

DESCRIPTION

BENZOFURYL-PYRONE DERIVATIVES5 Technical Field

 The present invention relates to novel benzofuryl- α -pyrone derivatives and to medicines containing them as active ingredients. More specifically, the invention relates to novel benzofuryl- α -pyrone derivatives and to
10 lipid metabolism enhancers, arteriosclerosis prophylactic agents, arteriosclerosis treatment agents, triglyceride biosynthesis inhibitors, blood triglyceride lowering agents or blood HDL elevating agents containing them as active ingredients.

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Background Art

 Blood cholesterol and triglycerides (TG) themselves are generally insoluble in blood, and they exist as lipoproteins by binding with apolipoproteins. In the
20 body, triglycerides are biosynthesized primarily in the liver from acetyl CoA as the starting substance which is produced from sugars, etc., by 6 different enzymes and one enzyme group (acetyl CoA carboxylase, the fatty acid synthase group, fatty acyl CoA synthase,
25 glycerophosphoric acid acyl transferase, lysophosphatidic acid acyl transferase, phosphatidic acid phosphatase and diacylglycerol acyl transferase), and are secreted from the liver into the blood as lipoproteins.

 The condition of a higher-than-normal cholesterol
30 and/or triglyceride blood level is known as hyperlipidemia. The condition termed hyperlipidemia is classified into 6 types based on the lipoproteins in the blood, according to the Fredrickson classification (WHO classification). Types I, IV and V are characterized by
35 increased triglycerides only, type IIa by increased cholesterol, and types IIb and III by increases in both

("Sogo Rinsho", 43, 871(1994)). This means that present hyperlipidemia drugs (that lower only cholesterol or that lower both cholesterol and triglycerides) cannot always be appropriately applied for all hyperlipidemia cases.

5 In particular, type IV accounts for 40 to 50% of male hyperlipidemia patients ("Rinsho to Kenkyu", 69, 318(1992)). Most secondary onset forms accompanying diabetes are also type IV ("Sogo Rinsho", 43, 878(1994)).

Hypertriglyceridemia is a condition in which blood
10 triglyceride levels are increased, and in the past few years it has been receiving attention among clinical physicians and pharmaceutical manufacturers as a risk factor in arteriosclerosis and ischemic diseases.

Because most attention in the field of
15 hyperlipidemia, which includes hypertriglyceridemia, has been focused on cholesterol alone, which is directly implicated in arteriosclerosis, few drugs have been developed with the aim of lowering triglycerides, and treatment of hypertriglyceridemia has been limited to the
20 use of clofibrate-based hypolipidemic drugs or nicotinic acid preparations as the existing hypolipidemic drugs. Because these must be used in high doses and many action sites have been reported, there are concerns about a number of related side-effects (The Lipid, 5, 65 to
25 72(1994)). It would therefore be highly desirable to find a new type of drug that has a triglyceride-lowering effect at low doses, exhibits few side-effects and has a clear action mechanism.

Hypertriglyceridemia occurs as a result of various
30 causes, including genetic background and, as mentioned above, secondary onset accompanying diabetes, etc. ("Sogo Rinsho", 43, 878(1994)); more specifically, it is attributed to:

A. accelerated triglyceride synthesis (secretion) in
35 the liver, and

B. delayed decomposition of synthesized triglycerides (present in the blood as lipoproteins) by

lipoprotein lipase (LPL) ("Rinsho to Kenkyu", 69, 340(1992)). In particular, for hypertriglyceridemia accompanying diabetes, A. is said to be the cause of non-insulin-dependent diabetes mellitus (NIDDM), while B. is
5 said to be the cause of insulin-dependent diabetes mellitus (IDDM) ("Rinsho to Kenkyu", 69, 379(1992)). Consequently, the action mechanism of therapeutic agents for hypertriglyceridemia is believed to be inhibition of triglyceride synthesis (secretion) in the liver and/or
10 accelerated decomposition of synthesized triglycerides (present in the blood as lipoproteins) by lipoprotein lipase (LPL).

In the prior art there have been known α -pyrone derivatives with substitution of a heteroaromatic ring at
15 the C-6 position, for example, in WO 9635664, WO 9514013, WO 9514014, EP 588137, US 4668803, FR 2665445, Japanese Unexamined Patent Publication SHO No. 49-5976, Japanese Unexamined Patent Publication No. 8-503216, Japanese Unexamined Patent Publication No. 9-505291, Japanese
20 Unexamined Patent Publication No. 9-505293, Japanese Unexamined Patent Publication No. 9-505294, Japanese Unexamined Patent Publication No. 9-505295, or for example, in Tetrahedron Letters, 37, 6461 (1996), J. Chem. Research (S), 86 (1994), Chem. Pharm. Bull., 32, 1665 (1984), Chem. Ber., 100, 658 (1967) and J. Org.
25 Chem., 54, 3985 (1989).

However, no explanation or suggestion has been published regarding a triglyceride biosynthesis inhibiting effect, blood triglyceride lowering effect or
30 blood HDL elevating effect for any of these α -pyrone derivatives of the prior art.

Of the prior art publications, WO 9635664 and EP 588137 describe compounds with a structural feature wherein phenyl is a substituent at the C-3 position of
35 the α -pyrone ring, but no description or suggestion is given regarding the use of an alkyl group instead of a

phenyl group as the substituent at the C-3 position of the α -pyrone ring.

Similarly, US 4668803 among the prior art publications describes α -pyrone derivatives wherein the substituent at the C-3 position is an acyl group of 2 to 11 carbons or a phenyl group, but no description or suggestion is given regarding the use of an alkyl group instead of an acyl group of 2 to 11 carbons or a phenyl group as the substituent at the C-3 position of the α -pyrone ring.

Also, FR 2665445 among the prior art publications describes α -pyrone derivatives with $-S(O)_n-R^1$ as a substituent at the C-4 position, wherein n is 1 or 2 and R^1 represents an alkyl group of 1 to 6 carbons, a benzyl group or a phenyl group. However, no description or suggestion is given regarding the use of OH, OCOR or OSO_2R instead of $-S(O)_n-R^1$ as the substituent at the C-4 position of the α -pyrone ring.

Likewise, Japanese Unexamined Patent Publication No. 49-5976 among the prior art publications describes α -pyrone derivatives with hydrogen, a lower alkyl group or phenyl as a substituent at the C-4 position, but no description or suggestion is given regarding the use of OH, OCOR or OSO_2R instead of hydrogen, a lower alkyl group or phenyl as the substituent at the C-4 position of the α -pyrone ring.

Likewise, Chem. Ber., 100, 658 (1967) among the prior art publications describes α -pyrone derivatives with hydrogen, methyl or ethyl as a substituent at the C-4 position, but no description or suggestion is given regarding the use of OH, OCOR or OSO_2R instead of hydrogen, methyl or ethyl as the substituent at the C-4 position of the α -pyrone ring.

Likewise, J. Chem. Research (S), 86(1994) among the

prior art publications describes α -pyrone derivatives with an SMe group as a substituent at the C-4 position, but no description or suggestion is given regarding the use of OH, OCOR or OSO₂R instead of an SMe group as the substituent at the C-4 position of the α -pyrone ring.

In addition, Tetrahedron Letters, 37, 6461 (1996), Chem. Pharm. Bull., 32, 1665 (1984) and J. Org. Chem., 54, 3985 (1989) among the prior art publications describe α -pyrone derivatives with a pyridyl group substituent at the C-6 position, but no description or suggestion is given regarding the use of a benzofuryl group instead of a pyridyl group as the substituent at the C-6 position of the α -pyrone ring.

Disclosure of the Invention

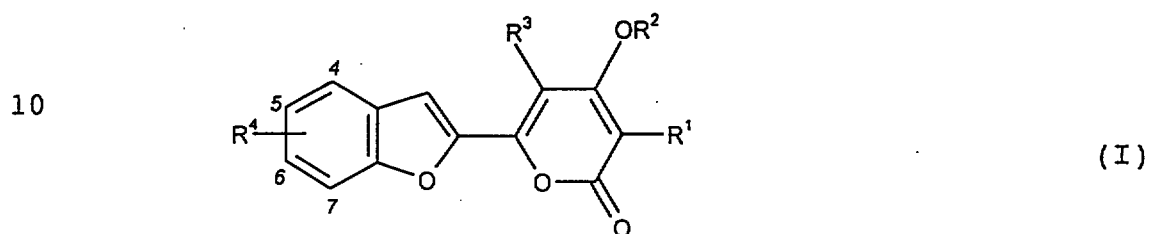
It is an object of the present invention to provide benzofuryl- α -pyrone derivatives, and especially novel benzofuryl- α -pyrone derivatives having a benzofuryl group as a substituent at the C-6 position of the α -pyrone ring.

It is another object of the invention to provide lipid metabolism enhancers, arteriosclerosis prophylactic agents or arteriosclerosis treatment agents, and especially to provide triglyceride biosynthesis inhibitors, blood triglyceride lowering agents or blood HDL elevating agents, that contain as active ingredients the novel benzofuryl- α -pyrone derivatives having a benzofuryl group as a substituent at the C-6 position of the α -pyrone ring.

The present inventors have conducted much research in light of the prior art cited above, and as a result the inventors have found that benzofuryl- α -pyrone derivatives, and especially benzofuryl- α -pyrone derivatives having a benzofuryl group as a substituent at the C-6 position of the α -pyrone ring, have a

triglyceride biosynthesis inhibiting effect, a blood triglyceride lowering effect and a blood HDL elevating effect; the present invention have been achieved after still further research on the same.

