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DESCRIPTION

ESTER COMPOUND AND MEDICAL USE THEREOF

5 **Technical Field**

 The present invention relates to a novel ester compound, and also relates to a pharmaceutical composition comprising a novel ester compound which selectively inhibits microsomal triglyceride transfer protein (MTP) in the small intestine or
10 a prodrug thereof, or a pharmaceutically acceptable salt of either. Further, the present invention relates to an agent for the treatment or prophylaxis of hyperlipidemia, arteriosclerosis, coronary artery diseases, obesity, diabetes or hypertension comprising a novel ester compound which
15 selectively inhibits MTP in the small intestine or a prodrug thereof, or a pharmaceutically acceptable salt of either as an active ingredient. In addition, the present invention relates to an agent for the treatment or prophylaxis of hyperlipidemia, arteriosclerosis, coronary artery diseases, obesity, diabetes
20 or hypertension, which has a novel function that has never been known before.

Background Art

 It has been said that hyperlipidemia, diabetes,
25 hypertension or the like is one of the risk factors for arteriosclerosis. Hyperlipidemia is a condition where the concentration of lipid such as cholesterol is abnormally elevated in the blood. Types of hyperlipidemia, depending on the cause, include primary hyperlipidemia caused by genetic

abnormality in enzyme, protein, lipoprotein and the like which participate in the metabolism of low-density lipoprotein (LDL), secondary hyperlipidemia due to various disease or drug administration, and acquired hyperlipidemia basically
5 resulting from overnutrition.

Meanwhile, lipid taken in from food is absorbed in the small intestine by the action of bile acid, and secreted as chylomicron in the blood via lymphatic vessels. The triglyceride moiety of the secreted chylomicrons is hydrolyzed
10 to free fatty acids by the action of lipoprotein lipase (LPL) existing in capillary vessels to become chylomicron remnants having a high content of cholesteryl ester (CE), which is then absorbed in the liver by the mediation of chylomicron remnant receptor in the liver. Further, in the liver, the absorbed
15 chylomicron remnant and free fatty acid are converted to CE and TG, respectively, which are then associated with apolipoprotein B synthesized on rough surfaced endoplasmic reticulum to form very low density lipoprotein (VLDL). The VLDL is transferred to the Golgi apparatus, modified and secreted outside cells,
20 and it becomes intermediate density lipoprotein (IDL) by the action of LPL. The IDL is converted to LDL by the action of hepatic triglyceride lipase (HTGL), and lipids are distributed to peripheral tissues.

It has long been indicated that, during the
25 above-mentioned formation of chylomicron in the small intestine or VLDL in the liver, a protein having TG- or CE-transfer activity is existing in microsomal fractions of the small intestine or liver. Meanwhile, the protein, i.e. MTP (microsomal triglyceride transfer protein) was purified and

separated from microsomal fractions of bovine liver by Wetterau
et al. in 1985 (Wetterau J.R. et al: Chem.Phys.Lipids 38,
205-222(1985)). MTP, however, began attracting a lot of
attention in the field of clinical medicine only after it was
5 reported in 1993 that the cause of abetalipoproteinemia lay in
the deficit of MTP. In other word, the disease is characterized
in that, while the genes related to apolipoprotein B are normal,
apolipoprotein B is hardly detected in the serum, the level of
serum cholesterol is 50mg/dL or lower, the level of serum
10 triglyceride is extremely low and, moreover, lipoproteins
including apolipoprotein B such as chylomicron, VLDL, LDL, etc.
do not at all exist in the blood. By this finding, it has been
shown that MTP is an integral protein involved in the
association between apolipoprotein B and TG or CE, i.e. the
15 formation of VLDL or chylomicron, and plays an essential role
in secretion thereof.

Since lipid is by nature insoluble in water, lipid in the
blood is combined with a hydrophilic protein known as
apolipoprotein and exists as so-called lipoprotein. All the
20 VLDL, IDL, LDL or chylomicron, etc. related to hyperlipidemia
are a lipoprotein.

MTP exists in the microsome fractions of hepatocytes and
intestinal epithelial cells, and catalyses the transfer of TG
or CE in cells. In the liver and small intestine, along with
25 the synthesis of apolipoprotein (apolipoprotein B100 in the
liver and apolipoprotein B48 in the small intestine), TG and
CE are combined with respective apolipoprotein B by the transfer
activity of MTP, and thus VLDL or chylomicron is formed. As
a result, those lipoproteins are secreted outside the cells as

VLDL in the liver or as chylomicron in the small intestine. It should be said that MTP is indispensable for the construction of those lipoproteins. Namely, if the activity of MTP is blocked, the transfer of lipid such as TG and CE, etc. to apolipoprotein is inhibited, whereby formation of a lipoprotein can be inhibited.

On the other hand, it has been elucidated that LDL in general is closely related to the progression of arteriosclerosis. That is, LDL permeating endothelium of blood vessels is deposited in intercellular matrix of vessel wall, where oxidative denaturation takes place and lipid peroxides or denaturated proteins induce a series of inflammation reactions. Consequently, macrophage invasion, leading to lipid deposit or foaming cells, migration or proliferation of smooth muscle cells and increase in intercellular matrix, etc. take place, which leads to the development of arteriosclerosis plaque. On the basis of the above, it is supposed to be possible to prevent or treat arteriosclerosis, coronary artery diseases or hypertension by reducing the level of LDL.

As already mentioned, it is possible to inhibit the formation of lipoprotein such as chylomicron, VLDL, LDL, etc. by inhibiting the action of MTP. Accordingly, it has been expected that it should become possible to control lipoprotein such as TG, cholesterol and LDL, etc. in blood and to control lipid in cells by adjusting the activity of MTP, and therefore, a novel agent for the treatment or prophylaxis of hyperlipidemia, arteriosclerosis, coronary artery diseases, diabetes, obesity, or hypertension, and further, an agent for the treatment or

prophylaxis of pancreatitis, hypercholesterolemia, hyperglyceridemia, etc. has been expected to be provided.

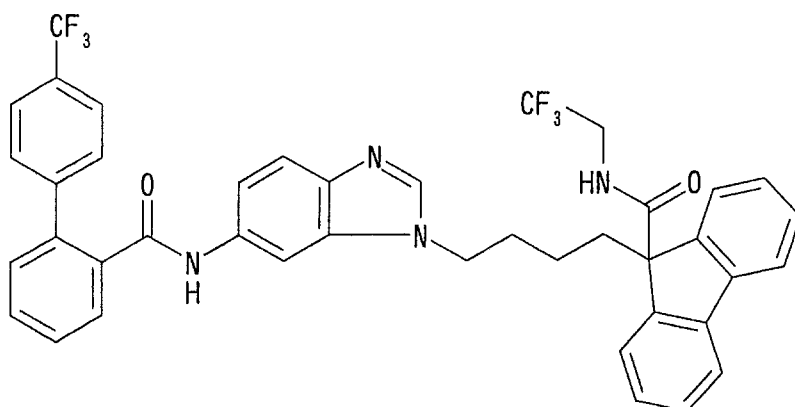
However, with the development of MTP inhibitors, some cases of fatty liver were reported and concern over
5 hepatotoxicity has been raised.

For these reasons, a novel MTP inhibitor causing no side effect such as a fatty liver, etc. has been strongly desired.

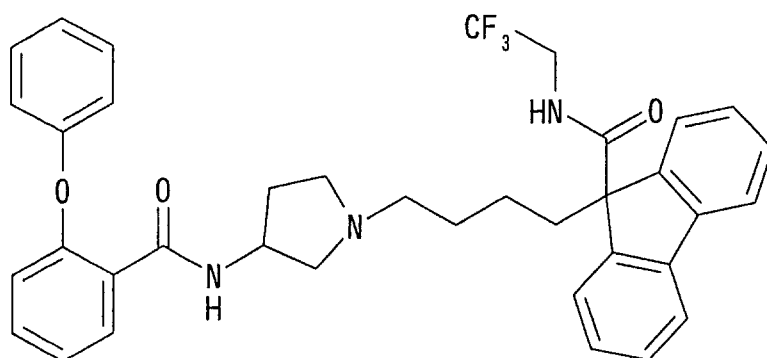
In the conventional manners, combined therapies of various combinations of different antihyperlipidemic drugs
10 have been tried. However, when, for example, a statin-type drug and a resin-type drug are given together, undesirable side effects such as increased GTO and GPT, constipation, blocking of absorption of vitamin A, D, E and K and the like are observed. On the other hand, when a statin-type drug and a fibrate drug
15 are given together, side effects such as rhabdomyolysis or increased CPK (creative phosphokinase) are observed. Thus, with regard to a combined therapy for hyperlipidemia, a medicament for a combined administration which can be administered in combination with a conventional
20 antihyperlipidemic drug without causing any above-mentioned side effect has been desired.

Meanwhile, examples of the known compound having MTP inhibitory activity with a similar structure of the compounds
25 of the present invention are described below.

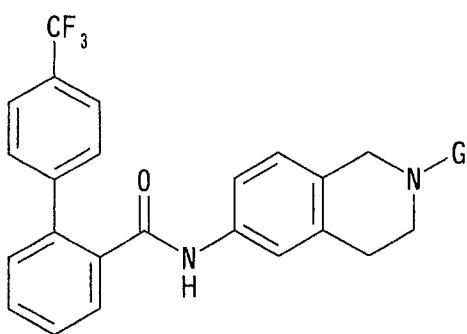
The following compound is disclosed in WO97/26240.



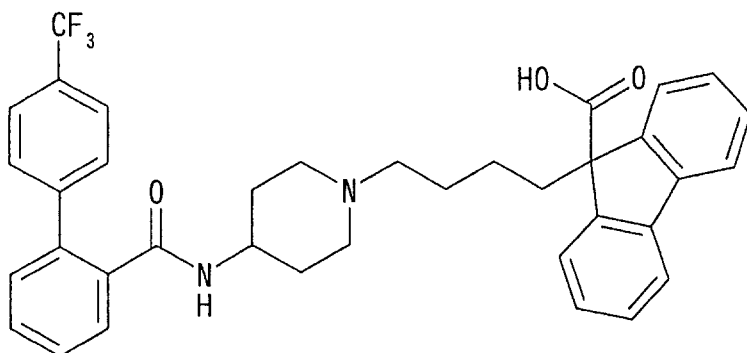
The following compound is disclosed in WO97/43257.



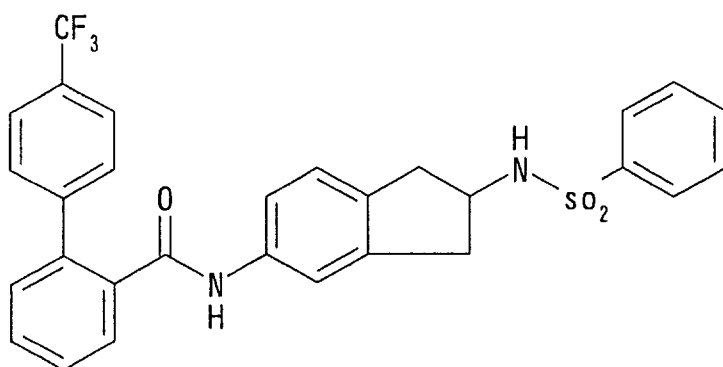
The following compound is disclosed in WO98/23593.



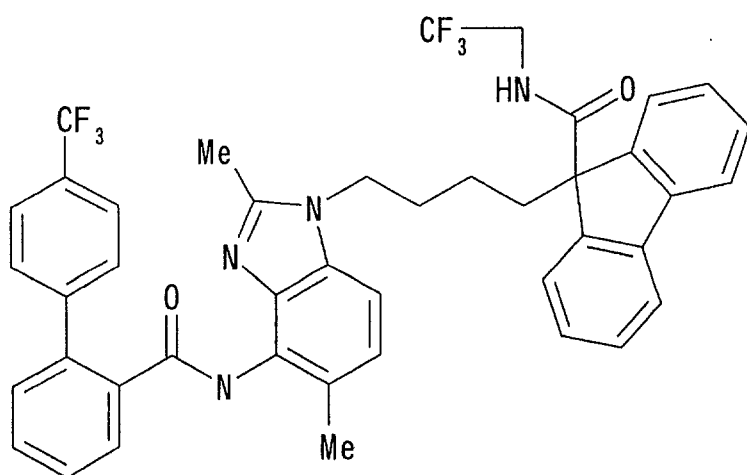
The following compound is disclosed in WO99/63929.



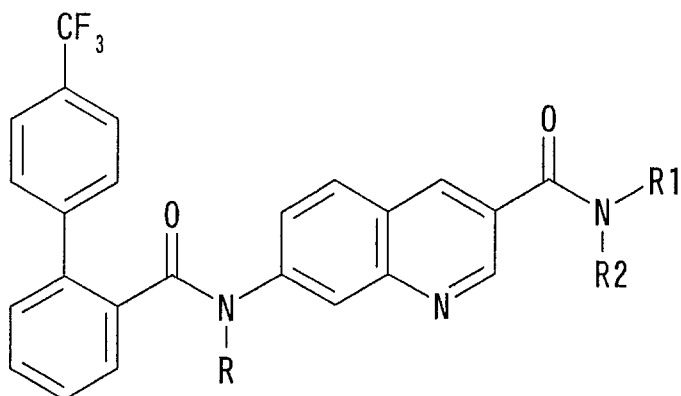
The following compound is disclosed in WO2000/5201.



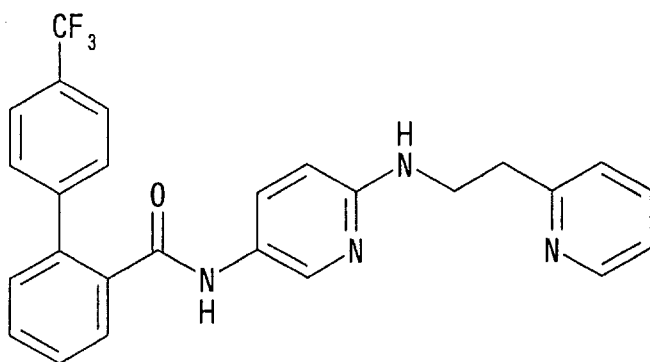
The following compound is disclosed in J. Med.
5 Chem.(2001), 44(6) p.851-856.



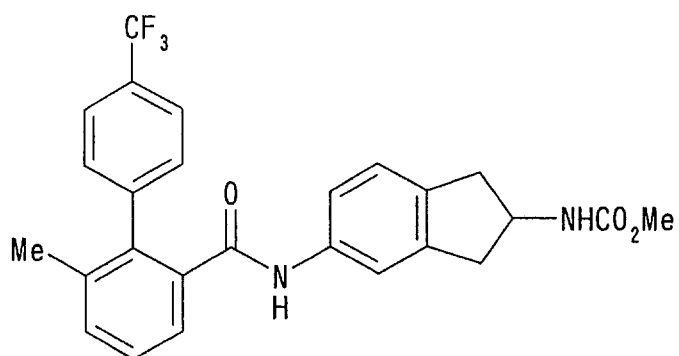
The following compound is disclosed in EP 1099701.



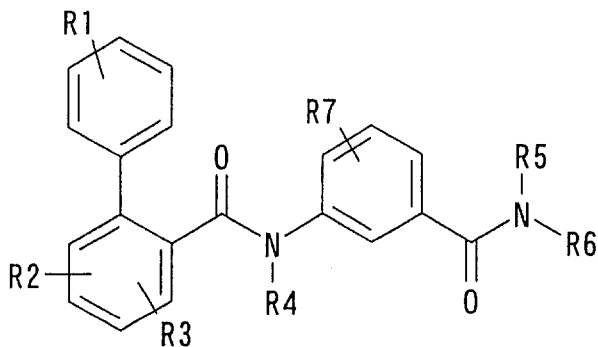
The following compound is disclosed in WO2001/77077.



The following compound is disclosed in J. Med.
 5 Chem.(2001), 44(6) p.4677-4687.



The following compound is disclosed in WO2002/4403.



In the above literatures, however, there is no disclosure of a compound comprising ester as the essential structure as that disclosed in the present invention, much less the disclosure of the data indicating that when a compound has the structure disclosed in the present invention, the compound selectively inhibits MTP in the small intestine while rarely affects MTP in the liver.

Disclosure of the Invention

Although the development of new antihyperlipidemic drugs working due to its MTP inhibitory activity has been advanced nowadays, those drugs are not satisfactory in terms of the level of action and the accompanying side effect such as a fatty liver, etc. Thus, the development of an antihyperlipidemic drug causing no side effect against the liver that is seen in the case of conventional MTP inhibitors and also having excellent MTP inhibitory activity has been strongly desired.

The inventors and those involved in the present invention have carried out intensive studies to provide a novel MTP inhibitor causing no above-mentioned side effect such as a fatty liver. As a result, they have found that an MTP inhibitor, which

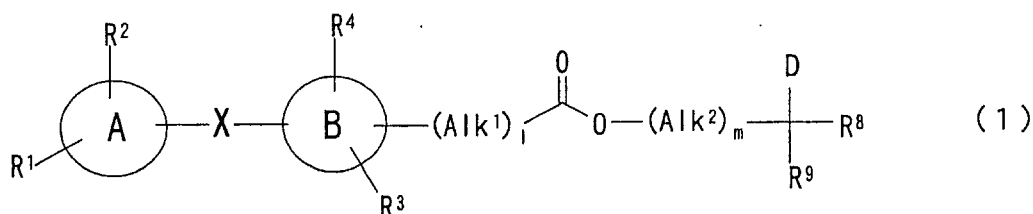
selectively inhibits MTP in the small intestine but substantially does not inhibit MTP in the liver, significantly lowers the level of unnecessary TG or cholesterol without causing a side effect such as a fatty liver, etc. Surprisingly, they have also found that the compound having ester structure represented by the below-mentioned formula (1) is immediately metabolized in the small intestine, blood or liver, which makes it possible for the compound to selectively affect MTP in the small intestine without substantially inhibiting MTP in the liver.

To be more specific, according to the conventional drug design concept for the preparation of a prodrug, the carboxylic acid which is the active principle is esterified to improve the absorption rate in the small intestine and is immediately metabolized in blood to reproduce carboxylic acid which is the active principle. On the other hand, a drug design concept that is different from the above concept for the preparation of a prodrug is used in the present invention. Namely, by introducing at least one ester in a molecular body of a compound having MTP inhibitory activity, the compound is, after it exerts MTP inhibitory activity on mucous membranes of the small intestine, immediately metabolized by an esterase or a metabolic enzyme, etc. in the small intestine, portal (blood) and liver to be transformed to corresponding carboxylic acid and alcohol which do not have MTP inhibitory activity. This is completely a new concept, by means of which MTP in the liver is not substantially affected and MTP in the small intestine is selectively inhibited. Further, the compounds of the present invention show strong MTP inhibitory activity in vitro,

thus potently inhibit MTP in the small intestine and significantly lower triglyceride and cholesterol in blood. In addition, the compounds of the present invention significantly lower non-HDL cholesterol and, surprisingly, increase plasma HDL cholesterol.

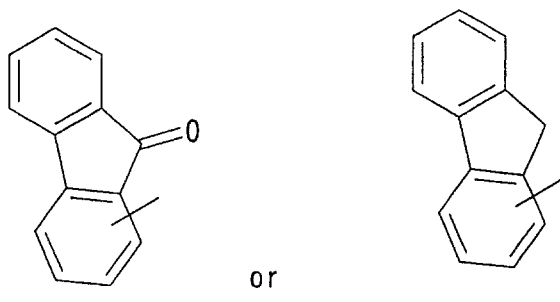
Accordingly, the inventors of the present invention have found that when a compound comprises the ester structure represented by the below-mentioned formula (1), the compound is immediately metabolized in the small intestine, blood or liver after it strongly inhibits MTP in the small intestine and hence MTP in the liver is not substantially inhibited, whereby they have completed the present invention.

Thus, the present invention relates to
 (1) An ester compound represented by the formula (1)



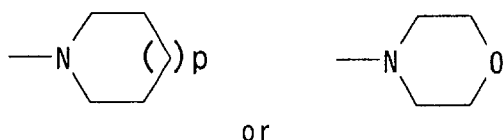
wherein

R^1 and R^2 are each hydrogen, C_1 - C_6 alkyl, C_3 - C_7 cycloalkyl, C_1 - C_6 alkoxy, halo C_1 - C_6 alkyl, halo C_1 - C_6 alkyloxy, optionally substituted C_6 - C_{14} aryl, optionally substituted C_7 - C_{16} aralkyl, optionally substituted C_6 - C_{14} aryloxy, optionally substituted C_7 - C_{16} aralkyloxy, optionally substituted C_7 - C_{15} arylcarbonyl, optionally substituted heterocycle, C_2 - C_7 alkoxy carbonyl, halogen, C_2 - C_6 alkenyl, $-\text{N}(\text{R}^{40})(\text{R}^{41})$ wherein R^{40} and R^{41} are each independently hydrogen or optionally substituted C_6 - C_{14} aryl;
 ring A is C_6 - C_{14} aryl, heterocycle, or

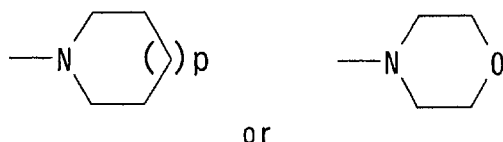


X is $-\text{COO}-(\text{CH}_2)_n-$, $-\text{CON}(\text{R}^{10})-(\text{CH}_2)_n-$ or $-\text{N}(\text{R}^{10})-\text{CO}-(\text{CH}_2)_n-$ wherein R^{10} is hydrogen, $\text{C}_1\text{-C}_6$ alkyl or $\text{C}_3\text{-C}_7$ cycloalkyl and n is an integer of 0 to 3;

5 R^3 and R^4 are each independently hydrogen, hydroxy, halogen, optionally substituted $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ alkoxy, halo $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_7\text{-C}_{16}$ aralkyloxy, $\text{C}_1\text{-C}_6$ acyl, optionally substituted heterocycle, $-\text{CON}(\text{R}^{11})(\text{R}^{12})$ (wherein R^{11} and R^{12} are each independently hydrogen, $\text{C}_1\text{-C}_6$ alkyl, optionally substituted $\text{C}_6\text{-C}_{14}$ aryl, optionally substituted $\text{C}_7\text{-C}_{16}$ aralkyl, $\text{C}_1\text{-C}_6$ alkoxy, or R^{11} and R^{12} may be taken together with the nitrogen to which they are attached to form



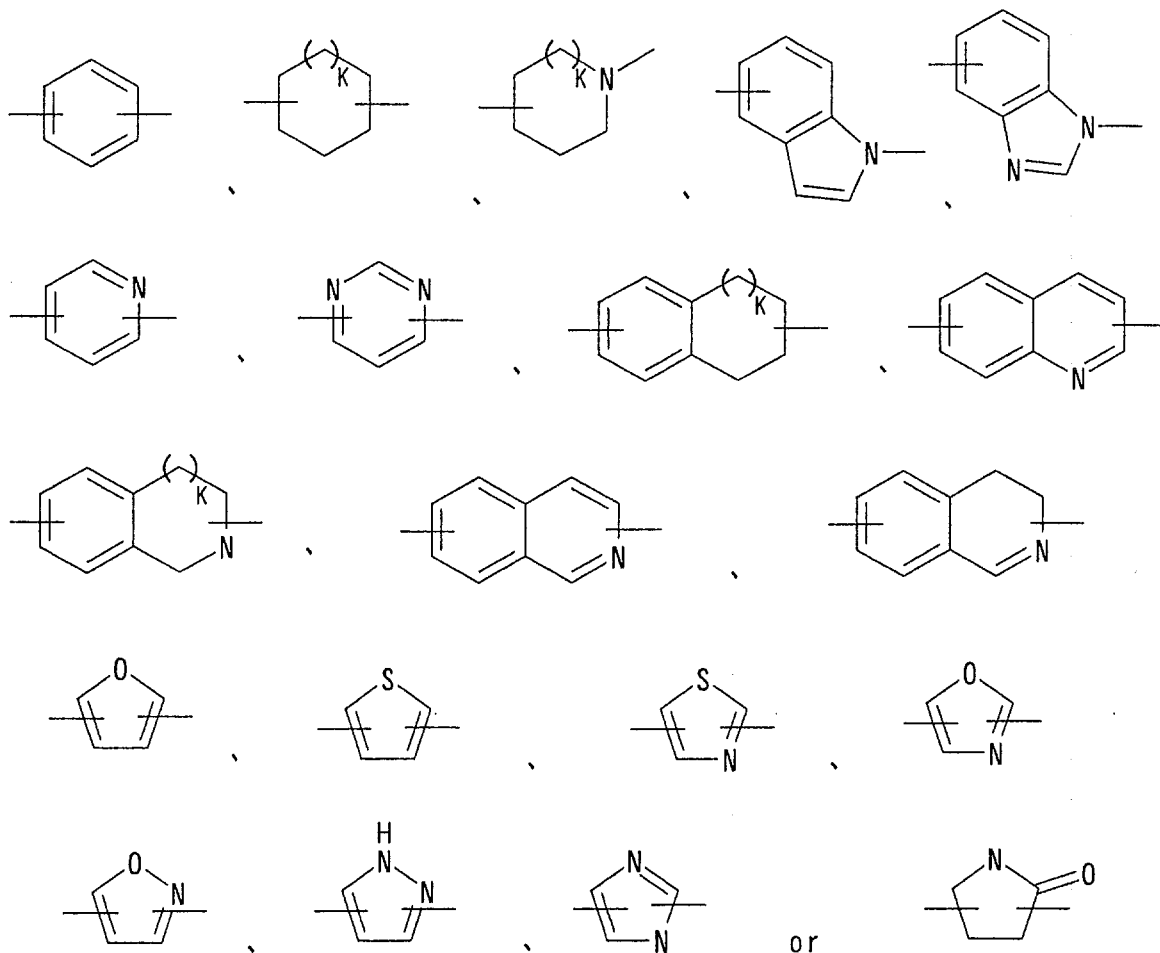
, wherein p is an integer of 0 to 2), $-(\text{CH}_2)_q-\text{N}(\text{R}^{13})(\text{R}^{14})$ (wherein 15 R^{13} and R^{14} are each independently hydrogen, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_2\text{-C}_7$ alkoxycarbonyl, $\text{C}_1\text{-C}_6$ acyl, or R^{13} and R^{14} may be taken together with the nitrogen to which they are attached to form



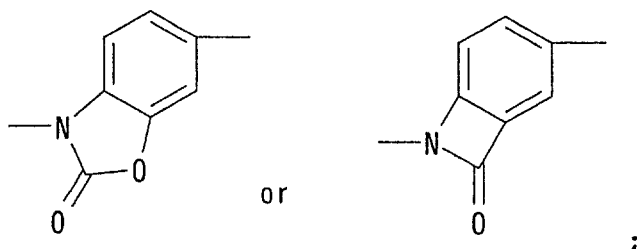
, wherein p has the same meaning as defined above and q is an 20 integer of 0 to 3), or $-\text{CO}(\text{R}^{15})$ (wherein R^{15} is hydroxy, $\text{C}_1\text{-C}_6$

alkoxy, optionally substituted C_6-C_{14} aryloxy, optionally substituted C_7-C_{16} aralkyloxy or C_1-C_6 alkyl);

ring B is



5 , wherein K is an integer of 0 to 2, or ring B may be taken together with R^3 , R^{10} and the nitrogen bound to R^{10} to form



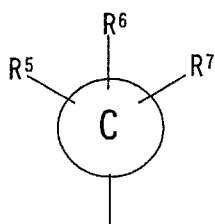
$Alk1^1$ is alkanediyl or alkenediyl;

$Alk1^2$ is alkanediyl or alkenediyl;

l is an integer of 0 to 3;

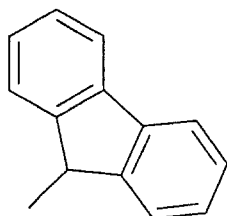
m is an integer of 0 to 3;

D is C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₇ alkoxy carbonyl, -N(R⁴²)-CO(R⁴³) (wherein R⁴² is hydrogen or C₁-C₆ alkyl and R⁴³ is C₆-C₁₄ aryl or C₇-C₁₆ aralkyl), or the group represented by the following formula



(wherein R⁵, R⁶ and R⁷ are each independently hydrogen, C₁-C₆ alkyl, C₁-C₆ alkoxy, C₂-C₇ alkoxy carbonyl, carboxyl, halogen, cyano, nitro, halo C₁-C₆ alkyl, C₁-C₆ acyl, hydroxy, amino, optionally substituted C₆-C₁₄ aryl, or -(CH₂)_r-CON(R¹⁶)(R¹⁷) (wherein R¹⁶ and R¹⁷ are each independently hydrogen, C₁-C₆ alkyl or halo C₁-C₆ alkyl and r is an integer of 0 to 3);

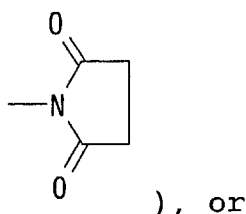
ring C is C₆-C₁₄ aryl, C₇-C₁₅ arylcarbonylamino, C₈-C₁₇ aralkylcarbonylamino, heterocycle residue, C₃-C₇ cycloalkyl or C₇-C₁₆ aralkyl, or ring C may be taken together with R⁷ and R⁸ to form



); and

R⁸ and R⁹ are each independently hydrogen, C₁-C₆ alkyl, optionally substituted C₆-C₁₄ aryl, hydroxy C₁-C₆ alkyl,

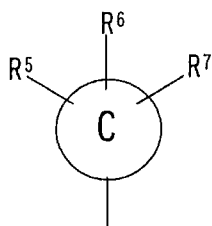
-CON(R¹⁸)(R¹⁹)(wherein R¹⁸ and R¹⁹ are each independently hydrogen, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, halo C₁-C₆ alkyl, C₂-C₁₂ alkoxyalkyl or optionally substituted C₆-C₁₄ aryl), -COO(R²⁰) or -(CH₂)_s-OCO(R²⁰)(wherein R²⁰ is hydrogen, C₁-C₆ alkyl or C₃-C₇ cycloalkyl; s is an integer of 0 to 3), -N(R²¹)(R²²)(wherein R²¹ and R²² are each independently hydrogen, C₁-C₆ alkyl, C₁-C₆ acyl, C₁-C₆ alkylsulfonyl, or R²¹ and R²² may be taken together with the nitrogen to which they are attached to form



10 R⁸ and R⁹ may be taken together to form C₃-C₇ cycloalkyl, or a prodrug thereof, or a pharmaceutically acceptable salt of either;

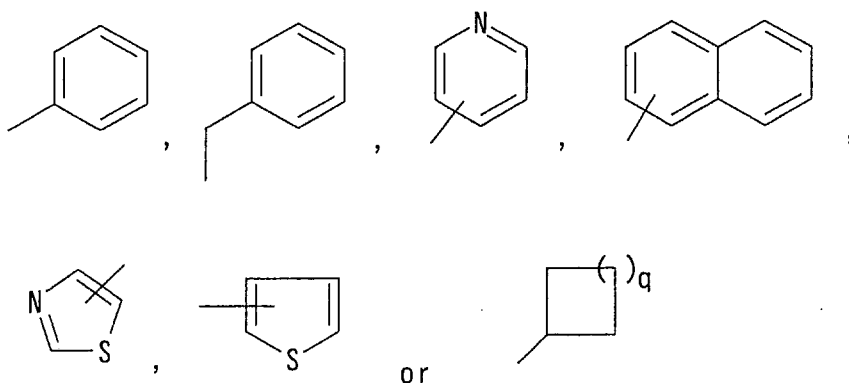
15 (2) The ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to the above (1), wherein D is C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₇ alkoxycarbonyl or -N(R⁴²)-CO(R⁴³) in which R⁴² and R⁴³ each has the same meaning as defined above;

20 (3) The ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to the above (1), wherein D is the group represented by the formula



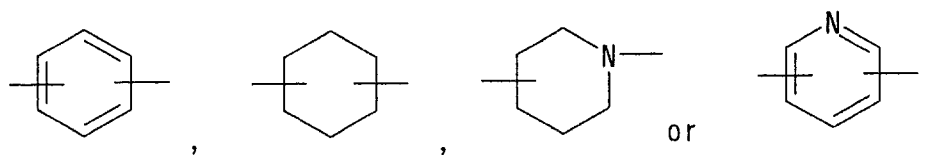
in which R⁵, R⁶ and R⁷ each has the same meaning as defined above;

- (4) The ester compound or a prodrug thereof, or a
5 pharmaceutically acceptable salt of either according to the
above (3), wherein the ring C is

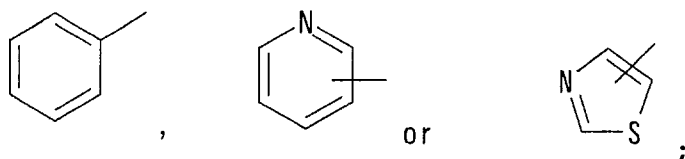


, in which q is an integer of 0 to 3;

- 10 (5) The ester compound or a prodrug thereof, or a
pharmaceutically acceptable salt of either according to the
above (2) or (4), wherein ring B is



- 15 (6) The ester compound or a prodrug thereof, or a
pharmaceutically acceptable salt of either according to the
above (5), wherein ring A is

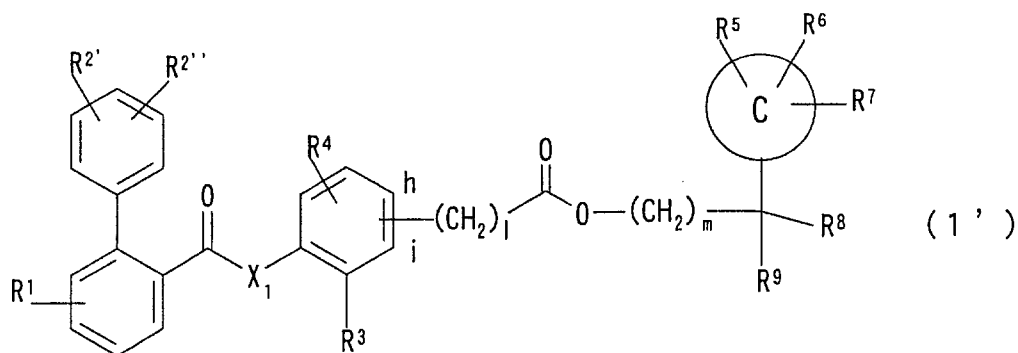


(7) The ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to the above (6), wherein X is $-\text{CON}(\text{R}^{10})-(\text{CH}_2)_n-$ in which R^{10} and n each has the same meaning as defined above;

(8) The ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to the above (6), wherein X is $-\text{COO}-(\text{CH}_2)_n-$ in which n has the same meaning as defined above;

(9) The ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to the above (7) or (8), wherein n is 0;

(10) The ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to the above (10), which is represented by the formula (1')



20

wherein

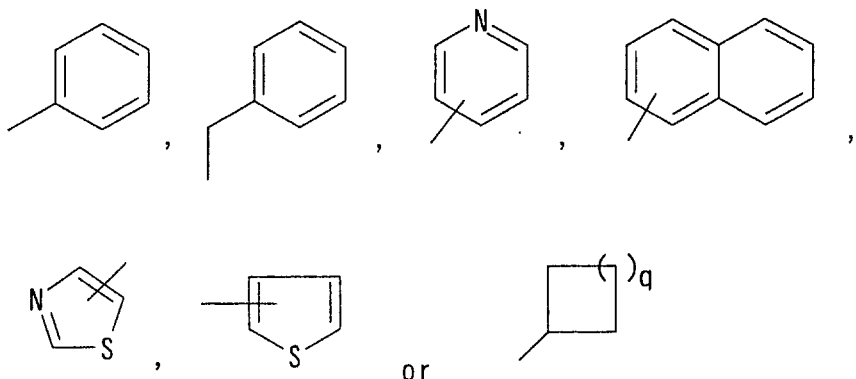
$R^{2'}$ and $R^{2''}$ are each independently hydrogen, C_1 - C_6 alkyl, C_3 - C_7 cycloalkyl, C_1 - C_6 alkoxy, halogen, halo C_1 - C_6 alkyl, C_1 - C_6 acyl, C_2 - C_6 alkenyl or cyano;

X_1 is -O- or -NR¹⁰- wherein R¹⁰ is hydrogen, C_1 - C_6 alkyl
5 or C_3 - C_7 cycloalkyl; and

R^1 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , ring C, l and m each has the same meaning as defined above, or a prodrug thereof, or a pharmaceutically acceptable salt of either;

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(11) The ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to the above (10), wherein the ring C is



15 , in which q is an integer of 0 to 3;

(12) The ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to the above (11), wherein X_1 is -NR¹⁰- in which R¹⁰ has the same meaning
20 as defined above;

(13) The ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to the

above (11), wherein X_1 is -O-;

(14) The ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to the
5 above (10) to (13), wherein the group $-(CH_2)_1-$ is located at the h-position of the benzene ring in the formula (1');

(15) The ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to the
10 above (10) to (13), wherein the group $-(CH_2)_1-$ is located at the i-position of the benzene ring in the formula (1');

(16) The ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to the
15 above (10) to (15), wherein R^8 and R^9 are each independently $-\text{CON}(R^{18})(R^{19})-$ in which R^{18} and R^{19} each has the same meaning as defined above;

(17) The ester compound or a prodrug thereof, or a
20 pharmaceutically acceptable salt of either according to the above (10) to (15), wherein R^8 and R^9 are each independently $-\text{COO}(R^{20})-$ in which R^{20} has the same meaning as defined above;

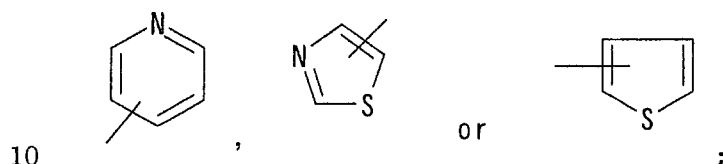
(18) The ester compound or a prodrug thereof, or a
25 pharmaceutically acceptable salt of either according to the above (12) to (17), wherein the ring C is C_6-C_{14} aryl;

(19) The ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to the

above (18), wherein C_6-C_{14} aryl is phenyl;

(20) The ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to the
5 above (12) to (17), wherein the ring C is C_3-C_7 cycloalkyl;

(21) The ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to the above (12) to (17), wherein the ring C is



(22) The ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to the above (1), which is selected from the group consisting of
15 {4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

2-phenyl-2-{2-[4-(4'-trifluoromethyl-biphenyl-2-carbonyloxy)-phenyl]-acetoxymethyl}-malonic acid diethyl
20 ester,

2-(2-{3-methyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{4-[methyl-(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic
25 acid diethyl ester,

{3-ethyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-

amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

5 {4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 9-(2,2,2-trifluoro-ethylcarbamoyl)-9h-fluoren-9-ylmethyl ester,

2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-propionic acid 9-(2,2,2-trifluoro-ethylcarbamoyl)-9h-fluoren-9-ylmethyl ester,

10 {4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2-(2,2,2-trifluoro-ethylcarbamoyl)-ethyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

15 {4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 1-(2,2,2-trifluoro-ethylcarbamoyl)-cyclopentylmethyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid
20 diisopropyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2,2-bis-(2,2,2-trifluoro-ethylcarbamoyl)-ethyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid
25 dimethyl ester,

2-cyclopentyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid
diethyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 1-(2,2,2-trifluoro-ethylcarbamoyl)-cyclohexylmethyl ester,

2-phenyl-2-{2-[4-(2-trifluoromethyl-benzoylamino)-phenyl]-acetoxymethyl}-malonic acid diethyl ester,

2-{2-[4-(2-phenoxy-benzoylamino)-phenyl]-acetoxymethyl}-2-phenyl-malonic acid diethyl ester,

2-{2-[4-(2-butoxy-benzoylamino)-phenyl]-acetoxymethyl}-2-phenyl-malonic acid diethyl ester,

10 2-phenyl-2-{2-[4-(2-trifluoromethyl-benzoyloxy)-phenyl]-acetoxymethyl}-malonic acid diethyl ester,

2-{2-[4-(2-benzoyl-benzoyloxy)-phenyl]-acetoxymethyl}-2-phenyl-malonic acid diethyl ester,

15 2-{2-[4-(2-benzoyl-benzoylamino)-phenyl]-acetoxymethyl}-2-phenyl-malonic acid diethyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid dicyclohexyl ester,

20 {4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-cyclohexylcarbamoyl-2-phenyl-ethyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2,2-bis-phenylcarbamoyl-ethyl ester,

25 {4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-isopropylcarbamoyl-2-phenyl-ethyl ester,

