-phenoxy)-3,5-dichloro-phenyl}-ethoxycarbonyl-amino}-acetic acid ethyl ester;

[{3,5-Dichloro-4-[4-methoxy-3-(3-methyl-benzoyl)-phenoxy]-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;

30 [{3,5-Dibromo-4-[3-(4-chloro-benzoyl)-4-methoxy-phenoxy]-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester;

{{3,5-Dibromo-4-[3-(4-chloro-benzoyl)-4-methoxy-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid ethyl ester;

({3,5-Dichloro-4-[4-methoxy-3-(4-methyl-benzoyl)-phenoxy]-phenyl}-ethoxycarbonyl-amino)-acetic acid ethyl ester;

[{3,5-Dichloro-4-[4-methoxy-3-(4-methyl-benzoyl)-phenoxy]-phenyl}-(4-methoxy-phenoxy-carbonyl)-amino]-acetic acid ethyl ester.

- 5 6. A pharmaceutical composition which comprises compounds of formula (I), as claimed in any preceding claims and a pharmaceutically acceptable carrier, diluent or excipients.
7. A method of preventing or treating diseases caused by dyslipidemia or obesity comprising administering an effective, non-toxic amount of compound of formula
10 (I) or suitable pharmaceutical composition as defined in any preceding claims to a patient in need thereof.
8. A medicine for treating/reducing dyslipidemia or obesity which comprises administering a compound of formula (I), as defined in any preceding claims and a pharmaceutically acceptable carrier, diluent or excipients to a patient in need
15 thereof.
9. Use of compounds of formula (I), their pharmaceutical compositions and medicines containing them as defined in any previous claims as a medicament suitable for the treatment of diseases mentioned in any of the aforesaid claims.

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