Specifically, the present invention provides benzofuryl- α -pyrone derivatives (and salts thereof) represented by the following structural formula (I)



wherein R¹ represents hydrogen or an alkyl group of 1 to 5 carbons;

R² represents hydrogen, -CO-R⁵ (wherein R⁵ represents hydrogen, an alkyl group of 1 to 5 carbons with optional substituents, a cycloalkyl group of 3 to 7 carbons, an aryl group of 6 to 10 carbons or a heterocycle), or -SO₂R⁶ (wherein R⁶ represents an optionally halogen-substituted alkyl group of 1 to 5 carbons or aryl group of 6 to 10 carbons);

R³ represents hydrogen, an alkyl group of 1 to 5 carbons, an alkenyl group of 2 to 5 carbons, an alkynyl group of 2 to 5 carbons, a cycloalkyl group of 3 to 7 carbons, a cycloalkyl group of 3 to 7 carbons-alkyl group of 1 to 5 carbons, an aryl group of 6 to 10 carbons, an aralkyl group of 7 to 20 carbons, an alkoxy group of 1 to 5 carbons or an aryloxy group of 6 to 10 carbons;

R⁴ is a substituent at the C-4 position, C-5 position, C-6 position or C-7 position of the benzofuran ring and represents:

R^{4a} which represents hydrogen, a nitro group, a cyano group, a halogen atom, a heterocycle, an alkenyl group of 2 to 5 carbons, an alkynyl group of 2 to 5 carbons, an aryl group of 6 to 10 carbons, A=CH(CH₂)_n- (wherein A represents an alicyclic heterocycle, "="

represents a double bond and n represents 0, 1 or 2),
A=CH(CH₂)_mO- (wherein A represents an alicyclic
heterocycle, "=" represents a double bond and m
represents 1, 2 or 3), A-SO₂-(CH₂)_m- (wherein A represents
5 an alicyclic heterocycle and m represents 1, 2 or 3),
-OR⁷ (wherein R⁷ represents hydrogen, a cycloalkyl group
of 3 to 7 carbons, an aryl group of 6 to 10 carbons, a
heterocycle, an optionally halogen-substituted
alkylsulfonyl group of 1 to 4 carbons, or an arylsulfonyl
10 group of 6 to 10 carbons), -O-CO-R⁸ (wherein R⁸
represents hydrogen, an alkyl group of 1 to 4 carbons, an
aryl group of 6 to 10 carbons, an aralkyl group of 7 to
20 carbons or a heterocycle), -NR⁹R¹⁰ (wherein R⁹ and R¹⁰
each independently represents hydrogen, an alkyl group of
15 1 to 4 carbons, an aralkyl group of 7 to 20 carbons, a
phenyl group, a heterocycle, -SO₂-R¹¹ (wherein R¹¹
represents an optionally halogen-substituted alkyl group
of 1 to 12 carbons, a heterocycle-substituted alkyl group
of 1 to 6 carbons, an aryl group of 6 to 10 carbons, a
20 heterocycle or an aralkyl group of 7 to 20 carbons) or
-CO-R¹² (wherein R¹² represents hydrogen, an alkyl group
of 1 to 12 carbons, an aryl group of 6 to 10 carbons, an
aralkyl group of 7 to 20 carbons, a heterocycle, an
alkoxy group of 1 to 10 carbons, a heterocycle-
25 substituted alkyl group of 1 to 6 carbons, an aryloxy
group of 6 to 10 carbons, a heteroaryloxy group or an
aralkyloxy group of 7 to 20 carbons)), -CO-R¹³ (wherein
R¹³ represents hydrogen, -OH, an alkyl group of 1 to 4
carbons, an aryl group of 6 to 10 carbons, a heterocycle,
30 an alkoxy group of 1 to 4 carbons, an aryloxy group of 6
to 10 carbons or an aralkyloxy group of 7 to 20 carbons),
or -CO-NR¹⁴R¹⁵ (wherein R¹⁴ and R¹⁵ each independently
represents hydrogen, an alkyl group of 1 to 4 carbons, a
cycloalkyl group of 3 to 7 carbons, an aryl group of 6 to
35 10 carbons, an aralkyl group of 7 to 20 carbons, a
heterocycle or a heterocycle-substituted alkyl group of 1
to 4 carbons);

R^{4b} which represents a saturated or unsaturated alkoxy group of 1 to 6 carbons optionally substituted with 1 to 3 groups selected from the group consisting of halogens, cycloalkyl groups of 3 to 7 carbons, phenyl, naphthyl, heterocycles, $-OR^{16}$ (wherein R^{16} represents hydrogen, an alkyl group of 1 to 4 carbons, a phenyl group, a naphthyl group, a benzyl group or a heterocycle), $-O-CO-R^{16}$ (wherein R^{16} represents hydrogen, an alkyl group of 1 to 4 carbons, a phenyl group, a naphthyl group, a benzyl group or a heterocycle), $-NR^{17}R^{18}$ (wherein R^{17} and R^{18} each independently represents hydrogen, an alkyl group of 1 to 4 carbons, a heterocycle, an alkylsulfonyl group of 1 to 4 carbons, a phenylsulfonyl group, $-SO_2$ -Het (wherein Het represents a heterocycle), an aminosulfonyl group, a methylaminosulfonyl group, a dimethylaminosulfonyl group, a diethylaminosulfonyl group, or an alkyl group of 1 to 4 carbons substituted with 1 or 2 groups selected from among phenyl, heterocycles, phenoxy, $-O$ -Het (wherein Het represents a heterocycle) and hydroxyl, $-NH-CO-R^{19}$ (wherein R^{19} represents hydrogen, an alkyl group of 1 to 4 carbons, a phenyl group, a naphthyl group, a benzyl group, a heterocycle, an alkoxy group of 1 to 4 carbons or a benzyloxy group), $-CO-R^{20}$ (wherein R^{20} represents hydrogen, a heterocycle, an alkoxy group of 1 to 4 carbons, a phenoxy group, a benzyloxy group or $-OR^{21}$ (wherein R^{21} represents hydrogen or a heterocycle)), and $-CO-NR^{22}R^{23}$ (wherein R^{22} and R^{23} each independently represents hydrogen, an alkyl group of 1 to 4 carbons, a benzyl group or a heterocycle); or

R^{4c} which represents an alkyl group of 1 to 4 carbons optionally substituted with 1 to 3 groups selected from the group consisting of halogens, cycloalkyl groups of 3 to 7 carbons, phenyl, naphthyl, heterocycles, $-SH$, $-OR^{16}$ (wherein R^{16} represents hydrogen, an alkyl group of 1 to 4 carbons, a phenyl group, a naphthyl group, a benzyl group or a heterocycle),

-O-CO-R¹⁶ (wherein R¹⁶ represents hydrogen, an alkyl group of 1 to 4 carbons, a phenyl group, a naphthyl group, a benzyl group or a heterocycle), -NR¹⁷R¹⁸ (wherein R¹⁷ and R¹⁸ each independently represents hydrogen, an alkyl group of 1 to 4 carbons, a heterocycle, an alkylsulfonyl group of 1 to 4 carbons, a phenylsulfonyl group, -SO₂-Het (wherein Het represents a heterocycle), an aminosulfonyl group, a methylaminosulfonyl group, a dimethylaminosulfonyl group, a diethylaminosulfonyl group, or an alkyl group of 1 to 4 carbons substituted with 1 or 2 groups selected from among phenyl, heterocycles, phenoxy, -O-Het (wherein Het represents a heterocycle) and hydroxyl, -NH-CO-R¹⁹ (wherein R¹⁹ represents hydrogen, an alkyl group of 1 to 4 carbons, a phenyl group, a naphthyl group, a benzyl group, a heterocycle, an alkoxy group of 1 to 4 carbons or a benzyloxy group), -CO-R²⁰ (wherein R²⁰ represents hydrogen, a heterocycle, an alkoxy group of 1 to 4 carbons, a phenoxy group, a benzyloxy group or -OR²¹ (wherein R²¹ represents hydrogen or a heterocycle)) and -CO-NR²²R²³ (wherein R²² and R²³ each independently represents hydrogen, an alkyl group of 1 to 4 carbons, a benzyl group or a heterocycle); and

the numbers in italics represents the positions on the benzofuran ring.

The present invention further provides pharmaceutical compositions comprising a therapeutically effective dose of the benzofuryl- α -pyrone derivatives represented by structural formula (I) above or their salts, with pharmaceutically acceptable carriers.

The invention still further provides lipid metabolism enhancers, triglyceride biosynthesis inhibitors, blood triglyceride lowering agents, blood HDL elevating agents, arteriosclerosis prophylactic agents and arteriosclerosis treatment agents containing as active ingredients the benzofuryl- α -pyrone derivatives

represented by structural formula (I) above or their salts.

Embodiment for Carrying Out the Invention

5 The terms used alone or in conjunction with other terms throughout the present specification will now be explained. However, the invention is in no way restricted by the specific examples listed below.

10 "Alkyl" means a linear or branched alkyl group such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, t-butyl, n-pentyl, isopentyl or 3-pentyl.

 "Alkenyl" means a linear or branched alkenyl group such as vinyl, 1-propenyl, aryl, isopropenyl, 2-butenyl, 3-butenyl, 1-pentenyl or 2-pentenyl.

15 "Alkynyl" means a linear or branched alkynyl group such as ethynyl, 1-propynyl, 2-propynyl, 1-butylnyl, 2-butylnyl, 3-butylnyl, 2-methyl-3-butylnyl, 1-pentylnyl, 2-pentylnyl, 3-pentylnyl or 4-pentylnyl.

20 "Cycloalkyl" means a cycloalkyl group of 3 to 7 carbons such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl.