2-benzyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl

ester,

2-(2-{2-methyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

5 4'-trifluoromethyl-biphenyl-2-carboxylic acid 4-[2-phenyl-2,2-bis-(2,2,2-trifluoro-ethylcarbamoyl)-ethoxycarbonylmethyl]-phenyl ester,

biphenyl-2-carboxylic acid 4-[2-phenyl-2,2-bis-(2,2,2-trifluoro-ethylcarbamoyl)-ethoxycarbonylmethyl]-phenyl
10 ester,

2-butoxy-benzoic acid 4-[2-phenyl-2,2-bis-(2,2,2-trifluoro-ethylcarbamoyl)-ethoxycarbonylmethyl]-phenyl ester,

2-cyclohexyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl
15 ester,

{4-[(biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2,2-bis-(2,2,2-trifluoro-ethylcarbamoyl)-ethyl ester,

20 [4-(2-phenoxy-benzoylamino)-phenyl]-acetic acid 2-phenyl-2,2-bis-(2,2,2-trifluoro-ethylcarbamoyl)-ethyl ester,

2-phenyl-2-(2-{2-trifluoromethyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

25 {4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2,2-bis-propylcarbamoyl-ethyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-

phenyl}-acetic acid 2,2-bis-methylcarbamoyl-2-phenyl-ethyl ester,

2-pyridin-2-yl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid
5 diethyl ester,

2-pyridin-3-yl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid
diethyl ester,

4'-trifluoromethyl-biphenyl-2-carboxylic acid 4-(2,2-bis-ethylcarbamoyl-2-phenyl-ethoxycarbonylmethyl)-phenyl
10 ester,

2-phenyl-2-(2-{3-trifluoromethyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

15 [4-(2-butoxy-benzoylamino)-phenyl]-acetic acid
2-phenyl-2,2-bis-(2,2,2-trifluoro-ethylcarbamoyl)-ethyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-butylcarbamoyl-2-phenyl-ethyl
20 ester,

2-(2-{4-[(9-oxo-9h-fluorene-1-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{4-[(9h-fluorene-1-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

25 {3-methyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

2-(2-{4-[(4'-methyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

- 2-(2-{4-[(4'-methoxy-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
- {4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,
- {4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3-phenyl-3,3-bis-propylcarbamoyl-propyl ester,
- {4-[(biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,
- [4-(2-phenoxy-benzoylamino)-phenyl]-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,
- [4-(2-butoxy-benzoylamino)-phenyl]-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,
- 2-phenyl-2-(2-{4-[(3'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,
- 2-(2-{4-[2-(4-fluoro-benzoyl)-benzoylamino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
- 4'-trifluoromethyl-biphenyl-2-carboxylic acid 4-(2,2-bis-ethylcarbamoyl-2-phenyl-ethoxycarbonylmethyl)-2-chloro-phenyl ester,
- 2-phenyl-2-{2-[4-(2-thiophen-3-yl-benzoylamino)-phenyl]-acetoxymethyl}-malonic acid diethyl ester,
- 2-(2-{4-[(biphenyl-3-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
- 2-(2-{4-[isopropyl-(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{4-[cyclohexyl-(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-{2-[4-(2-isopropyl-benzoylamino)-phenyl]-acetoxymethyl}-2-phenyl-malonic acid diethyl ester,

2-{2-[4-(2-benzyl-benzoylamino)-phenyl]-acetoxymethyl}-2-phenyl-malonic acid diethyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid dipropyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diisobutyl ester,

2-phenyl-2-{2-[4-(2-trifluoromethoxy-benzoylamino)-phenyl]-acetoxymethyl}-malonic acid diethyl ester,

2-{2-[4-(2-butoxycarbonyl-benzoylamino)-phenyl]-acetoxymethyl}-2-phenyl-malonic acid diethyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-isobutylcarbamoyle-2-phenyl-ethyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-(3-methyl-butylcarbamoyle)-2-phenyl-ethyl ester,

2-(2-{4-[ethyl-(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

[4-(2-cyclohexyl-benzoylamino)-phenyl]-acetic acid 2,2-bis-ethylcarbamoyle-2-phenyl-ethyl ester,

{4-[(4'-chloro-biphenyl-2-carbonyl)-amino]-phenyl}-

acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{4-[(3',4'-dichloro-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

5 {3-methyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2,2-bis-propylcarbamoyl-ethyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-(2-methoxy-ethylcarbamoyl)-2-phenyl-ethyl ester,

2-[2-(4-{[2-methyl-4-(4-trifluoromethyl-phenyl)-thiazole-5-carbonyl]-amino}-phenyl)-acetoxymethyl]-2-phenyl-malonic acid diethyl ester,

(4-{[2-methyl-4-(4-trifluoromethyl-phenyl)-thiazole-5-carbonyl]-amino}-phenyl)-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

(4-{[2-(4-trifluoromethyl-phenyl)-pyridine-3-carbonyl]-amino}-phenyl)-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

20 (3-methyl-4-{[2-(4-trifluoromethyl-phenyl)-pyridine-3-carbonyl]-amino}-phenyl)-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

2-(2-{3-ethyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

{3-isopropyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

2-(2-{3-isopropyl-4-[(4'-trifluoromethyl-biphenyl-2-

carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

{3-ethyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-

5 3-phenyl-propyl ester,

{3-isobutyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

2-(2-{3-isobutyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-chloro-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

15 2-(2-{3-bromo-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-

20 ethylcarbamoyl-2-phenyl-ethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2,2-bis-propylcarbamoyl-ethyl ester,

{3-methylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

5 {3-benzylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 4,4-bis-ethylcarbamoyl-4-phenyl-butyl ester,

10 {3-diethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-diisopropylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

2-(2-{3-diethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

20 2-(2-{3-diisopropylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

{3-(isopropyl-methyl-carbamoyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

2-(2-{3-(ethyl-methyl-carbamoyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

{3-(ethyl-methyl-carbamoyl)-4-[(4'-trifluoromethyl-

biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-(ethyl-methyl-carbamoyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

{3-(piperidine-1-carbonyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-(pyrrolidine-1-carbonyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-(pyrrolidine-1-carbonyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-(methyl-propyl-carbamoyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-(methyl-propyl-carbamoyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-ethylcarbamoyl-2-phenyl-ethyl ester,

2-phenyl-2-(2-{3-(pyrrolidine-1-carbonyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-phenyl-2-(2-{3-(piperidine-1-carbonyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2-propionylamino-ethyl ester,

5 {3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2-propionylamino-ethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-(2,5-dioxo-pyrrolidin-1-yl)-2-phenyl-ethyl ester,

10 {3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-ethylcarbamoyl-benzyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-ethylcarbamoylmethyl-benzyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-isopropylamino-2-phenyl-ethyl ester hydrochloride,

20 [3-dimethylcarbamoyl-4-(2-trifluoromethyl-benzoylamino)-phenyl]-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

2-{2-[3-dimethylcarbamoyl-4-(2-trifluoromethyl-benzoylamino)-phenyl]-acetoxymethyl}-2-phenyl-malonic acid diethyl ester,

25 2-[2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-fluoro-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic

acid diethyl ester,

2-(2-{4-[(4'-bromo-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

5 {3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-acetylamino-2-phenyl-ethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-butyrylamino-2-phenyl-ethyl ester,

[4-(2-benzoyl-benzoylamino)-3-dimethylcarbamoyl-phenyl]-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

2-{2-[4-(2-benzoyl-benzoylamino)-3-dimethylcarbamoyl-phenyl]-acetoxymethyl}-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid dimethyl ester,

2-cyclopentyl-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy methyl)-malonic acid diethyl ester,

2-cyclohexyl-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy methyl)-malonic acid diethyl ester,

25 2-(2-{4-[(4'-chloro-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{4-[(4'-acetyl-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxymethyl)-2-phenyl-malonic

acid diethyl ester,

[3-dimethylcarbamoyl-4-(2-phenoxy-benzoylamino)-phenyl]-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

5 2-{2-[3-dimethylcarbamoyl-4-(2-phenoxy-benzoylamino)-phenyl]-acetoxymethyl}-2-phenyl-malonic acid diethyl ester,

2-(2-{4-[(4'-cyano-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

10 2-(2-{3-dimethylcarbamoyl-4-[(4-methyl-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(5-methyl-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

15 {3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-methanesulfonylamino-2-phenyl-ethyl ester,

3-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-2-phenyl-propionic acid ethyl ester,

20 {3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-(methyl-propionyl-amino)-2-phenyl-ethyl ester,

25 2-[3-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-propyl]-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(5-methoxy-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-

acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{4-[(5-chloro-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

5 2-(2-{3-dimethylcarbamoyl-4-[(6-methyl-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester),

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid di-2,2,2-trifluoroethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(2'-fluoro-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{5-dimethylcarbamoyl-2-fluoro-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-bromo-5-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

20 2-(2-{3-chloro-5-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(3'-fluoro-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

25 2-(2-{4-[(3'-chloro-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-

biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(5-nitro-pyridin-2-yl)-malonic acid diethyl ester,

2-(5-amino-pyridin-2-yl)-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-pyridin-2-yl-malonic acid diethyl ester,

2-(2-{3-chloro-5-dimethylcarbamoyl-2-fluoro-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-bromo-5-dimethylcarbamoyl-2-fluoro-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-ortho-tolyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-m-tolyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-p-tolyl-malonic acid diethyl ester,

2-(2-chloro-phenyl)-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-(3-chloro-phenyl)-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-(4-chloro-phenyl)-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

5 2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-succinic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(2-methoxy-phenyl)-malonic acid diethyl ester,

10 2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(3-methoxy-phenyl)-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(4-methoxy-phenyl)-malonic acid diethyl ester,

15 2-(2-{4-[(5,4'-bis-trifluoromethyl-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{4-[(6-chloro-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

20 2-(2-{3-dimethylcarbamoyl-4-[(6-fluoro-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

25 2-[2-(2-{3-dimethylcarbamoyl-4-[(5-methyl-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(5-ethoxy-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-

acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(5-isopropoxy-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

5 2-[2-(2-{4-[(5,4'-bis-trifluoromethyl-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(6-methoxy-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

10 2-(2-{3-dimethylcarbamoyl-4-[(3-methyl-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-{2-[4-(2,4-bis-trifluoromethyl-benzoylamino)-3-dimethylcarbamoyl-phenyl]-acetoxymethyl}-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-methyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

20 2-ethyl-4-trifluoromethyl-benzoylamino)-phenyl]-acetoxymethyl}-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-ethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

25 2-(2-{3-dimethylcarbamoyl-4-[(4'-isopropenyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-isopropyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic

acid diethyl ester,

2-{2-[3-dimethylcarbamoyl-4-(2-isopropenyl-4-trifluoromethyl-benzoylamino)-phenyl]-acetoxymethyl}-2-phenyl-malonic acid diethyl ester,

5 2-{2-[3-dimethylcarbamoyl-4-(2-isopropyl-4-trifluoromethyl-benzoylamino)-phenyl]-acetoxymethyl}-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[2-(3-trifluoromethyl-phenylamino)-benzoylamino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-{2-[3-dimethylcarbamoyl-4-(4'-trifluoromethyl-biphenyl-2-carbonyloxy)-phenyl]-acetoxymethyl}-2-phenyl-malonic acid diethyl ester,

15 2-(2-{3-dimethylcarbamoyl-4-[2-(3-trifluoromethyl-phenoxy)-benzoylamino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-ethyl-2-phenyl-butyl ester,

20 2-(2-{3-dimethylcarbamoyl-4-[2-(4-trifluoromethyl-phenoxy)-benzoylamino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 1-phenyl-cyclopropylmethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-diphenyl-ethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-

2-carbonyl)-amino]-phenyl}-acetic acid 1-phenyl-cyclopentylmethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3-hydroxy-2-

5 hydroxymethyl-2-phenyl-propyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3-acetoxy-2-acetoxymethyl-2-phenyl-propyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-thiophen-2-yl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-thiophen-3-yl-malonic acid diethyl ester,

15 2-(2-{4-dimethylcarbamoyl-5-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-pyridin-2-yl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(3-methyl-thiophen-2-yl)-malonic acid diethyl ester,

20 2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(5-methyl-thiophen-2-yl)-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-thiazol-2-yl-malonic acid diethyl ester,

25 2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-isopropyl-malonic acid diethyl ester,

2-sec-butyl-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-isobutyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-propyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-ethyl-malonic acid diethyl ester,

2-butyl-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-allyl-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

3-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-2,2-bis-ethoxycarbonyl-propionic acid ethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(1-methyl-butyl)-malonic acid diethyl ester,

2-(2-{3-ethoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

{3-hydroxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-

2-phenyl-ethyl ester,

{3-methoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

5 2-(2-{3-methoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

 {3-methoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2,2-bis-propylcarbamoyl-ethyl ester,

10

 {3-methoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

 {3-ethoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

15

 {3-ethoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

20 2-(2-{3-isopropoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

 {3-isopropoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

25

 {3-isopropoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

 {3-propoxy-4-[(4'-trifluoromethyl-biphenyl-2-

carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-
2-phenyl-ethyl ester,

{3-benzyloxy-4-[(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-
5 2-phenyl-ethyl ester,

2-(2-{3-benzyloxy-4-[(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic
acid diethyl ester,

2-(2-{3-hydroxy-4-[(4'-trifluoromethyl-biphenyl-2-
10 carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic
acid diethyl ester,

2-{2-[3-methoxy-4-(4'-trifluoromethyl-biphenyl-2-
carbonyloxy)-phenyl]-acetoxymethyl}-2-phenyl-malonic acid
diethyl ester,

15 {3-dimethylamino-4-[(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-
2-phenyl-ethyl ester,

{3-piperidin-1-yl-4-[(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-
20 2-phenyl-ethyl ester,

{3-pyrrolidin-1-yl-4-[(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-
2-phenyl-ethyl ester,

2-phenyl-2-(2-{3-piperidin-1-yl-4-[(4'-
25 trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
acetoxymethyl)-malonic acid diethyl ester,

2-phenyl-2-(2-{3-pyrrolidin-1-yl-4-[(4'-
trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
acetoxymethyl)-malonic acid diethyl ester,

2-(2-{3-dimethylamino-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-morpholin-4-yl-4-[(4'-trifluoromethyl-biphenyl-1-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-diethylamino-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-[2-(2-{2-methyl-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic acid diethyl ester,

2-phenyl-2-(2-{3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-phenyl-2-[2-(2-{3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-malonic acid diethyl ester,

{3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

{3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3-phenyl-3,3-bis-propylcarbamoyl-propyl ester,

2-[2-(2-{4-methyl-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic acid diethyl ester,

2-[2-(2-{2-methyl-5-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic

acid diethyl ester,

{3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-isopropylcarbamoyl-3-phenyl-propyl ester,

5 {2-methyl-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

{2-methyl-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 4,4-bis-ethylcarbamoyl-10 4-phenyl-butyl ester,

{2-methyl-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3-phenyl-3,3-bis-propylcarbamoyl-propyl ester,

{2-methoxy-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-15 3-phenyl-propyl ester,

2-[2-(2-{2-methoxy-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic acid diethyl ester,

20 {2-ethoxy-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

2-[2-(2-{2-ethoxy-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic acid diethyl ester, 25

2-[2-(2-{2-isopropoxy-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic acid diethyl ester,

2-[2-(2-{2-methoxycarbonyl-3-[(4'-trifluoromethyl-

biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic acid diethyl ester,

2-[2-(2-{2-ethoxy-5-methyl-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic acid diethyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid 2-[9-(2,2,2-trifluoro-ethylcarbamoyl)-9h-fluoren-9-yl]-ethyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid 2-(9h-fluoren-9-yl)-ethyl ester,

n-biphenyl-2-yl-terephthalamide acid 2-[9-(2,2,2-trifluoro-ethylcarbamoyl)-9h-fluoren-9-yl]-ethyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid 2-[(biphenyl-2-carbonyl)-amino]-ethyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid 2-(2-biphenyl-2-yl-acetyl-amino)-ethyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid 3-naphthalen-1-yl-3-(2,2,2-trifluoro-ethylcarbamoyl)-propyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid 3-[2-(2,2,2-trifluoro-ethylcarbamoyl)-naphthalen-1-yl]-propyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid 3,3-diphenyl-3-(2,2,2-trifluoro-ethylcarbamoyl)-propyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid 3-biphenyl-2-yl-3-(2,2,2-trifluoro-ethylcarbamoyl)-propyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-

benzoic acid 3-phenyl-3-(2,2,2-trifluoro-ethylcarbamoyl)-
propyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-
benzoic acid 2-[8-(2,2,2-trifluoro-ethylcarbamoyl)-
5 naphthalen-1-yl]-ethyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-
benzoic acid 3-(2,6-dichloro-phenyl)-3-(2,2,2-trifluoro-
ethylcarbamoyl)-propyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-
10 benzoic acid 3-(2-chloro-phenyl)-3-(2,2,2-trifluoro-
ethylcarbamoyl)-propyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-benzoyloxy}-ethyl)-malonic acid diethyl
ester,

15 2-(2-{3-methyl-4-[(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-benzoyloxy}-ethyl)-2-phenyl-malonic acid
diethyl ester,

2-(2-{2-chloro-4-[(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-benzoyloxy}-ethyl)-2-phenyl-malonic acid
20 diethyl ester,

2-phenyl-2-{2-[4-(4'-trifluoromethyl-biphenyl-2-
carbonyloxy)-benzoyloxy]-ethyl}-malonic acid diethyl ester,

2-{2-[4-(2-benzoyl-benzoyloxy)-benzoyloxy]-ethyl}-2-
phenyl-malonic acid diethyl ester,

25 4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-
benzoic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

4'-trifluoromethyl-biphenyl-2-carboxylic acid
4-(3,3-bis-ethylcarbamoyl-3-phenyl-propoxycarbonyl)-2-
chloro-phenyl ester,

4'-trifluoromethyl-biphenyl-2-carboxylic acid
4-(3,3-bis-ethylcarbamoyl-3-phenyl-propoxycarbonyl)-phenyl
ester,

4'-trifluoromethyl-biphenyl-2-carboxylic acid
5 4-(3,3-bis-ethylcarbamoyl-3-phenyl-propoxycarbonyl)-2,6-
dichloro-phenyl ester,

4-methyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-
amino]-cyclohexanecarboxylic acid 2-[9-(2,2,2-trifluoro-
ethylcarbamoyl)-9h-fluoren-9-yl]-ethyl ester,

10 4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-
cyclohexanecarboxylic acid 2-[9-(2,2,2-trifluoro-
ethylcarbamoyl)-9h-fluoren-9-yl]-ethyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-
cyclohexanecarboxylic acid 3-phenyl-3-(2,2,2-trifluoro-
15 ethylcarbamoyl)-propyl ester,

2-phenyl-2-{4-[(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-cyclohexanecarbonyloxymethyl}-malonic acid
diethyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-
20 carbonyl)-amino]-cyclohexanecarbonyloxy}-ethyl)-malonic
acid diethyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-piperidin-1-yl}-acetoxymethyl)-malonic
acid diethyl ester,

25 2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-indol-1-yl}-acetoxymethyl)-malonic acid
diethyl ester,

2-(2-{2-methyl-4-[(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-benzoimidazol-1-yl}-acetoxymethyl)-2-

phenyl-malonic acid diethyl ester,

[2-oxo-3-(4'-trifluoromethyl-biphenyl-2-carbonyl)-
2,3-dihydro-benzooxazol-6-yl]-acetic acid 2,2-bis-
ethylcarbamoyl-2-phenyl-ethyl ester,

5 2-(2-{3-ethoxycarbonyl-4-[(4'-trifluoromethyl-
biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-
phenyl-malonic acid diethyl ester,

2-(3-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-
biphenyl-2-carbonyl)-amino]-phenyl}-propionyloxymethyl)-2-
10 phenyl-malonic acid diethyl ester,

4-[[{(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-
methyl]-benzoic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl
ester,

3-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-
15 amino]-phenyl}-propionic acid ethylcarbamoyl-phenyl-methyl
ester,

5-(2,2-bis-ethylcarbamoyl-2-phenyl-ethoxycarbonyl-
methyl)-2-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-
benzoic acid benzyl ester,

20 5-(2,2-bis-ethylcarbamoyl-2-phenyl-ethoxycarbonyl-
methyl)-2-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-
benzoic acid,

5-(2,2-bis-ethylcarbamoyl-2-phenyl-ethoxycarbonyl-
methyl)-2-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-
25 benzoic acid ethyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-benzoimidazol-1-yl}-acetoxymethyl)-malonic
acid diethyl ester,

3-[[{(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-

methyl}-benzoic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

5-(2,2-bis-ethylcarbamoyl-2-phenyl-ethoxycarbonylmethyl)-2-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid methyl ester,

2-(2-{3-benzyloxycarbonyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-carboxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-{2-[2-oxo-3-(4'-trifluoromethyl-biphenyl-2-carbonyl)-2,3-dihydro-benzooxazol-6-yl]-acetoxymethyl}-2-phenyl-malonic acid diethyl ester,

2-{2-[8-oxo-7-(4'-trifluoromethyl-biphenyl-2-carbonyl)-7-aza-bicyclo[4.2.0]octa-1(6),2,4-trien-3-yl]-acetoxymethyl}-2-phenyl-malonic acid diethyl ester,

2-(2-{3-isopropoxycarbonyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-methoxycarbonyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-[2-(3-dimethylcarbamoyl-4-{[1-(2-nitro-4-trifluoromethyl-phenyl)-pyrrolidine-2-carbonyl]-amino}-phenyl)-acetoxymethyl]-2-phenyl-malonic acid diethyl ester,

2-(2-{3-acetylamino-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-methoxycarbonylamino-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-(4-methyl-thiazol-2-yl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-phenyl-2-(2-{6-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-biphenyl-3-yl}-acetoxymethyl)-malonic acid diethyl ester,

2-(2-{3-formyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylaminomethyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-(methoxy-methyl-carbamoyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-isobutyryl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester, and

2-(2-{3-(1-hydroxy-2-methyl-propyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester;

25

(23) The ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to the above (1), which is selected from the group consisting of

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-

phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

2-phenyl-2-{2-[4-[(4'-trifluoromethyl-biphenyl-2-carbonyloxy)-phenyl]-acetoxymethyl]-malonic acid diethyl
5 ester,

2-(2-{3-methyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{4-[methyl-(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic
10 acid diethyl ester,

{3-ethyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

15 {4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 9-(2,2,2-trifluoro-ethylcarbamoyl)-9h-fluoren-9-ylmethyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-propionic acid 9-(2,2,2-trifluoro-ethylcarbamoyl)-9h-fluoren-9-ylmethyl ester,
20

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2-(2,2,2-trifluoro-ethylcarbamoyl)-ethyl ester,

2-phenyl-2-(2-{4-[4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl
25 ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diisopropyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2,2-bis-(2,2,2-trifluoroethylcarbamoyl)-ethyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid dimethyl ester,

2-cyclopentyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid dicyclohexyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-cyclohexylcarbamoyl-2-phenyl-ethyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2,2-bis-phenylcarbamoyl-ethyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-isopropylcarbamoyl-2-phenyl-ethyl ester,

2-benzyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-(2-{2-methyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl-2-phenyl-malonic acid diethyl ester,

4'-trifluoromethyl-biphenyl-2-carboxylic acid 4-[2-phenyl-2,2-bis-(2,2,2-trifluoro-ethylcarbamoyl)-

ethoxycarbonylmethyl]-phenyl ester,

biphenyl-2-carboxylic acid 4-[2-phenyl-2,2-bis-(2,2,2-trifluoro-ethylcarbamoyl)-ethoxycarbonylmethyl]-phenyl ester,

5 2-cyclohexyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

{4-[(biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2,2-bis-(2,2,2-trifluoro-ethylcarbamoyl)-ethyl
10 ester,

2-phenyl-2-(2-{2-trifluoromethyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-methylcarbamoyl-2-phenyl-ethyl ester,

2-pyridin-2-yl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

20 2-pyridin-3-yl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

4'-trifluoromethyl-biphenyl-2-carboxylic acid 4-(2,2-bis-ethylcarbamoyl-2-phenyl-ethoxycarbonylmethyl)-phenyl
25 ester,

2-phenyl-2-(2-{3-trifluoromethyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-

phenyl}- acetic acid 2,2-bis-butylcarbamoyl-2-phenyl-ethyl ester,

{3-methyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-
5 2-phenyl-ethyl ester,

2-(2-{4-[(4'-methyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{4-[(4'-methoxy-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

10 {4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3-phenyl-3,3-bis-propylcarbamoyl-propyl
15 ester,

{4-[(biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

2-phenyl-2-(2-{4-[(3'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl
20 ester,

4'-trifluoromethyl-biphenyl-2-carboxylic acid 4-(2,2-bis-ethylcarbamoyl-2-phenyl-ethoxycarbonylmethyl)-2-chloro-phenyl ester,

2-(2-{4-[isopropyl-(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
25

2-(2-{4-[cyclohexyl-(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid dipropyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diisobutyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-isobutylcarbamoyl-2-phenyl-ethyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-(3-methyl-butylcarbamoyl-2-phenyl-ethyl ester,

2-(2-{4-[ethyl-(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

{4-[(4'-chloro-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-(ethylcarbamoyl-2-phenyl-ethyl ester,

{4-[(3',4'-dichloro-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-(ethylcarbamoyl-2-phenyl-ethyl ester,

{3-methyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2,2-bis-propylcarbamoyl-ethyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-(2-methoxy-ethylcarbamoyl)-2-phenyl-ethyl ester,

2-(2-{3-ethyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

{3-isopropyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

2-(2-{3-isopropyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

{3-ethyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

10 {3-isobutyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

2-(2-{3-isobutyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-chloro-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

20 2-(2-{3-bromo-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

25 {3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2,2-bis-propylcarbamoyl-ethyl ester,

{3-methylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-

ethylcarbamoyl-2-phenyl-ethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-ethyl ester,

5 2-(2-{3-diethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

{3-benzylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 4,4'-bis-ethylcarbamoyl-4-phenyl-butyl ester,

15 {3-diethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-diisopropylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

20 2-(2-{3-diethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

25 2-(2-{3-diisopropylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

{3-(isopropyl-methylcarbamoyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

2-(2-{3-(ethyl-methylcarbamoyl)-4-[(4'-trifluoro-

methyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-
2-phenyl-malonic acid diethyl ester,

{3-(ethyl-methylcarbamoyl)-4-[(4'-trifluoromethyl-
biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-
5 ethylcarbamoyl-2-phenyl-ethyl ester,

{3-(ethyl-methylcarbamoyl)-4-[(4'-trifluoromethyl-
biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-
ethylcarbamoyl-3-phenyl-propyl ester,

{3-(piperidine-1-carbonyl)-4-[(4'-trifluoromethyl-
10 biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-
ethylcarbamoyl-2-phenyl-ethyl ester,

{3-(pyrrolidine-1-carbonyl)-4-[(4'-trifluoromethyl-
biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-
ethylcarbamoyl-2-phenyl-ethyl ester,

15 {3-(methyl-propylcarbamoyl)-4-[(4'-trifluoromethyl-
biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-
ethylcarbamoyl-2-phenyl-ethyl ester,

{3-(methyl-propylcarbamoyl)-4-[(4'-trifluoromethyl-
biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-
20 ethylcarbamoyl-3-phenyl-ethyl ester,

{3-(dimethylcarbamoyl)-4-[(4'-trifluoromethyl-
biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-ethyl-
carbamoyl-2-phenyl-ethyl ester,

2-phenyl-2-(2-{3-(pyrrolidine-1-carbonyl)-4-[(4'-
25 trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
acetoxymethyl)-malonic acid diethyl ester,

2-phenyl-2-(2-{3-(piperidine-1-carbonyl)-4-[(4'-
trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
acetoxymethyl)-malonic acid diethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2-propionylamino-ethyl ester,

5 {3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2-propionylamino-ethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-(2,5-dioxo-pyrrolidin-1-yl)-2-phenyl-ethyl ester,

10 {3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-ethylcarbamoyl-benzyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-ethylcarbamoylmethyl-benzyl ester,

15 {3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-isopropylamino-2-phenyl-ethyl ester hydrochloride,

2-[2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-fluoro-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

25 2-(2-{4-[(4'-bromo-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-

acetylamino-2-phenyl-ethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-butrylamino-2-phenyl-ethyl ester,

5 2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid dimethyl ester,

2-cyclopentyl-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

10 2-cyclohexyl-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-(2-{4-[(4'-chloro-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

15 2-(2-{4-[(4'-acetyl-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

20 2-(2-{4-[(4'-cyano-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4-methyl-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

25 2-(2-{3-dimethylcarbamoyl-4-[(5-methyl-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-

biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-
methanesulfonylamino-2-phenyl-ethyl ester,

3-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-
biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-
5 propionic acid ethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-
biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-(methyl-
propionyl-amino)-2-phenyl-ethyl ester,

2-[3-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-
10 biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-
phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(5-methoxy-4'-
trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

15 2-(2-{4-[5-chloro-4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-
acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(6-methyl-4'-
trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
20 acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-
biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-
phenyl-malonic acid di-2,2,2-trifluoroethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(2'-fluoro-4'-
25 trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{5-dimethylcarbamoyl-2-fluoro-4-[(4'-
trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-bromo-5-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-chloro-5-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(3'-fluoro-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{4-(3'-chloro-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(5-nitro-pyridin-2-yl)-malonic acid diethyl ester,

2-(5-amino-pyridin-2-yl)-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-pyridin-2-yl-malonic acid diethyl ester,

2-(2-{3-chloro-5-dimethylcarbamoyl-2-fluoro-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-bromo-5-dimethylcarbamoyl-2-fluoro-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-o-

tolyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-m-tolyl-malonic acid diethyl ester,

5 2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-p-tolyl-malonic acid diethyl ester,

2-(2-chloro-phenyl)-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

10 2-(3-chloro-phenyl)-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-(4-chloro-phenyl)-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

15 2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-succinic acid diethyl ester,

20 2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(2-methoxy-phenyl)-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(3-methoxy-phenyl)-malonic acid diethyl ester,

25 2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(4-methoxy-phenyl)-malonic acid diethyl ester,

2-(2-{4-(5,4'-bis-trifluoromethyl-biphenyl-2-

- carbonyl)- amino]-3-dimethylcarbamoyl-phenyl}-
 acetoxymethyl)-2-phenyl}-malonic acid diethyl ester,
 2-(2-{4-(6-chloro-4'-trifluoromethyl-biphenyl-2-
 carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-
 5 acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
 2-(2-{3-dimethylcarbamoyl-4-[(6-fluoro-4'-
 trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
 acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
 2-[2-(2-{3-dimethylcarbamoyl-4-[(5-methyl-4'-
 10 trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
 acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
 2-(2-{3-dimethylcarbamoyl-4-[(5-ethoxy-4'-
 trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
 acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
 15 2-(2-{3-dimethylcarbamoyl-4-[(5-isopropoxy-4'-
 trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
 acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
 2-[2-(2-{4-[(5,4'-bis-4'-trifluoromethyl-biphenyl-
 2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxy)-
 20 ethyl]-2-phenyl-malonic acid diethyl ester,
 2-(2-{3-dimethylcarbamoyl-4-[(6-methoxy-4'-
 trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
 acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
 2-(2-{3-dimethylcarbamoyl-4-[(3-methyl-4'-
 25 trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
 acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
 2-{2-[4-(2,4-bis-trifluoromethyl-benzoylamino)-3-
 dimethylcarbamoyl-phenyl]-acetoxymethyl)-2-phenyl-malonic
 acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-methyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-{2-[3-dimethylcarbamoyl-4-(2-ethyl-4-trifluoromethyl-benzoylamino)-phenyl]-acetoxymethyl}-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-ethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-isopropenyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-isopropyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-{2-[3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyloxy)-phenyl]-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-ethyl-2-phenyl-butyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 1-phenyl-cyclopropylmethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-diphenyl-ethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 1-phenyl-

cyclopentylmethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3-hydroxy-2-hydroxymethyl-2-phenyl-propyl ester,

5 {3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3-acetoxy-2-acetoxymethyl-2-phenyl-propyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-thiophen-2-yl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-thiophen-3-yl-malonic acid diethyl ester,

2-(2-{4-dimethylcarbamoyl-5-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-pyridin-2-yl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(3-methyl-thiophen-2-yl)-malonic acid diethyl ester,

20 2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(5-methyl-thiophen-2-yl)-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-thiazol-2-yl-malonic acid diethyl ester,

2-(2-{3-ethoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

{3-hydroxy-4-[(4'-trifluoromethyl-biphenyl-2-

- carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl- 2-phenyl-ethyl ester,
 {3-methoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl- 2-phenyl-ethyl ester,
 5 2-(2-{3-methoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
 {3-methoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2,2-bis-propylcarbamoyl-ethyl ester,
 10 {3-methoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,
 15 {3-ethoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,
 {3-ethoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,
 20 2-(2-{3-isopropoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
 {3-isopropoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,
 25 {3-isopropoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

{3-propoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

5 {3-benzyloxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

2-(2-{3-benzyloxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

10 2-(2-{3-hydroxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-{2-[3-methoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyloxy)-phenyl]-acetoxymethyl}-2-phenyl-malonic acid
15 diethyl ester,

{3-dimethylamino-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-piperidin-1-yl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,
20

{3-pyrrolidin-1-yl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

25 2-phenyl-2-(2-{3-piperidin-1-yl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-phenyl-2-(2-{3-pyrrolidin-1-yl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-

acetoxymethyl)-malonic acid diethyl ester,

2-(2-{3-dimethylamino-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

5 (2-{3-morpholin-4-yl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-diethylamino-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

10 2-[2-(2-{2-methyl-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic acid diethyl ester,

2-phenyl-2-(2-{3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-phenyl-2-[2-(2-{3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-malonic acid diethyl ester,

20 {3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

{3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

25 {3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3-phenyl-3,3-bis-propylcarbamoyl-propyl ester,

2-[2-(2-{4-methyl-3-[(4'-trifluoromethyl-biphenyl-2-

carbonyl)-amino]-phenyl}-acetoxy-ethyl)-2-phenyl-malonic acid diethyl ester,

2-[2-(2-{2-methyl-5-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic
5 acid diethyl ester,

{3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-isopropylcarbamoyl-3-phenyl-propyl ester,

{2-methyl-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,
10

{2-methyl-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 4,4-bis-ethylcarbamoyl-4-phenyl-butyl ester,

{2-methyl-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3-phenyl-3,3-bis-propylcarbamoyl-propyl ester,
15

{2-methoxy-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,
20

2-[2-(2-{2-methoxy-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic acid diethyl ester,

{2-ethoxy-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,
25

2-[2-(2-{2-ethoxy-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic acid diethyl ester,

2-[2-(2-{2-isopropoxy-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic acid diethyl ester,

2-[2-(2-{2-methoxycarbonyl-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic acid diethyl ester,

2-[2-(2-{2-ethoxy-5-methyl-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic acid diethyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid 2-[9-(2,2,2-trifluoro-ethylcarbamoyl)-9h-fluoren-9-yl]-ethyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid 2-[9h-fluoren-9-yl]-ethyl ester,

n-biphenyl-2-yl-terephthalamic acid 2-[9-(2,2,2-trifluoro-ethylcarbamoyl)-9h-fluoren-9-yl]-ethyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid 2-[(biphenyl-2-carbonyl)-amino]-ethyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid 2-(2-biphenyl-2-yl-acetyl-amino)-ethyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid 3-naphthalen-1-yl-3-(2,2,2-trifluoro-ethylcarbamoyl)-propyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid 3-[2-(2,2,2-trifluoro-ethylcarbamoyl)-naphthalen-1-yl]-propyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid 3,3-diphenyl-3-(2,2,2-trifluoro-ethylcarbamoyl)-propyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-
benzoic acid 3-biphenyl-2-yl-3-(2,2,2-trifluoro-
ethylcarbamoyl)-propyl ester,

5 4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-
benzoic acid 3-phenyl-3-(2,2,2-trifluoro-
ethylcarbamoyl)-propyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-
benzoic acid 2-[8-(2,2,2-trifluoro-
ethylcarbamoyl)-naphthalen-1-yl]-ethyl ester,

10 4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-
benzoic acid 3-[(2,6-dichloro-phenyl)-3-
(2,2,2-trifluoro-ethylcarbamoyl)-propyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-
benzoic acid 3-(2-chloro-phenyl)-3-(2,2,2-trifluoro-
15 ethylcarbamoyl)-propyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-benzoyloxy}-ethyl)-malonic acid diethyl
ester,

2-(2-{3-methyl-4-[(4'-trifluoromethyl-biphenyl-2-
20 carbonyl)-amino]-benzoyloxy}-ethyl)-2-phenyl-malonic acid
diethyl ester,

2-(2-{2-chloro-4-[(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-benzoyloxy}-ethyl)-2-phenyl-malonic acid
diethyl ester,

25 2-phenyl-2-{2-[4-[(4'-trifluoromethyl-biphenyl-2-
carbonyloxy)-benzoyloxy]-ethyl]-malonic acid diethyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-
benzoic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

4'-trifluoromethyl-biphenyl-2-carboxylic acid 4-(3,3-

bis-ethylcarbamoyl-3-phenyl-propoxycarbonyl)-2-chloro-phenyl ester,

4'-trifluoromethyl-biphenyl-2-carboxylic acid 4-(3,3-bis-ethylcarbamoyl-3-phenyl-propoxycarbonyl)-phenyl ester,

5 4'-trifluoromethyl-biphenyl-2-carboxylic acid 4-(3,3-bis-ethylcarbamoyl-3-phenyl-propoxycarbonyl)-2,6-dichloro-phenyl ester,

2-(2-{3-ethoxycarbonyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(3-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-propionyloxymethyl)-2-phenyl-malonic acid diethyl ester,

15 2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-propionic acid ethylcarbamoyl-phenyl-methyl ester,

5-(2,2-bis-ethylcarbamoyl-2-phenyl-ethoxycarbonylmethyl)-2-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid benzyl ester,

20 5-(2,2-bis-ethylcarbamoyl-2-phenyl-ethoxycarbonylmethyl)-2-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid,

5-(2,2-bis-ethylcarbamoyl-2-phenyl-ethoxycarbonylmethyl)-2-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid ethyl ester,

25 5-(2,2-bis-ethylcarbamoyl-2-phenyl-ethoxycarbonylmethyl)-2-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid methyl ester,

2-(2-{3-benzyloxycarbonyl-4-[(4'-trifluoromethyl-

biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-carboxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic
5 acid diethyl ester,

2-(2-{3-isopropoxycarbonyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-methoxycarbonyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
10

2-(2-{3-acetylamino-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-methoxycarbonylamino-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
15

2-(2-{3-(4-methyl-thiazol-2-yl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
20

2-phenyl-2-(2-{6-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-biphenyl-3-yl}-acetoxymethyl)-malonic acid diethyl ester,

2-(2-{3-formyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
25

2-(2-{3-dimethylaminomethyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-3-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-methoxy-methylcarbamoyl}-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-3-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-isobutyryl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-3-acetoxymethyl)-2-phenyl-malonic acid diethyl ester, and

2-(2-{3-(1-hydroxy-2-methyl-propyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester;

10

(24) The ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to the above (1), which is selected from the group consisting of

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl)-2-phenyl-ethyl ester,

2-phenyl-2-{2-[4-[(4'-trifluoromethyl-biphenyl-2-carbonyloxy)-phenyl]-acetoxymethyl}-malonic acid diethyl ester,

2-(2-{3-methyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{4-[methyl-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl]-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

{3-ethyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-2-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-phenyl-ethyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-

carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid

5 diisopropyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2,2-bis-(2,2,2-trifluoro-ethylcarbamoyl)-ethyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid
10 dimethyl ester,

2-cyclopentyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid
15 dicyclohexyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-cyclohexylcarbamoyl-2-phenyl ethyl ester,
20

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2,2-bis-phenylcarbamoyl-ethyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-isopropylcarbamoyl-2-phenyl-ethyl ester,
25

2-benzyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-(2-{2-methyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

4'-trifluoromethyl-biphenyl-2-carboxylic acid 4-[2-phenyl-2,2-bis-(2,2,2-trifluoro-ethylcarbamoyl)-ethoxycarbonylmethyl]-phenyl ester,

biphenyl-2-carboxylic acid 4-[2-phenyl-2,2-bis-(2,2,2-trifluoro-ethylcarbamoyl)-ethoxycarbonylmethyl]-phenyl ester,

2-cyclohexyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

{4-[(biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2,2-bis-(2,2,2-trifluoro-ethylcarbamoyl)-ethyl ester,

2-phenyl-2-(2-{2-trifluoromethyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-methylcarbamoyl-2-phenyl-ethyl ester,