 A "cycloalkyl group of 3 to 7 carbons-alkyl group of 1 to 5 carbons" is a group comprising the aforementioned cycloalkyl group of 3 to 7 carbons and alkyl group of 1
25 to 5 carbons, and for example, there may be mentioned cyclopropylmethyl, cyclopentylmethyl, cyclopentylethyl, cyclohexylmethyl, cyclohexylethyl and cycloheptylmethyl.

 "Aryl" means an aromatic ring of 6 to 10 carbons such as phenyl or naphthyl.

30 A "heterocycle" is a heterocycle containing as constituents of the ring 1 to 4 hetero atoms selected from the group consisting of oxygen, nitrogen and sulfur, and it may be a 5- or 6-membered heteroaromatic group such as imidazolyl, thiazolyl, isothiazolyl, pyrazolyl,
35 triazolyl, tetrazolyl, pyrrolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, triazinyl, furyl, thienyl, oxazolyl or isoxazolyl, or a 5- to 7-membered

heteroalicyclic group such as thiazolidinyl,
oxazolidinyl, imidazolidinyl, pyrrolidinyl, piperidyl,
morpholinyl, piperazinyl, homopiperazinyl,
5 tetrahydrofuryl, tetrahydropyranyl, dioxolanyl, dioxanyl,
oxazinyl, thiazinyl, diazinyl or pyrazolidinyl; this also
includes bicyclic groups condensed onto benzene,
cycloalkyl groups of 3 to 7 carbons and other
heteroaromatic rings or heteroalicyclic rings, the
heteroaromatic ring or heteroalicyclic ring may also be
10 optionally substituted, and when chemically possible, the
nitrogen atom or sulfur atom may be in an oxidized form.

"Heteroaryl" means a heteroaromatic group of the
heterocycles defined above.

"Aralkyl" represents a group of 7 to 20 carbons
15 comprising the aforementioned alkyl group of 1 to 5
carbons and aryl group of 6 to 10 carbons, and for
example, there may be mentioned benzyl, phenethyl,
phenylpropyl, benzhydryl, trityl and naphthylmethyl.

"Alkoxy" means a linear or branched alkoxy group
20 such as methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy,
isobutoxy, sec-butoxy, t-butoxy, n-pentyloxy,
isopentyloxy, 3-pentyloxy, 2,2-dimethylpropoxy, n-
hexyloxy, 4-methylpentyloxy or 2-ethylbutoxy.

"Unsaturated alkoxy" means a linear or branched
25 unsaturated alkoxy group such as vinyloxy, allyloxy, 2-
propenyloxy, 2-propynyloxy, 2-methyl-2-propenyloxy, 1-
butenyloxy, 2-butenyloxy, 3-butenyloxy, 2-butynyloxy, 2-
pentyloxy, 3-hexenyloxy, 5-hexenyloxy or 5-hexynyloxy.

"Aryloxy" means an aryloxy group of 6 to 10 carbons
30 such as phenoxy or naphthyloxy.

"Aralkyloxy" represents a group comprising the
aforementioned alkoxy group of 1 to 5 carbons and aryl
group of 6 to 10 carbons, and for example, there may be
mentioned benzyloxy, phenethyloxy, phenylpropoxy,
35 trityloxy and naphthylmethyloxy.

"Cycloalkyloxy" means a cycloalkyloxy group of 3 to
7 carbons such as cyclopropyloxy, cyclobutyloxy,

cyclopentyloxy, cyclohexyloxy or cycloheptyloxy.

"Acyl" means a linear or branched acyl group of 1 to 6 carbons such as formyl, acetyl, propionyl, n-butyryl, isobutyryl, n-valeryl, trimethylacetyl or 3,3,3-trimethylpropionyl.

"Arylcarbonyl" means an arylcarbonyl group of 7 to 11 carbons such as benzoyl or naphthylcarbonyl.

"Alkylsulfonyl" means an alkylsulfonyl group of 1 to 5 carbons such as methanesulfonyl, ethanesulfonyl or n-propanesulfonyl.

"Arylsulfonyl" means an arylsulfonyl group of 6 to 10 carbons such as phenylsulfonyl or naphthalenesulfonyl.

The rings of the "aryl", "phenyl", "naphthyl" and "heterocycle" may be substituted with 1 to 4 substituents selected from the group consisting of, for example, -OH, carboxyl, cyano, phenyl, heterocycles, -SO₂NH₂, -SO₃H, alkylsulfamoyl groups such as methylsulfamoyl, ethylsulfamoyl, dimethylsulfamoyl, etc., phenylsulfamoyl, benzylsulfamoyl, morpholinesulfonyl, alkylsulfonyl groups such as methanesulfonyl, ethanesulfonyl, n-propanesulfonyl, etc., arylsulfonyl groups such as phenylsulfonyl, naphthalenesulfonyl, etc., amino, methylenedioxy, alkoxy groups of 1 to 5 carbons such as methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, isobutoxy, t-butoxy, n-pentyloxy, etc., alkylamino groups such as methylamino, dimethylamino, ethylamino, diethylamino, n-propylamino, isopropylamino, n-butylamino, isobutylamino, t-butylamino, etc., acylamino groups such as formamino, acetylamino, propionylamino, n-butyrylamino, etc., alkoxycarbonylamino groups such as methoxycarbonylamino, ethoxycarbonylamino, n-propoxycarbonylamino, n-butoxycarbonylamino, t-butoxycarbonylamino, etc., aralkyloxycarbonylamino groups such as benzyloxycarbonylamino, naphthylmethyloxycarbonylamino, etc., alkylsulfonylamino groups such as methanesulfonylamino, ethanesulfonylamino, n-propanesulfonylamino, etc., arylsulfonylamino groups

such as phenylsulfonylamino, naphthalenesulfonylamino, etc., nitro, hydroxymethyl, alkyl groups of 1 to 5 carbons such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, t-butyl, n-pentyl, etc., aralkyl groups
5 such as benzyl, phenethyl, trityl, naphthylmethyl, etc., aralkyloxy groups such as benzyloxy, phenethyloxy, phenylpropoxy, trityloxy, naphthylmethyloxy, etc., acyl groups such as formyl, acetyl, propionyl, n-butyryl, isobutyryl, n-valeryl, trimethylacetyl, 3,3,3-
10 trimethylpropionyl, etc., alkoxycarbonyl groups such as methoxycarbonyl, ethoxycarbonyl, n-propoxycarbonyl, isopropoxycarbonyl, n-butoxycarbonyl, t-butoxycarbonyl, etc., aryloxycarbonyl groups such as phenoxycarbonyl, naphthyloxycarbonyl, etc., aralkyloxycarbonyl groups such
15 as benzyloxycarbonyl, phenethyloxycarbonyl, trityloxycarbonyl, naphthylmethyloxycarbonyl, etc., carbamoyl, alkylcarbamoyl groups such as methylcarbamoyl, dimethylcarbamoyl, ethylcarbamoyl, diethylcarbamoyl, n-propylcarbamoyl, n-butylcarbamoyl, etc., halogenated
20 methyl groups such as chloromethyl, bromomethyl, trifluoromethyl, etc., and halogen atoms, i.e. fluorine, chlorine, bromine and iodine; when chemically possible, these may be substituted with 1 to 3 oxo groups or thiooxo groups.

25 In formula (I) above, R^1 represents hydrogen or an alkyl group of 1 to 5 carbons. As alkyl groups of 1 to 5 carbons there may be mentioned, for example, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, t-butyl, n-pentyl, isopentyl and 3-pentyl.

30 As preferred groups for R^1 there may be mentioned hydrogen, methyl, ethyl and isopropyl, and methyl may be mentioned as a particularly preferred group for R^1 .

In formula (I) above, R^2 represents hydrogen, $-CO-R^5$ (wherein R^5 represents hydrogen, an alkyl group of 1 to 5
35 carbons with optional substituents, a cycloalkyl group of 3 to 7 carbons, an aryl group of 6 to 10 carbons or a heterocycle), or $-SO_2R^6$ (wherein R^6 represents an

optionally halogen-substituted alkyl group of 1 to 5 carbons, or an aryl group of 6 to 10 carbons).

When R^2 is $-CO-R^5$ and the R^5 group is an alkyl group of 1 to 5 carbons with an optional substituent, the alkyl group of 1 to 5 carbons for R^5 may be, for example, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, t-butyl, n-pentyl, isopentyl, 3-pentyl, etc., among which methyl, ethyl and isopropyl are preferred.

Optional substituents of the alkyl group of 1 to 5 carbons for R^5 include all alkyl group substituents known to those skilled in the art and, for example, they include halogen atoms, $-OH$, carboxyl groups, formyl groups, acyl groups, cyano groups, nitro groups, amino groups, mercapto groups, sulfonate groups, aryl groups of 6 to 10 carbons, heterocycles, cycloalkyl groups of 3 to 7 carbons and their protected forms; more specifically, there may be mentioned $-OH$; hydroxyl protected with an alkyl group of 1 to 4 carbons, an aryl group of 6 to 10 carbons, an aralkyl group of 7 to 20 carbons, a heterocycle, an acyl group of 1 to 5 carbons, an arylcarbonyl group of 7 to 11 carbons or an aralkylcarbonyl group of 8 to 21 carbons; $-O-CO-Het$ (wherein Het represents a heterocycle); cycloalkyl groups of 3 to 7 carbons; aryl groups of 6 to 10 carbons; heterocycles; amino groups; amino groups protected with an alkyl group of 1 to 4 carbons, an aralkyl group of 7 to 20 carbons, an optionally halogen-substituted alkylsulfonyl group of 1 to 4 carbons, an arylsulfonyl group of 6 to 10 carbons, an acyl group of 1 to 5 carbons, an arylcarbonyl group of 7 to 11 carbons, an aralkylcarbonyl group of 8 to 21 carbons, an alkoxycarbonyl group of 2 to 5 carbons, an aralkyloxycarbonyl group of 8 to 21 carbons or a heterocycle; $-NH-CO-Het$ (wherein Het represents a heterocycle); acyl groups of 1 to 5 carbons; carboxyl groups; alkoxycarbonyl groups of 2 to 5 carbons; aryloxycarbonyl groups of 7 to 11 carbons;

aralkyloxycarbonyl groups of 8 to 21 carbons; -CO-O-Het (wherein Het represents a heterocycle); carbamoyl groups, alkylcarbamoyl groups of 2 to 5 carbons; aralkylcarbamoyl groups of 8 to 21 carbons; -CO-NH-Het (wherein Het represents a heterocycle); and -CO-Het (wherein Het represents a heterocycle). As preferred substituents among these there may be mentioned phenyl, aryloxy, amino, t-butoxycarbonylamino, benzyloxycarbonylamino, (benzyloxycarbonylamino)methylamino, acetylamino and morpholinylcarbonyl.

When R^2 is $-COR^5$ and the R^5 group is a cycloalkyl group of 3 to 7 carbons, the cycloalkyl group of 3 to 7 carbons for R^5 may be, for example, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, etc., among which cyclohexyl is preferred.

When R^2 is $-COR^5$ and the R^5 group is an aryl group of 6 to 10 carbons, the aryl group of 6 to 10 carbons for R^5 may be, for example, phenyl, naphthyl, etc., among which phenyl is preferred.

When R^2 is $-COR^5$ and the R^5 group is a heterocycle, the heterocycle for R^5 may be, for example, imidazolyl, thiazolyl, isothiazolyl, pyrazolyl, triazolyl, pyrrolyl, pyridyl, pyrimidinyl, pyrazinyl, furyl, thienyl, isoxazolyl, thiazolidinyl, oxazolidinyl, imidazolidinyl, pyrrolidinyl, piperidyl, morpholinyl, piperazinyl, tetrahydrofuryl, tetrahydropyranyl, etc., among which pyridyl, pyrrolidinyl and furyl are preferred.

As preferred groups for R^5 there may be mentioned alkyl groups of 1 to 5 carbons with optional substituents, among which there may be mentioned methyl, methyl or ethyl substituted with phenyl, aryloxy, amino, t-butoxycarbonylamino, benzyloxycarbonylamino, (benzyloxycarbonyl)-N-methylamino, acetylamino or morpholinylcarbonyl, and isopropyl; aryl groups of 6 to 10 carbons, among which there may be mentioned phenyl; and heterocycles, among which there may be mentioned pyridyl, pyrrolidinyl and furyl.

When R^2 is $-SO_2R^6$ and the R^6 group is an optionally halogen-substituted alkyl group of 1 to 5 carbons, the optionally halogen-substituted alkyl group of 1 to 5 carbons for R^6 may be, for example, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, t-butyl, n-pentyl, chloromethyl, bromomethyl, trifluoromethyl, etc., among which methyl and trifluoromethyl are preferred.

When R^2 is $-SO_2R^6$ and R^6 is an aryl group of 6 to 10 carbons, the aryl group of 6 to 10 carbons for R^6 may be, for example, phenyl, naphthyl, etc., among which phenyl is preferred.

As preferred groups for R^6 there may be mentioned optionally halogen-substituted alkyl groups of 1 to 5 carbons, and as particularly preferred groups for R^6 there may be mentioned methyl and trifluoromethyl.

As preferred groups for R^2 there may be mentioned hydrogen, $-COR^{70}$ (wherein R^{70} represents an alkyl group of 1 to 5 carbons with an optional substituent, an aryl group of 6 to 10 carbons or a heterocycle) and optionally halogen-substituted alkylsulfonyl groups of 1 to 5 carbons, and as particularly preferred groups for R^2 there may be mentioned hydrogen, $-COR^{71}$ (wherein R^{71} represents a methyl group; a methyl or ethyl group substituted with phenyl, aryloxy, amino, t-butoxycarbonylamino, benzyloxycarbonylamino, (benzyloxycarbonyl)-N-methylamino, acetylamino or morpholinylcarbonyl; an isopropyl group; a phenyl group; a pyridyl group; a pyrrolidinyl group; or a furyl group), methanesulfonyl and trifluoromethanesulfonyl.

In formula (I) above, R^3 represents hydrogen, an alkyl group of 1 to 5 carbons, an alkenyl group of 2 to 5 carbons, an alkynyl group of 2 to 5 carbons, a cycloalkyl group of 3 to 7 carbons, a cycloalkyl of 3 to 7 carbons-alkyl group of 1 to 5 carbons, an aryl group of 6 to 10 carbons, an aralkyl group of 7 to 20 carbons, an alkoxy group of 1 to 5 carbons or an aryloxy group of 6 to 10



carbons.

When R^3 is an alkyl group of 1 to 5 carbons, the alkyl group of 1 to 5 carbons may be, for example, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, t-butyl, n-pentyl, etc., among which methyl, ethyl, isopropyl and n-pentyl are preferred.

When R^3 is an alkenyl group of 2 to 5 carbons, the alkenyl group of 2 to 5 carbons may be vinyl, allyl, 1-propenyl, isopropenyl, 2-butenyl, 3-butenyl, 1-pentenyl, 2-pentenyl, etc., among which 2-butenyl is preferred.

When R^3 is an alkynyl group of 2 to 5 carbons, the alkynyl group of 2 to 5 carbons may be vinyl, allyl, 1-propenyl, isopropenyl, 2-butenyl, 3-butenyl, 1-pentenyl, 2-pentenyl, etc., among which 2-butenyl is preferred.

When R^3 is a cycloalkyl group of 3 to 7 carbons, the cycloalkyl group of 3 to 7 carbons may be, for example, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, etc., among which cyclohexyl is preferred.

When R^3 is a cycloalkyl of 3 to 7 carbons-alkyl group of 1 to 5 carbons, the cycloalkyl of 3 to 7 carbons-alkyl group of 1 to 5 carbons may be, for example, cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl, cyclohexylmethyl, cycloheptylmethyl, etc., among which cyclopentylmethyl is preferred.

When R^3 is an aryl group of 6 to 10 carbons, the aryl group of 6 to 10 carbons may be, for example, phenyl, naphthyl, etc., among which phenyl is preferred.

When R^3 is an aralkyl group of 7 to 20 carbons, the aralkyl group of 7 to 20 carbons may be, for example, benzyl, phenethyl, phenylpropyl, benzhydryl, trityl, naphthylmethyl, etc., among which benzyl is preferred.

When R^3 is an alkoxy group of 1 to 5 carbons, the alkoxy group of 1 to 5 carbons may be, for example, methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, isobutoxy, sec-butoxy, t-butoxy, etc., among which methoxy is preferred.

When R^3 is an aryloxy group of 6 to 10 carbons, the

aryloxy group of 6 to 10 carbons may be, for example, phenoxy, naphthyloxy, etc., among which phenoxy is preferred.

As preferred groups for R^3 there may be mentioned
5 alkyl groups of 1 to 5 carbons, alkenyl groups of 2 to 5 carbons, cycloalkyl groups of 3 to 7 carbons-alkyl groups of 1 to 5 carbons and aralkyl groups of 7 to 20 carbons, and as particularly preferred groups for R^3 there may be mentioned alkyl groups of 1 to 5 carbons, among which
10 methyl, ethyl, isopropyl and n-pentyl are preferred; cycloalkyl groups of 3 to 7 carbons-alkyl groups of 1 to 5 carbons, among which cyclopentylmethyl is preferred; and benzyl.

In formula (I) above, R^4 is a substituent at the C-4
15 position, C-5 position, C-6 position or C-7 position of the benzofuran ring and represents:

R^{4a} which represents hydrogen, a nitro group, a cyano group, a halogen atom, a heterocycle, an alkenyl group of 2 to 5 carbons, an alkynyl group of 2 to 5
20 carbons, an aryl group of 6 to 10 carbons, $A=CH(CH_2)_n-$ (wherein A represents an alicyclic heterocycle, "=" represents a double bond and n represents 0, 1 or 2), $A=CH(CH_2)_mO-$ (wherein A represents an alicyclic heterocycle, "=" represents a double bond and m
25 represents 1, 2 or 3), $A-SO_2-(CH_2)_m-$ (wherein A represents an alicyclic heterocycle and m represents 1, 2 or 3), $-OR^7$ (wherein R^7 represents hydrogen, a cycloalkyl group of 3 to 7 carbons, an aryl group of 6 to 10 carbons, a heterocycle or an optionally halogen-substituted
30 alkylsulfonyl group of 1 to 4 carbons or arylsulfonyl group of 6 to 10 carbons), $-O-CO-R^8$ (wherein R^8 represents hydrogen, an alkyl group of 1 to 4 carbons, an aryl group of 6 to 10 carbons, an aralkyl group of 7 to 20 carbons or a heterocycle), $-NR^9R^{10}$ (wherein R^9 and R^{10}
35 each independently represents hydrogen, an alkyl group of 1 to 4 carbons, an aralkyl group of 7 to 20 carbons, a phenyl group, a heterocycle, $-SO_2-R^{11}$ (wherein R^{11}

represents an optionally halogen-substituted alkyl group of 1 to 12 carbons, a heterocycle-substituted alkyl group of 1 to 6 carbons, an aryl group of 6 to 10 carbons, a heterocycle or an aralkyl group of 7 to 20 carbons) or
5 -CO-R¹² (wherein R¹² represents hydrogen, an alkyl group of 1 to 12 carbons, an aryl group of 6 to 10 carbons, an aralkyl group of 7 to 20 carbons, a heterocycle, an alkoxy group of 1 to 10 carbons, a heterocycle-substituted alkyl group of 1 to 6 carbons, an aryloxy group of 6 to 10 carbons, a heteroaryloxy group or an
10 aralkyloxy group of 7 to 20 carbons)), -CO-R¹³ (wherein R¹³ represents hydrogen, -OH, an alkyl group of 1 to 4 carbons, an aryl group of 6 to 10 carbons, a heterocycle, an alkoxy group of 1 to 4 carbons, an aryloxy group of 6
15 to 10 carbons or an aralkyloxy group of 7 to 20 carbons) or -CO-NR¹⁴R¹⁵ (wherein R¹⁴ and R¹⁵ each independently represents hydrogen, an alkyl group of 1 to 4 carbons, a cycloalkyl group of 3 to 7 carbons, an aryl group of 6 to 10 carbons, an aralkyl group of 7 to 20 carbons, a
20 heterocycle or a heterocycle-substituted alkyl group of 1 to 4 carbons);