2-pyridin-2-yl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-pyridin-3-yl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

4'-trifluoromethyl-biphenyl-2-carboxylic acid 4-(2,2-bis-ethylcarbamoyl)-2-phenyl-ethoxycarbonylmethyl)-

phenyl ester,

2-phenyl-2-(2-{3-trifluoromethyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

5 {4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-butylcarbamoyl-2-phenyl-ethyl ester,

{3-methyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-10 2-phenyl-ethyl ester,

2-(2-{4-[(4'-methyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{4-[(4'-methoxy-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

15 {4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3-phenyl-3,3-bis-propylcarbamoyl-propyl-20 ester,

{4-[(biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

2-phenyl-2-(2-{4-[(3'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl-25 ester,

4'-trifluoromethyl-biphenyl-2-carboxylic acid 4-(2,2-bis-ethylcarbamoyl)-2-phenyl-ethoxycarbonylmethyl)-2-chloro-phenyl ester,

2-(2-{4-[isopropyl-(4'-trifluoromethyl-biphenyl-2-

carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{4-[cyclohexyl-(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid dipropyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diisobutyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-isobutylcarbamoyl-2-phenyl-ethyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-(3-methyl-butylcarbamoyl)-2-phenyl-ethyl ester,

2-(2-{4-[ethyl-(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

{4-[(4'-chloro-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{4-[(3'4'-dichloro-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-methyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2,2-bis-propylcarbamoyl-ethyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-(2-methoxy-ethylcarbamoyl)-2-phenyl-ethyl ester,

2-(2-{3-ethyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

{3-isopropyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

10 2-(2-{3-isopropyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

{3-ethyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

{3-isobutyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

20 2-(2-{3-isobutyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-chloro-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

25 2-(2-{3-bromo-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-

phenyl-malonic acid diethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2,2-bis-propylcarbamoyl-ethyl ester,

5 {3-methylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

10 2-(2-{3-diethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

{3-benzylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 4,4-bis-ethylcarbamoyl-4-phenyl-butyl ester,

20 {3-diethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-diisopropylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

25 2-(2-{3-diethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-diisopropylcarbamoyl-4-[(4'-trifluoromethyl-

biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

{3-(isopropyl-methylcarbamoyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

2-(2-{3-(ethyl-methylcarbamoyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

{3-(ethyl-methylcarbamoyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-(ethyl-methylcarbamoyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

{3-(piperidin-1-carbonyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-(pyrrolidin-1-carbonyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-(methyl-propylcarbamoyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-(methyl-propylcarbamoyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-ethylcarbamoyl-2-phenyl-ethyl ester,

- 2-phenyl-2-(2-{3-pyrrolidin-1-carbonyl}-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,
- 2-phenyl-2-(2-{3-piperidin-1-carbonyl}-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,
- {3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2-propionylamino-ethyl ester,
- {3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-(2,5-dioxo-pyrrolidin-1-yl)-2-phenyl-ethyl ester,
- {3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-ethylcarbamoyl-benzyl ester,
- {3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-ethylcarbamoylmethyl-benzyl ester,
- {3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-isopropylamino-2-phenyl-ethyl ester hydrochloride,
- 2-[2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic acid diethyl ester,
- 2-(2-{3-dimethylcarbamoyl-4-[(4'-fluoro-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
- 2-(2-{4-[(4'-bromo-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxymethyl)-2-phenyl-malonic

acid diethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid
2-acethylamino-2-phenyl-ethyl ester,

5 {3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid
2-butyrylamino-2-phenyl-ethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-
10 2-phenyl-malonic acid dimethyl ester,

2-cyclopentyl-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-cyclohexyl-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

15 2-(2-{4-[(4'-chloro-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

20 2-(2-{4-[(4'-acetyl-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{4-[(4'-cyano-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxymethyl)-2-phenyl-malonic
25 acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4-methyl-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(5-methyl-4'-

- trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
 acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
 {3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-
 biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid
- 5 2-methanesulfonylamino-2-phenyl-ethyl ester,
 3-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-
 biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-
 propionic acid ethyl ester,
 {3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-
 10 biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-(methyl-
 propionyl-amino)-2-phenyl-ethyl ester,
 2-[3-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-
 -biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-propyl]-2-
 phenyl-malonic acid diethyl ester,
- 15 2-(2-{3-dimethylcarbamoyl-4-[(5-methoxy-4'-
 trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
 acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
 2-(2-{4-[(5-chloro-4'-trifluoromethyl-biphenyl-2-
 carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-
 20 acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
 2-(2-{3-dimethylcarbamoyl-4-[(6-methyl-4'-
 trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
 acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
 2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-
 25 -biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-
 phenyl-malonic acid di-2,2,2-trifluoroethyl ester,
 2-(2-{3-dimethylcarbamoyl-4-[(2'-fluoro-4'-
 trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
 acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

- 2-(2-{5-dimethylcarbamoyl-2-fluoro-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
- 2-(2-{3-bromo-5-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
- 5 2-(2-{3-chloro-5-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
- 10 2-(2-{3-dimethylcarbamoyl-4-[(3'-fluoro-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
- 2-(2-{4-[(3'-chloro-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
- 15 2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(5-nitro-pyridin-2-yl)-malonic acid diethyl ester,
- 2-(5-amino-pyridin-2-yl)-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,
- 20 2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-pyridin-2-yl-malonic acid diethyl ester,
- 25 2-(2-{3-chloro-5-dimethylcarbamoyl-2-fluoro-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
- 2-(2-{3-bromo-5-dimethylcarbamoyl-2-fluoro-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-

acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-ortho-tolyl-malonic acid diethyl ester,

5 2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-m-tolyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-p-
10 tolyl-malonic acid diethyl ester,

2-(2-chloro-phenyl)-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-(3-chloro-phenyl)-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,
15

2-(4-chloro-phenyl)-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

20 2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-succinic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(2-methoxy-phenyl)-malonic acid diethyl ester,
25

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(3-methoxy-phenyl)-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-

biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(4-methoxy-phenyl)-malonic acid diethyl ester,

2-(2-{4-[(5,4'-bis-trifluoromethyl-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl})-

5 acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{4-[(6-chloro-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl})-

acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(6-fluoro-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl})-

10 acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-[2-(2-{3-dimethylcarbamoyl-4-[(5-methyl-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl})-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

15 2-(2-{3-dimethylcarbamoyl-4-[(5-ethoxy-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl})-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(5-isopropoxy-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl})-

20 acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-[2-(2-{4-(5,4'-bis-trifluoromethyl-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl})-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-(6-methoxy-4'-

25 trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl})-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(3-methyl-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl})-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-{2-[4-(2,4-bis-trifluoromethyl-benzoylamino)-3-dimethylcarbamoyl-phenyl]-acetoxymethyl}-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-methyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-{2-[3-dimethylcarbamoyl-4-[(2-ethyl-4-trifluoromethyl-benzoylamino)-phenyl]-acetoxymethyl]-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-ethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-isopropenyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-isopropyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-{2-[3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyloxy)-phenyl]-acetoxymethyl]-2-phenyl-malonic acid diethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-ethyl-2-phenyl-butyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 1-phenyl-cyclopropylmethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-

diphenyl-ethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 1-phenyl-cyclopentylmethyl ester,

5 {3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3-hydroxy-2-hydroxymethyl-2-phenyl-propyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid
10 3-acetoxymethyl-2-phenyl-propyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-thiophen-2-yl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-
15 thiophen-3-yl-malonic acid diethyl ester,

2-(2-{4-dimethylcarbamoyl-5-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-pyridin-2-yl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

20 2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(3-methyl-thiophen-2-yl)-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(5-
25 methyl-thiophen-2-yl)-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-thiazol-2-yl-malonic acid diethyl ester,

2-(2-{3-ethoxy-4-[(4'-trifluoromethyl-biphenyl-2-

carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic
acid diethyl ester,

5 {3-hydroxy-4-[(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-
ethylcarbamoyl-2-phenyl-ethyl ester

{3-methoxy-4-[(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-
ethylcarbamoyl-2-phenyl-ethyl ester

10 2-(2-{3-methoxy-4-[(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic
acid diethyl ester,

{3-methoxy-4-[(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2,2-bis-
propylcarbamoyl-ethyl ester,

15 {3-methoxy-4-[(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-
ethylcarbamoyl-3-phenyl-propyl ester,

{3-ethoxy-4-[(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-
20 ethylcarbamoyl-2-phenyl-ethyl ester,

{3-ethoxy-4-[(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-
ethylcarbamoyl-3-phenyl-propyl ester,

25 2-(2-{3-isopropoxy-4-[(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic
acid diethyl ester,

{3-isopropoxy-4-[(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-
ethylcarbamoyl-2-phenyl-ethyl ester,

{3-isopropoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

5 {3-propoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-benzyloxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

10 2-(2-{3-benzyloxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-hydroxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

15 2-{2-[3-methoxy-4-(4'-trifluoromethyl-biphenyl-2-carbonyloxy)-phenyl]-acetoxymethyl}-2-phenyl-malonic acid diethyl ester,

{3-dimethylamino-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-piperidin-1-yl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

25 {3-pyrrolidin-1-yl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

2-phenyl-2-(2-{3-piperidin-1-yl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-

acetoxymethyl)- malonic acid diethyl ester,

2-phenyl-2-(2-{3-pyrrolidin-1-yl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)- malonic acid diethyl ester,

5 2-(2-{3-dimethylamino-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-morpholin-4-yl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

10 2-(2-{3-diethylamino-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-[2-(2-{2-methyl-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic acid diethyl ester,

15 2-phenyl-2-(2-{3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

20 2-phenyl-2-[2-(2-{3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-malonic acid diethyl ester,

{3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

25 {3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3-phenyl-3,3-bis-propylcarbamoyl-propyl ester,

2-[2-(2-{4-methyl-3-[(4'-trifluoromethyl-biphenyl-2-

carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic acid diethyl ester,

2-[2-(2-{2-methyl-5-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic
5 acid diethyl ester,

{3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-isopropylcarbamoyl-3-phenyl-propyl ester,

{2-methyl-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,
10

{2-methyl-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 4,4-bis-ethylcarbamoyl-4-phenyl-butyl ester,

{2-methyl-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3-phenyl-3,3-bis-propylcarbamoyl-propyl ester,
15

{2-methoxy-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,
20

2-[2-(2-{2-methoxy-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic acid diethyl ester,

{2-ethoxy-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,
25

2-[2-(2-{2-ethoxy-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic acid diethyl ester,

2-[2-(2-{2-isopropoxy-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic acid diethyl ester,

2-[2-(2-{2-methoxycarbonyl-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic acid diethyl ester,

2-[2-(2-{2-ethoxy-5-methyl-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic acid diethyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid 2-[(biphenyl-2-carbonyl)-amino]-ethyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid 2-(2-biphenyl-2-yl-acetyl-amino)-ethyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid 3-naphthalen-1-yl-3-(2,2,2-trifluoroethylcarbamoyl)-propyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid 3-[2-(2,2,2-trifluoroethylcarbamoyl)-naphthalen-1-yl]-propyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid 3,3-diphenyl-3-(2,2,2-trifluoroethylcarbamoyl)-propyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid 3-biphenyl-2-yl-3-(2,2,2-trifluoroethylcarbamoyl)-propyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid 3-phenyl-3-(2,2,2-trifluoroethylcarbamoyl)-propyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-

benzoic acid 2-[8-(2,2,2-trifluoro-ethylcarbamoyl)-naphthalen-1-yl]-ethyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid 3-(2,6-dichloro-phenyl)-3-(2,2,2-trifluoro-ethylcarbamoyl)-propyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid 3-(2-chloro-phenyl)-3-(2,2,2-trifluoro-ethylcarbamoyl)-propyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoyloxy}-ethyl)-malonic acid diethyl ester,

2-(2-{3-methyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoyloxy}-ethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{2-chloro-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoyloxy}-ethyl)-2-phenyl-malonic acid diethyl ester,

2-phenyl-2-{2-[4-(4'-trifluoromethyl-biphenyl-2-carbonyloxy)-benzoyloxy]-ethyl}-malonic acid diethyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

4'-trifluoromethyl-biphenyl-2-carboxylic acid 4-(3,3-bis-ethylcarbamoyl-3-phenyl-propoxycarbonyl)-2-chloro-phenyl ester,

4'-trifluoromethyl-biphenyl-2-carboxylic acid 4-(3,3-bis-ethylcarbamoyl-3-phenyl-propoxycarbonyl)-phenyl ester,

4'-trifluoromethyl-biphenyl-2-carboxylic acid 4-(3,3-bis-ethylcarbamoyl-3-phenyl-propoxycarbonyl)-2,6-dichloro-p

henyl ester,

2-(2-{3-ethoxycarbonyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

5 2-(3-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-propionyloxymethyl)-2-phenyl-malonic acid diethyl ester,

3-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-propionic acid ethylcarbamoyl-phenyl-
10 methyl ester,

5-(2,2-bis-ethylcarbamoyl-2-phenyl-ethoxycarbonylmethyl)-2-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid benzyl ester,

5-(2,2-bis-ethylcarbamoyl-2-phenyl-ethoxycarbonylmethyl)-2-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid,
15

5-(2,2-bis-ethylcarbamoyl-2-phenyl-ethoxycarbonylmethyl)-2-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid ethyl ester,

5-(2,2-bis-ethylcarbamoyl-2-phenyl-ethoxycarbonylmethyl)-2-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid methyl ester,
20

2-(2-{3-benzyloxycarbonyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-
25 2-phenyl-malonic acid diethyl ester,

2-(2-{3-carboxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-isopropoxycarbonyl-4-[(4'-trifluoromethyl-

biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-methoxycarbonyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)- 2-phenyl-malonic acid diethyl ester,

2-(2-{3-acetylamino-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-methoxycarbonylamino-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)- 2-phenyl-malonic acid diethyl ester,

2-(2-{3-(4-methyl-thiazol-2-yl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)- 2-phenyl-malonic acid diethyl ester,

2-phenyl-(2-{6-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-biphenyl-3-yl}-acetoxymethyl)- malonic acid diethyl ester,

2-(2-{3-formyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylaminomethyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-(methoxy-methylcarbonyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-isobutyryl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester, and

2-(2-{3-(1-hydroxy-2-methyl-propyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester;

- 5 (25) The ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to the above (1), which is selected from the group consisting of

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

10

{3-ethyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2,2-bis-(2,2,2-trifluoro-ethylcarbamoyl)-ethyl ester,

15

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-cyclohexylcarbamoyl-2-phenyl-ethyl ester,

20 {4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2,2-bis-phenylcarbamoyl-ethyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-isopropylcaramoyl-2-phenyl-ethyl ester,

25

4'-trifluoromethyl-biphenyl-2-carboxylic acid 4-[2-phenyl-2,2-bis-(2,2,2-trifluoro-ethylcarbamoyl)-ethoxycarbonylmethyl]-phenyl ester,

biphenyl-2-carboxylic acid 4-[2-phenyl-2,2-bis-

(2,2,2-trifluoro-ethylcarbamoyl)-ethoxycarbonylmethyl]-phenyl ester,

5 {4-[(biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid
2-phenyl-2,2-bis-(2,2,2-trifluoro-ethylcarbamoyl)-ethyl
ester,

2-phenyl-2-(2-{2-trifluoromethyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

10 {4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-methylcarbamoyl-2-phenyl-ethyl
ester,

4'-trifluoromethyl-biphenyl-2-carboxylic acid 4-(2,2-bis-ethylcarbamoyl-2-phenyl-ethoxycarbonylmethyl)-phenyl
ester,

15 {4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-butylcarbamoyl-2-phenyl-ethyl-
ester,

{3-methyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

20 {4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl
ester,

25 {4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3-phenyl-3,3-bis-propylcarbamoyl-propyl
ester,

{4-[(biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl ethyl ester,

4'-trifluoromethyl-biphenyl-2-carboxylic acid 4-(2,2-

bis-ethylcarbamoyl-2-phenyl-ethoxycarbonylmethyl)-2-chloro-phenyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-isobutylcarbamoyl-2-phenyl ethyl
5 ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-(3-methyl-butylcarbamoyl)-2-phenyl ethyl ester,

{4-[(4'-chloro-biphenyl-2-carbonyl)-amino]-phenyl}-
10 acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl ethyl ester,

{4-[(3',4'-dichloro-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl)-2-phenyl-ethyl ester,

{3-methyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2,2-bis-propylcarbamoyl)-ethyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-(2-methoxy-ethylcarbamoyl)-2-phenyl-ethyl ester,

20 {3-isopropyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-phenyl-ethyl ester,

{3-ethyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-
25 ethylcarbamoyl-3-phenyl-propyl ester,

{3-isobutyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-

- biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-
2,2-bis-propylcarbamoyl-ethyl ester,
- {3-methylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-
2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-
5 ethylcarbamoyl-2-phenyl-ethyl ester,
- {3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-
2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-
ethylcarbamoyl-3-phenyl-propyl ester,
- {3-benzylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-
10 carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-
ethylcarbamoyl-2-phenyl-ethyl ester,
- {3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-
biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 4,4-bis-
ethylcarbamoyl-4-phenyl-butyl ester,
- 15 {3-diethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-
2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-
ethylcarbamoyl-2-phenyl-ethyl ester,
- {3-diisopropylcarbamoyl-4-[(4'-trifluoromethyl-
biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-
20 ethylcarbamoyl-2-phenyl-ethyl ester,
- {3-(isopropyl-methylcarbamoyl)-4-[(4'-
trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic
acid 2,2-bis- ethylcarbamoyl-2-phenyl-ethyl ester,
- {3-(ethyl-methylcarbamoyl)-4-[(4'-trifluoromethyl-
25 biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-
ethylcarbamoyl-2-phenyl-ethyl ester,
- {3-(ethyl-methylcarbamoyl)-4-[(4'-trifluoromethyl-
biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-
ethylcarbamoyl-3-phenyl-propyl ester,

{3-(piperidin-1-carbonyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

5 {3-(pyrrolidin-1-carbonyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-(methyl-propylcarbamoyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

10 {3-(methyl-propylcarbamoyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

{3-hydroxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-methoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

20 {3-methoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2,2-bis-propylcarbamoyl-ethyl ester,

{3-methoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

25 {3-ethoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-ethoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-

- ethylcarbamoyl-3-phenyl-propyl ester,
 {3-isopropoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,
- 5 {3-isopropoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,
 {3-propoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,
- 10 {3-benzyloxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,
 {3-dimethylamino-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,
- 15 {3-piperidin-1-yl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,
 {3-pyrrolidin-1-yl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,
- 20 {3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,
- 25 {3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3-phenyl-3,3-bis-propylcarbamoyl-propyl ester,
 {3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-

phenyl}-acetic acid 3,3-bis-isopropylcarbamoyl-3-phenyl-propyl ester,

{2-methyl-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

{2-methyl-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 4,4-bis-ethylcarbamoyl-4-phenyl-butyl ester,

{2-methyl-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3-phenyl-3,3-bis-propylcarbamoyl-propyl ester,

{2-methoxy-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

{2-ethoxy-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

4'-trifluoromethyl-biphenyl-2-carboxylic acid 4-(3,3-bis-ethylcarbamoyl-3-phenyl-propoxycarbonyl)-2-chlorophenyl ester,

4'-trifluoromethyl-biphenyl-2-carboxylic acid 4-(3,3-bis-ethylcarbamoyl-3-phenyl-propoxycarbonyl)-phenyl ester,

4'-trifluoromethyl-biphenyl-2-carboxylic acid 4-(3,3-bis-ethylcarbamoyl-3-phenyl-propoxycarbonyl)-2,6-dichlorophenyl ester,

5-(2,2-bis-ethylcarbamoyl-2-phenyl-ethoxycarbonylmethyl)-2-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-

amino]-benzoic acid benzyl ester,

5-(2,2-bis-ethylcarbamoyl-2-phenyl-ethoxycarbonyl-methyl)-2-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid,

5 5-(2,2-bis-ethylcarbamoyl-2-phenyl-ethoxycarbonyl-methyl)-2-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid ethyl ester, and

5-(2,2-bis-ethylcarbamoyl-2-phenyl-ethoxycarbonyl-methyl)-2-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid methyl ester;

(26) The ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to the above (1), which is selected from the group consisting of

15 2-phenyl-2-{2-[4-(4'-trifluoromethyl-biphenyl-2-carbonyloxy)-phenyl]-acetoxymethyl}-malonic acid diethyl ester,

2-(2-{3-methyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{4-[methyl-(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diisopropyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid dimethyl ester,

2-cyclopentyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid dicyclohexyl ester,

2-benzyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-(2-{2-methyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-cyclohexyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-phenyl-2-(2-{2-trifluoromethyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-pyridin-2-yl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-pyridin-3-yl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-phenyl-2-(2-{3-trifluoromethyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-

acetoxymethyl)- malonic acid diethyl ester,

2-(2-{4-[(4'-methyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{4-[(4'-methoxy-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-phenyl-2-(2-{4-[(3'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-(2-{4-[isopropyl-(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{4-[cyclohexyl-(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid dipropyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diisobutyl ester,

2-(2-{4-[ethyl-(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-ethyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-isopropyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-isobutyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-chloro-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-bromo-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-diethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-diisopropylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-(ethyl-methylcarbamoyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

{3-(pyrrolidine-1-carbonyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

2-phenyl-2-(2-{3-(pyrrolidine-1-carbonyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-phenyl-2-(2-{3-(piperidine-1-carbonyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-

acetoxymethyl)-malonic acid diethyl ester,

2-[2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

5 2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{4-[(4'-bromo-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxymethyl)-2-phenyl-malonic
10 acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-cyclopentyl-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-cyclohexyl-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

20 2-(2-{4-[(4'-chloro-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{4-[(4'-acetyl-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

25 2-(2-{4-[(4'-cyano-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4-methyl-4'-

- trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
 acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
 2-(2-{3-dimethylcarbamoyl-4-[(5-methyl-4'-
 trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
 5 acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
 2-[3-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-
 biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-propyl]-2-
 phenyl-malonic acid diethyl ester,
 2-(2-{3-dimethylcarbamoyl-4-[(5-methoxy-4'-
 10 trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
 acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
 2-(2-{4-[(5-chloro-4'-trifluoromethyl-biphenyl-2-
 carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-
 acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
 15 2-(2-{3-dimethylcarbamoyl-4-[(6-methyl-4'-
 trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
 acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
 2-(2-{3-dimethylcarbamoyl-4-[4'-trifluoromethyl-
 biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-
 20 phenyl-malonic acid di-2,2,2-trifluoroethyl ester,
 2-(2-{3-dimethylcarbamoyl-4-[(2'-fluoro-4'-
 trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
 acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
 2-(2-{5-dimethylcarbamoyl-2-fluoro-4-[(4'-
 25 trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
 acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
 2-(2-{3-bromo-5-dimethylcarbamoyl-4-[(4'-
 trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
 acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

- 2-(2-{3-chloro-5-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
- 2-(2-{3-dimethylcarbamoyl-4-[(3'-fluoro-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
- 5 2-(2-{4-[(3'-chloro-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
- 10 2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(5-nitro-pyridin-2-yl)-malonic acid diethyl ester,
- 2-(5-amino-pyridin-2-yl)-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,
- 15 2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-pyridin-2-yl-malonic acid diethyl ester,
- 2-(2-{3-chloro-5-dimethylcarbamoyl-2-fluoro-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
- 20 2-(2-{3-bromo-5-dimethylcarbamoyl-2-fluoro-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
- 25 2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-ortho-tolyl-malonic acid diethyl ester,
- 2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-m-

tolyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-p-tolyl-malonic acid diethyl ester,

5 2-(3-chloro-phenyl)-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-(3-chloro-phenyl)-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

10 2-(4-chloro-phenyl)-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-succinic acid diethyl ester,

15 2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(2-methoxy-phenyl)-malonic acid diethyl ester,

20 2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(3-methoxy-phenyl)-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(4-methoxy-phenyl)-malonic acid diethyl ester,

25 2-(2-{4-[(5,4'-bis-trifluoromethyl-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{4-[(6-chloro-4'-trifluoromethyl-biphenyl-2-

- carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-
 acetoxymethyl)-2-phenyl)-malonic acid diethyl ester,
 2-(2-{3-dimethylcarbamoyl-4-[(6-fluoro-4'-
 trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
 5 acetoxymethyl)-2-phenyl)-malonic acid diethyl ester,
 2-[2-(2-{3-dimethylcarbamoyl-4-[(5-methyl-4'-
 trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
 acetoxy)-ethyl]-2-phenyl)-malonic acid diethyl ester,
 2-(2-{3-dimethylcarbamoyl-4-[(5-ethoxy-4'-
 10 trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
 acetoxymethyl)-2-phenyl)-malonic acid diethyl ester,
 2-(2-{3-dimethylcarbamoyl-4-[(5-isopropoxy-4'-
 trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
 acetoxymethyl)-2-phenyl)-malonic acid diethyl ester,
 15 2-[2-(2-{4-[(5,4'-bis-trifluoromethyl-biphenyl-2-
 carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxy)-
 ethyl]-2-phenyl-malonic acid diethyl ester,
 2-(2-{3-dimethylcarbamoyl-4-[(6-methoxy-4'-
 trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
 20 acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
 2-(2-{3-dimethylcarbamoyl-4-[(3-methyl-4'-
 trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
 acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
 2-{2-[4-(2,4-bis-trifluoromethyl-benzoylamino)-3-
 25 dimethylcarbamoyl-phenyl]-acetoxymethyl}-2-phenyl)-malonic
 acid diethyl ester,
 2-(2-{3-dimethylcarbamoyl-4-[(4'-methyl-biphenyl-2-
 carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic
 acid diethyl ester,

2-{2-[3-dimethylcarbamoyl-4-[(2-ethyl-4-trifluoromethyl-benzoylamino)-phenyl]-acetoxymethyl]-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-ethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-isopropenyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-isopropyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-{2-[3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyloxy)-phenyl]-acetoxymethyl]-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-thiophen-2-yl- malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-thiophen-3-yl- malonic acid diethyl ester,

2-(2-{4-dimethylcarbamoyl-5-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-pyridin-2-yl}-acetoxymethyl)-2-phenyl- malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(3-methyl-thiophen-2-yl)-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(5-

methyl-thiophen-2-yl)-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-thiazol-2-yl-malonic acid diethyl ester,

5 2-(2-{3-ethoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-methoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic
10 acid diethyl ester,

2-(2-{3-isopropoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-benzyloxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic
15 acid diethyl ester,

2-(2-{3-hydroxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

20 2-{2-[3-methoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyloxy)-phenyl]-acetoxymethyl]-2-phenyl-malonic acid diethyl ester,

2-phenyl-2-(2-{3-piperidin-1-yl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-
25 malonic acid diethyl ester,

2-phenyl-2-(2-{3-pyrrolidin-1-yl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-(2-{3-dimethylamino-4-[(4'-trifluoromethyl-

biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-morpholin-4-yl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-diethylamino-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-[2-(2-{2-methyl-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-ethyl]-2-phenyl-malonic acid diethyl ester,

2-phenyl-2-(2-{3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-phenyl-2-[2-(2-{3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-ethyl]-malonic acid diethyl ester,

2-[2-(2-{4-methyl-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-ethyl]-2-phenyl-malonic acid diethyl ester,

2-[2-(2-{2-methyl-5-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-ethyl]-2-phenyl-malonic acid diethyl ester,

2-[2-(2-{2-methoxy-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-ethyl]-2-phenyl-malonic acid diethyl ester,

2-[2-(2-{2-ethoxy-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-ethyl]-2-phenyl-malonic acid diethyl ester,

2-[2-(2-{2-isopropoxy-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic acid diethyl ester,

2-[2-(2-{2-methoxycarbonyl-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic acid diethyl ester,

2-[2-(2-{2-ethoxy-5-methyl-3-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic acid diethyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoyloxy}-ethyl)-malonic acid diethyl ester,

2-(2-{3-methyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoyloxy}-ethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{2-chloro-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoyloxy}-ethyl)-2-phenyl-malonic acid diethyl ester,

2-phenyl-2-{2-[4-(4'-trifluoromethyl-biphenyl-2-carbonyloxy)-benzoyloxy]-ethyl}-malonic acid diethyl ester,

2-(2-{3-ethoxycarbonyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(3-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-propionyloxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-benzyloxycarbonyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-carboxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

5 2-(2-{3-isopropoxycarbonyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-methoxycarbonyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

10 2-(2-{3-acetyl-amino-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

15 2-(2-{3-methoxycarbonylamino-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-(4-methyl-thiazol-2-yl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

20 2-phenyl-2-(2-{6-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-biphenyl-3-yl}-acetoxymethyl)-malonic acid diethyl ester,

2-(2-{3-formyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

25 2-(2-{3-dimethylaminomethyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-(methoxy-methylcarbamoyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-

2-phenyl-malonic acid diethyl ester,

2-(2-{3-isobutyryl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester, and

5 2-(2-{3-(1-hydroxy-2-methyl-propyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester;

(27) The ester compound or a prodrug thereof, or a
10 pharmaceutically acceptable salt of either according to the above (1), which is selected from the group consisting of

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

15 {3-ethyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2,2-bis-(2,2,2-trifluoro-ethylcarbamoyl)-ethyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-cyclohexylcarbamoyl-2-phenyl-ethyl ester,

25 {4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2,2-bis-phenylcarbamoyl-ethyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-isopropylcarbamoyl-2-phenyl-ethyl ester,

{4-[(biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid
2-phenyl-2,2-bis-(2,2,2-trifluoro-ethylcarbamoyl)-ethyl
ester,

2-phenyl-2-(2-{2-trifluoromethyl-4-[(4'-trifluoro-
5 methyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-
malonic acid diethyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-
phenyl}-acetic acid 2,2-bis-methylcarbamoyl-2-phenyl-ethyl
ester,

10 {4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-
phenyl}-acetic acid 2,2-bis-butylcarbamoyl-2-phenyl-ethyl
ester,

{3-methyl-4-[(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethyl-
15 carbamoyl-2-phenyl-ethyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-
phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl-
ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-
20 phenyl}-acetic acid 3-phenyl-3,3-bis-propyl- carbamoyl-
propyl ester,

{4-[(biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid
2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-
25 phenyl}-acetic acid 2,2-bis-isobutylcarbamoyl-2-phenyl-
ethyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-
phenyl}-acetic acid 2,2-bis-(3-methyl-butylcarbamoyl)-2-
phenyl-ethyl ester,

{4-[(4'-chloro-biphenyl-2-carbonyl)-amino]-phenyl}-
acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{4-[(3',4'-dichloro-biphenyl-2-carbonyl)-amino]-
phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl
5 ester,

{3-methyl-4-[(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2,2-bis-
propylcarbamoyl-ethyl ester,

{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-
10 phenyl}-acetic acid 2,2-bis-(2-methoxy-ethylcarbamoyl)-
2-phenyl-ethyl ester,

{3-isopropyl-4-[(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-
2-phenyl-ethyl ester,

15 {3-ethyl-4-[(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethyl-
carbamoyl-3-phenyl-propyl ester,

{3-isobutyl-4-[(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethyl-
20 carbamoyl-2-phenyl-ethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-
biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-
2,2-bis-propylcarbamoyl-ethyl ester,

{3-methylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-
25 2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-
ethylcarbamoyl-2-phenyl-ethyl ester,

{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-
biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-
ethylcarbamoyl-3-phenyl-propyl ester,

{3-benzylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

5 {3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 4,4-bis-ethylcarbamoyl-4-phenyl-butyl ester,

{3-diethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

10 {3-diisopropylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-(isopropyl-methylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid
15 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-(ethyl-methylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

20 {3-(piperidine-1-carbonyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-(pyrrolidine-1-carbonyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,
25

{3-(methyl-propylcarbamoyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-(methyl-propylcarbamoyl)-4-[(4'-trifluoromethyl-

biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

{3-hydroxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-methoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-methoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2-phenyl-2,2-bis-propylcarbamoyl-ethyl ester,

{3-methoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

{3-ethoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-ethoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

{3-isopropoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-isopropoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

{3-propoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-benzyloxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

5 {3-dimethylamino-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-piperidin-1-yl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

10 {3-pyrrolidin-1-yl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid 3,3-bis-ethylcarbamoyl-3-phenyl-propyl ester,

15 5-(2,2-bis-ethylcarbamoyl-2-phenyl-ethoxycarbonylmethyl)-2-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid benzyl ester,

5-(2,2-bis-ethylcarbamoyl-2-phenyl-ethoxycarbonylmethyl)-2-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid,

5-(2,2-bis-ethylcarbamoyl-2-phenyl-ethoxycarbonylmethyl)-2-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid ethyl ester, and

25 5-(2,2-bis-ethylcarbamoyl-2-phenyl-ethoxycarbonylmethyl)-2-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid methyl ester;

(28) The ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to the

above (1), which is selected from the group consisting of

2-(2-{3-methyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

5 2-(2-{4-[methyl-(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid
10 diethyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid
diisopropyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid
15 dimethyl ester,

2-cyclopentyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid
diethyl ester,

20 2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid
dicyclohexyl ester,

2-benzyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid
25 diethyl ester,

2-(2-{2-methyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-cyclohexyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-

2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid
diethyl ester,

2-phenyl-2-(2-{2-trifluoromethyl-4-[(4'-trifluoro-
methyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-
5 malonic acid diethyl ester,

2-pyridin-2-yl-2-(2-{4-[(4'-trifluoromethyl-
biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)- malonic
acid diethyl ester,

2-pyridin-3-yl-2-(2-{4-[(4'-trifluoromethyl-
10 biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)- malonic
acid diethyl ester,

2-phenyl-2-(2-{3-trifluoromethyl-4-[(4'-trifluoro-
methyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-
malonic acid diethyl ester,

15 2-(2-{4-[(4'-methyl-biphenyl-2-carbonyl)-amino]-
phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{4-[(4'-methoxy-biphenyl-2-carbonyl)-amino]-
phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-phenyl-2-(2-{4-[(3'-trifluoromethyl-biphenyl-2-
20 carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl
ester,

2-(2-{4-[isopropyl-(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic
acid diethyl ester,

25 2-(2-{4-[cyclohexyl-(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic
acid diethyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid

dipropyl ester,

2-phenyl-2-(2-{4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diisobutyl ester,

5 2-(2-{4-[ethyl-(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-ethyl-4-(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic
10 acid diethyl ester,

2-(2-{3-isopropyl-4-(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-isobutyl-4-(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic
15 acid diethyl ester,

2-(2-{3-chloro-4-(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

20 2-(2-{3-bromo-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,
25

2-(2-{3-diethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-diisopropylcarbamoyl-4-[(4'-trifluoromethyl-

biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-(ethyl-methylcarbamoyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

{3-(ethyl-methylcarbamoyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

{3-(pyrrolidine-1-carbonyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetic acid 2,2-bis-ethylcarbamoyl-2-phenyl-ethyl ester,

2-phenyl-2-(2-{3-(pyrrolidine-1-carbonyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-phenyl-2-(2-{3-(piperidine-1-carbonyl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-[2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-fluoro-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{4-[(4'-bromo-biphenyl-2-carbonyl)-amino]}-3-dimethylcarbamoyl-phenyl)-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid dimethyl ester,

2-cyclopentyl-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-cyclohexyl-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-(2-{4-[(4'-chloro-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{4-[(4'-acetyl-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{4-[(4'-cyano-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4-methyl-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(5-methyl-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-[3-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-propyl]-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(5-methoxy-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{4-[(5-chloro-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-

acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(6-methyl-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-

acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

5 2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid 2,2,2-trifluoroethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(2'-fluoro-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-

10 acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{5-dimethylcarbamoyl-2-fluoro-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-bromo-5-dimethylcarbamoyl-4-[(2'-fluoro-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

15 2-(2-{3-chloro-5-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

20 2-(2-{3-dimethylcarbamoyl-4-[(3'-fluoro-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{4-[(3'-chloro-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-

25 acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(5-nitro-pyridin-2-yl)-malonic acid diethyl ester,

2-(5-amino-pyridin-2-yl)-2-(2-{3-dimethylcarbamoyl-

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-
phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-
biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-
5 pyridin-2-yl-malonic acid diethyl ester,

2-(2-{3-chloro-5-dimethylcarbamoyl-2-fluoro-4-[(4'-
trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-bromo-5-dimethylcarbamoyl-2-fluoro-4-[(4'-
10 trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-
biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-o-
tolyl-malonic acid diethyl ester,

15 2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-
biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-m-
tolyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-
biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-p-
20 tolyl-malonic acid diethyl ester,

2-(2-chloro-phenyl)-2-(2-{3-dimethylcarbamoyl-4-
[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
acetoxymethyl)-malonic acid diethyl ester,

2-(3-chloro-phenyl)-2-(2-{3-dimethylcarbamoyl-4-
25 [(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
acetoxymethyl)-malonic acid diethyl ester,

2-(4-chloro-phenyl)-2-(2-{3-dimethylcarbamoyl-4-
[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
acetoxymethyl)-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-succinic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(2-methoxy-phenyl)-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(3-methoxy-phenyl)-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(4-methoxy-phenyl)-malonic acid diethyl ester,

2-(2-{4-[(5,4'-bis-trifluoromethyl-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{4-[(6-chloro-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-3-dimethylcarbamoyl-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(6-fluoro-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-[2-(2-{3-dimethylcarbamoyl-4-[(5-methyl-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-ethyl]-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(5-ethoxy-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(5-isopropoxy-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-

acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-[2-(2-{4-(5,4'-bis-trifluoromethyl-biphenyl-2-carbonyl)-amino}-3-dimethylcarbamoyl-phenyl)-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

5 2-(2-{3-dimethylcarbamoyl-4-(6-methoxy-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino}-phenyl)-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-(3-methyl-4'-trifluoromethyl-biphenyl-2-carbonyl)-amino}-phenyl)-acetoxymethyl)-
10 2-phenyl-malonic acid diethyl ester,

2-{2-{4-(2,4-bis-trifluoromethyl-benzoylamino)-3-dimethylcarbamoyl-phenyl]-acetoxymethyl}-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-methyl-biphenyl-2-carbonyl)-amino]-phenyl)-acetoxymethyl)-2-phenyl-malonic
15 acid diethyl ester,

2-{2-[3-dimethylcarbamoyl-4-(2-ethyl-4-trifluoromethyl-benzoylamino)-phenyl]-acetoxymethyl}-2-phenyl-malonic acid diethyl ester,

20 2-(2-{3-dimethylcarbamoyl-4-[(4'-ethyl-biphenyl-2-carbonyl)-amino]-phenyl)-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-isopropenyl-biphenyl-2-carbonyl)-amino]-phenyl)-acetoxymethyl)-2-
25 phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-isopropyl-biphenyl-2-carbonyl)-amino]-phenyl)-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-

biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-thiophen-2-yl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-thiophen-3-yl-malonic acid diethyl ester,

2-(2-{4-dimethylcarbamoyl-5-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-pyridin-2-yl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(3-methyl-thiophen-2-yl)-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(5-methyl-thiophen-2-yl)-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-thiazol-2-yl-malonic acid diethyl ester,

2-(2-{3-ethoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-methoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-isopropoxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-benzyloxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-hydroxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-phenyl-2-(2-{3-piperidin-1-yl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-phenyl-2-(2-{3-pyrrolidin-1-yl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-(2-{3-dimethylamino-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-morpholin-4-yl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-diethylamino-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{2-chloro-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoyloxy}-ethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-ethoxycarbonyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(3-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-propionyloxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-benzyloxycarbonyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-

phenyl-malonic acid diethyl ester,

2-(2-{3-carboxy-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

5 2-(2-{3-isopropoxycarbonyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-methoxycarbonyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

10 2-(2-{3-acetyl-amino-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-methoxycarbonylamino-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

15 2-(2-{3-(4-methyl-thiazol-2-yl)-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

20 2-phenyl-2-(2-{6-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-biphenyl-3-yl}-acetoxymethyl)-malonic acid diethyl ester,

2-(2-{3-formyl-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

25 2-(2-{3-dimethylaminomethyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic acid diethyl ester,

2-(2-{3-(methoxy-methylcarbamoyl)-4-[(4'-trifluoro-

methyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-
2-phenyl-malonic acid diethyl ester,

2-(2-{3-isobutyryl-4-[(4'-trifluoromethyl-biphenyl-2-
carbonyl)-amino]-phenyl}-acetoxymethyl)-2-phenyl-malonic
5 acid diethyl ester, and

2-(2-{3-(1-hydroxy-2-methyl-propyl)-4-[(4'-
trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-
acetoxymethyl)-2-phenyl-malonic acid diethyl ester;