R^{4b} which represents a saturated or unsaturated alkoxy group of 1 to 6 carbons optionally substituted with 1 to 3 groups selected from the group consisting of
25 halogens, cycloalkyl groups of 3 to 7 carbons, phenyl, naphthyl, heterocycles, -OR¹⁶ (wherein R¹⁶ represents hydrogen, an alkyl group of 1 to 4 carbons, a phenyl group, a naphthyl group, a benzyl group or a heterocycle), -O-CO-R¹⁶ (wherein R¹⁶ represents hydrogen,
30 an alkyl group of 1 to 4 carbons, a phenyl group, a naphthyl group, a benzyl group or a heterocycle), -NR¹⁷R¹⁸ (wherein R¹⁷ and R¹⁸ each independently represents hydrogen, an alkyl group of 1 to 4 carbons, a heterocycle, an alkylsulfonyl group of 1 to 4 carbons, a
35 phenylsulfonyl group, -SO₂-Het (wherein Het represents a heterocycle), an aminosulfonyl group, a methylaminosulfonyl group, a dimethylaminosulfonyl group,

a diethylaminosulfonyl group, or an alkyl group of 1 to 4 carbons substituted with 1 or 2 groups selected from among phenyl, heterocycles, phenoxy, -O-Het (wherein Het represents a heterocycle) and hydroxyl, -NH-CO-R¹⁹ (wherein R¹⁹ represents hydrogen, an alkyl group of 1 to 4 carbons, a phenyl group, a naphthyl group, a benzyl group, a heterocycle, an alkoxy group of 1 to 4 carbons or a benzyloxy group), -CO-R²⁰ (wherein R²⁰ represents hydrogen, a heterocycle, an alkoxy group of 1 to 4 carbons, a phenoxy group, a benzyloxy group or -OR²¹ (wherein R²¹ represents hydrogen or a heterocycle)) and -CO-NR²²R²³ (wherein R²² and R²³ each independently represents hydrogen, an alkyl group of 1 to 4 carbons, a benzyl group or a heterocycle); or

R^{4c} which represents an alkyl group of 1 to 4 carbons optionally substituted with 1 to 3 groups selected from the group consisting of halogens, cycloalkyl groups of 3 to 7 carbons, phenyl, naphthyl, heterocycles, -SH, -OR¹⁶ (wherein R¹⁶ represents hydrogen, an alkyl group of 1 to 4 carbons, a phenyl group, a naphthyl group, a benzyl group or a heterocycle), -O-CO-R¹⁶ (wherein R¹⁶ represents hydrogen, an alkyl group of 1 to 4 carbons, a phenyl group, a naphthyl group, a benzyl group or a heterocycle), -NR¹⁷R¹⁸ (wherein R¹⁷ and R¹⁸ each independently represents hydrogen, an alkyl group of 1 to 4 carbons, a heterocycle, an alkylsulfonyl group of 1 to 4 carbons, a phenylsulfonyl group, -SO₂-Het (wherein Het represents a heterocycle), an aminosulfonyl group, a methylaminosulfonyl group, a dimethylaminosulfonyl group, a diethylaminosulfonyl group, or an alkyl group of 1 to 4 carbons substituted with 1 or 2 groups selected from among phenyl, heterocycles, phenoxy, -O-Het (wherein Het represents a heterocycle) and hydroxyl, -NH-CO-R¹⁹ (wherein R¹⁹ represents hydrogen, an alkyl group of 1 to 4 carbons, a phenyl group, a naphthyl group, a benzyl group, a heterocycle, an alkoxy group of 1 to 4 carbons or a

benzyloxy group), $-\text{CO}-\text{R}^{20}$ (wherein R^{20} represents hydrogen, a heterocycle, an alkoxy group of 1 to 4 carbons, a phenoxy group, a benzyloxy group or $-\text{OR}^{21}$ (wherein R^{21} represents hydrogen or a heterocycle)) and
5 $-\text{CO}-\text{NR}^{22}\text{R}^{23}$ (wherein R^{22} and R^{23} each independently represents hydrogen, an alkyl group of 1 to 4 carbons, a benzyl group or a heterocycle).

When R^4 is R^{4a} , there may be mentioned as specific examples of R^{4a} , hydrogen; nitro; cyano; halogen atoms
10 such as fluorine, chlorine, bromine and iodine; heterocycles such as imidazolyl, thiazolyl, isothiazolyl, pyrazolyl, triazolyl, pyrrolyl, pyridyl, pyrimidinyl, pyrazinyl, furyl, thienyl, isoxazolyl, thiazolidinyl, oxazolidinyl, imidazolidinyl, 6-oxo-4,5-benzo-1,3-oxazin-
15 2-yl, 1-oxoisoindolin-2-yl, pyrrolidinyl, 2,5-dioxopyrrolidinyl, piperidyl, 2,6-dioxopiperidyl, 1-(4-bromobenzoyl)piperidin-4-yl, morpholinyl, piperazinyl, 2,3-dioxopiperazinyl, homopiperazinyl, tetrahydrofuryl and tetrahydropyranyl; alkenyl groups such as vinyl,
20 allyl, 1-propenyl, isopropenyl, 2-butenyl, 3-butenyl, 1-pentenyl and 2-pentenyl; alkynyl groups such as ethynyl, 1-propynyl, 2-propynyl, 1-butyne, 2-butyne, 3-butyne, 2-methyl-3-butyne, 1-pentyne, 2-pentyne, 3-pentyne and 4-pentyne; aryl groups such as phenyl and naphthyl;
25 hydroxyl; cycloalkyloxy groups such as cyclopropyloxy, cyclobutyloxy, cyclopentyloxy, cyclohexyloxy and cycloheptyloxy; aryloxy groups such as phenoxy and naphthyloxy; groups represented by $-\text{O}-\text{Het}$ (wherein Het represents a heterocycle), such as imidazolyloxy,
30 thiazolyloxy, isothiazolyloxy, pyrazolyloxy, triazolyloxy, pyrrolyloxy, pyridyloxy, pyrimidinyl, pyrazinyl, furyloxy, thienyl, isoxazolyloxy, thiazolidinyloxy, oxazolidinyloxy, imidazolidinyloxy, pyrrolidinyl, piperidyloxy, morpholinyl, piperazinyl, tetrahydrofuryloxy and
35 tetrahydropyranyloxy; optionally halogen-substituted alkylsulfonyloxy groups such as methanesulfonyloxy,

ethanesulfonyloxy, n-propanesulfonyloxy and trifluoromethanesulfonyloxy; arylsulfonyloxy groups such as phenylsulfonyloxy and naphthalenesulfonyloxy; acyloxy groups such as formyloxy, acetyloxy, propionyloxy, 5 butyryloxy, isobutyryloxy and trimethylacetyloxy; arylcarboxy groups such as benzoyloxy and naphthylcarboxy; aralkylcarboxy groups such as phenylacetyloxy, 2-phenylpropionyloxy, 3-phenylbutyryloxy, diphenylacetyloxy and 10 naphthylacetyloxy; groups represented by -O-CO-Het (wherein Het represents a heterocycle), such as imidazolylcarboxy, thiazolylcarboxy, isothiazolylcarboxy, pyrazolylcarboxy, triazolylcarboxy, pyrrolylcarboxy, pyridylcarboxy, pyrimidinylcarboxy, pyrazinylcarboxy, 15 furylcarboxy, thienylcarboxy, isoxazolylcarboxy, thiazolidinylcarboxy, oxazolidinylcarboxy, imidazolidinylcarboxy, pyrrolidinylcarboxy, piperidylcarboxy, morpholinylcarboxy, piperazinylcarboxy, tetrahydrofurylcarboxy and tetrahydropyranylcarboxy; 20 amino; alkylamino groups such as methylamino, dimethylamino, ethylamino, diethylamino, propylamino, dipropylamino, isopropylamino, diisopropylamino and dibutylamino; aralkylamino groups such as benzylamino and dibenzylamino; heterocycle-substituted amino groups such 25 as imidazolylamino, N-methyl-N-imidazolylamino, thiazolylamino, N-methyl-N-thiazolylamino, isothiazolylamino, pyrazolylamino, triazolylamino, N-methyl-N-triazolylamino, pyrrolylamino, pyridylamino, N-methyl-N-pyridylamino, dipyridylamino, pyrimidinylamino, 30 pyrazinylamino, furylamino, thienylamino, isoxazolylamino, thiazolidinylamino, oxazolidinylamino, imidazolidinylamino, pyrrolidinylamino, N-methyl-N-pyrrolidinylamino, piperidylamino, morpholinylamino, N-methyl-N-morpholinylamino, tetrahydrofurylamino and 35 tetrahydropyranylamino; optionally halogen-substituted alkylsulfonylamino groups such as methanesulfonylamino, N-methyl-N-methanesulfonylamino, ethanesulfonylamino, n-

propanesulfonylamino and trifluoromethanesulfonylamino;
arylsulfonylamino groups such as phenylsulfonylamino, N-
methyl-N-phenylsulfonylamino, N-(4-chlorophenylsulfonyl)-
N-methylamino and naphthalenesulfonylamino; acylamino
5 groups such as formylamino, acetylamino, N-methyl-N-
acetylamino, propionylamino, butyrylamino,
isobutyrylamino, N-methyl-N-isobutyrylamino and
trimethylacetylamino; arylcarbonylamino groups such as
benzoylamino, N-methyl-N-benzoylamino and
10 naphthylcarbonylamino; aralkylcarbonylamino groups such
as phenylacetylamino, N-methyl-N-phenylacetylamino, 2-
phenylpropionylamino, 3-phenylbutyrylamino,
diphenylacetylamino and naphthylacetylamino; amino groups
substituted with a group represented by -CO-Het (wherein
15 Het represents a heterocycle), such as
imidazolylcarbonylamino, N-methyl-N-
imidazolylcarbonylamino, thiazolylcarbonylamino, N-
methyl-N-thiazolylcarbonylamino, pyridylcarbonylamino, N-
methyl-N-pyridylcarbonylamino, pyrimidinylcarbonylamino,
20 N-methyl-N-pyrimidinylcarbonylamino,
pyrazinylcarbonylamino, N-methyl-N-
pyrazinylcarbonylamino, furylcarbonylamino,
thienylcarbonylamino, N-methyl-N-thienylcarbonylamino, N-
methyl-N-oxazolylcarbonylamino, N-methyl-N-
25 tetrazolylcarbonylamino, thiazolidinylcarbonylamino,
oxazolidinylcarbonylamino, imidazolidinylcarbonylamino,
pyrrolidinylcarbonylamino and piperidylcarbonylamino;
alkoxycarbonylamino groups such as methoxycarbonylamino,
ethoxycarbonylamino, n-propoxycarbonylamino,
30 isopropoxycarbonylamino, t-butoxycarbonylamino and N-
methyl-N-(t-butoxycarbonyl)amino; aryloxycarbonylamino
groups such as phenoxycarbonylamino and
naphthyloxycarbonylamino; aralkyloxycarbonylamino groups
such as benzyloxycarbonylamino,
35 phenethyloxycarbonylamino, phenylpropoxycarbonylamino,
benzhydryloxycarbonylamino and
naphthylmethoxycarbonylamino; formyl; carboxyl;

alkoxycarbonyl groups such as methoxycarbonyl, ethoxycarbonyl, n-propoxycarbonyl, isopropoxycarbonyl and t-butoxycarbonyl; aryloxycarbonyl groups such as phenoxycarbonyl and naphthyloxycarbonyl;

5 aralkyloxycarbonyl groups such as benzyloxycarbonyl, phenethyloxycarbonyl, phenylpropoxycarbonyl, benzhydryloxycarbonyl and naphthylmethoxycarbonyl; acyl groups such as acetyl, propionyl, butyryl and isobutyryl; arylcarbonyl groups such as benzoyl and naphthylcarbonyl;

10 groups represented by -CO-Het (wherein Het represents a heterocycle), such as imidazolylcarbonyl, thiazolylcarbonyl, isothiazolylcarbonyl, pyrazolylcarbonyl, triazolylcarbonyl, pyrrolylcarbonyl, pyridylcarbonyl, pyrimidinylcarbonyl, pyrazinylcarbonyl,

15 furylcarbonyl, thienylcarbonyl, isoxazolylcarbonyl, thiazolidinylcarbonyl, oxazolidinylcarbonyl, imidazolidinylcarbonyl, pyrrolidinylcarbonyl, piperidylcarbonyl, morpholinylcarbonyl, piperazinylcarbonyl and 1,3,4-trihydroisoquinon-2-ylcarbonyl; carbamoyl groups such as carbamoyl,

20 methylcarbamoyl, dimethylcarbamoyl, ethylcarbamoyl, diethylcarbamoyl, propylcarbamoyl, dipropylcarbamoyl, cyclopropylcarbamoyl, cyclopentylcarbamoyl, cyclohexylcarbamoyl, phenylcarbamoyl, 4-bromo-2-

25 cyanophenylcarbamoyl, N-methyl-N-phenylcarbamoyl, benzylcarbamoyl, N-benzyl-N-methylcarbamoyl, N-methyl-N-phenethylcarbamoyl, dibenzylcarbamoyl, imidazolylcarbamoyl, N-imidazolyl-N-methylcarbamoyl, N-benzimidazolyl-N-methylcarbamoyl, thiazolylcarbamoyl, N-

30 methyl-N-thiazolylcarbamoyl, benzothiazolylcarbamoyl, N-benzothiazolyl-N-methylcarbamoyl, isothiazolylcarbamoyl, oxazolylcarbamoyl, N-methyl-N-oxazolylcarbamoyl, benzoxazolylcarbamoyl, N-benzoxazolyl-N-methylcarbamoyl, pyrazolylcarbamoyl, triazolylcarbamoyl,

35 pyrrolylcarbamoyl, pyridylcarbamoyl, N-methyl-N-pyridylcarbamoyl, N-methyl-N-(pyridylmethyl)carbamoyl, pyrimidinylcarbamoyl, pyrazinylcarbamoyl, furylcarbamoyl,

thienylcarbamoyl, isoxazolylcarbamoyl,
thiazolidinylcarbamoyl, oxazolidinylcarbamoyl,
imidazolidinylcarbamoyl, pyrrolidinylcarbamoyl,
piperidylcarbamoyl, tetrahydrofurylcarbamoyl and
5 tetrahydropyranylcarbamoyl; groups represented by
 $A=CH(CH_2)_n-$ (wherein A represents an alicyclic
heterocycle, "=" represents a double bond and n
represents 0, 1, or 2), such as (3,5-dioxo-2,4-
thiazolidinylidene)methyl, (3,5-dioxo-2,4-
10 oxazolidinylidene)methyl, (2,5-dioxoimidazolidin-4-
ylidene)methyl, (5-oxo-3-thioxo-2,4-
thiazolidinylidene)methyl, (2,4,6-trioxo-3,5-
diazaperhydroinylidene)methyl and (3,5-dimethyl-2,4,6-
trioxo-3,5-diazaperhydroinylidene)methyl; groups
15 represented by $A=CH(CH_2)_mO-$ (wherein A represents an
alicyclic heterocycle, "=" represents a double bond and m
represents 1, 2, or 3), such as 2-(3,5-dioxo-2,4-
thiazolidinylidene)ethoxy, 2-(3,5-dioxo-2,4-
oxazolidinylidene)ethoxy, 2-(2,5-dioxoimidazolidin-4-
20 ylidene)ethoxy, 2-(5-oxo-3-thioxo-2,4-
thiazolidinylidene)ethoxy, 2-(2,4,6-trioxo-3,5-
diazaperhydroinylidene)ethoxy and 2-(3,5-dimethyl-2,4,6-
trioxo-3,5-diazaperhydroinylidene)ethoxy; and groups
represented by $A-SO_2-(CH_2)_m-$ (wherein A represents an
25 alicyclic heterocycle and m represents 1, 2, or 3), such
as (3,5-dioxo-2,4-thiazolidinyl)sulfonylmethyl, (3,5-
dioxo-2,4-oxazolidinyl)sulfonylmethyl, (2,5-
dioxoimidazolidin-4-yl)sulfonylmethyl, and (5-oxo-3-
thioxo-2,4-thiazolidinyl)sulfonylmethyl.

30 As preferred groups for R^{4a} there may be
specifically mentioned, for example, hydrogen, nitro,
cyano, bromine, imidazolyl, thiazolyl, pyridyl,
pyrimidinyl, furyl, thienyl, morpholinyl, piperazinyl,
hydroxyl, pyrrolidinyloxy, piperidyloxy,
35 methanesulfonyloxy, trifluoromethanesulfonyloxy,
phenylsulfonyloxy, acetyloxy, benzoyloxy,
imidazolylcarboxy, thiazolylcarboxy, pyridylcarboxy,

pyrimidinylcarboxy, pyrazinylcarboxy, dimethylamino,
ethylamino, diethylamino, dibenzylamino, imidazolylamino,
thiazolylamino, pyridylamino, pyrimidinylamino, N-methyl-
N-methanesulfonylamino, phenylsulfonylamino, N-methyl-N-
5 phenylsulfonylamino, N-methyl-N-acetylamino, N-methyl-N-
isobutyrylamino, N-methyl-N-benzoylamino, N-methyl-N-
phenylacetylamino, N-methyl-N-imidazolylcarbonylamino, N-
methyl-N-thiazolylcarbonylamino, N-methyl-N-
thienylcarbonylamino, N-methyl-N-oxazolylcarbonylamino,
10 N-methyl-N-tetrazolylcarbonylamino, N-methyl-N-
pyridylcarbonylamino, N-methyl-N-pyrazinylcarbonylamino,
N-methyl-N-pyrimidinylcarbonylamino, N-methyl-N-(t-
butoxycarbonyl)amino, dimethylcarbamoyl,
cyclohexylcarbamoyl, phenylcarbamoyl, N-methyl-N-
15 phenylcarbamoyl, N-benzyl-N-methylcarbamoyl,
imidazolylcarbamoyl, benzimidazolylcarbamoyl,
thiazolylcarbamoyl, N-methyl-N-thiazolylcarbamoyl,
benzothiazolylcarbamoyl, isothiazolylcarbamoyl,
pyrazolylcarbamoyl, triazolylcarbamoyl,
20 pyrrolylcarbamoyl, pyridylcarbamoyl, N-methyl-N-
pyridylcarbamoyl, pyrimidinylcarbamoyl,
pyrazinylcarbamoyl, isoxazolylcarbamoyl,
piperidylcarbamoyl, 1,3,4-trihydroisoquinolin-2-
ylcarbonyl, formyl, carboxyl, methoxycarbonyl,
25 ethoxycarbonyl, n-propoxycarbonyl, isopropoxycarbonyl, t-
butoxycarbonyl, acetyl, benzoyl, (3,5-dioxo-2,4-
thiazolidinylidene)methyl, (3,5-dioxo-2,4-
oxazolidinylidene)methyl, (2,5-dioxoimidazolidin-4-
ylidene)methyl, (5-oxo-3-thioxo-2,4-
30 thiazolidinylidene)methyl, 2-(3,5-dioxo-2,4-
thiazolidinylidene)ethoxy, 2-(3,5-dioxo-2,4-
oxazolidinylidene)ethoxy, 2-(2,5-dioxoimidazolidin-4-
ylidene)ethoxy, 2-(5-oxo-3-thioxo-2,4-
thiazolidinylidene)ethoxy, (3,5-dioxo-2,4-
35 thiazolidinyl)sulfonylmethyl, (3,5-dioxo-2,4-
oxazolidinyl)sulfonylmethyl, (2,5-dioxoimidazolidin-4-
yl)sulfonylmethyl and (5-oxo-3-thioxo-2,4-

thiazolidinyl)sulfonylmethyl.