10 (29) The ester compound or a prodrug thereof, or a
pharmaceutically acceptable salt of either according to the
above (1), which is selected from the group consisting of

4'-trifluoromethyl-biphenyl-2-carboxylic acid 4-[2-
phenyl-2,2-bis-(2,2,2-trifluoro-ethylcarbamoyl)-
15 ethoxycarbonylmethyl]-phenyl ester,

biphenyl-2-carboxylic acid 4-[2-phenyl-2,2-bis-
(2,2,2-trifluoro-ethylcarbamoyl)-ethoxycarbonylmethyl]-
phenyl ester,

4'-trifluoromethyl-biphenyl-2-carboxylic acid 4-(2,2-
20 bis-ethylcarbamoyl-2-phenyl-ethoxycarbonylmethyl)-phenyl
ester,

4'-trifluoromethyl-biphenyl-2-carboxylic acid 4-(2,2-
bis-ethylcarbamoyl-2-phenyl-ethoxycarbonylmethyl)-2-
chloro-phenyl ester,

25 4'-trifluoromethyl-biphenyl-2-carboxylic acid 4-(3,3-
bis-ethylcarbamoyl-3-phenyl-propoxycarbonylmethyl)-2-
chloro-phenyl ester,

4'-trifluoromethyl-biphenyl-2-carboxylic acid 4-(3,3-
bis-ethylcarbamoyl-3-phenyl-propoxycarbonyl)-phenyl ester,

and

4'-trifluoromethyl-biphenyl-2-carboxylic acid 4-(3,3-bis-ethylcarbamoyl-3-phenyl-propoxycarbonyl)-2,6-dichloro-phenyl ester;

5

(30) The ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to the above (1), which is selected from the group consisting of

2-phenyl-2-{2-[4-(4'-trifluoromethyl-biphenyl-2-carbonyloxy)-phenyl]-acetoxymethyl}-malonic acid diethyl ester,

2-{2-[3-dimethylcarbamoyl-4-(4'-trifluoromethyl-biphenyl-2-carbonyloxy)-phenyl]-acetoxymethyl}-2-phenyl-malonic acid diethyl ester,

15 2-{2-[3-methoxy-4-(4'-trifluoromethyl-biphenyl-2-carbonyloxy)-phenyl]-acetoxymethyl}-2-phenyl malonic acid diethyl ester, and

4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-benzoic acid 3-[2-(2,2,2-trifluoro-ethylcarbamoyl)-naphthalen-1-yl]-propyl ester;

20

(31) The ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to the above (1), which is selected from the group consisting of

25 2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-isopropyl-malonic acid diethyl ester,

2-sec-butyl-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-

acetoxymethyl)-2-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-isobutyl-malonic acid diethyl ester,

5 2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-propyl-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-ethyl-malonic acid diethyl ester,

2-butyl-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-allyl-2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-malonic acid diethyl ester,

2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxy)-2,2-bis-ethoxycarbonyl-propionic acid ethyl ester, and

20 2-(2-{3-dimethylcarbamoyl-4-[(4'-trifluoromethyl-biphenyl-2-carbonyl)-amino]-phenyl}-acetoxymethyl)-2-(1-methyl-butyl)-malonic acid diethyl ester;

(32) A pharmaceutical composition, which comprises the ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to any of the above (1) to (31) and a pharmaceutically acceptable carrier;

(33) An MTP (microsomal triglyceride transfer protein)

inhibitor, which comprises the ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to any of the above (1) to (31) as an active ingredient;

5 (34) An agent for the treatment or prophylaxis of hyperlipidemia, which comprises the ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to any of the above (1) to (31) as an active ingredient;

10 (35) An agent for the treatment or prophylaxis of arteriosclerosis, which comprises the ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to any of the above (1) to (31) as an active ingredient;

15

(36) An agent for the treatment or prophylaxis of coronary artery diseases, which comprises the ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to any of the above (1) to (31) as an active ingredient;

20

(37) An agent for the treatment or prophylaxis of obesity, which comprises the ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to any of the above (1) to (31) as an active ingredient;

25

(38) An agent for the treatment or prophylaxis of diabetes, which comprises the ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to any of the above (1) to (31) as an active ingredient;

(39) An agent for the treatment or prophylaxis of hypertension, which comprises the ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to any of
5 the above (1) to (31) as an active ingredient;

(40) An agent for the treatment or prophylaxis of hyperlipidemia, arteriosclerosis, coronary artery diseases, obesity, diabetes or hypertension, which comprises MTP inhibitor selectively
10 inhibiting MTP (microsomal triglyceride transfer protein) in the small intestine and a pharmaceutically acceptable carrier;

(41) The agent for the treatment or prophylaxis according to the above (40), wherein the MTP inhibitor does not substantially
15 inhibit MTP in the liver but substantially inhibits only MTP in the small intestine;

(42) The agent for the treatment or prophylaxis according to the above (41), wherein after the administered MTP inhibitor
20 inhibits MTP in the small intestine, it is metabolized in the small intestine, blood and liver to the amount at which the remaining MTP inhibitor in the liver does not substantially inhibit the MTP in the liver;

(43) The agent for the treatment or prophylaxis according to the above (42), wherein the remaining MTP inhibitor in the liver is metabolized to the state where TG-releasing activity of the liver is kept at the level of about 80% or more of the normal
25 level;

(44) The agent for the treatment or prophylaxis according to the above (40) to (43), wherein the MTP inhibitor is a compound having at least one ester bond;

5

(45) The agent for the treatment or prophylaxis according to the above (44), wherein after the compound having at least one ester bond exerts MTP inhibitory activity, the ester moiety of the compound is metabolized in blood to become an inactive substance;

10

(46) The agent for the treatment or prophylaxis according to the above (40) to (45), wherein the MTP inhibitor is the ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either mentioned in any of the above (1) to (31);

15

(47) A method for the treatment or prophylaxis of hyperlipidemia, arteriosclerosis, coronary artery diseases, obesity, diabetes or hypertension, which comprises administering a compound selectively inhibiting MTP (microsomal triglyceride transfer protein) in the small intestine;

20

(48) The method according to the above (47), wherein after the compound inhibits MTP in the small intestine, it is metabolized in the small intestine, blood and liver to the amount at which remaining said compound in the liver does not substantially inhibit MTP in the liver;

25

(49) The method according to the above (47), wherein the

remaining compound in the liver is metabolized to the state where TG-releasing activity of the liver is kept at the level of about 80% or more of the normal level;

5 (50) The method according to the above (47) to (49), wherein the compound has at least one ester bond;

(51) The method according to the above (50), wherein after the compound having at least ester bond exerts MTP inhibitory
10 activity, the ester moiety of the compound is metabolized in blood to become an inactive substance;

(52) The method according to the above (47) to (52), wherein the compound is the ester compound or a prodrug thereof, or a
15 pharmaceutically acceptable salt of either mentioned in any of the above (1) to (31);

(53) The agent for the treatment or prophylaxis according to the above (40) to (46), wherein the agent is an agent for the
20 treatment or prophylaxis of hyperlipidemia which is used in combination with other antihyperlipidemic drug(s);

(54) The agent for the treatment or prophylaxis according to the above (53), wherein other antihyperlipidemic drug is a
25 statin-type drug;

(55) The agent for the treatment or prophylaxis according to the above (54), wherein the statin-type drug is one or more drug(s) selected from the group consisting of lovastatin,

simvastatin, pravastatin, fluvastatin, atorvastatin and cerivastatin;

(56) The agent for the treatment or prophylaxis according to
5 the above (40) to (46), wherein the agent is an agent for the treatment or prophylaxis of obesity which is used in combination with other anti-obesity drug(s);

(57) The agent for the treatment or prophylaxis according to
10 the above (56), wherein other anti-obesity drug is mazindol or/and orlistat;

(58) The agent for the treatment or prophylaxis according to
15 the above (40) to (46), wherein the agent is an agent for the treatment or prophylaxis of diabetes which is used in combination with other anti-diabetic drug(s);

(59) The agent for the treatment or prophylaxis according to
20 the above (58), wherein other anti-diabetic drug is one or more drug(s) selected from the group consisting of insulin preparations, sulfonylurea drugs, insulin secretagogues, sulfonamide drugs, biguanide drugs, α -glucosidase inhibitors and insulin resistance-improving drugs;

25 (60) The agent for the treatment or prophylaxis according to the above (59), wherein other anti-diabetic drug is one or more drug(s) selected from the group consisting of insulin, glibenclamide, tolbutamide, glyclopyramide, acetohexamide, glimepiride, tolazamide, gliclazide, nateglinide, glybuzole,

metformin hydrochloride, buformin hydrochloride, boglibose, acarbose and pioglitazone hydrochloride;

(61) The agent for the treatment or prophylaxis according to
5 the above (40) to (46), wherein the agent is an agent for the treatment or prophylaxis of hypertension which is used in combination with other anti-hypertension drug(s);

(62) The agent for the treatment or prophylaxis according to
10 the above (61), wherein other anti-hypertension drug is one or more drug(s) selected from the group consisting of loop diuretics, angiotensin converting enzyme inhibitors, angiotensin II receptor antagonists, calcium antagonists, β -blockers, α,β -blockers and α -blockers;

15

(63) The agent for the treatment or prophylaxis according to the above (62), wherein other anti-hypertension drug is one or more drug(s) selected from the group consisting of furosemide delayed release, captopril, captopril delayed release,
20 enalapril maleate, alacepril, delapril hydrochloride, silazapril, lisinopril, benazepril hydrochloride, imidapril hydrochloride, temocapril hydrochloride, quinapril hydrochloride, trandolapril, perindopril erbumine, losartan potassium, candesartan cilexetil, nicardipine hydrochloride,
25 nicardipine hydrochloride delayed release, nilvadipine, nifedipine, nifedipine delayed release, benidipine hydrochloride, diltiazem hydrochloride, diltiazem hydrochloride delayed release, nisoldipine, nitrendipine, manidipine hydrochloride, barnidipine hydrochloride,

efonidipine hydrochloride, amlodipine besylate, felodipine, cilnidipine, aranidipine, propranolol hydrochloride, propranolol hydrochloride delayed release, pindolol, pindolol delayed release, indenolol hydrochloride, carteolol
5 hydrochloride, carteolol hydrochloride delayed release, bunitrolol hydrochloride, bunitrolol hydrochloride delayed release, atenolol, asebutilol hydrochloride, metoprolol tartrate, metoprolol tartrate delayed release, nipradilol, penbutolol sulfate, tilisolol hydrochloride, carvedilol,
10 bisoprolol fumarate, betaxolol hydrochloride, celiprolol hydrochloride, bopindolol malonate, bevantolol hydrochloride, labetalol hydrochloride, arotinolol hydrochloride, amosulalol hydrochloride, prazosin hydrochloride, terazosin hydrochloride, doxazosin mesylate, bunazocin hydrochloride,
15 bunazocin hydrochloride delayed release, urapidil and phentolamine mesylate;

(64) Use of the agent for the treatment or prophylaxis according to the above (34) to (46) and other antihyperlipidemic drug(s)
20 for the treatment or prophylaxis of hyperlipidemia;

(65) The use according to the above (64), wherein other antihyperlipidemic drug is a statin-type drug;

25 (66) The use according to the above (64), wherein the statin-type drug is one or more drug(s) selected from the group consisting of lovastatin, simvastatin, pravastatin, fluvastatin, atorvastatin and cerivastatin;

(67) Use of the agent for the treatment or prophylaxis according to the above (34) to (46) and other anti-obesity drug(s) for the treatment or prophylaxis of obesity;

5 (68) The use according to the above (67), wherein other anti-obesity drug is mazindol or/and orlistat;

(69) Use of the agent for the treatment or prophylaxis according to the above (34) to (46) and other anti-diabetic drug(s) for
10 the treatment or prophylaxis of diabetes;

(70) The use according to the above (69), wherein other anti-diabetic drugs are one or more drug(s) selected from the group consisting of insulin preparations, sulfonylurea drugs,
15 insulin secretagogues, sulfonamide drugs, biguanide drugs, α -glucosidase inhibitors and insulin resistance improving drugs;

(71) The use according to the above (70), wherein other
20 anti-diabetic drug is one or more drug(s) selected from the group consisting of insulin, glibenclamide, tolbutamide, glyclopyramide, acetohexamide, glimepiride, tolazamide, gliclazide, nateglinide, glybuzole, metformin hydrochloride, buformin hydrochloride, boglibose, acarbose and pioglitazone
25 hydrochloride;

(72) Use of the agent for the treatment or prophylaxis according to the above (34) to (46) and other anti-hypertension drug(s) for the treatment or prophylaxis of hypertension;

(73) The use according to the above (72), wherein other anti-hypertension drug is one or more drug(s) selected from the group consisting of loop diuretics, angiotension converting
5 enzyme inhibitors, angiotension II receptor antagonists, calcium antagonists, beta-blockers, alpha/beta blockers and alpha blockers;

(74) The use according to the above (73), wherein other
10 anti-hypertension drug is one or more drug(s) selected from the group consisting of furosemide delayed release, captopril, captopril delayed release, enalapril maleate, alacepril, delapril hydrochloride, silazapril, lisinopril, benazepril hydrochloride, imidapril hydrochloride, temocapril
15 hydrochloride, quinapril hydrochloride, trandolapril, perindopril erbumine, losartan potassium, candesartan cilexetil, nicardipine hydrochloride, nicardipine hydrochloride delayed release, nilvadipine, nifedipine, nifedipine delayed release, benidipine hydrochloride,
20 diltiazem hydrochloride, diltiazem hydrochloride delayed release, nisoldipine, nitrendipine, manidipine hydrochloride, barnidipine hydrochloride, efonidipine hydrochloride, amlodipine besylate, felodipine, cilnidipine, aranidipine, propranolol hydrochloride, propranolol hydrochloride delayed
25 release, pindolol, pindolol delayed release, indenolol hydrochloride, carteolol hydrochloride, carteolol hydrochloride delayed release, bunitrolol hydrochloride, bunitrolol hydrochloride delayed release, atenolol, asebutilol hydrochloride, metoprolol tartrate, metoprolol

tartrate delayed release, nipradilol, penbutolol sulfate, tilisolol hydrochloride, carvedilol, bisoprolol fumarate, betaxolol hydrochloride, celiprolol hydrochloride, bopindolol malonate, bevantolol hydrochloride, labetalol hydrochloride, arotinolol hydrochloride, amosulalol hydrochloride, prazosin hydrochloride, terazosin hydrochloride, doxazosin mesylate, bunazocin hydrochloride, bunazocin hydrochloride delayed release, urapidil and phentolamine mesylate;

10 (75) A pharmaceutical composition comprising an effective amount of the ester compound or a prodrug thereof, or a pharmaceutically acceptable salt of either according to any of the above (1) to (31), a pharmaceutically acceptable, appropriate amount of ethanol and propylene glycol fatty acid ester;

(76) The pharmaceutical composition according to the above (75), which comprises 25 to 35% by weight of ethanol and 65 to 75% by weight of propylene glycol fatty acid ester;

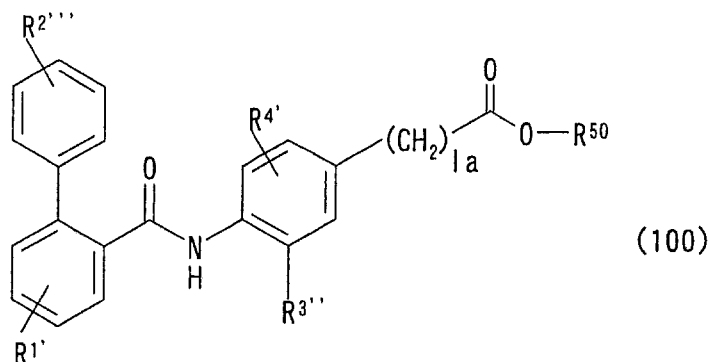
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(77) A capsule formulation comprising the pharmaceutical composition according to the above (75) or (76);

(78) The capsule formulation according to the above (77), wherein the capsule formulation is a hard capsule or soft capsule;

25

(79) A biphenyl compound represented by the formula (100)

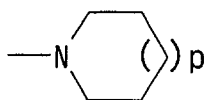


wherein

$R^{1'}$ is hydrogen, C_1 - C_6 alkyl, halogen, halo C_1 - C_6 alkyl or C_1 - C_6 alkoxy;

5 $R^{2'''}$ is hydrogen, C_1 - C_6 alkyl, halogen, halo C_1 - C_6 alkyl or C_2 - C_6 alkenyl;

$R^{3''}$ is $-\text{CON}(R^{11a})(R^{12a})$ wherein R^{11a} and R^{12a} are each independently hydrogen, C_1 - C_6 alkyl, optionally substituted C_6 - C_{14} aryl, optionally substituted C_7 - C_{16} aralkyl, C_1 - C_6 alkoxy, 10 or R^{11a} and R^{12a} may be taken together with the nitrogen to which they are attached to form



(in which p is an integer of 0 to 2);

$R^{4'}$ is hydrogen, halogen, C_1 - C_6 alkyl or halo C_1 - C_6 alkyl;

15 R^{50} is hydrogen, C_1 - C_6 alkyl, optionally substituted C_6 - C_{14} aryl or optionally substituted C_7 - C_{16} aralkyl; and

$1a$ is an integer of 1 to 3,

or a prodrug thereof, or a pharmaceutically acceptable salt of either; and

20

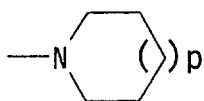
(80) The biphenyl compound according to the above (79),

wherein

$R^{1'}$ is hydrogen,

$R^{2''}$ is halo C_1 - C_6 alkyl,

$R^{3''}$ is $-\text{CON}(R^{11b})(R^{12b})$ wherein R^{11b} and R^{12b} are each
 5 independently hydrogen or C_1 - C_6 alkyl, or R^{11b} and R^{12b} may be taken
 together with the nitrogen to which they are attached to form



(in which p is an integer of 0 to 2),

$R^{4'}$ is hydrogen, and

10 R^{50} is hydrogen or C_1 - C_6 alkyl,

or a prodrug thereof, or a pharmaceutically acceptable salt of
 either.

The definitions of each substituent used in the present
 15 invention are as follows.

" C_1 - C_6 alkyl" refers to a straight- or branched-chain
 alkyl group having 1 to 6 carbon atom(s), and its example
 includes methyl, ethyl, propyl, isopropyl, butyl, isobutyl,
 sec-butyl, tert-butyl, pentyl, isopentyl, neopentyl,
 20 tert-pentyl or hexyl, etc., preferably a straight- or
 branched-chain alkyl group having 1 to 4 carbon atom(s), more
 preferably methyl, ethyl or isopropyl. Preferable examples
 for R^1 , R^2 , $R^{2'}$ and $R^{2''}$ include methyl, ethyl or isopropyl;
 preferable examples for R^3 and R^4 include methyl, ethyl, propyl,
 25 isopropyl, butyl or isobutyl; a preferable example for R^5 , R^6
 and R^7 includes methyl; preferable examples for R^8 and R^9 include
 methyl or ethyl; preferable examples for R^{10} include methyl,

ethyl or isopropyl; preferable examples for R^{11} and R^{12} include methyl, ethyl, propyl or isopropyl; preferable examples for R^{13} and R^{14} include methyl or ethyl; a preferable example for R^{15} includes isopropyl; preferable examples for R^{16} and R^{17} include
 5 methyl or ethyl; preferable examples for R^{18} and R^{19} include methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, tert-butyl, pentyl or isopentyl, more preferably ethyl; preferable examples for R^{20} include methyl, ethyl, propyl, isopropyl or isobutyl, more preferably ethyl; a preferable
 10 example for R^{21} and R^{22} includes methyl; and preferable examples for D include ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, sec-pentyl, etc.

Examples of the substituent for "optionally substituted C_1 - C_6 alkyl" include halogen, carboxyl, hydroxy, amino, nitro,
 15 cyano, C_1 - C_6 alkoxy, C_7 - C_{16} aralkyloxy, C_2 - C_7 alkoxycarbonyl, C_6 - C_{14} aryl, C_1 - C_6 alkylthio, C_1 - C_6 alkylsulfinyl, C_1 - C_6 alkylsulfonyl, C_1 - C_6 alkylamino, acylamino and the like, among which hydroxy is preferable. The number of the substituents is 1 to 5, preferably 1 to 3.

20 " C_3 - C_7 cycloalkyl" refers to a cycloalkyl having 3 to 7 carbon atoms, specifically cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, 1-methylcyclohexyl or cycloheptyl. Preferable examples thereof include a cycloalkyl having 3 to 6 carbon atoms, specifically cyclopropyl, cyclobutyl,
 25 cyclopentyl or cyclohexyl. More preferable examples thereof include cyclopropyl or cyclohexyl. A preferable example for R^1 and R^2 includes cyclohexyl; a preferable example for R^{10} includes cyclohexyl; a preferable example for R^{18} and R^{19} includes cyclohexyl; a preferable example for R^{20} includes

cyclohexyl; and preferable examples for ring C include cyclopentyl or cyclohexyl. It is also preferable that R⁸ and R⁹ are taken together to form cyclopentyl or cyclohexyl.

"C₁-C₆ alkoxy" refers to a straight- or branched-chain
 5 alkoxy group having 1 to 6 carbon atom(s), and its example includes methoxy, ethoxy, propoxy, isopropoxy, butoxy, tert-butoxy, pentyloxy, tert-pentyloxy or hexyloxy, etc., preferably an alkoxy having 1 to 4 carbon atom(s), such as methoxy, ethoxy, isopropoxy, butoxy or tert-butoxy, and more
 10 preferably methoxy or ethoxy. Preferable examples for R¹, R², R^{2'} and R^{2''} include methoxy, isopropoxy or butoxy; preferable examples for R³ and R⁴ include methoxy, ethoxy, propoxy or isopropoxy; preferable examples for R⁵, R⁶ and R⁷ include methoxy or ethoxy; a preferable example for R¹¹ and R¹² includes methoxy;
 15 and preferable examples for R¹⁵ include methoxy, ethoxy, propoxy or isopropoxy.

"Halogen" refers to chlorine, bromine, fluorine or the like. Preferable examples for R¹ include fluorine or chlorine; preferable examples for R^{2'} and R^{2''} include fluorine, chlorine
 20 or bromine; preferable examples for R³ and R⁴ include chlorine or bromine; and preferable examples for R⁵, R⁶ and R⁷ include fluorine or chlorine.

"Halo C₁-C₆ alkyl" refers to said C₁-C₆ alkyl substituted with said halogen, and its example includes chloromethyl,
 25 bromomethyl, fluoromethyl, trifluoromethyl, trichloromethyl, tribromomethyl, trichloroethyl, pentafluoropropyl or chlorobutyl, etc., preferably chloromethyl, bromomethyl, fluoromethyl, trifluoromethyl, trifluoroethyl or trichloromethyl, and more preferably trifluoromethyl. A

preferable example for R^1 , R^2 , $R^{2'}$ and $R^{2''}$ includes trifluoromethyl; a preferable example for R^3 and R^4 includes trifluoromethyl; a preferable example for R^5 , R^6 and R^7 includes trifluoromethyl; preferable examples for R^{16} and R^{17} include
 5 trifluoromethyl or trifluoroethyl; and preferable examples for R^{18} and R^{19} include trifluoromethyl or trifluoroethyl.

"Halo C_1 - C_6 alkyloxy" refers to, for example, chloromethyloxy, bromomethyloxy, fluoromethyloxy, trifluoromethyloxy, trichloromethyloxy, tribromomethyloxy,
 10 trichloroethyloxy, pentafluoropropyloxy or chlorobutyloxy, etc., preferably chloromethyloxy, bromomethyloxy, fluoromethyloxy, trifluoromethyloxy or trichloromethyloxy, and more preferably trifluoromethyloxy. A preferable example for R^1 , R^2 , $R^{2'}$ and $R^{2''}$ includes trifluoromethyloxy.

15 " C_2 - C_{12} alkoxyalkyl" refers to an alkoxyalkyl of which alkoxy moiety has the same meaning as said alkoxy and alkyl moiety has the same meaning as said alkyl, and its example includes methoxymethyl, ethoxymethyl, propoxymethyl, butoxymethyl, pentyloxymethyl, hexyloxymethyl, ethoxyethyl or
 20 methoxyethyl, etc. A preferable example for R^{18} and R^{19} includes methoxyethyl.

" C_2 - C_7 alkylcarbonyl" refers to acetyl, propionyl, butyryl or pivaloyl, etc., and a preferable example for R^{21} and R^{22} includes acetyl.

25 " C_1 - C_7 alkylsulfonyl" refers to methanesulfonyl, ethanesulfonyl, propylsulfonyl, butylsulfonyl, pentylsulfonyl or hexylsulfonyl, etc., and a preferable example for R^{21} and R^{22} includes methylsulfonyl.

" C_2 - C_7 alkoxycarbonyl" refers to an alkoxycarbonyl of

which alkyl moiety has 1 to 6 carbon atom(s) such as methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, isopropoxycarbonyl, butoxycarbonyl, isobutoxycarbonyl, tert-butoxycarbonyl, pentyloxycarbonyl, tert-pentyloxycarbonyl or hexyloxycarbonyl, etc. Preferable examples thereof include methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl or butoxycarbonyl. A preferable example for R^2 includes butoxycarbonyl; a preferable example for R^5 , R^6 and R^7 includes methoxycarbonyl; a preferable example for R^{13} and R^{14} includes methoxycarbonyl; and a preferable example for D includes ethoxycarbonyl.

" C_1 - C_6 acyl" refers to formyl having one carbon atom, or an alkanoyl having 2 to 6 carbon atoms such as acetyl, propionyl, butyryl or pivaloyl, etc., and its preferable examples include formyl, acetyl or pivaloyl. A preferable example for R^2 and $R^{2'}$ includes acetyl; a preferable example for R^3 includes formyl; a preferable example for R^5 , R^6 and R^7 includes acetyl; a preferable example for R^{13} and R^{14} includes acetyl; and a preferable example for R^{21} and R^{22} includes acetyl.

"Alkanediyl" has preferably 1 to 6 carbon atom(s), and its example includes methylene, ethane-1,2-diyl, ethane-1,1-diyl, propane-1,3-diyl, butane-1,4-diyl, pentane-1,5-diyl, hexane-1,6-diyl, 1,1-dimethylethane-1,2-diyl, 1,1-diethylethane-1,2-diyl, 2,2-dimethylethane-1,2-diyl, 2,2-diethylethane-1,2-diyl, 1,1-dimethylpropane-1,3-diyl, 1,1-diethylpropane-1,3-diyl, 2,2-dimethylpropane-1,3-diyl, 2,2-diethylpropane-1,3-diyl, 3,3-dimethylpropane-1,3-diyl or 3,3-diethylpropane-1,3-diyl, etc. Preferable examples for Alk^1 and Alk^2 include methylene,

ethane-1,2-diyl, ethane-1,1-diyl, propane-1,3-diyl, etc.

"Alkenediyl" has preferably 2 to 6 carbon atom(s), and its example includes ethylene-1,2-diyl, 1-propene-1,3-diyl, 2-propene-1,3-diyl, 1-butene-1,4-diyl, 2-butene-1,4-diyl, 5 3-butene-1,4-diyl or 1,3-butadiene-1,4-diyl, etc. Preferable examples for Alk¹ and Alk² include ethylene-1,2-diyl, 1-propene-1,3-diyl, 2-propene-1,3-diyl, etc.

"C₆-C₁₄ aryl" refers to phenyl, naphthyl or biphenyl, etc., preferably phenyl.

10 In the "optionally substituted C₆-C₁₄ aryl", the substituent(s) is/are not particularly limited, and may be the same or different each other and is/are arbitrarily positioned. The number of substituents is not particularly limited so long as they are chemically acceptable, while the number is 15 preferably around 1 to 3. Specifically, examples of the substituent include C₁-C₆ alkyl (e.g. methyl, ethyl, propyl, isopropyl, butyl, tert-butyl, etc.), hydroxy, C₁-C₆ alkoxy (e.g. methoxy, ethoxy, propoxy, butoxy, etc.), halogen (e.g. fluorine, chlorine, bromine, etc.), nitro, cyano, C₁-C₆ acyl (e.g. formyl, 20 acetyl, propionyl, etc.), C₁-C₆ acyloxy (e.g. formyloxy, acetoxo, propionyloxy, etc.), mercapto, C₁-C₆ alkylthio (e.g. methylthio, ethylthio, propylthio, butylthio, isobutylthio, etc.), amino, C₁-C₆ alkylamino (e.g. methylamino, ethylamino, propylamino, butylamino, etc.), di(C₁-C₆ alkyl)amino (e.g. 25 dimethylamino, diethylamino, dipropylamino, dibutylamino, etc.), carboxyl, C₂-C₇ alkoxycarbonyl (e.g. methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, etc.), amido, trifluoromethyl, C₁-C₆ alkylsulfonyl (e.g. methylsulfonyl, ethylsulfonyl, etc.), aminosulfonyl, C₃-C₇ cycloalkyl (e.g.

cyclopentyl, cyclohexyl, etc.), phenyl, acylamido (e.g. acetamido, propionylamido, etc.) and the like, among which hydroxy, C₁-C₆ alkyl, C₁-C₆ alkoxy, mercapto, C₁-C₆ alkylthio, halogen, trifluoromethyl, C₁-C₆ acyl, C₂-C₇ alkoxycarbonyl and
 5 acylamido are preferable.

A preferable example for R¹ and R² includes phenyl which may be substituted with halo C₁-C₆ alkyl (e.g. trifluoromethyl, etc.), C₁-C₆ alkyl (e.g. methyl, ethyl, etc.), halogen (e.g. fluorine, chlorine, bromine, etc.), C₁-C₆ alkoxy (e.g. methoxy, etc.), C₁-C₆ acyl (e.g. acetyl, etc.), C₂-C₆ alkenyl
 10 (e.g. isopropenyl, etc.) or cyano; a preferable example for R⁵, R⁶ and R⁷ includes phenyl which may be substituted with halo C₁-C₆ alkyl (e.g. trifluoromethyl, etc.), C₁-C₆ alkyl (e.g. methyl, etc.), halogen (e.g. chlorine, etc.) or C₁-C₆ alkoxy (e.g. methoxy, etc.); a preferable example for R⁸ and R⁹ includes
 15 phenyl; a preferable example for R¹¹ and R¹² includes phenyl; a preferable example for R¹⁸ and R¹⁹ includes phenyl; a preferable example for R⁴³ includes biphenyl; a preferable example for ring A includes phenyl; and preferable examples for ring C include
 20 phenyl or naphthyl.

"C₇-C₁₆ aralkyl" refers to an arylalkyl, of which aryl moiety is phenyl (which may be substituted with 1 to 3 substituent(s) mentioned in the above description of aryl) and alkyl moiety is alkyl having 1 to 6 carbon atom(s). Examples
 25 thereof include benzyl, phenethyl, phenylpropyl, phenylbutyl or phenylhexyl, etc., among which benzyl or phenylethyl is preferable. A preferable example for R¹ and R² includes benzyl; a preferable example for R¹¹ and R¹² includes benzyl; and a preferable example for ring C includes benzyl.

"C₆-C₁₄ aryloxy" refers to phenoxy, naphthyloxy, etc. (where the phenyl group or naphthyl group may be substituted with 1 to 3 substituent(s) mentioned in the above description of aryl), preferably phenoxy. A preferable example for R¹ and
 5 R² includes phenoxy, and a preferable example for R¹⁵ includes phenoxy.

"C₇-C₁₆ aralkyloxy" refers to an arylalkoxy of which alkoxy moiety has 1 to 4 carbon atom(s) (where the aryl group may be substituted with 1 to 3 substituent(s) mentioned in the above
 10 description of aryl), and example thereof includes benzyloxy, phenethyloxy, phenylpropyloxy, phenylbutyloxy, etc., preferably benzyloxy. A preferable example for R¹ and R² includes benzyloxy; a preferable example for R³ includes benzyloxy; and a preferable example for R¹⁵ includes benzyloxy.

15 "C₇-C₁₅ arylcarbonyl" refers to benzoyl, naphthoyl, etc. (where the phenyl group or naphthyl group may be substituted with 1 to 3 substituent(s) mentioned in the above description of aryl), preferably benzoyl. A preferable example for R¹ and R² includes benzoyl.

20 "C₇-C₁₅ arylcarbonylamino" refers to phenylcarbonylamino, naphthylcarbonylamino, etc. (where the phenyl group or naphthyl group may be substituted with 1 to 3 substituent(s) mentioned in the above description of aryl), preferably benzoyl. A preferable example for ring C includes phenylcarbonylamino.

25 "C₈-C₁₆ aralkylcarbonylamino" refers to benzylcarbonylamino, naphthylcarbonylamino, etc. (where the phenyl group or naphthyl group may be substituted with 1 to 3 substituent(s) mentioned in the above description of aryl), preferably benzylcarbonylamino. A preferable example for ring

C includes benzylcarbonylamino.

"heterocycle" refers to a 5- to 6-membered heteroaromatic ring, a 5- to 6-membered saturated heterocycle or a 5- to 6-membered unsaturated heterocycle, any of which contains 1 to 3 heteroatom(s) selected from nitrogen, oxygen and sulfur as an atom constituting the ring other than carbon atom, or a fused heterocyclic ring in which said heterocycle and benzene ring are fused. Specifically, its example includes thiophen-2-yl, thiophen-3-yl, furan-2-yl, furan-3-yl, pyrrol-1-yl, pyrrol-2-yl, pyrrol-3-yl, imidazol-1-yl, imidazol-2-yl, imidazol-4-yl, imidazol-5-yl, pyrazol-1-yl, pyrazol-3-yl, pyrazol-4-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, oxazol-2-yl, oxazol-4-yl, oxazol-5-yl, isoxazol-3-yl, isoxazol-4-yl, isoxazol-5-yl, pyrimidin-2-yl, pyrimidin-4-yl, pyrimidin-5-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyrrolidin-2-yl, pyrrolidin-3-yl, benzothiophen-2-yl, benzothiophen-3-yl, benzofuran-2-yl, benzofuran-3-yl, indol-2-yl, indol-3-yl, benzimidazol-1-yl, benzimidazol-2-yl, benzothiazol-2-yl, benzoxazol-2-yl, quinolin-2-yl, quinolin-3-yl, quinolin-4-yl, isoquinolin-1-yl, isoquinolin-3-yl, isoquinolin-4-yl, 1,3,4-thiadiazol-2-yl, morpholin-4-yl, etc.

A preferable example for R^1 and R^2 includes thiophen-3-yl; preferable examples for ring A include imidazol-5-yl, thiazol-5-yl, pyridin-3-yl or pyrrolidin-2-yl; a preferable example for R^3 includes thiazol-2-yl; and preferable examples for ring C include pyridin-2-yl, pyridin-3-yl, thiophen-2-yl, thiophen-3-yl or thiazol-2-yl.

With regard to a substituent in "optionally substituted

heterocycle", the same substituents as those mentioned in the above description of aryl may be exemplified. The number of substituents is not particularly limited so long as they are chemically acceptable, while the number is preferably around
 5 1 to 3.

"C₂-C₆ alkenyl" refers to a straight- or branched-chain alkenyl group having 2 to 6 carbon atoms, and its example includes vinyl, n-propenyl, isopropenyl, n-butenyl, isobutenyl, sec-butenyl, tert-butenyl, n-pentenyl,
 10 isopentenyl, neopentenyl, 1-methylpropenyl, n-hexenyl, isohexenyl, 1,1-dimethylbutenyl, 2,2-dimethylbutenyl, 3,3-dimethylbutenyl, 3,3-dimethylpropenyl, 2-ethylbutenyl, etc. A preferable example for R² and R^{2'} includes n-propenyl, and a preferable example for D includes n-propenyl.

15 "Prodrug" of the compound refers to a derivative of the compound of the present invention, which has a group capable of being chemically or metabolically converted and shows pharmaceutical activity after it is hydrolyzed or solvolyzed or converted under physiological conditions.

20 For example, there may be listed a derivative in which a substituent such as -CO-C₁-C₆ alkyl, -CO₂-C₁-C₆ alkyl, -CONH-C₁-C₆ alkyl, -CO-C₂-C₆ alkenyl, -CO₂-C₂-C₆ alkenyl, -CONH-C₂-C₆ alkenyl, -CO-C₆-C₁₄ aryl, -CO₂-C₆-C₁₄ aryl, -CONH-C₆-C₁₄ aryl, -CO-heterocycle, -CO₂-heterocycle,
 25 -CONH-heterocycle, etc. (wherein any of said C₁-C₆ alkyl, C₂-C₆ alkenyl, C₆-C₁₄ aryl and heterocycle may be substituted with halogen, C₁-C₆ alkyl, hydroxy, C₁-C₆ alkoxy, carboxyl, amino, amino acid residue, -PO₃H₂, -SO₃H, -CO-polyethyleneglycol residue,
 -CO₂-polyethyleneglycol residue,

-CO-polyethyleneglycol monoalkyl ether residue or -CO₂-polyethyleneglycol monoalkyl ether residue) is attached to the hydroxy group of the compound.

Also, there may be exemplified a derivative in which a
 5 substituent such as -CO-C₁-C₆ alkyl, -CO₂-C₁-C₆ alkyl, -CO-C₂-C₆ alkenyl, -CO₂-C₂-C₆ alkenyl, -CO₂-C₆-C₁₄ aryl, -CO-C₆-C₁₄ aryl, -CO-heterocycle, -CO₂-heterocycle, etc. (wherein any of said C₁-C₆ alkyl, C₂-C₆ alkenyl, C₆-C₁₄ aryl and heterocycle may be substituted with halogen, C₁-C₆ alkyl, hydroxy, C₁-C₆ alkoxy,
 10 carboxyl, amino, amino acid residue, -PO₃H₂, -SO₃H, -CO-polyethyleneglycol residue, -CO₂-polyethyleneglycol residue, -CO-polyethyleneglycol monoalkyl ether residue, -CO₂-polyethyleneglycol monoalkyl ether residue or -PO₃H₂, etc.) is attached to the amino group of the compound.

15 Furthermore, there may be exemplified a derivative in which a substituent such as C₁-C₆ alkoxy, C₆-C₁₄ aryloxy, etc. (wherein said C₁-C₆ alkoxy or C₆-C₁₄ aryloxy may be substituted with halogen, C₁-C₆ alkyl, hydroxy, C₁-C₆ alkoxy, carboxyl, amino, amino acid residue, -PO₃H₂, -SO₃H, polyethyleneglycol residue
 20 or polyethyleneglycol monoalkyl ether residue, etc.) is attached to the carboxyl group of the compound.

"Pharmaceutically acceptable salt" includes various inorganic acid addition salts such as hydrochloride, hydrobromide, sulphate, phosphate or nitrate, etc.; various
 25 organic acid addition salts such as acetate, propionate, succinate, glycolate, lactate, malate, oxalate, tartrate, citrate, maleate, fumarate, methanesulfonate, benzensulfonate, p-toluenesulfonate or ascorbate, etc.; or various salts with an amino acid such as aspartate or glutamate, etc., although

it is not limited thereto. It may be hydrated compound, hydrate or solvate depending on the circumstances.

"MTP in the small intestine" refers to the MTP existing in small intestinal epithelial cells.

5 "MTP in the liver" refers to the MTP existing in hepatic cells.

The expression "selectively inhibit MTP in the small intestine" means the level of inhibition is at least about 5 times higher, preferably about 10 times higher, than MTP
10 inhibition in other parts of body such as liver and heart, especially liver. To be more specific, on the basis of S9 metabolic stability test, it means that in the test using human or hamster S9 the remaining rate of unaltered form 10 minutes after the treatment with small intestine S9 is about 10 times
15 or more higher than that in the case of the treatment with liver S9 (see Test Example 7).

The expression "it is metabolized to the amount at which the remaining MTP inhibitor in the liver does not substantially inhibit the MTP in the liver" means that almost all of the orally
20 administered MTP inhibitors are metabolized to an inactive metabolite before arriving at the liver or at the moment of arriving at the liver and show substantially no MTP inhibitory activity in the liver, i.e. the MTP inhibitors are converted to those that do not substantially inhibit TG release from the
25 liver. More specifically, it means the condition where TG-releasing activity of the liver is kept at the level of about 80% or more, preferably about 90% or more, more preferably 100% of the normal level. In terms of metabolism, it means that the ratio of inactive metabolite to unaltered form in portal vein

blood is approximately 8 or more to 1 one hour after the oral administration to hamsters, i.e. about 80% or more of the agent (compound) is metabolized before arriving at the liver (see Test Example 6), or on the basis of liver S9 metabolic stability test, it means that 10 minutes after the test using human or hamster S9 the remaining rate of unaltered form is about 20% or less, preferably about 10% or less, more preferably about 8% or less (see Test Example 7).

The expression "MTP inhibitor does not substantially inhibit MTP in the liver" has essentially the same meaning with the above "it is metabolized to the amount at which the remaining MTP inhibitor in the liver does not substantially inhibit the MTP in the liver", and means the condition where TG-releasing activity of the liver is kept at the level of about 80% or more, preferably about 90% or more, more preferably 100% of the normal level.

As "pharmaceutically acceptable carrier", various organic or inorganic carrier materials which are conventionally used as formulation material are used, and it is formulated as excipient, lubricant, binder, disintegrating agent, solvent, solubilizer, suspending agent, isotonizing agent, buffer, soothing agent, etc. If desired, pharmaceutical additives such as preservative, antioxidant, coloring agent, sweetening agent, etc. may be also used. Preferable examples of said excipient include lactose, sucrose, D-mannitol, starch, crystalline cellulose, light anhydrous silicic acid, etc. Preferable examples of said lubricant include magnesium stearate, calcium stearate, talc, colloidal silica, etc. Preferable examples of said binder include crystalline

cellulose, sucrose, D-mannitol, dextrin, hydroxypropyl cellulose, hydroxypropyl methylcellulose, polyvinylpyrrolidone, etc. Preferable examples of said disintegrating agent include starch, carboxymethylcellulose, 5 carboxymethylcellulose calcium, crosscarmellose sodium, sodium carboxymethylstarch, etc. Preferable examples of said solvent include water for injection, alcohol, propylene glycol, macrogol, sesame-seed oil, corn oil, propylene glycol fatty acid ester, etc. Preferable examples of said solubilizer 10 include polyethyleneglycol, propyleneglycol, D-mannitol, benzyl benzoate, ethanol, trisaminomethane, cholesterol, triethanolamine, sodium carbonate, sodium citrate, etc. Preferable examples of said suspending agent include surfactants (e.g. stearyl triethanolamine, sodium lauryl 15 sulfate, lauryl aminopropionic acid, lecithin, benzalkonium chloride, benzethonium chloride, glycerin monostearate, etc), polyvinyl alcohol, polyvinylpyrrolidone, carboxymethylcellulose sodium, methylcellulose, hydroxymethyl cellulose, etc. Preferable examples of said 20 isotonizing agent include sodium chloride, glycerin, D-mannitol, etc. Preferable examples of said buffer include phosphate, acetate, carbonate, citrate, etc. Preferable examples of said soothing agent include benzyl alcohol, etc. Preferable examples of said preservative include 25 paraoxybenzoic acid esters, chlorobutanol, benzyl alcohol, phenethyl alcohol, dehydroacetic acid, sorbic acid, etc. Preferable examples of said antioxidant include sulfites, ascorbic acid, etc. Preferable examples of said sweetening agent include aspartame, saccharin sodium, stevia, etc.

Preferable examples of said coloring agent include food colors such as food yellow No. 5, food red No. 2 and food blue No. 2, lake colors for food, iron oxide, etc.

5 Best mode for carrying out the invention

Detailed description is given below with respect to various substituents.

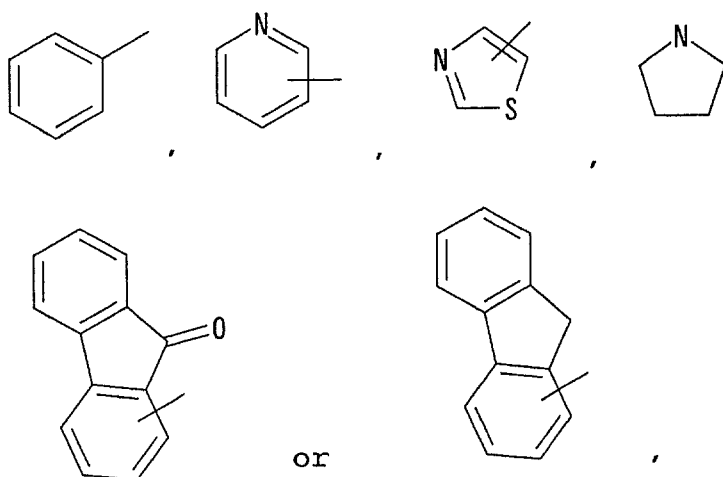
R^1 is preferably hydrogen; C_1-C_6 alkyl such as methyl, ethyl, etc.; C_1-C_6 alkoxy such as methoxy, isopropoxy, etc.;
 10 halogen such as fluorine, chlorine, etc.; halo C_1-C_6 alkyl such as trifluoromethyl, etc.; or C_2-C_6 alkenyl such as isopropenyl, etc.

R^2 is preferably phenyl (which may be substituted with halo C_1-C_6 alkyl such as trifluoromethyl, etc.; C_1-C_6 alkyl
 15 such as methyl, ethyl, etc.; halogen such as fluoro, chlorine, bromine, etc.; C_1-C_6 alkoxy such as methoxy, etc.; C_1-C_6 acyl such as acetyl, etc.; C_2-C_6 alkenyl such as isopropenyl, etc.; or cyano); C_1-C_6 alkyl such as ethyl, isopropyl, etc.; C_3-C_7 cycloalkyl such as cyclohexyl, etc.; C_1-C_6 alkoxy such as butoxy,
 20 etc.; halo C_1-C_6 alkyl such as trifluoromethyl, etc.; halo C_1-C_6 alkyloxy such as trifluoromethoxy, etc.; C_7-C_{16} aralkyl such as benzyl, etc.; C_6-C_{14} aryloxy such as phenoxy (of which aryl moiety may be substituted with halo C_1-C_6 alkyl such as trifluoromethyl, etc.), etc.; C_7-C_{15} arylcarbonyl such as
 25 benzoyl (of which aryl moiety may be substituted with halogen such as chlorine, etc.), etc.; heterocycle such as thiophen-3-yl, etc.; C_2-C_7 alkoxy carbonyl such as butoxy carbonyl, etc.; $-N(R^{40})(R^{41})$ (wherein R^{40} and R^{41} are each independently hydrogen or optionally substituted phenyl).

$R^{2'}$ is preferably hydrogen or halogen such as chlorine, etc.

$R^{2''}$ is preferably hydrogen, halo C_1 - C_6 alkyl such as trifluoromethyl, etc.; C_1 - C_6 alkyl such as methyl, ethyl, etc.;
 5 halogen such as fluorine, chlorine, bromine, etc.; C_1 - C_6 alkoxy such as methoxy, etc.; C_1 - C_6 acyl such as methylcarbonyl, etc.; C_2 - C_6 alkenyl such as isopropenyl, etc.; or cyano.

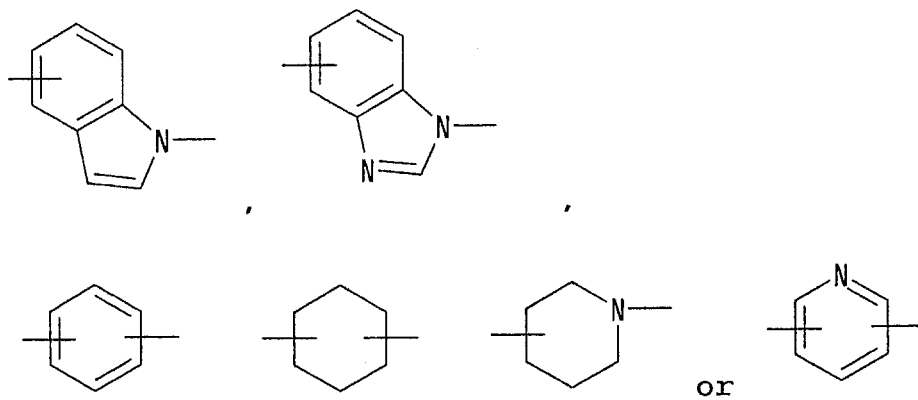
Ring A is preferably



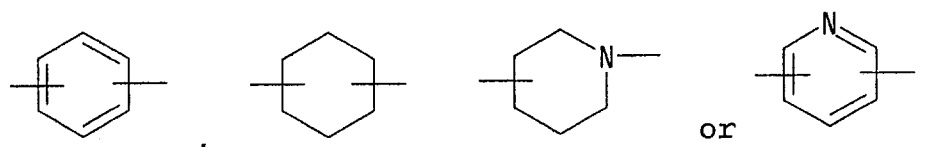
10 among which phenyl is especially preferred.

X is preferably $-\text{COO}-$, $-\text{N}(\text{R}^{10})\text{CO}-$ or $-\text{CON}(\text{R}^{10})-$ (wherein R^{10} is hydrogen; C_1 - C_6 alkyl such as methyl, isopropyl, etc.; or C_3 - C_7 cycloalkyl such as cyclohexyl, etc.), among which $-\text{COO}-$ or $-\text{CONH}-$ is especially preferred.

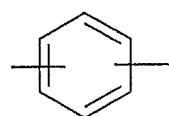
15 Ring B is preferably



or more preferably



or most preferably

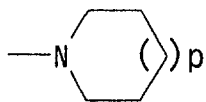


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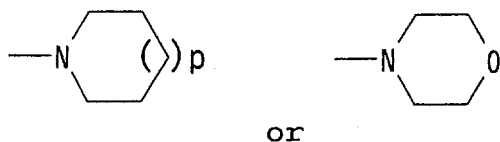
R^3 is preferably hydrogen; hydroxy; halogen such as chlorine, bromine, etc.; C_1 - C_6 alkyl such as methyl, ethyl, isopropyl, isobutyl, etc.; substituted C_1 - C_6 alkyl such as isobutyl substituted with hydroxy, etc.; C_1 - C_6 alkoxy such as methoxy, ethoxy, propoxy, isopropoxy, etc.; halo C_1 - C_6 alkyl such as trifluoromethyl, etc.; C_7 - C_{16} aralkyloxy such as benzyloxy, etc.; C_1 - C_6 acyl such as formyl, etc.; optionally substituted heterocycle such as 4-methyl-thiazol-2-yl, etc.; -CON(R^{11})(R^{12}) (wherein R^{11} and R^{12} are each independently

10 such as hydrogen; C_1 - C_6 alkyl such as methyl, ethyl, propyl, isopropyl, etc.; C_6 - C_{14} aryl such as phenyl, etc.; C_7 - C_{16} aralkyl such as benzyl, etc.; C_1 - C_6 alkoxy such as methoxy, etc.; or R^{11} and R^{12} may be taken together with the nitrogen to form

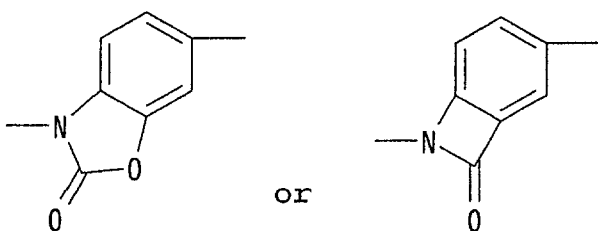
15



(wherein p is an integer of 0 or 1)); $-N(R^{13})(R^{14})$ or $-CH_2-N(R^{13})(R^{14})$ (wherein R^{13} and R^{14} are each independently hydrogen; C_1 - C_6 alkyl such as methyl, ethyl, etc.; C_2 - C_7 alkoxy carbonyl such as methoxycarbonyl, etc.; C_1 - C_6 acyl such as acetyl, etc.; or R^{13} and R^{14} may be taken together with the nitrogen to which they are attached to form



(wherein p has the same meaning as defined above)); or $-CO(R^{15})$ (wherein R^{15} is C_1 - C_6 alkyl such as isopropyl, etc.; C_1 - C_6 alkoxy such as methoxy, ethoxy, propoxy, isopropoxy, etc.; C_7 - C_{16} aralkyloxy such as benzyloxy, etc.; or hydroxy). Alternatively, R^3 and R^{10} may be taken together with the nitrogen to which R^{10} is attached and ring B to form



R^4 is preferably hydrogen or halogen such as fluorine, chlorine, bromine, etc.

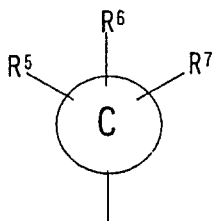
$Alk1^1$ is preferably methylene or ethane-1,1-diyl.

l is preferably 0, 1 or 2.

$Alk1^2$ is preferably methylene.

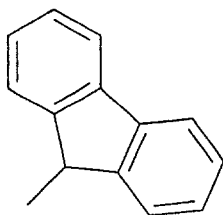
m is preferably 0 or an integer of 1 to 3.

D is preferably C₁-C₆ alkyl such as ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, sec-pentyl, etc.; C₂-C₆ alkenyl such as n-propenyl, etc.; C₂-C₇ alkoxy carbonyl such as ethoxycarbonyl, etc.; -N(R⁴²)-CO(R⁴³) (wherein R⁴² is hydrogen or C₁-C₆ alkyl; R⁴³ is C₆-C₁₄ aryl such as biphenyl, etc.; or C₇-C₁₆ aralkyl); or a group of the formula shown below:



(wherein ring C, R⁵, R⁶ and R⁷ each has the same meaning as defined above).

10 Ring C is preferably C₆-C₁₄ aryl such as phenyl, naphthyl, etc.; C₃-C₇ cycloalkyl such as cyclopentyl, cyclohexyl, etc.; C₇-C₁₆ aralkyl such as benzyl, etc.; or heterocycle such as pyridine-3-yl, thiophen-3-yl, thiazol-2-yl, etc. Alternatively, ring C may be take together with R⁷ and R⁸ to
15 form



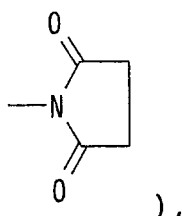
R⁵ is preferably hydrogen; C₁-C₆ alkyl such as methyl, etc.; C₁-C₆ alkoxy such as methoxy, etc.; halogen such as chlorine, etc.; nitro; amino; C₆-C₁₄ aryl such as phenyl, etc.;
20 or -CON(R¹⁶)(R¹⁷) or -CH₂-CON(R¹⁶)(R¹⁷) (wherein R¹⁶ and R¹⁷ are each independently hydrogen; C₁-C₆ alkyl such as ethyl, etc.,

or halo-C₁-C₆ alkyl such as 2,2,2-trifluoroethyl, etc.).

R⁶ is preferably hydrogen or halogen such as chlorine, etc.

R⁷ is preferably hydrogen.

5 R⁸ and R⁹ are each independently preferably hydrogen; C₁-C₆ alkyl such as ethyl, etc.; C₆-C₁₄ aryl such as phenyl, etc.; hydroxy-C₁-C₆ alkyl such as hydroxymethyl, etc.; -CON(R¹⁸)(R¹⁹)(wherein R¹⁸ and R¹⁹ are each independently hydrogen; C₁-C₆ alkyl such as methyl, ethyl, propyl, isopropyl, 10 butyl, isobutyl, etc.; C₃-C₇ cycloalkyl such as cyclohexyl, etc.; halo C₁-C₆ alkyl such as 2,2,2-trifluoroethyl, etc.; C₂-C₁₂ alkoxyalkyl such as methoxyethyl, etc.; or C₆-C₁₄ aryl such as phenyl, etc.); -COO(R²⁰) or -(CH₂)_n-OCO(R²⁰) (wherein R²⁰ is hydrogen; C₁-C₆ alkyl such as methyl, ethyl, propyl, isopropyl, 15 isobutyl, etc.; or C₃-C₇ cycloalkyl such as cyclohexyl, etc., and n is an integer of 0 or 1); -N(R²¹)(R²²)(wherein R²¹ and R²² are each independently hydrogen; C₁-C₆ alkyl such as methyl, isopropyl, etc.; C₁-C₆ acyl such as acetyl, propionyl, butyryl, etc.; C₁-C₆ alkylsulfonyl such as methylsulfonyl, etc.; or R²¹ 20 and R²² may be taken together with the nitrogen atom to which they are attached to form



or R⁸ and R⁹ taken together may form C₃-C₇ cycloalkyl such as cyclopropyl, cyclohexyl, etc.

substitution site will be illustrated below.

R^1 is preferably hydrogen, halo C_1 - C_6 alkyl or C_1 - C_6 alkyl, among which hydrogen is especially preferred.

R^2 is preferably phenyl (which may be substituted with
5 halo C_1 - C_6 alkyl such as trifluoromethyl, etc.; C_1 - C_6 alkyl such as methyl, etc.; halogen such as chlorine, etc.; or C_1 - C_6 alkoxy such as methoxy, etc.).

$R^{2'}$ is preferably hydrogen.

$R^{2''}$ is preferably hydrogen, halo- C_1 - C_6 alkyl, halogen,
10 C_1 - C_6 alkyl or C_1 - C_6 alkoxy, and trifluoromethyl is especially preferred.

X is preferably $-COO-$ or $-CON(R^{10})-$ (R^{10} has the same meaning as defined above), among which $-CONH-$ is especially preferred.

15 Ring B is preferably phenyl.

R^3 is preferably C_1 - C_6 alkyl, C_1 - C_6 alkoxy, $-CON(R^{11})(R^{12})$ (wherein R^{11} and R^{12} are each independently preferably hydrogen or C_1 - C_6 alkyl) or $-CO(R^{15})$ (wherein R^{15} is preferably C_1 - C_6 alkoxy).

20 R^4 is preferably hydrogen or methyl, and especially preferably methyl.

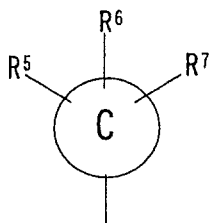
Alk^1 is preferably methylene.

Alk^2 is preferably methylene.

l is preferably 0 or 1, especially 1.

25 m is preferably 1 or 2, especially 1 or 2.

D is preferably C_1 - C_6 alkyl or a group of the formula shown below:



(wherein ring C, R^5 , R^6 and R^7 each has the same meaning as defined above).

Ring C is preferably phenyl, pyridin-3-yl, thiophen-3-yl,
 5 thiophen-2-yl and thiazol-2-yl, among which phenyl is especially preferred.

R^5 , R^6 and R^7 each is preferably hydrogen, halogen or C_1 - C_6 alkyl, among which hydrogen is especially preferred.

R^8 and R^9 each is preferably hydrogen, C_1 - C_6 alkyl, C_6 - C_{14}
 10 aryl, $-\text{CON}(R^{18})(R^{19})$ (wherein R^{18} and R^{19} each is preferably hydrogen or C_1 - C_6 alkyl) or $-\text{COO}(R^{20})$ (wherein R^{20} is preferably hydrogen or C_1 - C_6 alkyl), among which $-\text{CON}(R^{18})(R^{19})$ (wherein R^{18} and R^{19} each is preferably hydrogen or C_1 - C_6 alkyl) or $-\text{COO}(R^{20})$ (wherein R^{20} is preferably hydrogen or C_1 - C_6 alkyl) are
 15 more preferred, and $-\text{COO}(R^{20})$ (wherein R^{20} is preferably C_1 - C_6 alkyl) is especially preferred.

The substitution site of $-(\text{CH}_2)_1-$ on the benzene ring in the formula (1') is preferably i-position.

20 The compounds of the present invention may include hydrates or solvates, depending on the case, and may further include their metabolites. Furthermore, the compounds of the present invention include racemates and optically active compounds. The optically active compounds are preferably
 25 those wherein one of enantiomers is in enantiomer excess of

about 90% or higher, more preferably in enantiomer excess of about 99% or higher.

When the compounds of the present invention are used as
5 an agent for the treatment or prophylaxis of hyperlipidemia or arteriosclerosis, they can be administered systemically or locally, and orally or parenterally. Though the dose may vary depending on the age, body weight, symptoms, therapeutic effect, etc., the daily dose per adult is in the range of 0.1 mg to 1g
10 per one dose and can be administered one to several times per day. Also, the compounds of the present invention can be administered to human beings as well as animals other than human beings, especially mammals, for the treatment or prevention of said diseases. The compounds of the present invention can be
15 used in the same way for the treatment or prevention of coronary artery diseases, obesity, diabetes or hypertension.

In the formulation of the compounds of the present invention into solid compositions and liquid compositions for oral administration or injections, etc., for parenteral
20 administration, there may be added appropriate additives such as diluents, dispersants, adsorbents, solubilizers, etc. In addition, the composition of the present invention may take the known form such as tablets, pills, powders, granules, suppositories, injections, eye drops, solutions, capsules,
25 troches, aerosols, elixirs, suspensions, emulsions, syrups, etc.

When the compounds of the present invention are formulated into solid preparations such as tablets, pills, powders, granules, etc., examples of such an additive include

lactose, mannitol, glucose, hydroxypropyl cellulose, microcrystalline cellulose, starch, polyvinylpyrrolidone, magnesium aluminometasilicate or powdery silicic anhydride. In the case where the compounds of the present invention are
5 formulated into tablets or pills, they may be coated with a gastroenteric or enteric coating film containing a substance such as sucrose, gelatin, hydroxypropyl cellulose or hydroxymethyl cellulose phthalate. Furthermore, the tablets or pills may be multi-layered tablets comprising two or more
10 layers.

As the pharmaceutical compositions of the present invention, there are also exemplified capsules in which are filled liquid, semi-solid or solid contents prepared by dissolving the compounds of the present invention in a solvent
15 and adding an additive thereto. Examples of said solvents are purified water, ethanol, vegetable oil, etc., among which ethanol or a mixture of purified water and ethanol is preferably used. Any additives commonly used in the preparation of capsules can be used without any particular limitation. Such
20 additives include, for example, propylene glycol fatty acid esters; low molecular weight polyethylene glycols such as polyethylene glycol 200 to 600, etc., glycerine fatty acid esters thereof, and medium chain fatty acid triglycerides thereof; alcohols/polyols such as stearyl alcohol, cetanol,
25 polyethylene glycol, etc., or esters thereof; lipids such as sesame oil, soy bean oil, peanut oil, corn oil, hydrogenated oil, paraffin oil, bleached wax; fatty acids such as triethyl citrate, triacetin, stearic acid, palmitic acid, myristic acid, etc., and derivatives thereof. These additives are suitable

for preparing liquid or semi-solid contents. In the capsules of the present invention, propylene glycol fatty acid esters are preferable as such an additive. Examples of the propylene glycol fatty acid esters are propylene glycol monocaprylate (Capmul PG-8 (Brand name), Sefol 218 (Brand name), Capryo 190 (Brand name)), propylene glycol monolaurate (Lauroglycol FCC (Brand name)), propylene glycol monooleate (Myverol P-06 (Brand name)), propylene glycol myristate, propylene glycol monostearate, propylene glycol lisinolate (Propymuls (Brand name)), propylene glycol dicaprylate/dicaprate (Captex (Trademark) 200 (Brand name)) propylene glycol dilaurate, propylene glycol distearate and propylene glycol dioctanoate (Captex (Trademark) 800 (Brand name)). Although there is no particular limitation to the materials constituting the capsules of the present invention, they include, for example, polysaccharides derived from natural products such as agar, alginic acid salt, starch, xanthan, dextran, etc; proteins such as gelatin, casein, etc.; chemically processed products such as hydroxystarch, pullulan, hydroxypropyl cellulose, hydroxypropyl methylcellulose, polyvinyl alcohol or derivatives thereof, polyacryl derivatives, polyvinylpyrrolidone or derivatives thereof, polyethylene glycol, etc.

In the case where the pharmaceutical compositions of the present invention are liquid formulations for oral administration such as pharmaceutically acceptable emulsions, solubilizers, suspensions, syrups or elixirs, etc., diluents to be used include, for example, purified water, ethanol, vegetable oils, emulsifiers, etc. In addition to such diluents,

auxiliary agents such as wetting agents, suspending agents, sweeteners, condiments, flavors or antiseptics may be added to said liquid formulations.

In the case where the pharmaceutical compositions of the present invention are parenteral formulations such as injections, there are employed sterilized aqueous or non-aqueous solutions, solubilizers, suspending agents, emulsifiers, etc. Examples of the aqueous solutions, solubilizers and suspending agents include distilled water for injections, physiological saline, cyclodextrin, and derivatives thereof; organic amines such as triethanolamine, diethanolamine, monoethanolamine, triethylamine, etc.; and inorganic alkaline solutions. When aqueous solutions are employed, for example, propylene glycol, polyethylene glycol or vegetable oils such as olive oil, or alcohols such as ethanol may be further added. Further, surfactants (for mixed micelle formation) such as polyoxyethylene hydrogenated castor oils, sucrose fatty acid esters, or lecithin or hydrogenated lecithin (for liposome formation), etc. can be used as a solubilizer. Furthermore, with regard to the parenteral formulations of the present invention, they may be formulated into emulsions comprising non-aqueous solubilizers such as vegetable oils, together with lecithin, polyoxyethylene hydrogenated castor oil or polyoxyethylene-polyoxypropylene glycol, etc.

Further, the present invention provides a novel agent for the treatment or prophylaxis of hyperlipidemia, arteriosclerosis, coronary artery diseases, obesity, diabetes or hypertension with new functions that have never been known before. The agents of the present invention for the treatment

or prevention of said diseases are characterized in that they selectively inhibit MTP (microsomal triglyceride transfer protein) in the small intestine. Among these agents, an agent which does not substantially inhibit MTP in the liver, while
5 inhibits only MTP in the small intestine is desirable. Specifically, it is preferable that MTP inhibition of the agent in the liver is approximately 1/3 or less, preferably 1/100 or less when compared to that in the small intestine as estimated in terms of ED₅₀ or ED₂₀. As one preferred embodiment of the
10 therapeutic or prophylactic agents of the present invention for said diseases, they inhibit MTP in the small intestine, and they are then metabolized in the small intestine, blood, and liver to the amount at which the residual agent arriving at the liver does not substantially inhibit MTP in the liver. It is
15 particularly preferable that, when 300mg/kg of the compound of the present invention is administered orally, the rate of liver TG release inhibition exerted by the residual compound reaching the liver is about 20% or less, preferably less than about 10%, more preferably about 0%. Specifically, it is desirable that
20 the agent has about 40% or less, preferably about 20% or less inhibition rate of liver TG release when assayed by the method of Test Example 4 which will be hereinafter mentioned.

The pharmaceutical compositions or agents of the present
25 invention can be used in combination with other pharmaceutical compositions or agents. As other agents, there may be exemplified drugs for the treatment or prophylaxis of hyperlipidemia, arteriosclerosis, coronary artery disease, obesity, diabetes, or hypertension, and they can be used solely

or in combination with two or more kinds of said drugs. Examples of the antihyperlipidemic drugs include a statin-type drug, more specifically, lovastatin, simvastatin, pravastatin, fluvastatin, atorvastatin or cerivastatin. Examples of the
5 anti-obesity drugs include mazindol or olristat. Examples of the anti-diabetic drugs include insulin preparations, sulfonylurea drugs, insulin secretion-promotor drugs, sulfonamide drugs, biguanide drugs, α -glucosidase inhibitors, insulin resistance-improving drugs, etc., more specifically
10 insulin, glibenclamid, tolbutamide, glyclopyramide, acetohexamide, glimepiride, tolazamide, gliclazide, nateglinide, glibuzol, metformin hydrochloride, buformin hydrochloride, voglibose, acarbose, pioglitazone hydrochloride, etc. Examples of the anti-hypertension drugs
15 include loop diuretics, angiotensin converting enzyme inhibitors, angiotensin II receptor antagonists, Calcium antagonists, β -blockers, α , β -blockers and α -blockers, and more specifically, furosemide delayed release, captopril, captopril delayed release, enalapril maleate, alacepril,
20 delapril hydrochloride, silazapril, lisinopril, benazepril hydrochloride, imidapril hydrochloride, temocapril hydrochloride, quinapril hydrochloride, trandolapril, perindopril erbumine, losartan potassium, candesartan cilexetil, nicardipine hydrochloride, nicardipine
25 hydrochloride delayed release, nilvadipine, nifedipine, nifedipine delayed release, benidipine hydrochloride, diltiazem hydrochloride, diltiazem hydrochloride delayed release, nisoldipine, nitrendipine, manidipine hydrochloride, barnidipine hydrochloride, efonidipine hydrochloride,

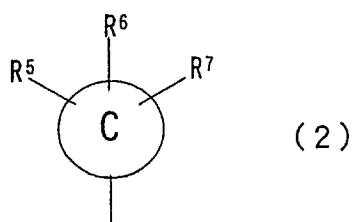
amlodipine besylate, felodipine, cilnidipine, aranidipine, propranolol hydrochloride, propranolol hydrochloride delayed release, pindolol, pindolol delayed release, indenolol hydrochloride, carteolol hydrochloride, carteolol hydrochloride delayed release, bunitrolol hydrochloride, bunitrolol hydrochloride delayed release, atenolol, asebutolol hydrochloride, metoprolol tartrate, metoprolol tartrate delayed release, nipradilol, penbutolol sulfate, tilisolol hydrochloride, carvedilol, bisoprolol fumarate, betaxolol hydrochloride, celiprolol hydrochloride, bopindolol malonate, bevantolol hydrochloride, labetalol hydrochloride, arotinolol hydrochloride, amosulalol hydrochloride, prazosin hydrochloride, terazosin hydrochloride, doxazosin mesylate, bunazocin hydrochloride, bunazocin hydrochloride delayed release, urapidil, and phentolamine mesylate, etc.

There is no particular limitation to the timing for the administration of pharmaceutical compositions or agents and other drugs for combination use according to the present invention, and they may be administered simultaneously or intermittently.

The amount of such drugs for combination use can be determined based on their clinical doses, and can be chosen depending on the age, weight, condition, medication time, dosage form, method of administration, combination, etc.

There is no particular limitation to the dosage form of the drugs for combination use, and it may be sufficient that the pharmaceutical compositions or agents and other drugs for combination use according to the present invention are combined at the time of administration.

Next, a process for preparing an ester compound represented by the formula (1) will be illustrated below as an example, but the process of the present invention is not limited thereto. In the process mentioned below, D is a group of the formula (2):



(wherein ring C, R⁵, R⁶ and R⁷ each has the same meaning as defined above), and when D is C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₇ alkoxycarbonyl or -N(R⁴²)-CO(R⁴³) (R⁴² and R⁴³ each has the same meaning as defined above), the compound can be prepared in the same.

In addition, the functional groups other than those to be reacted may be optionally protected in a previous stage and may be deprotected in an appropriate stage.

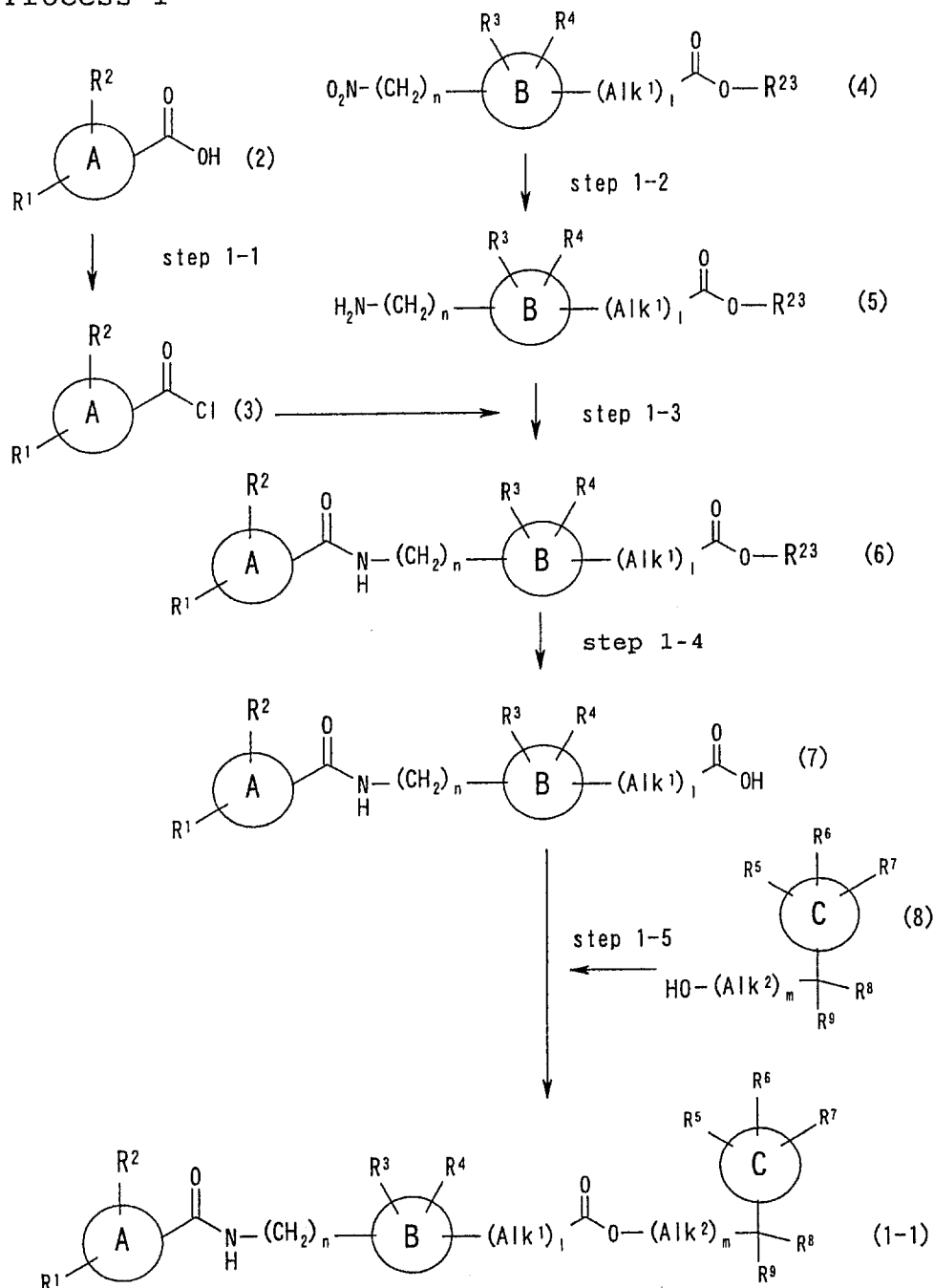
Further, the reaction in each step may be carried out in the usual manner, and separation and purification may be conducted by the appropriate selection or combination of conventional methods such as crystallization, recrystallization, column chromatography, preparative HPLC, etc.

Process 1

Among the compounds represented by the formula (1), a process for preparing compounds in which X is -CONH-(CH₂)_n-

will be illustrated below.

Process 1



In the above reaction scheme, $\text{R}^1, \text{R}^2, \text{R}^3, \text{R}^4, \text{R}^5, \text{R}^6, \text{R}^7, \text{R}^8, \text{R}^9, l, m, n, \text{Alk}^1, \text{Alk}^2$, ring A, ring B, and ring C each has the same meaning as defined above and R^{23} is $\text{C}_1\text{--C}_6$ alkyl.

Step 1-1

A carboxylic acid of the formula (2) is reacted with oxalyl chloride or thionyl chloride in a solvent to give an acid chloride of the formula (3).

5 The solvent used in the reaction includes, for example, ethers such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme, etc.; hydrocarbons such as benzene, toluene, hexane, xylene, etc.; halogenated hydrocarbons such as methylene chloride, chloroform, carbon
10 tetrachloride, 1,2-dichloroethane, etc.; and esters such as ethyl acetate, methyl acetate, butyl acetate, etc., and they may be used solely or in combination thereof. Preferred solvents in the present reaction include methylene chloride, chloroform or toluene, all of which contain a catalytic amount
15 of N,N-dimethylformamide.

The reaction temperature is about -20°C to 120°C , preferably about 0°C to room temperature.

The reaction time is about 10 minutes to 8 hours, preferably about 30 minutes to 4 hours.

20 Step 1-2

This step is a general reduction process for the nitro group attached directly to the aromatic ring. A nitro compound of the formula (4) is hydrogenated in a solvent in the presence of a catalyst to give a compound of the formula (5).

25 The solvent used in the reaction includes, for example, ethers such as tetrahydrofuran, dioxane, 1,2-dimethoxyethane, etc.; alcohols such as methanol, ethanol, isopropyl alcohol, t-butanol, etc.; and esters such as ethyl acetate, methyl acetate, butyl acetate, etc.; and they are used solely or in

combination thereof. Preferred solvents in the present reaction include alcohols such as methanol, ethanol, isopropyl alcohol, t-butanol, etc., and a mixture of said alcohol solvent and tetrahydrofuran and/or water.

5 The catalyst used in the reaction includes, for example, palladium-carbon, palladium hydroxide, Raney-Ni, platinum oxide, and among which palladium-carbon or reduced iron is preferred.

10 The reaction temperature is about 0°C to 120°C, preferably about room temperature to 100°C.

 The reaction time is about 30 minutes to 8 days, preferably about one hour to 96 hours.

Step 1-3

15 This step is a general condensation reaction between acid chlorides and amines. An acid chloride of the formula (3) is condensed with an amine of the formula (5) in a solvent in the presence of a base to give a compound of the formula (6).

20 The solvent used in the reaction includes, for example, ethers such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme, etc.; hydrocarbons such as benzene, toluene, hexane, xylene, etc.; halogenated hydrocarbons such as methylene chloride, chloroform, carbon tetrachloride, 1,2-dichloroethane, etc.; and esters such as ethyl acetate, methyl acetate, butyl acetate, etc., and they
25 can be used solely or in combination thereof. Preferred solvents in the present reaction include methylene chloride, chloroform, toluene, ethyl acetate or tetrahydrofuran.

 Examples of the bases used in the present invention include organic bases such as triethylamine, pyridine,

N-methylmorpholine, etc.; alkali metal hydroxides such as lithium hydroxide, sodium hydroxide, potassium hydroxide, etc.; and alkali metal carbonates such as sodium carbonate, potassium carbonate, sodium bicarbonate, potassium bicarbonate, etc., among which triethylamine, sodium hydroxide or sodium bicarbonate is preferable.

The reaction temperature is about 0°C to 80°C, preferably about 0°C to room temperature.

The reaction time is about 10 minutes to 48 hours, preferably about 30 minutes to 24 hours.

In the case of a compound of the formula (5) wherein R²³ is hydrogen, a compound of the formula (7) can be prepared by one step of condensation between an aminocarboxylic acid and an acid chloride (Schotten-Baumann reaction).

Alternatively, a compound of the formula (6) can be prepared by using a condensing agent (e.g. WSC-HOBT, DCC-HOBT) for a compound of the formula (2) and a compound of the formula (5). Further, a compound of the formula (6) may be provided by converting a compound of the formula (2) into its mixed anhydride, followed by the reaction in the presence of a base.

Step 1-4

This step is a general ester hydrolysis reaction using alkali. A compound of the formula (6) is hydrolysed in a solvent in the presence of a base to give a compound of the formula (7).

The solvent used in the reaction includes, for example, ethers such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme, etc.; and alcohols such as methanol, ethanol, isopropyl alcohol, etc.; and they can be used solely or in combination thereof. Preferred solvents in the

present reaction include a mixture of tetrahydrofuran and ethanol or methanol. Examples of the bases are aqueous solutions of alkali metal carbonates such as sodium carbonate, potassium carbonate, etc., or aqueous solutions of alkali metal hydroxides such as lithium hydroxide, sodium hydroxide, potassium hydroxide, etc., among which sodium hydroxide or lithium hydroxide is preferable.

The reaction temperature is about 0°C to 120°C, preferably about room temperature to 80°C.

The reaction time is about 1 hour to 24 hours, preferably about 2.5 hours to 12 hours.

Step 1-5

This step is a general condensation reaction of a carboxylic acid with an alcohol.

A carboxylic acid of the formula (7) is condensed with an alcohol of the formula (8) in a solvent in the presence of a base and a condensing agent to give a compound of the formula (1-1) which is one of the objective compounds.

The solvent used in the reaction includes, for example, ethers such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme, etc.; hydrocarbons such as benzene, toluene, hexane, xylene, etc.; halogenated hydrocarbons such as methylene chloride, chloroform, carbon tetrachloride, 1,2-dichloroethane, etc.; esters such as ethyl acetate, methyl acetate, butyl acetate, etc.; polar solvents such as acetone, N,N-dimethylformamide, dimethyl sulfoxide, etc.; and they can be used solely or in combination thereof. Preferred solvents in the present reaction include tetrahydrofuran, acetone, methylene chloride or

N,N-dimethylformamide.

Examples of the bases used in the reaction include organic bases such as triethylamine, pyridine, dimethylaminopyridine, N-methylmorpholine, etc., among which dimethylaminopyridine
5 is preferred.

Examples of the condensing agents used in the reaction include 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide hydrochloride (WSC.HCl), dicyclohexylcarbodiimide (DCC), etc. among which 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide
10 hydrochloride is preferred.

The reaction temperature is about 0°C to 80°C, preferably about 0°C to room temperature.