As particularly preferred groups for R^{4a} there may be specifically mentioned, for example, hydrogen, nitro, cyano, bromine, thienyl, piperazinyl,
5 trifluoromethanesulfonyloxy, phenylsulfonyloxy, acetyloxy, dimethylamino, dibenzylamino, N-methyl-N-methanesulfonylamino, N-methyl-N-phenylsulfonylamino, N-methyl-N-acetylamino, N-methyl-N-isobutyrylamino, N-methyl-N-benzoylamino, N-methyl-N-phenylacetylamino, N-
10 methyl-N-thienylcarbonylamino, N-methyl-N-oxazolylcarbonylamino, N-methyl-N-thiazolylcarbonylamino, N-methyl-N-pyridylcarbonylamino, thiazolylcarbamoyl, benzothiazolylcarbamoyl, benzimidazolylcarbamoyl, N-methyl-N-phenylcarbamoyl, 1,3,4-trihydroisoquinolin-2-
15 ylcarbonyl, methoxycarbonyl, isopropoxycarbonyl, and (3,5-dioxo-2,4-thiazolidinylidene)methyl.

When R^4 is R^{4b} , there may be mentioned as specific examples of substituents on the alkoxy groups of 1 to 4 carbons for R^{4a} , for example, halogen atoms such as
20 fluorine, chlorine, bromine and iodine; cycloalkyl groups of 3 to 7 carbons such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and cycloheptyl; aryl groups of 6 to 10 carbons such as phenyl, aminophenyl and naphthyl; heterocycles such as imidazolyl, N-tosylimidazolyl,
25 thiazolyl, 2-(morpholinesulfonyl)thiazolyl, isothiazolyl, pyrazolyl, triazolyl, tetrazolyl, pyrrolyl, pyridyl, 2-methoxypyridyl, 5-hydroxypyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, triazinyl, furyl, thienyl, 2-(morpholinesulfonyl)thienyl, oxazolyl, 2-phenyloxazolyl,
30 isoxazolyl, thiazolidinyl, oxazolidinyl, imidazolidinyl, pyrrolidinyl, piperidyl, morpholinyl, piperazinyl, tetrahydrofuryl, tetrahydropyranyl and dioxolanyl; -OH; alkoxy groups of 1 to 4 carbons such as methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, isobutoxy, sec-butoxy,
35 t-butoxy, n-pentyloxy, isopentyloxy, 3-pentyloxy, 2,2-dimethylpropoxy, n-hexyloxy, 4-methylpentyloxy and 2-ethylbutoxy; aryloxy groups of 6 to 10 carbons such as

phenoxy and naphthyloxy; benzyloxy; groups represented by
-O-Het (wherein Het represents a heterocycle), such as
pyridyloxy and piperidyloxy; acyloxy groups of 1 to 5
carbons such as formyloxy, acetyloxy, propionyloxy,
5 butyryloxy, isobutyryloxy and trimethylacetyloxy;
arylcarboxy groups of 7 to 11 carbons such as benzoyloxy
and naphthylcarboxy; phenylacetyloxy; groups represented
by -O-CO-Het (wherein Het represents a heterocycle), such
as imidazolylcarboxy, thiazolylcarboxy,
10 isothiazolylcarboxy, pyrazolylcarboxy, triazolylcarboxy,
pyrrolylcarboxy, pyridylcarboxy, pyrimidinylcarboxy,
pyrazinylcarboxy, furylcarboxy, thienylcarboxy,
isoxazolylcarboxy, thiazolidinylcarboxy,
oxazolidinylcarboxy, imidazolidinylcarboxy,
15 pyrrolidinylcarboxy, piperidylcarboxy,
morpholinylcarboxy, piperazinylcarboxy,
tetrahydrofurylcarboxy and tetrahydropyranylcarboxy;
amino; monosubstituted or disubstituted amino groups such
as methylamino, dimethylamino, ethylamino, diethylamino,
20 propylamino, dipropylamino, isopropylamino,
diisopropylamino, dibutylamino, benzylamino,
dibenzylamino, 2-hydroxy-2-phenethylamino, 2-hydroxy-3-
phenoxypropylamino, imidazolylamino, thiazolylamino,
isothiazolylamino, pyrazolylamino, triazolylamino,
25 pyrrolylamino, pyridylamino, dipyridylamino,
pyrimidinylamino, pyrazinylamino, furylamino,
thienylamino, isoxazolylamino, thiazolidinylamino,
oxazolidinylamino, imidazolidinylamino,
pyrrolidinylamino, piperidylamino, tetrahydrofurylamino
30 and tetrahydropyranylamino; optionally halogen-
substituted alkylsulfonylamino groups of 1 to 4 carbons
such as methanesulfonylamino, ethanesulfonylamino, n-
propanesulfonylamino and trifluoromethanesulfonylamino;
phenylsulfonylamino; acylamino groups of 1 to 5 carbons
35 such as dimethylaminosulfonylamino,
methylaminosulfonylamino, formylamino, acetylamino,
propionylamino, butyrylamino, isobutyrylamino and

trimethylacetyl-amino; arylcarbonylamino groups of 7 to 11 carbons such as benzoylamino and naphthylcarbonylamino; phenylacetyl-amino; groups represented by -NH-CO-Het (wherein Het represents a heterocycle), such as

5 imidazolylcarbonylamino, thiazolylcarbonylamino, isoxazolylcarbonylamino, pyridylcarbonylamino, pyrimidinylcarbonylamino, pyrazinylcarbonylamino, furylcarbonylamino, thienylcarbonylamino, pyrrolidinylcarbonylamino, piperidylcarbonylamino and

10 morpholinylcarbonylamino; alkoxycarbonylamino groups of 2 to 5 carbons such as methoxycarbonylamino, ethoxycarbonylamino, n-propoxycarbonylamino, isopropoxycarbonylamino and t-butoxycarbonylamino; benzyloxycarbonylamino; formyl; carboxy; alkoxycarbonyl

15 groups of 2 to 5 carbons such as methoxycarbonyl, ethoxycarbonyl, n-propoxycarbonyl, isopropoxycarbonyl and t-butoxycarbonyl; phenoxycarbonyl; benzyloxycarbonyl; acyl groups of 2 to 5 carbons such as acetyl, propionyl, butyryl and isobutyryl; groups represented by -CO-Het

20 (wherein Het represents a heterocycle) such as imidazolylcarbonyl, thiazolylcarbonyl, isothiazolylcarbonyl, pyrazolylcarbonyl, triazolylcarbonyl, pyrrolylcarbonyl, pyridylcarbonyl, pyrimidinylcarbonyl, pyrazinylcarbonyl, furylcarbonyl,

25 thienylcarbonyl, isoxazolylcarbonyl, thiazolidinylcarbonyl, oxazolidinylcarbonyl, imidazolidinylcarbonyl, pyrrolidinylcarbonyl, piperidylcarbonyl, morpholinylcarbonyl and piperazinylcarbonyl; groups represented by -CO-O-Het

30 (wherein Het represents a heterocycle), such as pyridyloxycarbonyl and piperidyloxycarbonyl; and carbamoyl groups such as carbamoyl, methylcarbamoyl, dimethylcarbamoyl, ethylcarbamoyl, diethylcarbamoyl, propylcarbamoyl, dipropylcarbamoyl, benzylcarbamoyl,

35 dibenzylcarbamoyl, imidazolylcarbamoyl, thiazolylcarbamoyl, isothiazolylcarbamoyl, pyrazolylcarbamoyl, triazolylcarbamoyl,

pyrrolylcarbamoyl, pyridylcarbamoyl,
pyrimidinylcarbamoyl, pyrazinylcarbamoyl, furylcarbamoyl,
thienylcarbamoyl, isoxazolylcarbamoyl,
thiazolidinylcarbamoyl, oxazolidinylcarbamoyl,
5 imidazolidinylcarbamoyl, pyrrolidinylcarbamoyl,
piperidylcarbamoyl, tetrahydrofurylcarbamoyl and
tetrahydropyranylcarbamoyl.