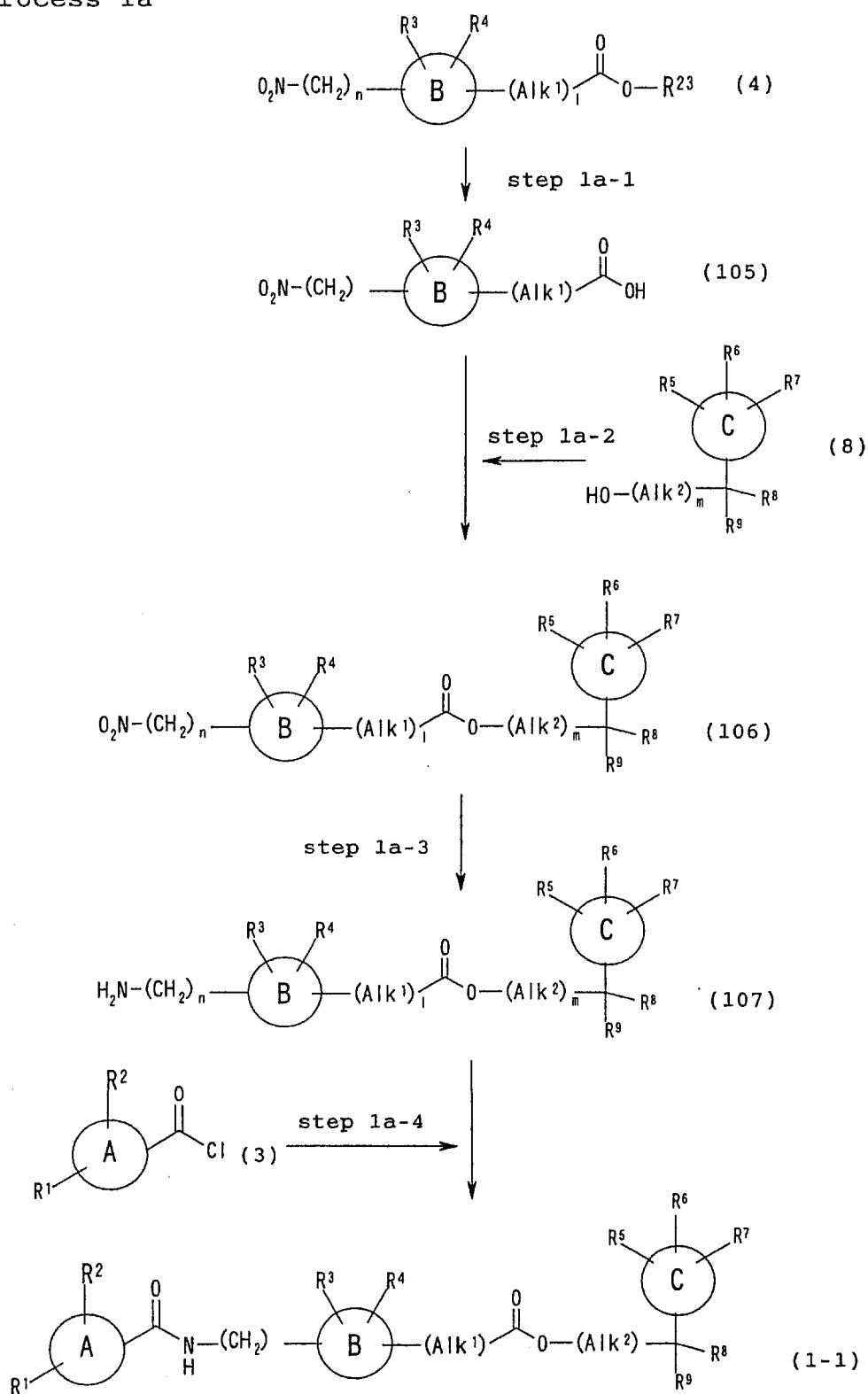
The reaction time is about 1 hour to 48 hours, preferably about 3 hours to 24 hours.

15 As an alternative process, a carboxylic acid of the formula (7) may be converted into its mixed anhydride and then reacted with an alcohol of the formula (8) in the presence of a base.

20 Process 1a

Process 1a as shown below is an alternative of Process 1.

Process 1a



In the above reaction scheme, R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , R^{23} , l , m , n , Alk^1 , Alk^2 , ring A, ring B and ring C each has the same meaning as defined above.

5 Step 1a-1

A compound of the formula (105) can be prepared from a compound of the formula (4) in a similar manner to Step 1-4 of Process 1.

Step 1a-2

10 A compound of the formula (106) can be prepared by condensing a carboxylic acid of the formula (105) with an alcohol of the formula (8) in a similar manner to Step 1-5 of Process 1.

Step 1a-3

15 A compound of the formula (107) can be prepared from a compound of the formula (106) in a similar manner to Step 1-2 of Process 1.

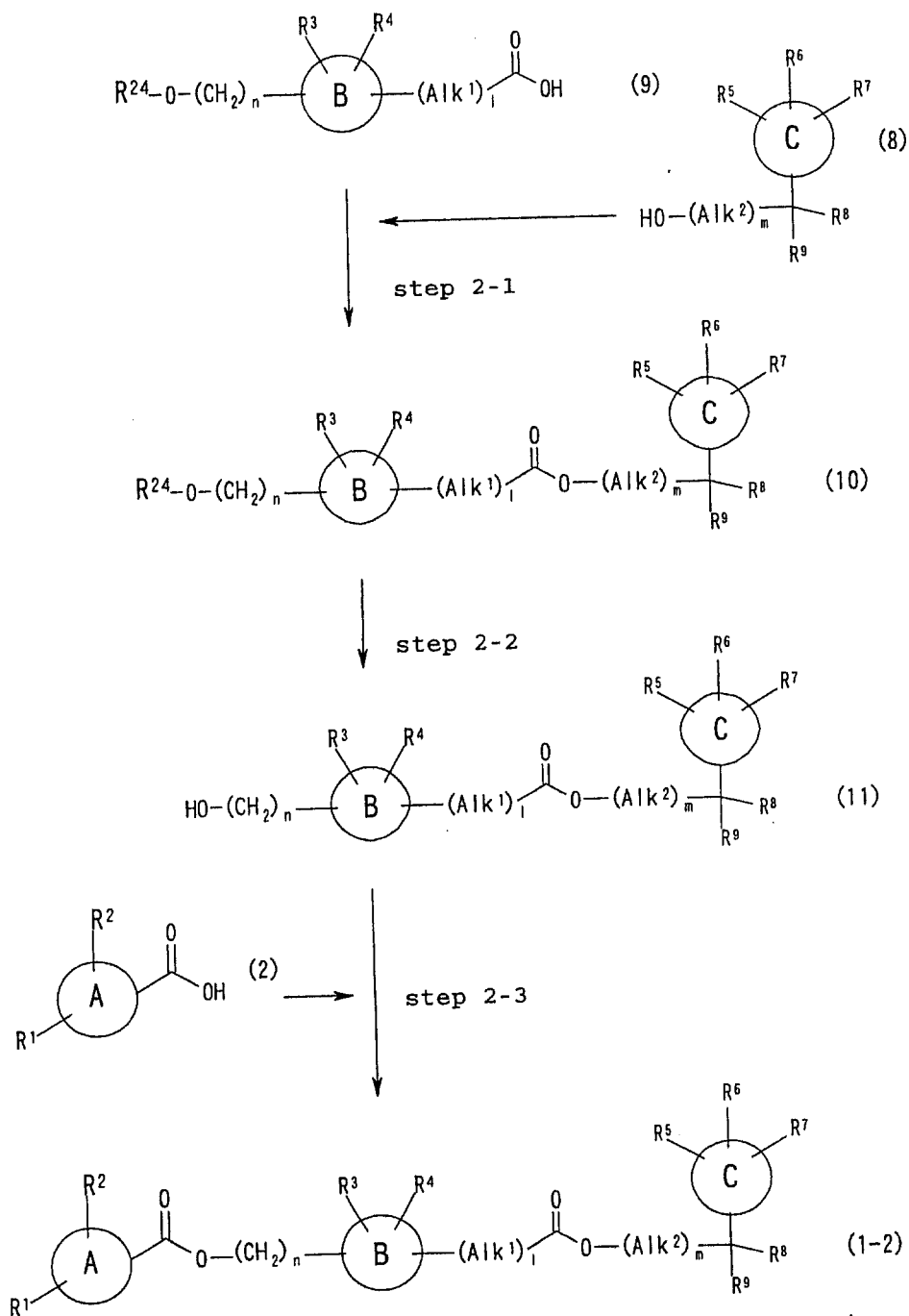
Step 1a-4

20 A compound of the formula (1-1) which is one of the objective compounds can be prepared by condensing an amine of the formula (107) with an acid chloride of the formula (3) in a similar manner to Step 1-3 of Process 1.

Process 2

25 Among the compounds represented by the formula (1), a process for preparing compounds in which X is $-COO-(CH_2)_n-$ will be illustrated below.

Process 2



In the above reaction scheme, $R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, 1, m, n, Alk^1, Alk^2$, ring A, ring B and ring C each has the same meaning as defined above, and R^{24} is a hydroxy-protecting group (for example, benzyl, p-methoxybenzyl, tert-butyl, trialkylsilyl, etc.).

Step 2-1

This step is a condensation reaction of a carboxylic acid with an alcohol similar to Step 1-5 of Process 1. A compound of the formula (10) can be prepared by condensing a carboxylic acid of the formula (9) with an alcohol of the formula (8) in
5 a solvent in the presence of a base and a condensing agent.

The solvent used in the reaction includes, for example, ethers such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme, etc.; hydrocarbons such as
10 benzene, toluene, hexane, xylene, etc.; halogenated hydrocarbons such as methylene chloride, chloroform, carbon tetrachloride, 1,2-dichloroethane, etc.; esters such as ethyl acetate, methyl acetate, butyl acetate, etc.; polar solvents such as acetone, N,N-dimethylformamide, dimethyl sulfoxide,
15 water, etc.; and they can be used solely or in combination thereof. Preferred solvents in the present reaction include tetrahydrofuran, methylene chloride or N,N-dimethylformamide.

Examples of the bases used in the reaction include organic bases such as triethylamine, pyridine, dimethylaminopyridine,
20 N-methylmorpholine, etc., among which dimethylaminopyridine is preferred.

Examples of the condensing agents used in the reaction include 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide hydrochloride (WSC·HCl), dicyclohexylcarbodiimide (DCC), etc.,
25 among which 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide hydrochloride is preferred.

The reaction temperature is about 0°C to 80°C, preferably about 0°C to room temperature.

The reaction time is about 2 hours to 48 hours, preferably

about 6 hours to 24 hours.

Step 2-2

This step is a general deprotection method for hydroxy groups. For example, when R^{24} is benzyl in a compound of the formula (10), the compound of the formula (10) is hydrogenated
5 in a solvent in the presence of a catalyst to give a compound of the formula (11).

The solvent used in the reaction includes, for example, ethers such as tetrahydrofuran, dioxane, 1,2-dimethoxyethane,
10 diglyme, etc.; alcohols such as methanol, ethanol, isopropyl alcohol, t-butanol, etc.; and esters such as ethyl acetate, methyl acetate, butyl acetate, etc.; and they can be used solely or in combination thereof. Preferred solvents in the present reaction are alcohols such as methanol, ethanol,
15 isopropyl alcohol, t-butanol, etc.

Examples of the catalyst used in the reaction include palladium carbon, palladium hydroxide, Raney-Ni, platinum oxide, etc., among which palladium carbon is preferred.

The reaction temperature is about 0°C to 80°C, preferably
20 about 0°C to room temperature.

The reaction time is about 1 hour to 16 hours, preferably about 2 hours to 8 hours.

Step 2-3

This step is a condensation reaction between a carboxylic
25 acid and an alcohol similar to Step 1-5 of Process 1. A compound of the formula (11) is condensed with an alcohol of the formula (2) in a solvent in the presence of a base and a condensing agent to give a compound of the formula (1-2) which is one of the objective compounds.

The solvent used in the reaction includes, for example, ethers such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme, etc.; hydrocarbons such as benzene, toluene, hexane, xylene, etc.; halogenated hydrocarbons such as methylene chloride, chloroform, carbon tetrachloride, 1,2-dichloroethane, etc.; esters such as ethyl acetate, methyl acetate, butyl acetate, etc.; and polar solvents such as acetone, N,N-dimethylformamide, dimethyl sulfoxide, etc., and they can be used solely or in combination thereof. Preferred solvents in the present reaction are tetrahydrofuran, methylene chloride, dimethylformamide, etc.

Examples of the bases used in the reaction include organic bases such as triethylamine, pyridine, dimethylaminopyridine, N-methylmorpholine, etc., among which dimethylaminopyridine is preferred.

Examples of the condensing agents used in the reaction include 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide hydrochloride (WSC.HCl), dicyclohexylcarbodiimide (DCC), etc., among which 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide hydrochloride is preferred.

The reaction temperature is about 0°C to 80°C, preferably about 0°C to room temperature.

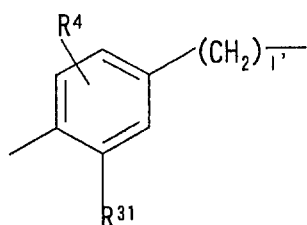
The reaction time is about 2 hours to 48 hours, preferably about 6 hours to 24 hours.

As an alternative process of Process 2, a phenol or an alcohol derivative derived from a compound of the formula (9) (wherein R^{24} is p-methoxybenzyl and the carboxyl group is protected by benzyl ester) is subjected to removal of the p-methoxybenzyl group with 2,3-dichloro-5,6-

dicyanobenzoquinone (DDQ), etc., followed by condensation with a compound of the formula (2). After removal of the benzyl group from the resulting compound, the deprotected compound is condensed with a compound of the formula (8) to give a compound of the formula (1-2) which is one of the objective compounds.

Process A

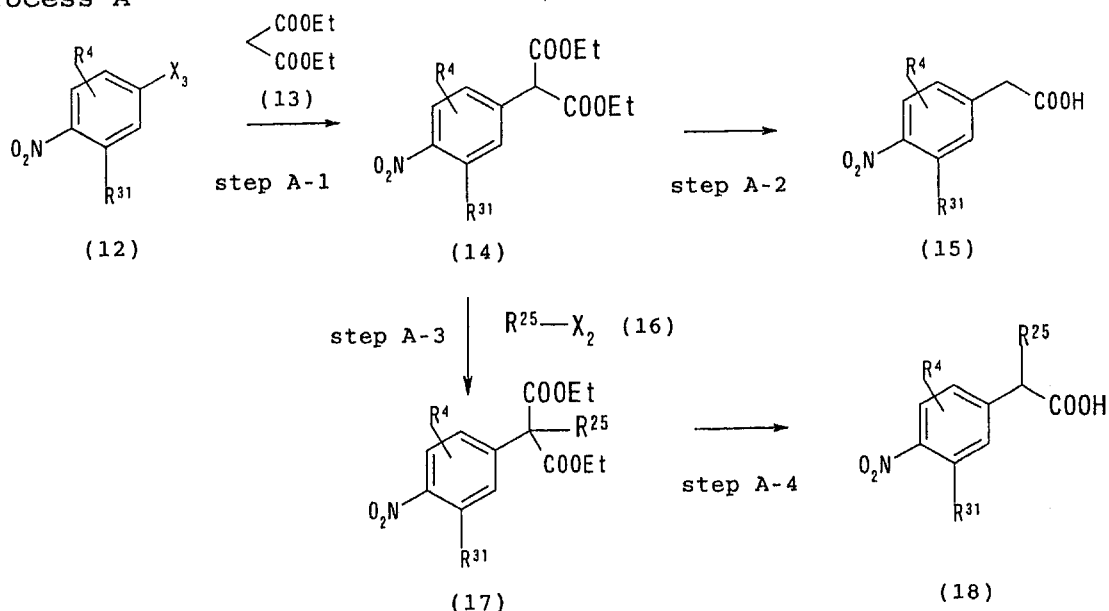
The following is an example of the process for preparing a compound of the formula (1) wherein ring B is



10

(wherein R^4 has the same meaning as defined above, R^{31} is C_1 - C_6 alkyl, and $1'$ is 1).

Process A



In the above reaction scheme, R^{31} and R^4 each has the same meaning as defined above, R^{25} is C_1 - C_6 alkyl, X_2 and X_3 each is halogen, and Et is ethyl.

Step A-1

A compound of the formula (14) can be prepared by reacting a compound of the formula (12) with a malonic acid ester of the formula (13) in a solvent in the presence of a base.

5 The solvent used in the reaction includes, for example, ethers such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme, etc.; hydrocarbons such as benzene, toluene, hexane, xylene, etc.; alcohols such as methanol, ethanol, isopropyl alcohol, t-butanol, etc.; and
10 polar solvents such as N,N-dimethylformamide, dimethyl sulfoxide, etc., and they can be used solely or in combination thereof. A preferred solvent in the present reaction is N,N-dimethylformamide.

 Examples of the bases used in the reaction include alkali
15 metal hydrides such as sodium hydride, potassium hydride, etc.; alkali metal alkoxides such as sodium ethoxide, sodium methoxide, potassium t-butoxide, etc.; alkali metal amides such as sodium amide, lithium bistrimethylsilylamide, etc.; and
20 alkali metal carbonates such as sodium carbonate, potassium carbonate, etc., among which sodium hydride is preferable.

 The reaction temperature is about 0°C to 120°C, preferably about room temperature to 100°C

 The reaction time is about 30 minutes to 24 hours, preferably about 1 hour to 12 hours.

25 Step A-2

 This step is a hydrolysis reaction of esters, followed by decarboxylation. A compound of the formula (15) can be prepared by stirring a compound of the formula (14) under heating in a solvent in the presence of a base.

The solvent used in the reaction includes, for example, ethers such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme, etc.; alcohols such as methanol, ethanol, isopropyl alcohol, t-butanol, etc.; and water; and
5 they can be used solely or in combination thereof. Preferred solvents in the present reaction are mixtures of an alcohol and water.

Examples of the bases used in the reaction include alkali metal carbonates such as sodium carbonate, potassium carbonate, etc., and alkali metal hydroxides such as lithium hydroxide,
10 sodium hydroxide, potassium hydroxide, etc., among which sodium hydroxide or potassium hydroxide is preferred.

The reaction temperature is about 0°C to 150°C, preferably about 60°C to 120°C

15 The reaction time is about 10 minutes to 12 hours, preferably about 30 minutes to 6 hours.

In accordance with the Steps 1a-2, 1a-3 and 1a-4 of the Process 1a, compounds of the present invention can be prepared from a compound of the formula (15) obtained in the above Step
20 A-2.

An example in the case where Alk^1 is a branched alkanediyl or alkenediyl will be illustrated below.

Step A-3

A compound of the formula (17) can be prepared by reacting
25 a compound of the formula (14) with a compound of the formula (16) in a solvent in the presence of a base.

The solvent used in the reaction includes, for example, ethers such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme, etc.; hydrocarbons such as

benzene, toluene, hexane, xylene, etc.; alcohols such as methanol, ethanol, isopropyl alcohol, t-butanol, etc.; and polar solvents such as N,N-dimethylformamide, dimethyl sulfoxide, etc., and they can be used solely or in combination thereof. Preferred solvents in the present reaction are N,N-dimethylformamide, etc.

Examples of the bases used in the reaction include alkali metal hydrides such as sodium hydride, potassium hydride, etc.; alkali metal alkoxides such as sodium ethoxide, sodium methoxide, potassium t-butoxide, etc.; alkali metal carbonates such as sodium carbonate, potassium carbonate, sodium bicarbonate, potassium bicarbonate, etc.; alkali metal hydroxides such as lithium hydroxide, sodium hydroxide, potassium hydroxide, etc.; alkali metal carboxylates such as sodium acetate, potassium acetate, etc.; and alkali metal phosphates such as sodium phosphate, potassium phosphate, etc., among which sodium hydride is preferred.

The reaction temperature is about 0°C to 120°C, preferably about room temperature to 100°C

The reaction time is about 10 minutes to 24 hours, preferably about 30 minutes to 12 hours.

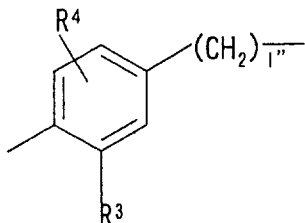
Step A-4

In a similar manner to Step A-2, a compound of the formula (18) can be prepared from a compound of the formula (17).

In accordance with the Steps 1a-2, 1a-3 and 1a-4 of the Process 1a, the compounds of the present invention can be prepared from a compound of the formula (18) obtained in the above Step A-4.

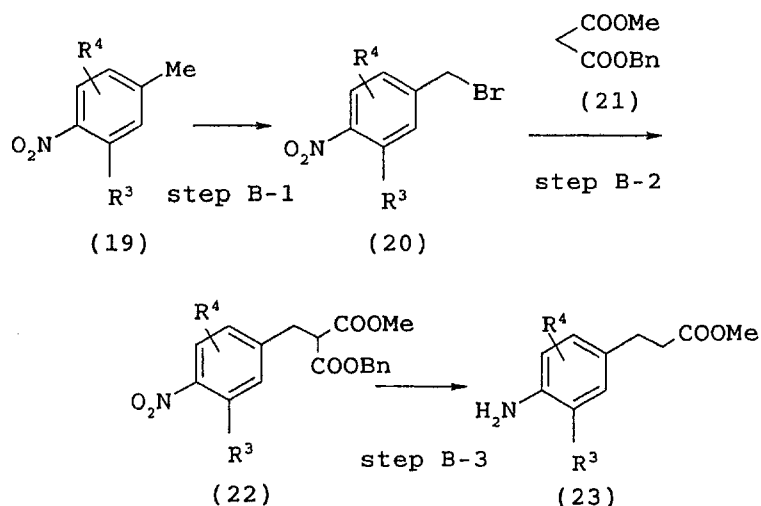
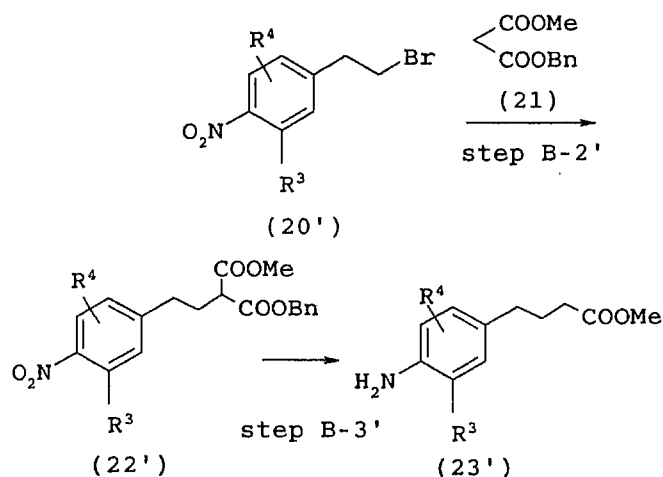
Process B

The following is an example of the process for preparing a compound of the formula (1) wherein ring B is



- 5 (wherein R³ and R⁴ each has the same meaning as defined above, and l'' is 2 or 3).

Process B

in case of $l''=2$ in case of $l''=3$ 

In the above reaction scheme, R^3 and R^4 each has the same meaning as defined above, Me is methyl, and Bn is benzyl.

Step B-1

- 5 A compound of the formula (20) can be prepared by reacting a compound of the formula (19) with a brominating agent in a solvent in the presence of a radical initiator (for example, 2,2'-azobisisobutyronitrile or benzoyl peroxide).

The solvent used in the reaction includes, for example,

hydrocarbons such as benzene, etc., and halogenated hydrocarbons such as methylene chloride, chloroform, carbon tetrachloride, 1,2-dichloroethane, etc., and they can be used solely or in combination thereof. Preferred solvents in the present reaction are methylene chloride or carbon tetrachloride.

The brominating agent used in the reaction includes, for example, bromine, N-bromosuccinimide, etc., among which N-bromosuccinimide is preferred.

The reaction temperature is about room temperature to 120°C, preferably about 60°C to 100°C

The reaction time is about 10 minutes to 8 hours, preferably about 30 minutes to 4 hours.

Step B-2

In a similar manner to Step A-1 of Process A, a compound of the formula (22) can be prepared by reacting a compound of the formula (20) with a compound of the formula (21).

Step B-2'

In a similar manner to Step A-1 of Process A, a compound of the formula (22') can be prepared by reacting a compound of the formula (20') (prepared from a compound of the formula (15) and a compound of the formula (22) via several steps) with a compound of the formula (21).

Step B-3

A compound of the formula (23) can be prepared by hydrogenating a compound of the formula (22) for debenzylation in a solvent, followed by decarboxylation.

The solvent used in the reaction includes, for example, ethers such as diethyl ether, tetrahydrofuran, dioxane,

1,2-dimethoxyethane, diglyme, etc.; alcohols such as methanol, ethanol, isopropyl alcohol, t-butanol, etc.; and water; and they can be used solely or in combination thereof. Preferred solvents in the present reaction are alcohols.

5 Examples of the catalyst used for the debenzylation include palladium carbon, palladium hydroxide, Raney-Ni, platinum oxide, etc., among which palladium carbon is preferred.

10 The reaction temperature in the debenzylation is preferably about room temperature to 80°C, and the reaction temperature in the decarboxylation is preferably 10°C to 150°C.

15 The reaction time in the debenzylation is about 1 hour to 16 hours, preferably about 2 hours to 8 hours, and the reaction time in the decarboxylation is about 5 minutes to 4 hours, preferably about 10 minutes to 2 hours.

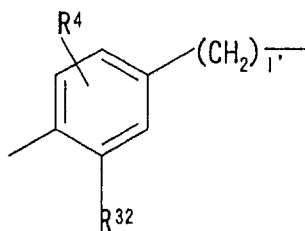
Step B-3'

 In a similar manner to Step B-3 of Process B, a compound of the formula (23') can be prepared from a compound of the formula (22').

20 In accordance with the Steps 1-3, 1-4 and 1-5 of the process 1, the compounds of the present invention can be prepared from a compound of the formula (23) or (23') obtained in Step B-3 or B-3'.

25 Process C

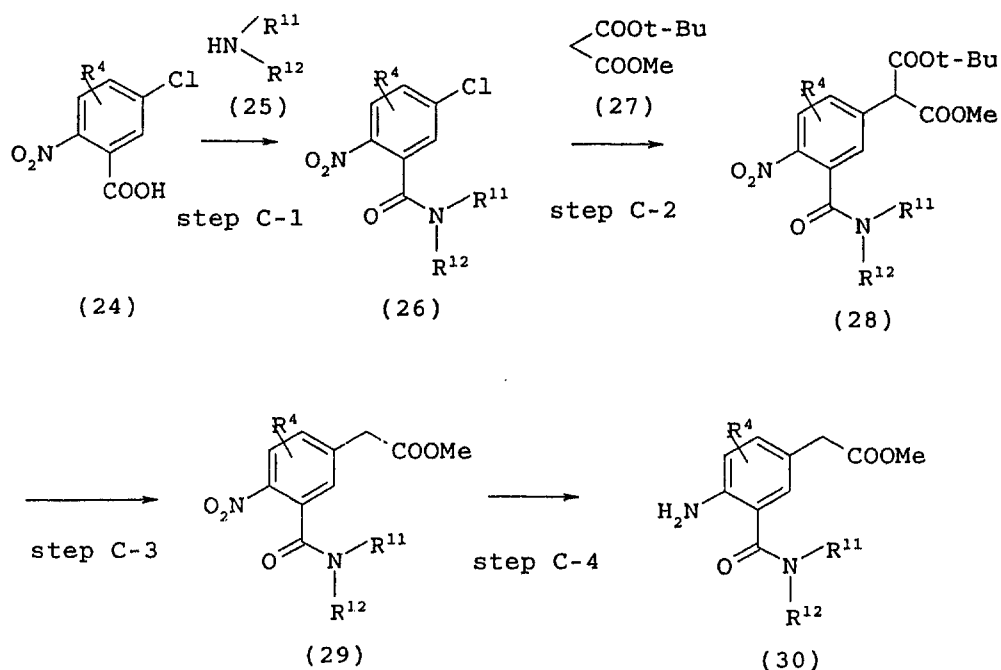
 The following is an example of the process for preparing a compound of the formula (1) wherein ring B is



(wherein R^4 has the same meaning as defined above, R^{32} is $-\text{CON}(R^{11})(R^{12})$ in which R^{11} and R^{12} each has the same meaning as defined above, and $1'$ is 1).

5

Process C



In the above reaction scheme, R^4 , R^{11} and R^{12} each has the same meaning as defined above, Me is methyl and t-Bu is tert-butyl.

10 Step C-1

An acid chloride can be prepared from a compound of the formula (24) in a similar manner to Step 1-1 of Process 1. The resulting acid chloride is reacted with a compound of the formula (25) in a similar manner to Step 1-3 of Process 1 to

give a compound of the formula (25).

Also, a compound of the formula (26) can be prepared by condensing a compound of the formula (24) with a compound of the formula (25) using a condensing agent (for example, WSC, HOBT). Alternatively, a compound of the formula (24) is converted into its mixed anhydride, followed by reaction with a compound of the formula (25) in the presence of a base, to give a compound of the formula (26).

Step C-2

10 In a similar manner to Step A-1 of Process A, a compound of the formula (28) can be prepared by reacting a compound of the formula (26) with a compound of the formula (27).

Step C-3

15 A compound of the formula (29) can be prepared by treating a compound of the formula (28) with an acid (trifluoroacetic acid, toluenesulfonic acid, methanesulfonic acid, etc.) in the presence or absence of a solvent under heating or at room temperature to convert the tert-butyl ester moiety into the carboxylic acid moiety, followed by decarboxylation.

20 The solvent used in the reaction includes, for example, ethers such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme, etc.; hydrocarbons such as benzene, toluene, hexane, xylene, etc.; alcohols such as methanol, ethanol, isopropyl alcohol, t-butanol, etc.;
25 halogenated hydrocarbons such as methylene chloride, chloroform, carbon tetrachloride, 1,2-dichloroethane, etc.; and water; and they can be used solely or in combination thereof. Preferred solvents in the present reaction are methylene chloride, chloroform or toluene.

The reaction temperature is about 0°C to 120°C, preferably about room temperature to 100°C

The reaction time is about 1 hour to 24 hours, preferably about 2 hours to 12 hours.

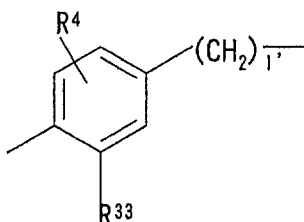
5 Step C-4

In a similar manner to Step 1-2 of Process 1, a compound of the formula (30) can be prepared from a compound of the formula (29).

10 In accordance with the Steps 1-3, 1-4 and 1-5 of Process 1, the compounds of the present invention can be prepared from a compound of the formula (30) obtained in the above Step C-4.

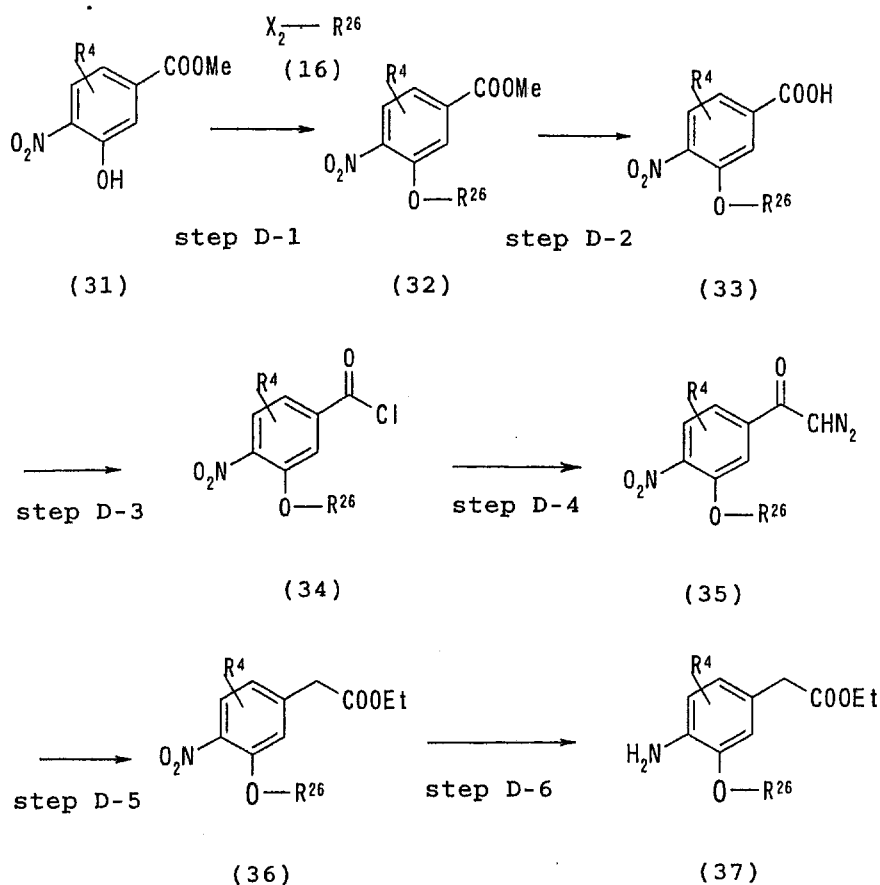
Process D

15 The following is an example of the process for preparing a compound of the formula (1) wherein ring B is



(wherein R⁴ has the same meaning as defined above, R³³ is C₁₋₆ alkoxy or C₇₋₁₆ aralkyloxy, and l' is 1).

Process D



In the above reaction scheme, R^4 , X_2 , Me and Et each has the same meaning as defined above and R^{26} is C_{1-6} alkyl or C_{7-16} aralkyl.

5 Step D-1

A compound of the formula (32) can be prepared by reacting a compound of the formula (31) with a compound of the formula (16) in a solvent in the presence of a base.

The solvent used in the reaction includes, for example,
 10 ethers such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme, etc.; hydrocarbons such as benzene, toluene, hexane, xylene, etc.; esters such as ethyl acetate, methyl acetate, butyl acetate, etc.; and polar solvents such as acetone, N,N-dimethylformamide, dimethyl

sulfoxide, etc.; and they can be used solely or in combination thereof. A preferred solvents in the present reaction is N,N-dimethylformamide.

Examples of the bases used in the reaction include alkali
5 metal hydrides such as sodium hydride, potassium hydride, etc.,
and alkali metal carbonates such as sodium carbonate, potassium
carbonate, sodium bicarbonate, potassium bicarbonate, etc.,
among which sodium hydride is preferred.

The reaction temperature is about 0°C to 100°C, preferably
10 about room temperature to 80°C

The reaction time is about 2 hour to 48 hours, preferably
about 6 hours to 24 hours.

Step D-2

A compound of the formula (33) can be prepared by
15 hydrolyzing the ester moiety of a compound of the formula (32)
in a solvent in the presence of a base.

The solvent used in the reaction includes, for example,
ethers such as diethyl ether, tetrahydrofuran, dioxane,
1,2-dimethoxyethane, diglyme, etc.; alcohols such as methanol,
20 ethanol, isopropyl alcohol, etc.; and water, and they can be
used solely or in combination thereof. Preferred solvents in
the present reaction are tetrahydrofuran or a mixture of
tetrahydrofuran and ethanol or methanol.

Examples of the bases used in the reaction include alkali
25 metal carbonates such as sodium carbonate, potassium carbonate,
etc.; aqueous solutions of alkali metal hydroxides such as
lithium hydroxide, sodium hydroxide, potassium hydroxide, etc.,
among which sodium hydroxide is preferred.

The reaction temperature is about 0°C to 120°C, preferably

about room temperature to 80°C

The reaction time is about 1 hour to 24 hours, preferably about 2.5 hours to 12 hours.

Step D-3

5 In a similar manner to Step 1-1 of Process 1, a compound of the formula (34) can be prepared from a compound of the formula (33).

Step D-4

10 This process is a conversion reaction from acid chlorides to diazoketones. A compound of the formula (35) can be prepared by reacting a compound of the formula (34) with diazomethane in a solvent in the presence of a base.

 The solvent used in the reaction includes, for example, ethers such as diethyl ether, tetrahydrofuran, dioxane, 15 1,2-dimethoxyethane, diglyme, etc., and they can be used solely or in combination thereof. Preferred solvents in the present reaction are diethyl ether or tetrahydrofuran.

 Examples of the bases used in the reaction include organic bases such as triethylamine, pyridine, dimethylaminopyridine, 20 N-methylmorpholine, etc., among which triethylamine is preferred.

 The reaction temperature is about -20°C to 50°C, preferably about 0°C to room temperature.

 The reaction time is about 2 hours to 48 hours, preferably 25 about 6 hours to 24 hours.

Step D-5

 This process is one carbon homologation (Arndt-Eistert synthesis) by α -diazoketone rearrangement (Wolff rearrangement). A compound of the formula (35) is reacted by

use of a silver catalyst (for example, silver benzoate, silver oxide) in an alcohol in the presence of a base to give a compound of the formula (36).

The solvent (also served as the reaction reagents) used
5 in the reaction includes, for example, alcohols such as methanol, ethanol, isopropyl alcohol, t-butanol, etc., and they can be used solely or in combination thereof. Preferred solvents (also served as the reaction reagents) in the present reaction are methanol or ethanol.

10 Examples of the bases used in the reaction include organic bases such as triethylamine, pyridine, dimethylaminopyridine, N-methylmorpholine, etc., among which triethylamine is preferred.

The reaction temperature is about room temperature to
15 120°C, preferably about 60°C to 120°C.

The reaction time is about 2 hours to 36 hours, preferably about 4 hours to 18 hours.

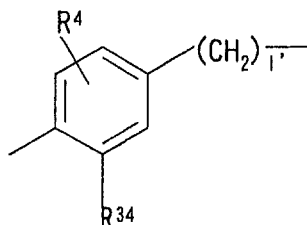
Step D-6

In a similar manner to Step 1-2 of Process 1, a compound
20 of the formula (37) can be prepared from a compound of the formula (36).

In accordance with the Steps 1-3, 1-4 and 1-5 of the above Process 1, the compounds of the present invention can be prepared from a compound of the formula (37) obtained in the
25 above Step D-6. The resulting compound of the present invention is further subjected to the reactions of Step 2-2 of Process 2, whereby the substituent $-OR^{26}$ can be converted into $-OH$.

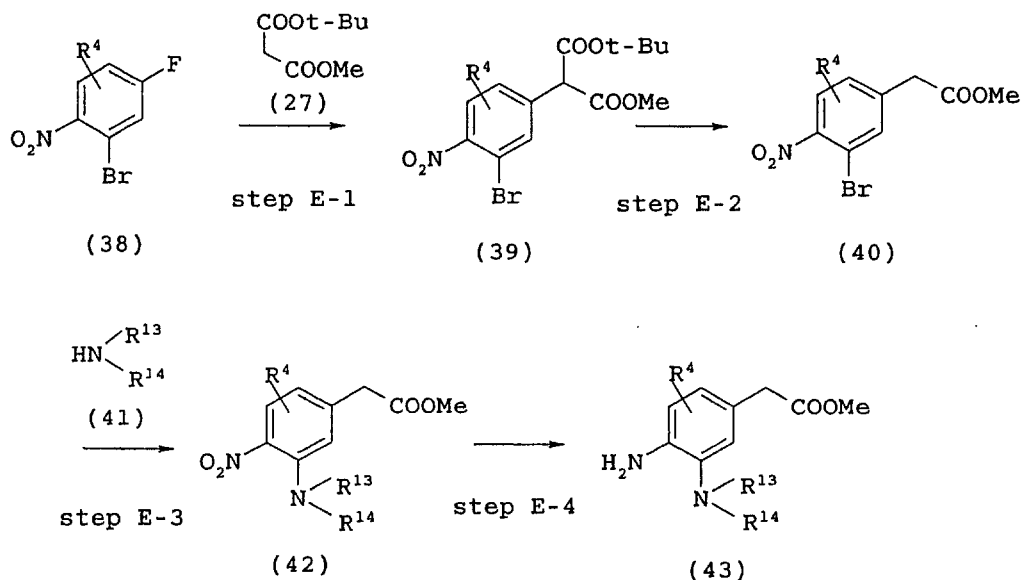
Process E

The following is an example of the process for preparing a compound of the formula (1) wherein ring B is



(wherein R^4 has the same meaning as defined above, R^{34} is
 5 $-N(R^{13})(R^{14})$ in which R^{13} and R^{14} each has the same meaning as defined above), and l' is 1).

Process E



In the above reaction scheme, R^4 , R^{13} , R^{14} , Me and t-Bu each has the same meaning as defined above.

10 Step E-1

In a similar manner to Step A-1 of Process A, a compound of the formula (39) can be prepared by reacting a compound of the formula (38) with a compound of the formula (27).

Step E-2

15 In a similar manner to Step C-3 of Process C, a compound of the formula (40) can be prepared from a compound of the formula

(39).

Step E-3

A compound of the formula (42) can be prepared by reacting a compound of the formula (40) with a compound of the formula
5 (41) without or in a solvent and in the presence of a base.

The solvent used in the reaction includes, for example, ethers such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme, etc.; hydrocarbons such as benzene, toluene, hexane, xylene, etc.; halogenated
10 hydrocarbons such as methylene chloride, chloroform, carbon tetrachloride, 1,2-dichloroethane, etc.; alcohols such as methanol, ethanol, isopropyl alcohol, t-butanol, etc.; esters such as ethyl acetate, methyl acetate, butyl acetate, etc.; and polar solvents such as N,N-dimethylformamide, dimethyl
15 sulfoxide, etc.; and they can be used solely or in combination thereof. A preferred solvent in the present reaction is tetrahydrofuran.

Examples of the bases used in the reaction include organic bases such as triethylamine, pyridine, dimethylaminopyridine,
20 N-methylmorpholine, etc., among which triethylamine or a mixture of triethylamine and dimethylaminopyridine is preferred.

The reaction temperature is about 0°C to 120°C, preferably about room temperature to 100°C.

25 The reaction time is about 2 hours to 48 hours, preferably about 6 hours to 24 hours.

Step E-4

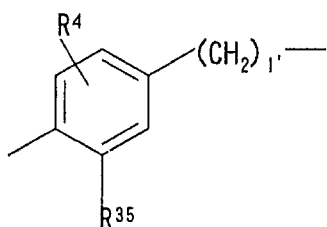
In a similar manner to Step 1-2 of Process 1, a compound of the formula (43) can be prepared from a compound of the formula

(42).

In accordance with the Steps 1-3, 1-4 and 1-5 of the above Process 1, the compounds of the present invention can be prepared from a compound of the formula (43) obtained in the above Step E-4.

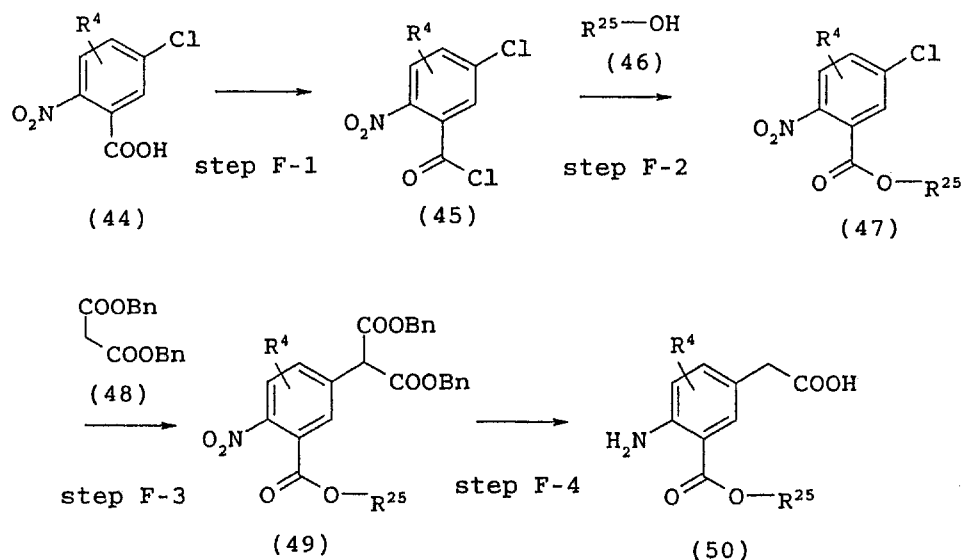
Process F

The following is an example of the process for preparing a compound of the formula (1) wherein ring B is



(wherein R^4 has the same meaning as defined above and R^{35} is $-\text{COO}(R^{25})$ in which R^{25} is $\text{C}_1\text{-C}_6$ alkyl, and $1'$ is 1).

Process F



In the above reaction scheme, R^4 , R^{25} and Bn each has the same meaning as defined above.

Step F-1

In a similar manner to Step 1-1 of Process 1, a compound of the formula (45) can be prepared from a compound of the formula (44).

Step F-2

5 A compound of the formula (47) can be prepared by reacting a compound of the formula (45) with a compound of the formula (46) in a solvent in the presence of a base.

 The solvent used in the reaction includes, for example, ethers such as diethyl ether, tetrahydrofuran, dioxane,
10 1,2-dimethoxyethane, diglyme, etc.; hydrocarbons such as benzene, toluene, hexane, xylene, etc.; halogenated hydrocarbons such as methylene chloride, chloroform, carbon tetrachloride, 1,2-dichloroethane, etc.; and esters such as ethyl acetate, methyl acetate, butyl acetate, etc.; and they
15 can be used solely or in combination thereof. A preferred solvent in the present reaction is tetrahydrofuran.

 Examples of the bases used in the reaction include organic bases such as triethylamine, pyridine, dimethylaminopyridine, N-methylmorpholine, etc., among which triethylamine is
20 preferred.

 The reaction temperature is about -30°C to 80°C , preferably about -20°C to room temperature.

 The reaction time is about 2 hours to 48 hours, preferably about 6 hours to 24 hours.

25 Step F-3

 In a similar manner to Step A-1 of Process A, a compound of the formula (49) can be prepared by reacting a compound of the formula (47) with a compound of the formula (48).

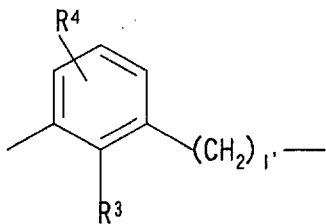
Step F-4

A compound of the formula (49) was reacted in a similar manner to Step 1-2 of Process 1, followed by debenzylation and decarboxylation to give a compound of the formula (50).

In accordance with the alternative process described in Step 1-3 and Step 1-5 of Process 1, the compounds of the present invention can be prepared from a compound of the formula (50) obtained in the above Step F-4.

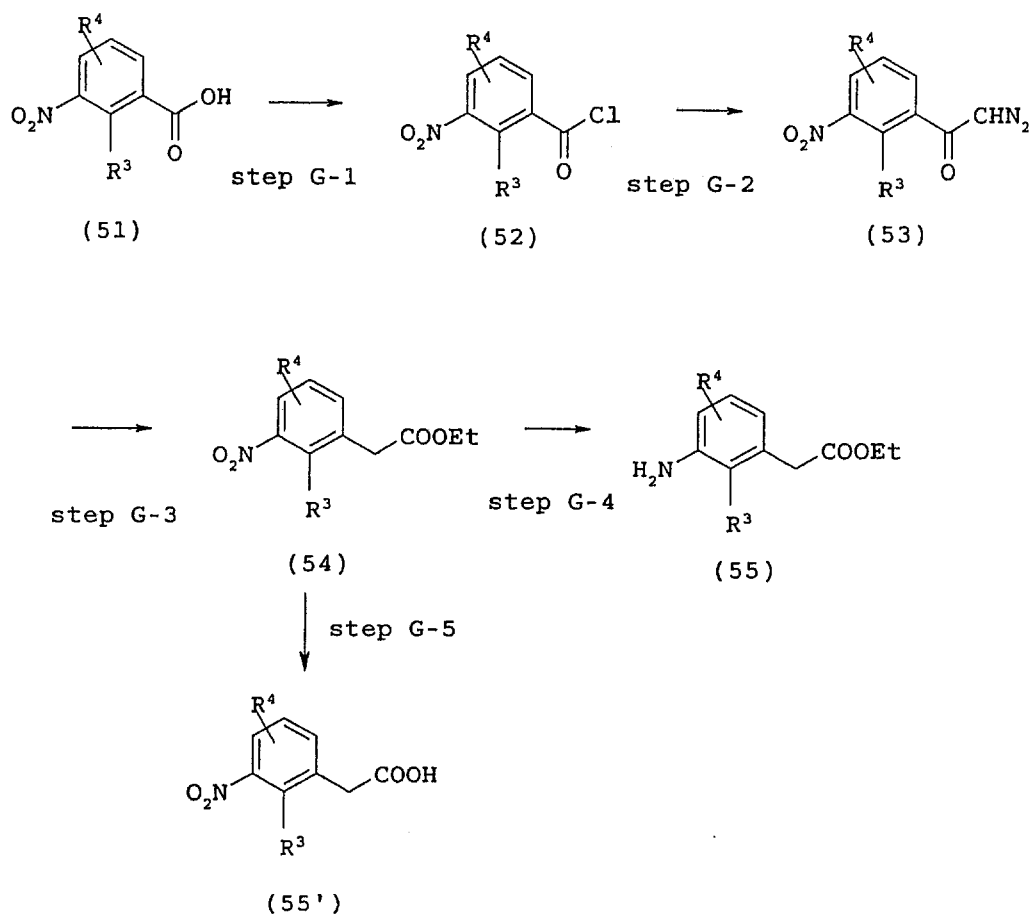
Process G

The following is an example of the process for preparing a compound of the formula (1) wherein ring B is



(wherein R³ and R⁴ each has the same meaning as defined above and l' is 1).

Process G



In the above reaction scheme, R^3 , R^4 and Et each has the same meaning as defined above.

Step G-1

- 5 In a similar manner to Step 1-1 of Process 1, a compound of the formula (52) can be prepared from a compound of the formula (51).

Step G-2

- 10 In a similar manner to Step D-4 of Process D, a compound of the formula (53) can be prepared from a compound of the formula (52).

Step G-3

In a similar manner to Step D-5 of Process D, a compound

of the formula (54) can be prepared from a compound of the formula (53).

Step G-4

In a similar manner to Step D-6 of Process D, a compound
5 of the formula (55) can be prepared from a compound of the formula (54).

In accordance with Steps 1-3, 1-4 and 1-5 of the above Process 1, the compounds of the present invention can be prepared from a compound of the formula (55) obtained above in
10 Step G-4.

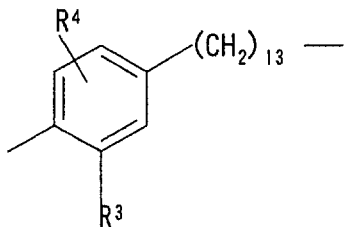
Step G-5

In a similar manner to Step 1-4 of the above Process 1, a compound of the formula (55') can be prepared from a compound of the formula (54).

15 In accordance with Steps 1a-2, 1a-3 and 1a-4 of the above Process 1a, the compounds of the present invention can be prepared from a compound of the formula (55') obtained in the above Step G-5.

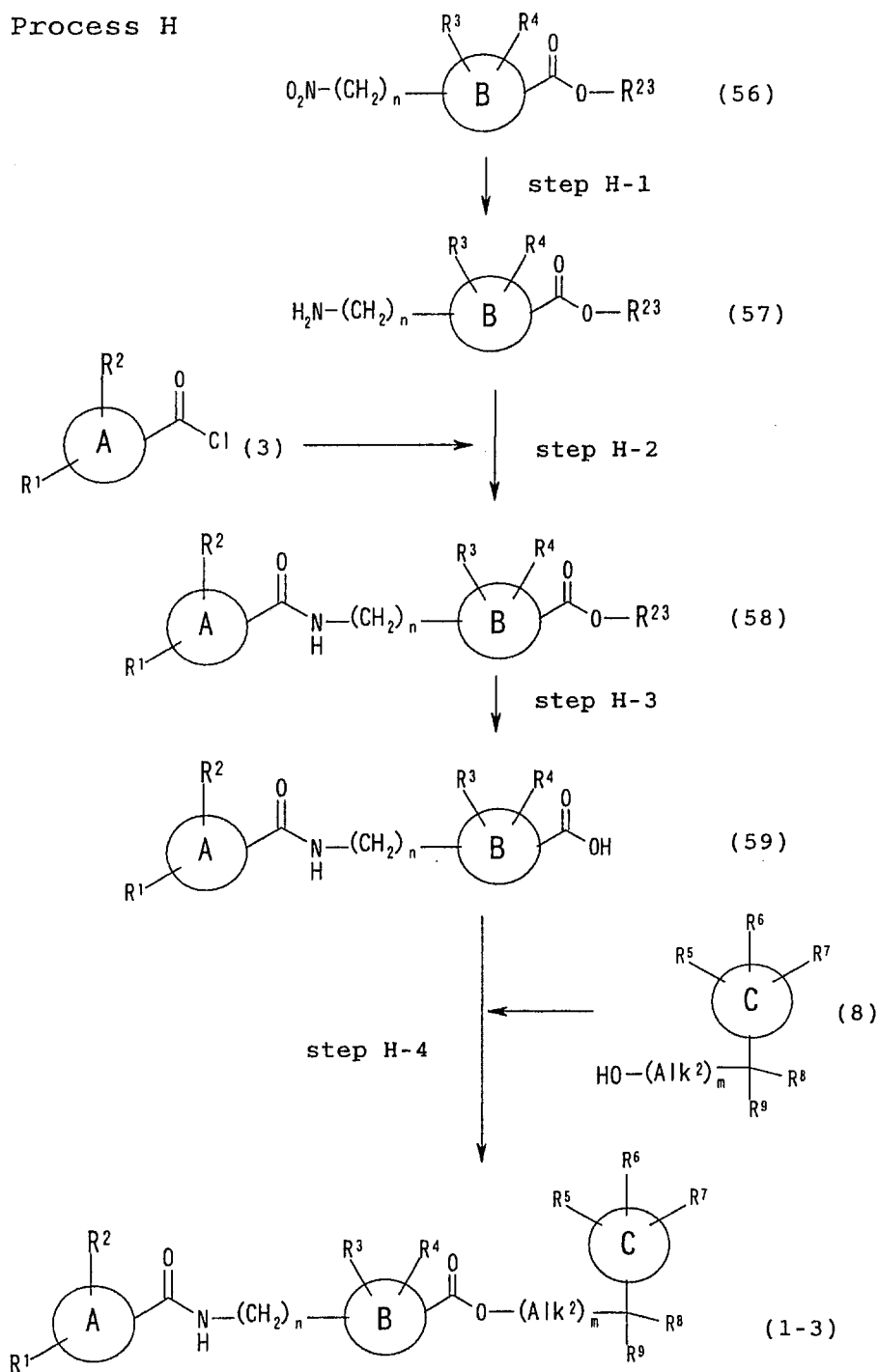
20 Process H

The following is an example of the process for preparing a compound of the formula (1) wherein ring B is



(wherein R³ and R⁴ each has the same meaning as defined above
25 and 13 is 0).

Process H



In the above reaction scheme, R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , R^{23} , Alk^2 , ring A, ring B, ring C, m and n each has the same meaning as defined above.

5 Step H-1

In a similar manner to Step 1-2 of Process 1, a compound of the formula (57) can be prepared from a compound of the formula (56).

Step H-2

- 5 In a similar manner to Step 1-3 of Process 1, a compound of the formula (58) can be prepared by reacting a compound of the formula (57) obtained in Step of H-1 (or commercially available product) with a compound of the formula (3).

Step H-3

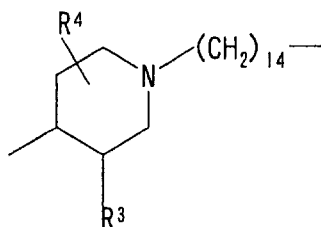
- 10 In a similar manner to Step 1-4 of Process 1, a compound of the formula (59) can be prepared from a compound of the formula (58).

Step H-4

- 15 In a similar manner to Step 1-5 of Process 1, a compound of the formula (1-3) which is one of the objective compounds can be prepared by reacting a compound of the formula (59) with a compound of the formula (8).

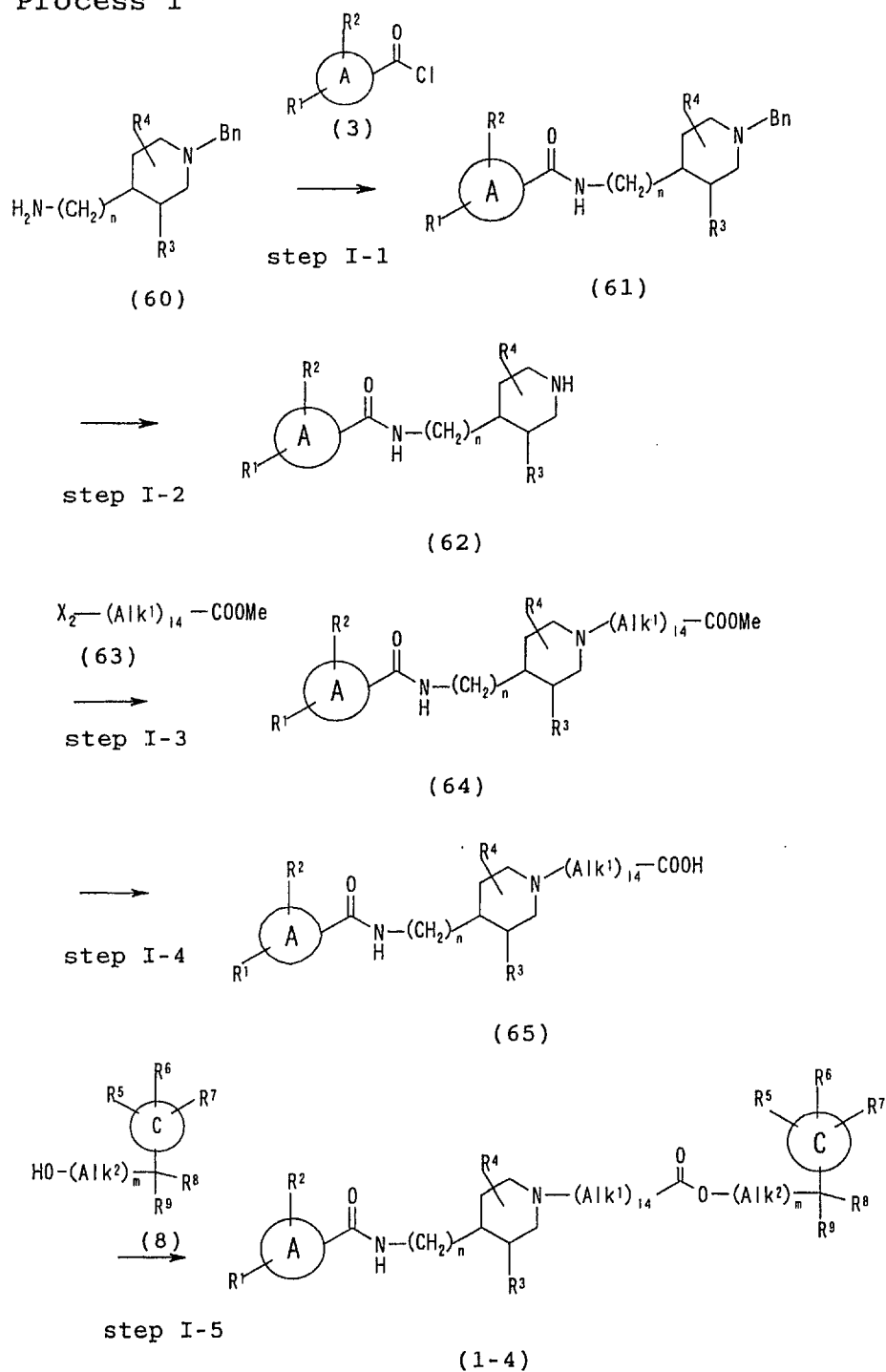
Process I

- 20 The following is an example of the process for preparing a compound of the formula (1) wherein ring B is



(wherein R^3 and R^4 each has the same meaning as defined above and 14 is 1 to 3).

Process I



In the above reaction scheme, R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, 14, m, n, ring A, ring C, Bn, Me, Alk¹, Alk² and X₂ each

has the same meaning as defined above.

Step I-1

In a similar manner to Step 1-3 of Process 1, a compound of the formula (61) can be prepared by reacting a compound of the formula (60) with a compound of the formula (3).

Step I-2

Under conditions similar to Step 1-2 of Process 1, with the proviso that palladium hydroxide is used as a catalyst, a compound of the formula (62) can be prepared from a compound of the formula (61).

Step I-3

A compound of the formula (64) can be prepared by reacting a compound of the formula (62) with a compound of the formula (63) in a solvent in the presence of a base. Alternatively, $X_2-(Alk^1)_{14}-COOEt$ (in the formula, X_2 , Alk^1 , 14 and Et each has the same meaning as defined above) may be used in place of a compound of the formula (63).

The solvent used in the reaction includes, for example, ethers such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme, etc.; hydrocarbons such as benzene, toluene, hexane, xylene, etc.; alcohols such as methanol, ethanol, isopropyl alcohol, t-butanol, etc.; esters such as ethyl acetate, methyl acetate, butyl acetate, etc.; polar solvents such as acetone, N,N-dimethylformamide, dimethyl sulfoxide, etc.; and they can be used solely or in combination thereof. A preferred solvent in the present reaction is N,N-dimethylformamide.

Examples of the bases used in the reaction include alkali metal hydrides such as sodium hydride, potassium hydride, etc.;

alkali metal alkoxides such as sodium ethoxide, sodium methoxide, potassium t-butoxide, etc.; alkali metal carbonates such as sodium carbonate, potassium carbonate, etc.; alkali metal hydroxides such as lithium hydroxide, sodium hydroxide, 5 potassium hydroxide, etc.; alkali metal carboxylates such as sodium acetate, potassium acetate, etc.; and alkali metal phosphates such as sodium phosphate, potassium phosphate, etc., among which potassium carbonate or sodium hydride is preferred.

The reaction temperature is about 0°C to 150°C, preferably 10 about room temperature to 100°C.

The reaction time is about 1 hour to 48 hours, preferably about 2 hours to 24 hours.

Step I-4

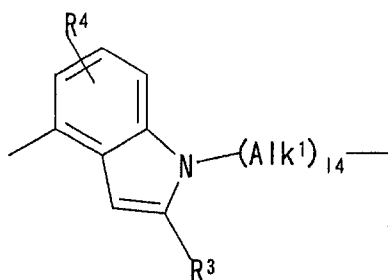
In a similar manner to Step 1-4 of Process 1, a compound 15 of the formula (65) can be prepared from a compound of the formula (64).

Step I-5

In a similar manner to Step 1-5 of Process 1, a compound of the formula (1-4) which is one of the objective compounds 20 can be prepared by reacting a compound of the formula (65) with a compound of the formula (8).

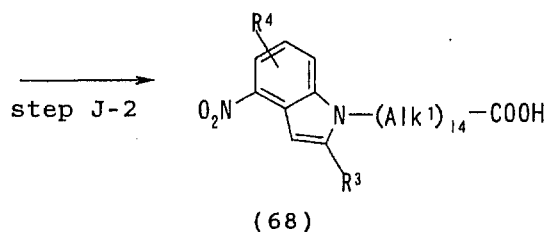
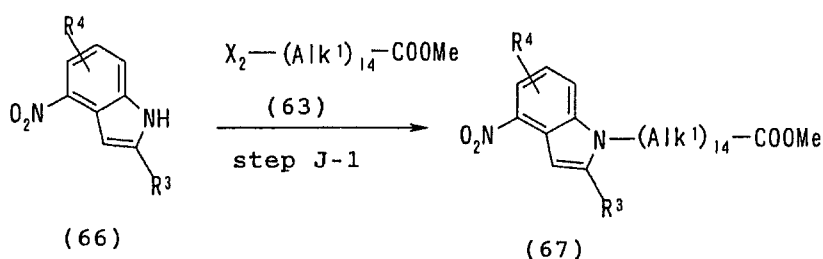
Process J

The following is an example of the process for preparing 25 a compound of the formula (1) wherein ring B is



(wherein R^3 , R^4 and Alk^1 each has the same meaning as defined above and 14 is 1 to 3).

Process J



- 5 In the above reaction scheme, R^3 , R^4 , Me, Alk^1 , 14 and X_2 each has the same meaning as defined above.

Step J-1

In a similar manner to Step I-3 of Process I, a compound of the formula (67) can be prepared by reacting a compound of the formula (66) with a compound of the formula (63).
 10 the formula (66) with a compound of the formula (63). Alternatively, $X_2-(Alk^1)_{14}-COOEt$ (in the formula X_2 , Alk^1 , 14 and Et each has the same meaning as defined above) may be used in place of a compound of the formula (63).

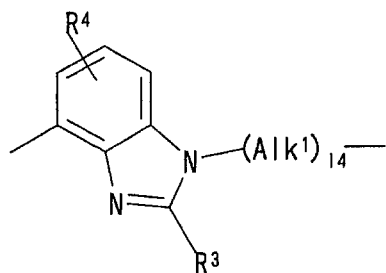
Step J-2

In accordance with the Step I-4 of Process I, a compound of the formula (68) can be prepared from a compound of the formula (67).

In a similar manner to Steps 1a-2, 1a-3 and 1a-4 of Process 5 1a, the compounds of the present invention can be prepared from a compound of the formula (68) obtained in the above Step J-2.

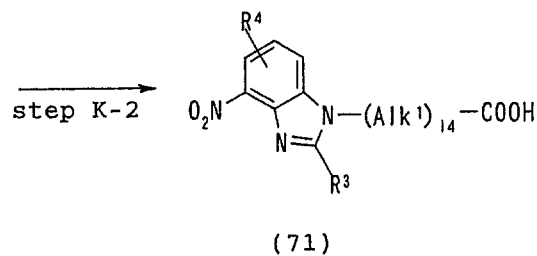
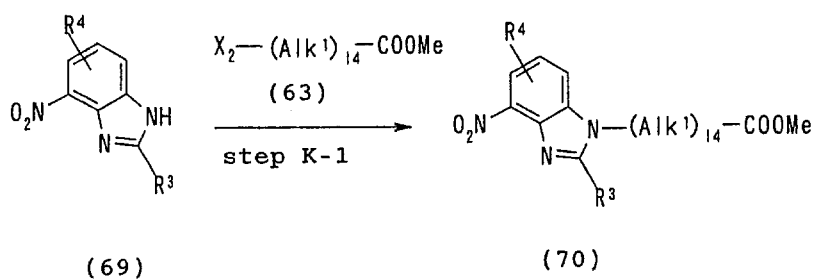
Process K

The following is an example of the process for preparing 10 a compound of the formula (1) wherein ring B is



(wherein R^3 , R^4 , 14 and Alk^1 each has the same meaning as defined above).

Process K



In the above reaction scheme, R^3 , R^4 , Me, 14, Alk^1 and X_2 each has the same meaning as defined above.

Step K-1

In a similar manner to Step I-3 of Process I, a compound
5 of the formula (70) can be prepared by reacting a compound of the formula (69) with a compound of the formula (63). Alternatively, $X_2-(Alk^1)_{14}-COOEt$ (in the formula X_2 , Alk^1 , 14 and Et each has the same meaning as defined above) may be used in place of a compound of the formula (63).

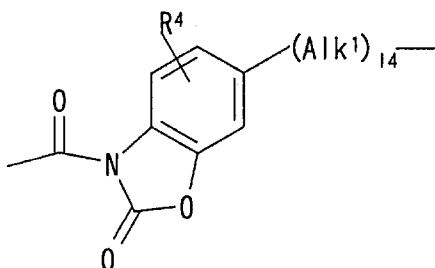
10 Step K-2

In a similar manner to Step I-4 of Process I, a compound of the formula (71) can be prepared from a compound of the formula (70).

In accordance with the Steps 1a-2, 1a-3 and 1a-4 of the
15 above Process 1a, the compounds of the present invention can be prepared from a compound of the formula (71) obtained in the above Step K-2.

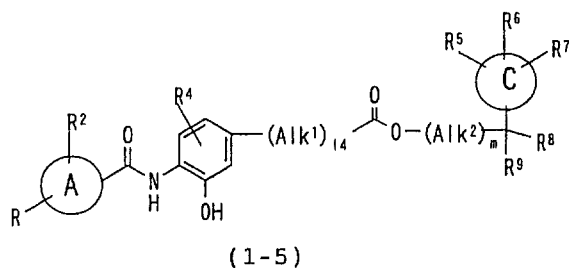
Process L

20 The following is an example of the process for preparing a compound of the formula (1) wherein R^3 of the ring B, and R^{10} of the X are taken together to form

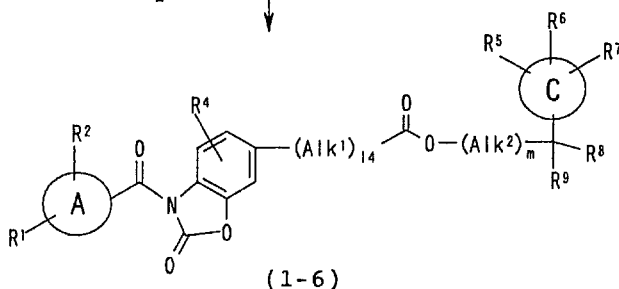


(wherein R^4 , 14 and Alk^1 each has the same meaning as defined
25 above).

Process L



step L-1
↓



In the above reaction scheme, R^1 , R^2 , R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , 14, m , ring A, ring C, Alk^1 and Alk^2 each has the same meaning as defined above.

5 Step L-1

A compound of the formula (1-5) obtained by debenzylation of a compound (wherein R^{26} is benzyl) obtained in the Process 1 and the Process D is reacted with a phosgene equivalent reagent (for example, triphosgene or diphosgene, etc.) in a solvent in
10 the presence of a base to give a compound of the formula (1-6).

The solvent used in the reaction includes, for example, ethers such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme, etc.; hydrocarbons such as benzene, toluene, hexane, xylene, etc.; halogenated
15 hydrocarbons such as methylene chloride, chloroform, carbon tetrachloride, 1,2-dichloroethane, etc.; and they can be used solely or in combination thereof. A preferred solvent in the present reaction is chloroform.

Examples of the bases used in the reaction include organic bases such as triethylamine, pyridine, dimethylaminopyridine, N-methylmorpholine, etc., among which triethylamine is preferred.

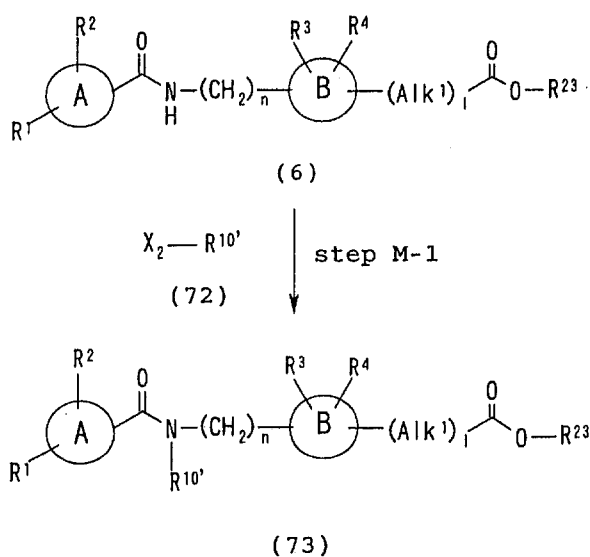
- 5 The reaction temperature is about -20°C to 100°C , preferably about 0°C to room temperature.

The reaction time is about 10 minutes to 4 hours, preferably about 30 minutes to 2 hours.

10 Process M

The following is an example of the process for preparing a compound of the formula (1) wherein R^{10} is other than hydrogen.

Process M



- In the above reaction scheme, R^1 , R^2 , R^3 , R^4 , R^{23} , l , n ,
 15 X_2 , ring A, ring B, and Alk^1 each has the same meaning as defined above, and $\text{R}^{10'}$ is $\text{C}_1\text{-C}_6$ alkyl or $\text{C}_3\text{-C}_7$ cycloalkyl).

Step M-1

A compound of the formula (73) can be prepared by reacting

a compound of the formula (6) obtained in the Step 1-3 of Process 1 with a compound of the formula (72) in a solvent in the presence of a base.

The solvent used in the reaction includes, for example,
5 ethers such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme, etc.; hydrocarbons such as benzene, toluene, hexane, xylene, etc.; esters such as ethyl acetate, methyl acetate, butyl acetate, etc.; and polar solvents such as acetone, N,N-dimethylformamide, dimethyl
10 sulfoxide, etc.; and they can be used solely or in combination thereof. A preferred solvent in the present reaction is N,N-dimethylformamide.

Examples of the bases used in the reaction include alkali metal hydrides such as sodium hydride, potassium hydride, etc.;
15 alkali metal alkoxides such as sodium ethoxide, sodium methoxide, potassium t-butoxide, etc.; alkali metal carbonates such as sodium carbonate, potassium carbonate, etc.; alkali metal carboxylates such as sodium acetate, potassium acetate, etc.; and alkali metal phosphates such as sodium phosphate,
20 potassium phosphate, etc., among which sodium hydride is preferred.

The reaction temperature is about 0°C to 100°C, preferably about room temperature to 80°C.

The reaction time is about 1 hour to 24 hours, preferably
25 about 2 hours to 8 hours.

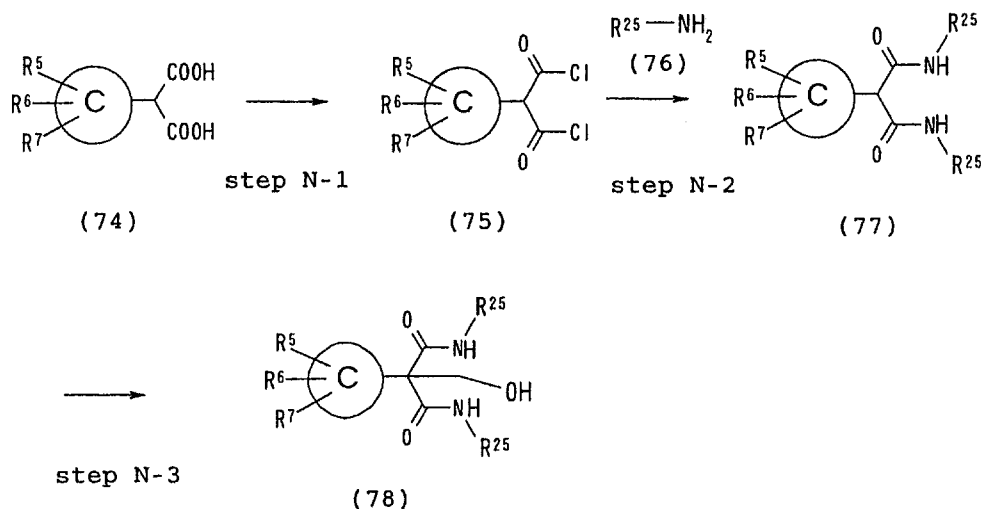
In accordance with the above Steps 1-4 and 1-5, the compounds of the present invention can be prepared from a compound of the formula (73) obtained in the above Step M-1.

Process N

The following is an example of the process for preparing a compound of the formula (1) wherein R^8 and R^9 are each $-\text{CONH}(R^{19'})$ (wherein $R^{19'}$ is $\text{C}_1\text{-C}_6$ alkyl).

5

Process N



In the above reaction scheme, R^5 , R^6 , R^7 , R^{25} and ring C each has the same meaning as defined above.

Step N-1

10 A compound of the formula (75) can be prepared by reacting a compound of the formula (74) with thionyl chloride or oxalyl chloride in a solvent.

The solvent used in the reaction includes, for example, ethers such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme, etc.; hydrocarbons such as benzene, toluene, hexane, xylene, etc.; halogenated hydrocarbons such as methylene chloride, chloroform, carbon tetrachloride, 1,2-dichloroethane, etc.; and esters such as ethyl acetate, methyl acetate, butyl acetate, etc.; and they
 15
 20 can be used solely or in combination thereof. A preferred

solvent used in the present reaction is toluene containing a catalytic amount of N,N-dimethylformamide.

The reaction temperature is about room temperature to 120°C, preferably about 50°C to 100°C.

5 The reaction time is about 10 minutes to 6 hours, preferably about 30 minutes to 3 hours.

Step N-2

A compound of the formula (77) can be prepared by reacting a compound of the formula (75) with a compound of the formula
10 (76) in a solvent in the presence of a base.

The solvent used in the reaction includes, for example, ethers such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme, etc.; hydrocarbons such as benzene, toluene, hexane, xylene, etc.; halogenated
15 hydrocarbons such as methylene chloride, chloroform, carbon tetrachloride, 1,2-dichloroethane, etc.; and esters such as ethyl acetate, methyl acetate, butyl acetate, etc.; and they can be used solely or in combination thereof. Preferred solvents in the present reaction are methylene chloride or
20 tetrahydrofuran.

Examples of the bases used in the reaction include organic bases such as triethylamine, pyridine, dimethylaminopyridine, N-methylmorpholine, etc., among which triethylamine is preferred.

25 The reaction temperature is about -40°C to 60°C, preferably about -30°C to room temperature.

The reaction time is about 2 hours to 48 hours, preferably about 6 hours to 24 hours.

Step N-3

A compound of the formula (78) can be prepared by reacting a compound of the formula (77) with paraformaldehyde or formalin without or in a solvent in the presence of a catalytic amount of a base.

5 The solvent used in the reaction includes, for example, ethers such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme, etc.; hydrocarbons such as benzene, toluene, hexane, xylene, etc.; halogenated hydrocarbons such as methylene chloride, chloroform, carbon
10 tetrachloride, 1,2-dichloroethane, etc.; alcohols such as methanol, ethanol, isopropyl alcohol, t-butanol, etc.; esters such as ethyl acetate, methyl acetate, butyl acetate, etc.; and polar solvents such as N,N-dimethylformamide, dimethyl sulfoxide, etc.; and they can be used solely or in combination
15 thereof. A preferred solvent in the present reaction is tetrahydrofuran.

 Examples of the bases used in the reaction include alkali metal hydrides such as sodium hydride, potassium hydride, etc.; alkali metal alkoxides such as sodium ethoxide, sodium
20 methoxide, potassium t-butoxide, etc.; alkali metal hydroxides such as sodium hydroxide, potassium hydroxide, lithium hydroxide, etc.; alkali metal carbonates such as sodium carbonate, potassium carbonate, etc.; and organic bases such as triethylamine, diethylamine, pyridine, etc., among which
25 potassium t-butoxide, sodium ethoxide or potassium hydroxide is preferred.

The reaction temperature is about 0°C to 100°C, preferably about room temperature to 80°C.

The reaction time is about 10 minutes to 24 hours,

preferably about 30 minutes to 12 hours.

In accordance with the above Processes 1, 1a and 2, the compounds of the present invention can be prepared using a compound of the formula (78) obtained in the above Step N-3 in place of a compound of the formula (8).

Process O

The following is an example of the process for preparing a compound of the formula (1) wherein R^8 and R^9 are each $-\text{COOR}^{25}$ (wherein R^{25} is $\text{C}_1\text{-C}_6$ alkyl).

Process O



In the above reaction scheme, R^5 , R^6 , R^7 , R^{25} and ring C each has the same meaning as defined above.

Step O-1

In a similar manner to Step N-3 of Process N, a compound of the formula (80) can be prepared from a compound of the formula (79).

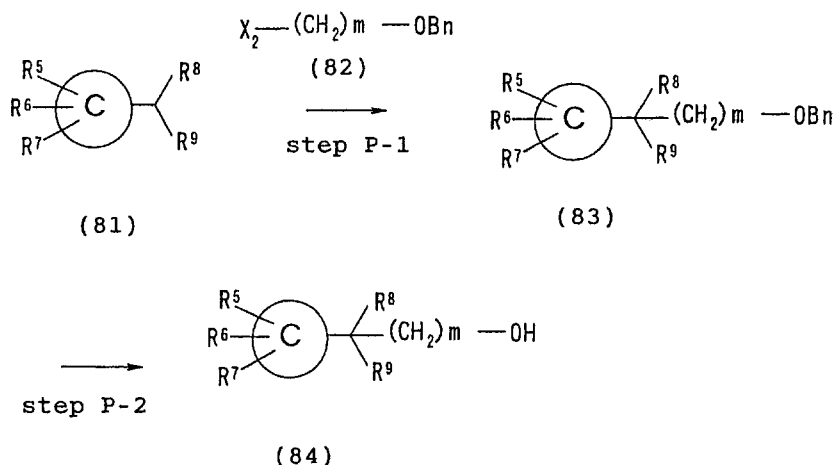
In accordance with the above Processes 1, 1a and 2, the compounds of the present invention can be prepared using a compound of the formula (80) obtained in the above Step O-1 in place of a compound of the formula (8).

Process P

The following is an example of the process for preparing

a compound of the formula (1) wherein m is 2 or 3. In this process, tert-butyldimethylsilyl (TBS) may be used in place of benzyl (Bn).

Process P



5 In the above reaction scheme, R⁵, R⁶, R⁷, R⁸, R⁹, X₂, m, Bn and ring C each has the same meaning as defined above.

Step P-1

A compound of the formula (83) can be prepared by reacting a compound of the formula (81) with a compound of the formula
10 (82) in a solvent in the presence of a base.

The solvent used in the reaction includes, for example, ethers such as diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane, diglyme, etc.; hydrocarbons such as benzene, toluene, hexane, xylene, etc.; halogenated
15 hydrocarbons such as methylene chloride, chloroform, carbon tetrachloride, 1,2-dichloroethane, etc.; alcohols such as methanol, ethanol, isopropyl alcohol, t-butanol, etc.; esters such as ethyl acetate, methyl acetate, butyl acetate, etc.; and polar solvents such as N,N-dimethylformamide, dimethyl
20 sulfoxide, etc.; and they can be used solely or in combination

thereof. Preferred solvents in the present reaction are N,N-dimethylformamide or tetrahydrofuran.

Examples of the bases used in the reaction include alkali metal hydrides such as sodium hydride, potassium hydride, etc.;
5 alkali metal alkoxides such as sodium ethoxide, sodium methoxide, potassium t-butoxide, etc.; alkali metal carbonates such as sodium carbonate, potassium carbonate, etc.; and organoalkali metals such as lithium diisopropylamide, etc., among which sodium hydride or lithium diisopropylamide is
10 preferred.

The reaction temperature is about 0°C to 100°C, preferably about room temperature to 80°C

The reaction time is about 30 minutes to 48 hours, preferably about 2 hours to 24 hours.

15 Step P-2

In a similar manner to Step 2-2 of Process 2, a compound of the formula (84) can be prepared from a compound of the formula (83).

In accordance with the above Processes 1, 1a and 2, the
20 compounds of the present invention can be prepared using a compound of the formula (84) obtained in the above Step P-2 in place of a compound of the formula (8).

Examples

25 The present invention is illustrated in more detail by Examples given below, but it goes without saying that the present invention is not limited thereto. In the Examples, Me is methyl, Et is ethyl, tBu is t-butyl and TBS is tert-butyldimethylsilyl.

Example 1

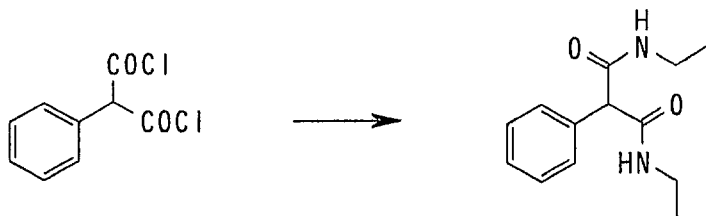
4-[(4'-Trifluoromethylbiphenyl-2-carbonyl)amino]phenyl-
acetic acid 2,2-bisethylcarbamoyl-2-phenylethyl ester

5 a) phenylmalonic acid dichloride



Thionyl chloride (13.7 mL) was added dropwise to a mixture
of phenylmalonic acid (11.31 g), dimethylformamide (230 μ L)
and toluene (27 mL) under ice-cooling. The mixture was
10 stirred at 80°C for 70 minutes, and the solvent was removed
off by evaporation. After azeotropic distillation with
toluene, the residue was dried in vacuo to give the title
compound (11.61 g).

b) Phenylmalonic acid diethylamide

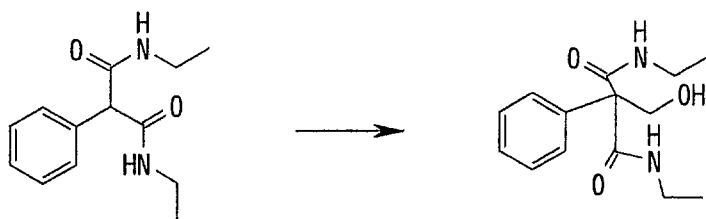


15

To a mixed solution of ethylamine in tetrahydrofuran (2M,
45.5 mL), triethylamine (13.9 mL) and methylene chloride (80
mL) was dropwise added the phenylmalonic acid dichloride (8.99
g) obtained in Example 1-a) at -20°C. The mixture was stirred
20 overnight while the temperature was raised to room temperature,
and then diluted with ethyl acetate after addition of 3N
hydrochloric acid. The organic layer was washed with
saturated brine, saturated aqueous sodium bicarbonate and

saturated brine, dried over sodium sulfate and concentrated. The resulting solid was washed with ethyl acetate and hexane to give the title compound (4.85 g) as a white powder.

c) 2-Hydroxymethyl-2-phenylmalonic acid diethylamide

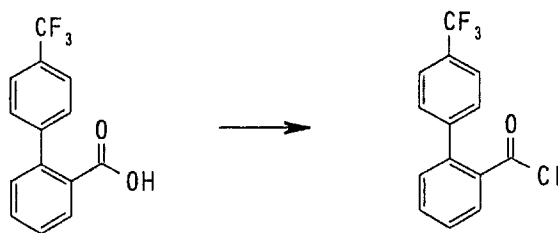


5

The phenylmalonic acid diethylamide (2.34 g) obtained in Example 1-b) and paraformamide (390 mg) were suspended in tetrahydrofuran (20 ml), and to this suspension was added potassium hydroxide (catalytic amount) at 60°C. The mixture was stirred for 5 hours and concentrated to remove the solvent. The residue was chromatographed on a column of silica gel with ethyl acetate:hexane=1:1 to give the title compound (2.31 g).

10

d) 4'-Trifluoromethylbiphenyl-2-carboxylic acid chloride

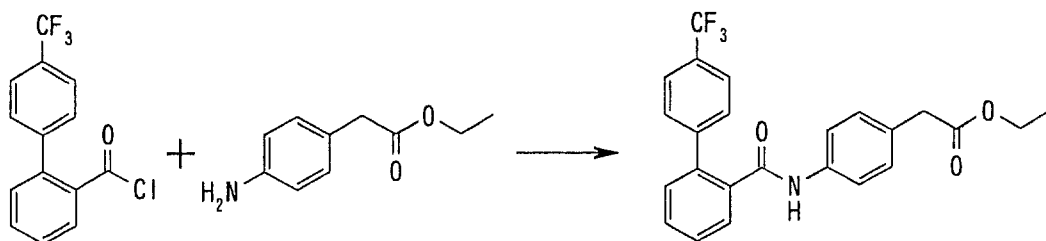


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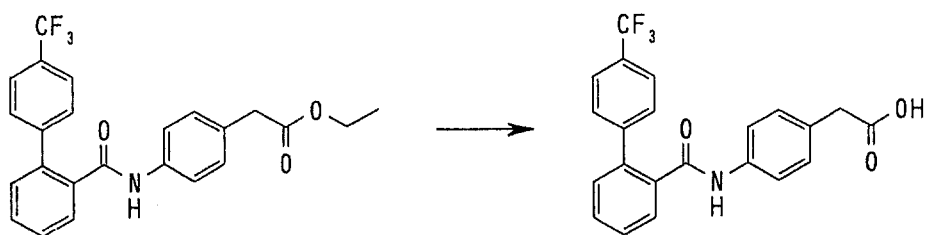
To a mixture of 4'-trifluoromethylbiphenyl-2-carboxylic acid (5.06 g), dimethylformamide (catalytic amount) and methylene chloride (30 mL) was added dropwise oxalyl chloride (2.43 mL) under ice-cooling. The mixture was stirred at room temperature for 100 minutes and the solvent was removed by evaporation. After azeotropic distillation with toluene, the residue was dried in vacuo to give the title compound (5.40 g).

20

e) 4-[(4'-Trifluoromethylbiphenyl-2-carbonyl)amino]phenylacetic acid ethyl ester



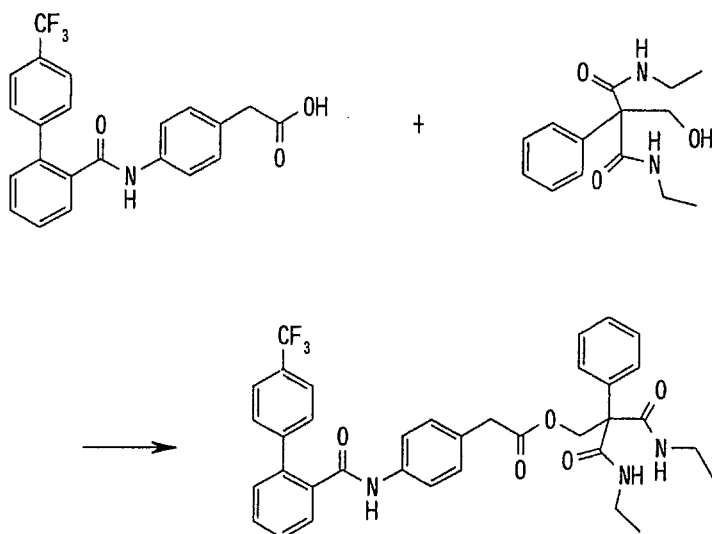
To a mixture of 4-aminophenylacetic acid ethyl ester
 5 (3.41 g), triethylamine (3.2 mL) and methylene chloride (30 mL)
 was added dropwise a solution of the 4'-
 trifluoromethylbiphenyl-2-carboxylic acid chloride (5.40 g)
 obtained in Example 1-d) in methylene chloride (10 mL) under
 ice-cooling, and the mixture was stirred at room temperature
 10 overnight. After addition of 1N hydrochloric acid, the
 reaction mixture was diluted with ethyl acetate, and the organic
 layer was washed with saturated brine, saturated aqueous sodium
 bicarbonate and saturated brine, dried over sodium sulfate, and
 then concentrated to give the title compound (8.12 g).
 15 f) 4-[(4'-Trifluoromethylbiphenyl-2-carbonyl)amino]phenyl-
 acetic acid



The 4-[(4'-Trifluoromethylbiphenyl-2-
 carbonyl)amino]phenylacetic acid ethyl ester (8.12 g) obtained
 20 in Example 1-e) was dissolved in 40 mL of tetrahydrofuran and
 20 mL of ethanol. After addition of 4N sodium hydroxide (5 mL),

the solution was stirred at room temperature for 5 hours and concentrated. The powder formed upon addition of 1N hydrochloric acid was collected by filtration and dried in vacuo to give the title compound (7.48 g).

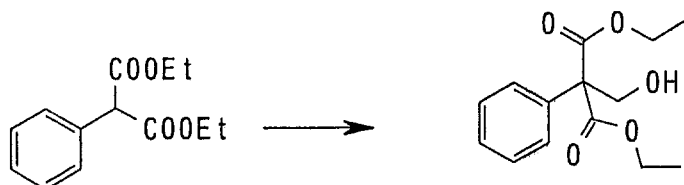
- 5 g) 4-[(4'-Trifluoromethylbiphenyl-2-carbonyl)amino]phenylacetic acid 2,2-bisethylethylcarbamoyl-2-phenylethyl ester



- The 4-[(4'-Trifluoromethylbiphenyl-2-carbonyl)amino]phenylacetic acid (519 mg) obtained in Example 1-f), the 2-hydroxymethyl-2-phenylmalonic acid diethylamide (317 mg) obtained in Example 1-c), dimethylaminopyridine (171 mg) and 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide hydrochloride (WSC.HCl)(268 mg) were dissolved in methylene chloride (5 ml). The solution was stirred at room temperature for 6 hours and the solvent was removed off by evaporation. The residue was purified by column chromatography on silica gel with ethyl acetate:hexane=1:1 to 3:2 to give the title compound (725 mg)(see Table 1).

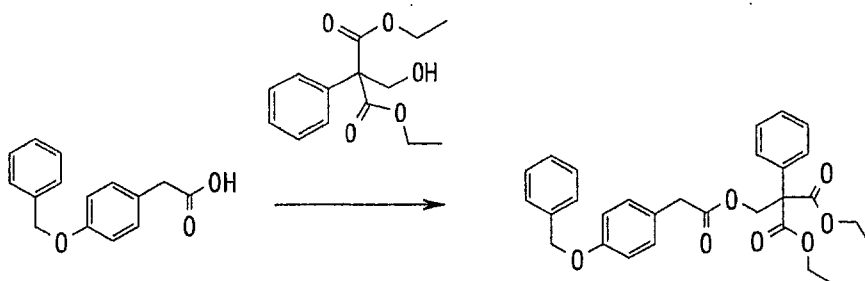
2-Phenyl-2-{2-[4-(4'-trifluoromethylbiphenyl-2-carbonyloxy)phenyl]acetoxymethyl}malonic acid diethyl ester

a) 2-Hydroxymethyl-2-phenylmalonic acid diethyl ester



5 Paraformaldehyde (720 mg) was suspended in phenylmalonic acid diethyl ester (4.73 g), and a catalytic amount of potassium hydroxide was added thereto at 60°C. After stirring for 1.5 hours, the reaction mixture was purified by column chromatography on silica gel with ethyl acetate:hexane=1:5 to 1:2 to give the title compound (4.96 g).

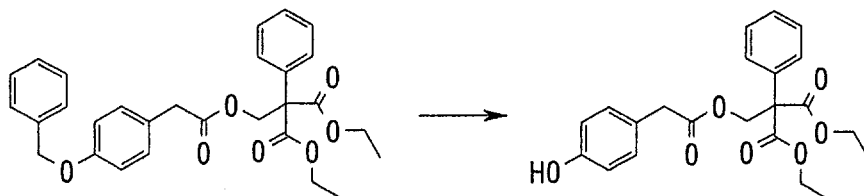
b) 2-[2-(4-(Benzyloxyphenyl)acetoxymethyl)]-2-phenylmalonic acid diethyl ester



15 4-Benzyloxyphenylacetic acid (1.09 g) was suspended in methylene chloride (50 mL) and the suspension was dissolved by addition of dimethylaminopyridine (0.511 g). To the solution was added the 2-hydroxymethyl-2-phenylmalonic acid diethyl ester (1.20 g) obtained in Example 1-2 a), and 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide
20 hydrochloride (0.864 g) was portionwise added thereto. The mixture was stirred at room temperature overnight and then

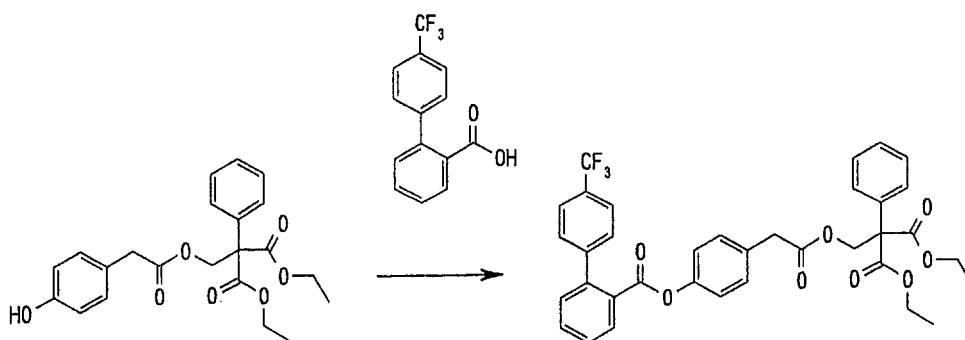
concentrated. The residue was purified by column chromatography on silica gel with ethyl acetate:hexane=1:4 to give the title compound (1.95 g) as a colorless oil.

c) 2-[2-(4-(Hydroxyphenyl)acetoxymethyl)-2-phenylmalonic acid diethyl ester



The 2-[2-(4-(Benzyloxyphenyl)acetoxymethyl)-2-phenylmalonic acid diethyl ester (1.95 g) obtained in Example 1-2 b) was dissolved in methanol (2.5 mL). The solution was subjected to hydrogenation in the presence of 7.5% palladium-carbon (0.200 g) under normal pressure for 4 hours. The reaction solution was filtered through a Celite pad and concentrated to give the title compound (1.71 g) as a colorless oil.

d) 2-Phenyl-2-{2-[4-(4'-trifluoromethylbiphenyl-2-carboxyloxy)phenyl]acetoxymethyl}malonic acid diethyl ester



4'-Trifluoromethylbiphenyl-2-carboxylic acid (0.266 g) was suspended in methylene chloride (10 mL), and the suspension was dissolved by addition of 4-dimethylaminopyridine (0.122 g). To the solution was added the

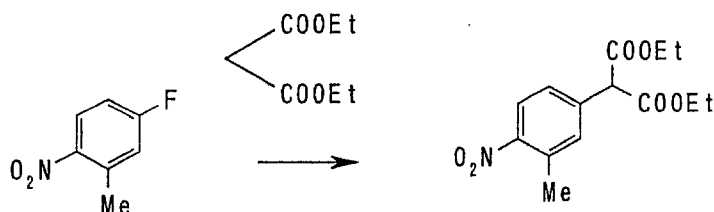
2-[2-(4-(hydroxyphenyl)acetoxymethyl)-2-phenylmalonic acid diethyl ester (0.400 g) obtained in Example 1-2 c), and 1-ethyl-3-(3'- dimethylaminopropyl)carbodiimide hydrochloride (0.192 g) was portionwise added thereto. The mixture was stirred at room temperature overnight and then concentrated. The residue was purified by column chromatography on silica gel with ethyl acetate:hexane=1:3 to give the title compound (0.55 g) as an amorphous powder (see Table 1).

10

Example 1-3

2-(2-{3-Methyl-4-[(4'-trifluoromethylbiphenyl-2-carbonyl)amino]phenyl}acetoxymethyl)-2-phenylmalonic acid diethyl ester

15 a) 2-(3-Methyl-4-nitrophenyl)malonic acid diethyl ester

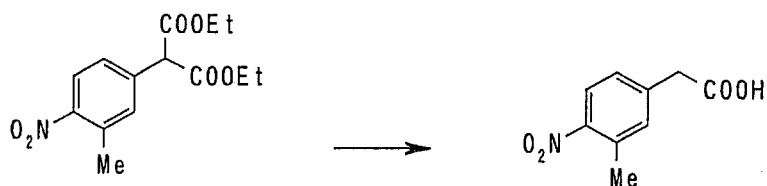


Sodium hydride (60% mineral oil; 0.599 g) was suspended in dimethylformamide (10 mL), and a solution of malonic acid diethyl ester (2.00 g) in dimethylformamide (10 mL) was added dropwise thereto under ice-cooling. After foam generation is stopped, a solution of 4-fluoro-2-methylnitrobenzene (1.94 g) in dimethylformamide (5 mL) was added thereto, and the reaction temperature was raised to 100°C, followed by stirring for 6 hours. The reaction mixture was concentrated, acidified with 1N hydrochloric acid and extracted with ethyl acetate. The extract was washed successively with water and saturated brine,

25

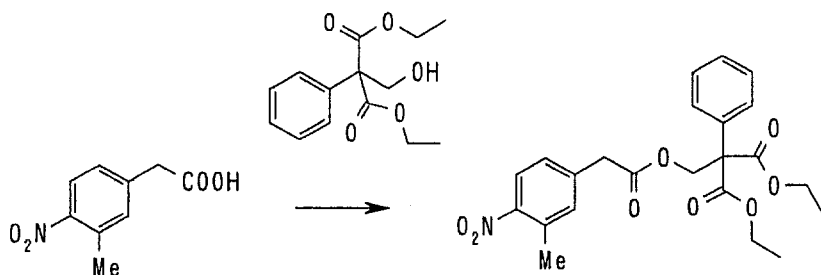
dried over sodium sulfate and concentrated. The residue was purified by column chromatography on silica gel with ethyl acetate:hexane=1:5 to give the title compound (1.65 g) as a yellow oil.

5 b) (3-Methyl-4-nitrophenyl)acetic acid



Potassium hydroxide (0.168 g) was dissolved in 7 mL of methanol and 1 mL of water, and the 2-(3-methyl-4-nitrophenyl)malonic acid diethyl ester (0.250 g) obtained in
 10 Example 1-3 a) was dissolved in the solution. The solution was stirred at 100°C for 2 hours and concentrated. The residue was acidified with 2N hydrochloric acid and extracted with ethyl acetate. The extract was washed with saturated brine, dried over sodium sulfate and concentrated to give the title compound
 15 (0.143 g) as a yellow solid.

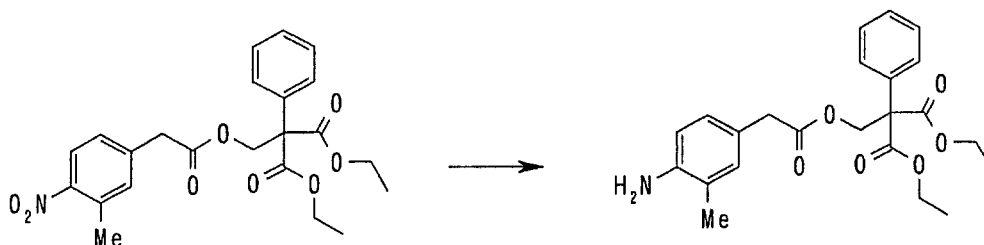
c) 2-[2-(3-Methyl-4-nitrophenyl)acetoxymethyl]-2-phenyl-malonic acid diethyl ester



The (3-Methyl-4-nitrophenyl)acetic acid (0.143 g)
 20 obtained in Example 1-3 b) was dissolved in methylene chloride (5 mL). To the solution were added 2-(3-methyl-4-nitrophenyl)malonic acid diethyl ester (0.195

g) obtained in Example 1-2 a), 4-dimethylaminopyridine (0.090 g) and 1-ethyl-3-(3'- dimethylaminopropyl)carbodiimide hydrochloride (0.141 g), and the mixture was stirred at room temperature overnight. The reaction mixture was concentrated and the residue was purified by column chromatography on silica gel with ethyl acetate:hexane=1:4 to give the title compound (0.219 g) as a yellow oil.

d) 2-[2-(4-Amino-3-methylphenyl)acetoxymethyl]-2-phenyl-malonic acid diethyl ester

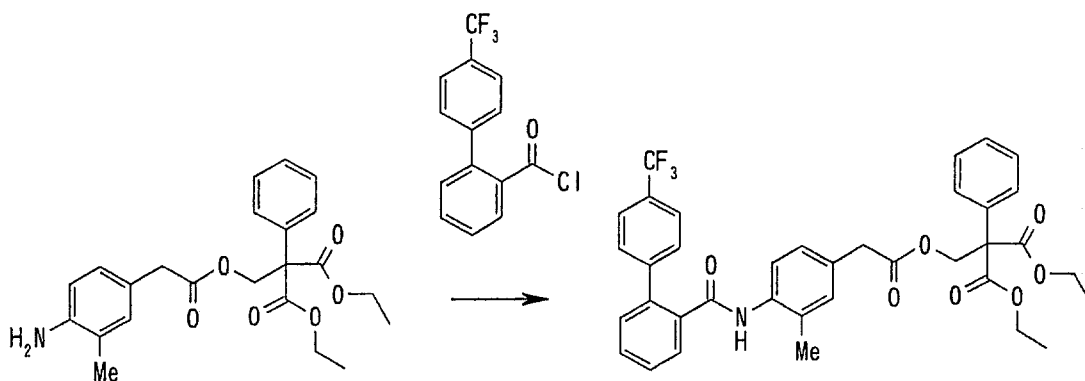


10

The 2-[2-(3-Methyl-4-nitrophenyl)acetoxymethyl]-2-phenyl-malonic acid diethyl ester (0.219 g) obtained in Example 1-3 c) was dissolved in methanol (3 mL). The solution was subjected to hydrogenation in the presence of 7.5% palladium-carbon (0.030 g) under normal pressure to give the title compound (0.197 g) as a yellow oil.

15

e) 2-(2-{3-Methyl-4-[(4'-trifluoromethylbiphenyl-2-carbonyl)amino]phenyl}acetoxymethyl)-2-phenylmalonic acid diethyl ester

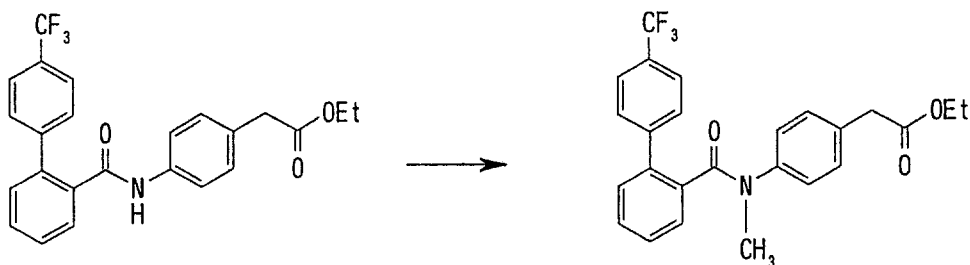


In a similar manner to Example 1 d), 4'-trifluoro-
methyl-2-biphenylcarboxylic acid (0.124 g) was converted into
its corresponding acid chloride. On the other hand, the title
5 compound (0.215 g) was obtained as a colorless amorphous from
the 2-[2-(4-amino-3-methylphenyl)acetoxymethyl]-2-
phenylmalonic acid diethyl ester (0.197 g) obtained in Example
1-3 d) in a similar manner to Example 1 e)(see Table 1).

10 Example 1-4

2-(2-{4-[Methyl-(4'-trifluoromethylbiphenyl-2-
carbonyl)amino]phenyl}acetoxymethyl)-2-phenylmalonic acid
diethyl ester

a) {4-[Methyl-(4'-trifluoromethylbiphenyl-2-
15 carbonyl)amino]phenyl}acetic acid ethyl ester

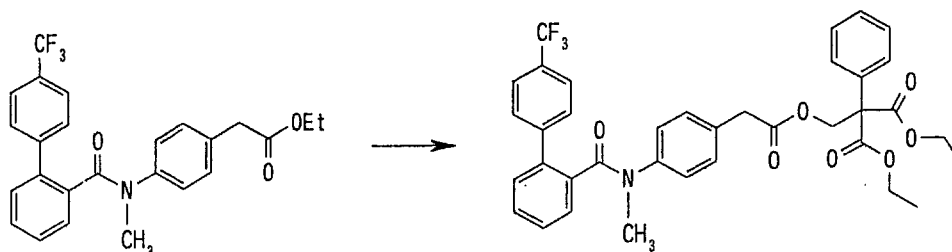


Sodium hydride (51 mg) was dissolved in dimethylformamide
(5 mL), and the solution was cooled to 0°C. To the solution
was added the 4-[(4'-trifluoromethylbiphenyl-2-

carbonyl)amino]phenylacetic acid ethyl ester (500 mg) obtained in Example 1 e), and the mixture was stirred for one hour. After addition of iodomethane (183 mg), the mixture was stirred at room temperature for 3 hours and water was then added.

5 The reaction solution was concentrated, diluted with ethyl acetate, and washed with water. The resulting solution was dried over sodium sulfate and purified by column chromatography on silica gel with hexane:ethyl acetate=4:1 to give the title compound (141 mg).

10 b) 2-(2-{4-[Methyl-(4'-trifluoromethylbiphenyl-2-carbonyl)amino]phenyl}acetoxymethyl)-2-phenylmalonic acid diethyl ester



15 The {4-[Methyl-(4'-trifluoromethylbiphenyl-2-carbonyl)amino]phenyl}acetic acid ethyl ester (141 mg) obtained in Example 1-4 a) was subjected to reactions similar to those in Examples 1 f) and 1 g) to give the title compound (56 mg)(see Table 1).

20

Example 1-5

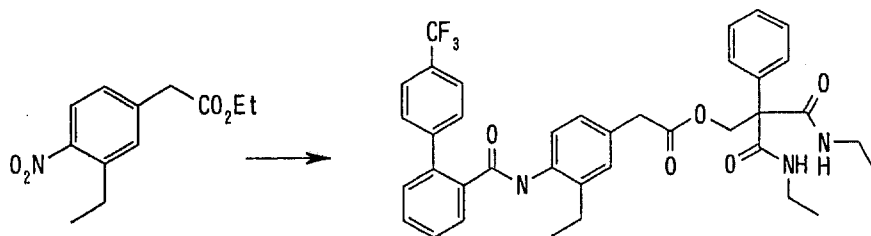
{3-Ethyl-4-[(4'-trifluoromethylbiphenyl-2-carbonyl)amino]phenyl}acetic acid 2,2-bisethylester

25 a) 3-Ethyl-4-nitrophenylacetic acid ethyl ester



To a solution of 4-nitrophenylacetic acid ethyl ester (1.63 g) in tetrahydrofuran (100 mL) was dropwise added 2M ethyl magnesium chloride in tetrahydrofuran (3 mL) at -15°C under argon atmosphere, and the mixture was stirred at the same temperature for 30 minutes. After further dropwise addition of 2M ethyl magnesium chloride in tetrahydrofuran (3 mL), the mixture was stirred at -15°C for one hour, and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (3.0 g) was added thereto at the same temperature. The mixture was stirred overnight, and water (300 mL) was added thereto, followed by extraction with chloroform (150 mL x 3). The organic layers were combined, washed with saturated brine, dried over sodium sulfate and purified by column chromatography on silica gel with hexane:ethyl acetate=10:1 to give the title compound (1.09 g).

b) {3-Ethyl-4-[(4'-trifluoromethylbiphenyl-2-carbonyl)amino]phenyl}acetic acid 2,2-bisethylester



The 3-ethyl-4-nitrophenylacetic acid ethyl ester (1.05 g) obtained in Example 1-5 a) was subjected to reactions similar to those in Example 1-3 d), Example 1 e), Example 1 f) and Example

1 g) to give the title compound (1.60 g)(see Table 1).

Examples 1-6 to 1-83

Compounds of Examples 1-6 to 1-85 were obtained in a similar
5 manner to Examples 1 to 1-5. The compounds obtained were shown
in Tables 2 to 17.

Table 1

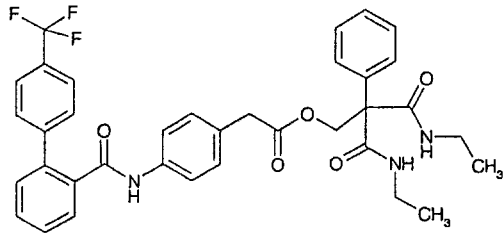
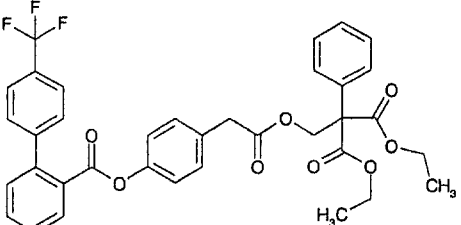
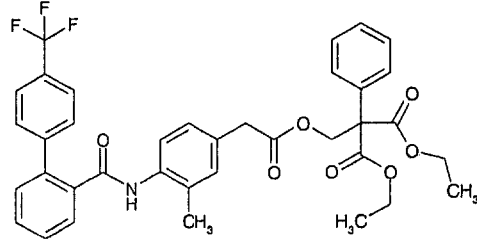
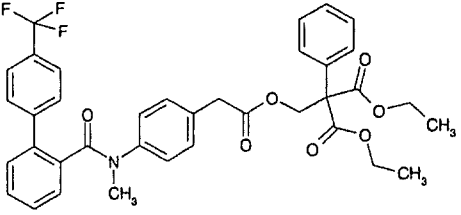
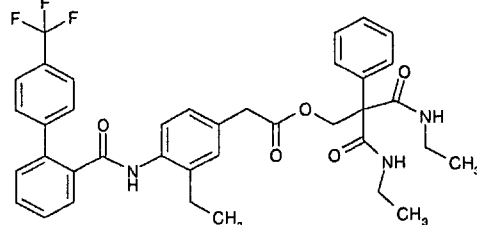
Example	Structure	NMR (δ , 300MHz, CDCl ₃)
1	 m.p. 88.4-91.2	1.05(6H, t, J=7.3Hz), 3.18-3.29(4H, m), 3.53(2H, s), 4.83(2H, s), 6.95(1H, br-s), 7.02-7.23(8H, m), 7.27-7.36(3H, m), 7.41-7.47(1H, m), 7.49-7.63(4H, m), 7.65-7.72(2H, m), 7.77-7.84(1H, m)
1-2		1.19(6H, t, J=9.2Hz), 3.53(2H, s), 4.18(4H, q, J=9.2Hz), 4.82(2H, s), 6.79(2H, d, J=12Hz), 7.14(2H, d, J=12Hz), 7.29(5H, brs), 7.38-7.73(7H, m), 8.09(1H, dd, J=1.2Hz, J=7.5Hz).
1-3		1.21(6H, t, J=7.1Hz), 1.67(3H, s), 3.47(2H, s), 4.20(4H, q, J=7.1Hz), 4.82(2H, s), 6.89(1H, brs), 6.92(1H, brs), 7.00(1H, d, J=10.6Hz), 7.30(5H, brs), 7.42-7.84(9H, m).
1-4		1.22(6H, t, J=7.2Hz), 3.23(3H, s), 3.40(2H, s), 4.21(4H, q, J=7.2Hz), 4.83(2H, s), 6.10(2H, d, J=8.3Hz), 6.70(2H, d, J=8.3Hz), 7.07-7.61(13H, m)
1-5	 m.p. 105-109	0.93(3H, t, J=7.5Hz), 1.05(6H, t, J=7.3Hz), 1.94(2H, q, J=7.5Hz), 3.13-3.28(4H, m), 3.53(2H, s), 4.83(2H, s), 6.80-7.84(19H, m)

Table 3

Example	Structure	NMR (δ , 300MHz, CDCl ₃)
1-11		1.18(6H, d, J=6.4Hz), 1.20(6H, d, J=6.0Hz), 3.50(2H, s), 4.80(2H, s), 5.08(1H, sept, J=6.4Hz), 5.08(1H, sept, J=6.0Hz), 6.92(1H, s), 7.05-7.16(4H, m), 7.27-7.32(5H, m), 7.41-7.47(1H, m), 7.49-7.63(4H, m), 7.65-7.72(2H, m), 7.80(1H, dd, J=1.5, 7.1Hz)
1-12		3.53(2H, s), 3.74-3.97(4H, m), 4.87(2H, s), 6.94(1H, s), 7.00-7.07(2H, m), 7.09-7.20(4H, m), 7.31-7.47(6H, m), 7.49-7.64(4H, m), 7.65-7.72(2H, m), 7.80(1H, dd, J=1.5, 7.5Hz)
1-13		3.51(2H, s), 3.71(6H, s), 4.81(2H, s), 6.92(1H, br-s), 7.05-7.16(4H, m), 7.22-7.35(5H, m), 7.41-7.46(1H, m), 7.49-7.63(4H, m), 7.65-7.71(2H, m), 7.81(1H, dd, J=1.5, 7.2Hz)
1-14		1.20(6H, t, J=7.1Hz), 1.29-1.81(10H, br), 2.40-2.53(1H, m), 3.52(2H, s), 4.13(4H, q, J=7.1Hz), 4.48(2H, s), 6.93(1H, brs), 7.14(4H, brs), 7.39-7.83(8H, m).
1-15	 m.p. 108.8 - 112.4	1.27-1.44(5H, m), 1.46-1.61(3H, m), 1.79-1.90(2H, m), 3.57(2H, s), 3.72-3.87(2H, m), 4.07(2H, s), 5.71-5.81(1H, m), 6.94(1H, br-s), 7.10-7.21(4H, m), 7.40-7.47(1H, m), 7.49-7.63(4H, m), 7.65-7.72(2H, m), 7.77-7.83(1H, m)

Table 4

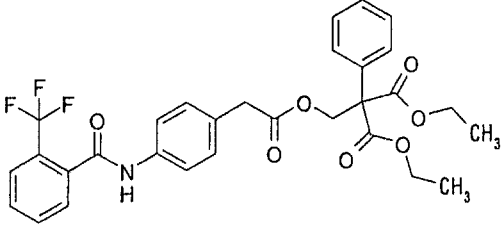
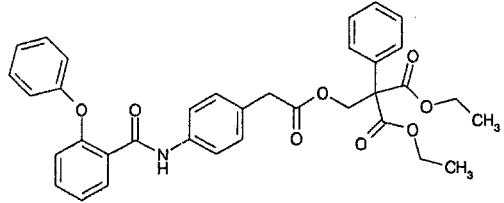
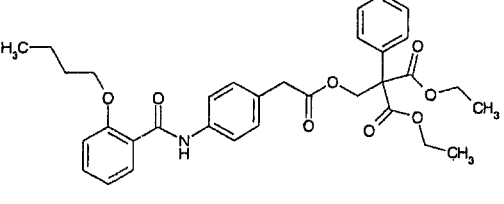
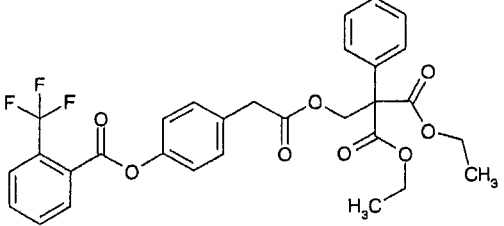
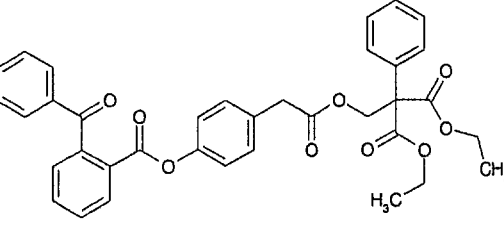
Example	Structure	NMR (δ , 300MHz, CDCl ₃)
1-16	 m.p. 93-95	1.22(6H, t, J=7.2Hz), 3.57(2H, s), 4.21(4H, q, J=7.2Hz), 4.83(2H, s), 7.20(1H, d, J=8.5Hz), 7.28-7.67(12H, m), 7.76(1H, d, J=7.4)
1-17	 m.p. 99-103	1.20(6H, t, J=7.1Hz), 3.53(2H, s), 4.19(4H, q, J=7.1Hz), 4.82(2H, s), 6.91(1H, d, J=8.3Hz), 7.11-7.56(16H, m), 8.33(1H, dd, J=7.8, 1.8Hz), 9.62(1H, br.s)
1-18		1.05(3H, m), 1.22(6H, t, J=7.2Hz), 1.58(2H, m), 1.99(2H, m), 3.57(2H, s), 4.21(6H, m), 4.85(2H, s), 7.04-7.60(12H, m), 8.30(1H, m), 10.07(1H, br.s)
1-19		1.22(6H, t, J=6.9Hz), 3.60(2H, s), 4.20(4H, q, J=6.9Hz), 4.85(2H, s), 7.12-7.37(9H, m), 7.63-7.73(2H, m), 7.79-7.86(1H, m), 7.90-8.00(1H, m).
1-20		1.18(6H, t, J=6.8Hz), 3.51(2H, s), 4.17(4H, q, J=6.8Hz), 4.80(2H, s), 6.70(2H, d, J=12Hz), 7.09(2H, d, J=12Hz), 7.27(5H, brs), 7.41-7.83(8H, m), 8.21(1H, d, J=10Hz).

Table 5

Example	Structure	NMR (δ , 300MHz, CDCl_3)
1-21		1.18(6H, t, $J=7.2\text{Hz}$), 3.49(2H, s), 4.15(4H, q, $J=7.2\text{Hz}$), 4.80(2H, s), 7.07(1H, d, $J=8.6\text{Hz}$), 7.27-7.54(17H, m), 7.88(1H, d, $J=6.2\text{Hz}$)
1-22		1.16-1.83(20H, m), 3.50(2H, s), 4.80-4.91(2H, m), 4.82(2H, s), 6.93(1H, br-s), 7.05-7.17(4H, m), 7.27-7.34(5H, m), 7.41-7.47(1H, m), 7.49-7.63(4H, m), 7.65-7.72(2H, m), 7.80(1H, dd, $J=1.5, 7.2\text{Hz}$)
1-23		0.95-1.22(6H, m), 1.23-1.43(4H, m), 1.50-1.71(6H, m), 1.71-1.90(4H, m), 3.52(2H, s), 3.69-3.83(2H, m), 4.84(2H, s), 6.95(1H, br-s), 7.04-7.35(11H, m), 7.41-7.48(1H, m), 7.49-7.65(4H, m), 7.66-7.73(2H, m), 7.77-7.84(1H, m)
1-24		3.58(2H, s), 5.06(2H, s), 6.81(1H, br-s), 6.99-7.05(4H, m), 7.08-7.16(2H, m), 7.24-7.47(14H, m), 7.50-7.67(6H, m), 7.80(1H, dd, $J=1.5, 7.5\text{Hz}$), 9.08(2H, br-s)
1-25		1.04(6H, d, $J=6.4\text{Hz}$), 1.09(6H, d, $J=6.8\text{Hz}$), 3.52(2H, s), 3.95-4.09(2H, m), 4.83(2H, s), 6.92-7.03(3H, m), 7.03-7.10(2H, m), 7.11-7.23(4H, m), 7.27-7.36(3H, m), 7.41-7.47(1H, m), 7.49-7.64(4H, m), 7.65-7.72(2H, m), 7.80(1H, dd, $J=1.5, 7.5\text{Hz}$)