As preferred groups for R^{4b} there may be
specifically mentioned, for example, saturated or
10 unsaturated alkoxy groups such as methoxy, 2-propynyloxy,
2-butyloxy, 3-hexenyloxy, 5-hexenyloxy and 2,2-
dimethylpropoxy; halogen-substituted alkoxy groups such
as 2-bromoethoxy and 2-chloroethoxy; cycloalkyl-alkoxy
groups such as cyclopentylmethoxy and cyclohexylmethoxy;
15 aryl-alkoxy groups such as benzyloxy, aminobenzyloxy,
chlorobenzyloxy, fluorobenzyloxy, bromobenzyloxy,
nitrobenzyloxy, (trifluoromethyl)benzyloxy,
dichlorobenzyloxy, dimethylbenzyloxy, methoxybenzyloxy,
sulfamoylbenzyloxy, (methylenedioxy)benzyloxy,
20 carboxybenzyloxy, (methoxycarbonyl)benzyloxy, n-
butoxybenzyloxy, 3-phenylpropoxy,
di(methoxyphenyl)methoxy, 2,2-diphenylethoxy, 1-methyl-1-
phenylethoxy and naphthylmethoxy; heterocycle-substituted
alkoxy groups such as thienylmethoxy, 2-
25 (morpholinesulfonyl)thienylmethoxy, pyridylmethoxy, (5-
hydroxypyridyl)methoxy, (2-methoxypyridyl)methoxy, 2-
(pyridyl)ethoxy, pyrazinylmethoxy, pyrimidinylmethoxy, N-
tosylimidazolylmethoxy, oxazolylmethoxy, 2-
phenyloxazolylmethoxy, thiazolylmethoxy, 2-
30 (morpholinesulfonyl)thiazolylmethoxy, (3,5-dioxo-2,4-
thiazolidinyl)methoxy, N-methylpiperidylmethoxy, N-t-
butoxycarbonylpiperidylmethoxy, N-acetylpiperidylmethoxy,
N-methanesulfonylpiperidylmethoxy, (4-oxachroman-2-
yl)methoxy, (3,3-dimethyl-2,4-dioxolanyl)methoxy, (1-
35 methyl-3-oxetanyl)methoxy and 2-(morpholin-4-yl)ethoxy;
alkoxy-alkoxy groups such as methoxymethyl and 2-
ethoxyethoxy; benzyloxy-alkoxy groups such as 2-

(benzyloxy)ethoxy; acyloxy-alkoxy groups such as 2-(acetyloxy)ethoxy; alkylamino-alkoxy groups such as bis(dimethylaminomethyl)methoxy; alkoxycarbonylamino-alkoxy groups such as 4-(t-butoxycarbonylamino)butoxy;
5 and alkoxycarbonyl-alkoxy groups such as ethoxycarbonylmethoxy, 2-(methoxycarbonyl)ethoxy and 5-(ethoxycarbonyl)pentyloxy.

As particularly preferred groups for R^{4b} there may be specifically mentioned, for example, methoxy, 2-
10 propynyloxy, benzyloxy, aminobenzyloxy, chlorobenzyloxy, fluorobenzyloxy, (trifluoromethyl)benzyloxy, dichlorobenzyloxy, dimethylbenzyloxy, methoxybenzyloxy, sulfamoylbenzyloxy, (methylenedioxy)benzyloxy, carboxybenzyloxy, (methoxycarbonyl)benzyloxy, n-
15 butoxybenzyloxy, thienylmethoxy, 2-(morpholinesulfonyl)thienylmethoxy, pyridylmethoxy, (2-methoxypyridyl)methoxy, (5-hydroxypyridyl)methoxy, 2-(pyridyl)ethoxy, pyrazinylmethoxy, pyrimidinylmethoxy, N-tosylimidazolylmethoxy, oxazolylmethoxy, 2-
20 phenyloxazolylmethoxy, thiazolylmethoxy, 2-(morpholinesulfonyl)thiazolylmethoxy, (3,5-dioxo-2,4-thiazolidinyl)methoxy, N-methylpiperidylmethoxy and methoxymethyl.

When R^4 is R^{4c} , there may be mentioned as specific
25 examples of substituents on the alkoxy groups of 1 to 4 carbons for R^{4c} , for example, halogen atoms such as fluorine, chlorine, bromine, iodine; cycloalkyl groups of 3 to 7 carbons such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and cycloheptyl; aryl groups of 6
30 to 10 carbons such as phenyl and naphthyl; heterocycles such as imidazolyl, thiazolyl, isothiazolyl, pyrazolyl, triazolyl, tetrazolyl, pyrrolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, triazinyl, furyl, thienyl, oxazolyl, isoxazolyl, thiazolidinyl, oxazolidinyl, 3,5-dioxooxazolidinyl, imidazolidinyl, 2-oxoimidazolidinyl,
35 pyrrolidinyl, piperidyl, morpholinyl, pyrazolidinyl, 3,5-dioxopyrazolidinyl, piperazinyl, 2,5-dioxopiperazinyl,

tetrahydrofuryl, tetrahydropyranyl and dioxolanyl; -SH; -OH; alkoxy groups of 1 to 4 carbons such as methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, isobutoxy, sec-butoxy, t-butoxy, n-pentyloxy, isopentyloxy, 3-pentyloxy, 2,2-dimethylpropoxy, n-hexyloxy, 4-methylpentyloxy and 2-ethylbutoxy; aryloxy groups of 6 to 10 carbons such as phenoxy and naphthyloxy; benzyloxy; groups represented by -O-Het (wherein Het represents a heterocycle), such as pyridyloxy and piperidyloxy; acyloxy groups of 1 to 5 carbons such as formyloxy, acetyloxy, propionyloxy, butyryloxy, isobutyryloxy and trimethylacetyloxy; arylcarboxy groups of 7 to 11 carbons such as benzoyloxy and naphthylcarboxy; phenylacetyloxy; groups represented by -O-CO-Het (wherein Het represents a heterocycle), such as imidazolylcarboxy, thiazolylcarboxy, isothiazolylcarboxy, pyrazolylcarboxy, triazolylcarboxy, pyrrolylcarboxy, pyridylcarboxy, pyrimidinylcarboxy, pyrazinylcarboxy, furylcarboxy, thienylcarboxy, isoxazolylcarboxy, thiazolidinylcarboxy, oxazolidinylcarboxy, imidazolidinylcarboxy, pyrrolidinylcarboxy, piperidylcarboxy, morpholinylcarboxy, piperazinylcarboxy, tetrahydrofurylcarboxy and tetrahydropyranylcarboxy; amino; monosubstituted or disubstituted amino groups such as methylamino, dimethylamino, ethylamino, 2-hydroxy-2-phenethylamino, 2-hydroxy-3-phenoxypropylamino, diethylamino, propylamino, dipropylamino, isopropylamino, diisopropylamino, dibutylamino, benzylamino, dibenzylamino, imidazolylamino, thiazolylamino, isothiazolylamino, pyrazolylamino, triazolylamino, pyrrolylamino, pyridylamino, dipyridylamino, pyrimidinylamino, pyrazinylamino, furylamino, thienylamino, isoxazolylamino, thiazolidinylamino, oxazolidinylamino, imidazolidinylamino, pyrrolidinylamino, piperidylamino, tetrahydrofurylamino and tetrahydropyranylamino; optionally halogen-substituted alkylsulfonylamino groups of 1 to 4 carbons

such as methanesulfonylamino, ethanesulfonylamino, n-propanesulfonylamino and trifluoromethanesulfonylamino; phenylsulfonylamino; acylamino groups of 1 to 5 carbons such as formylamino, acetylamino, propionylamino, butyrylamino, isobutyrylamino and trimethylacetylamino; arylcarbonylamino groups of 7 to 11 carbons such as benzoylamino, 4-chlorobenzoylamino and naphthylcarbonylamino; phenylacetylamino; groups represented by -NH-CO-Het (wherein Het represents a heterocycle), such as imidazolylcarbonylamino, thiazolylcarbonylamino, pyridylcarbonylamino, pyrimidinylcarbonylamino, pyrazinylcarbonylamino, furylcarbonylamino, thienylcarbonylamino, thiazolidinylcarbonylamino, oxazolidinylcarbonylamino, imidazolidinylcarbonylamino, pyrrolidinylcarbonylamino and piperidylcarbonylamino; alkoxycarbonylamino groups of 2 to 5 carbons such as methoxycarbonylamino, ethoxycarbonylamino, n-propoxycarbonylamino, isopropoxycarbonylamino and t-butoxycarbonylamino; benzyloxycarbonylamino; formyl; carboxyl; alkoxycarbonyl groups of 2 to 5 carbons such as methoxycarbonyl, ethoxycarbonyl, n-propoxycarbonyl, isopropoxycarbonyl and t-butoxycarbonyl; phenoxycarbonyl; benzyloxycarbonyl; acyl groups of 2 to 5 carbons such as acetyl, propionyl, butyryl and isobutyryl; groups represented by -CO-Het (wherein Het represents a heterocycle), such as imidazolylcarbonyl, thiazolylcarbonyl, isothiazolylcarbonyl, pyrazolylcarbonyl, triazolylcarbonyl, pyrrolylcarbonyl, pyridylcarbonyl, pyrimidinylcarbonyl, pyrazinylcarbonyl, furylcarbonyl, thienylcarbonyl, isoxazolylcarbonyl, thiazolidinylcarbonyl, oxazolidinylcarbonyl, imidazolidinylcarbonyl, pyrrolidinylcarbonyl, piperidylcarbonyl, morpholinylcarbonyl and piperazinylcarbonyl; groups represented by -CO-O-Het (wherein Het represents a heterocycle), such as pyridyloxycarbonyl and piperidyloxycarbonyl; and

carbamoyl groups such as carbamoyl, methylcarbamoyl, dimethylcarbamoyl, ethylcarbamoyl, diethylcarbamoyl, propylcarbamoyl, dipropylcarbamoyl, benzylcarbamoyl, dibenzylcarbamoyl, imidazolylcarbamoyl, 5 thiazolylcarbamoyl, isothiazolylcarbamoyl, pyrazolylcarbamoyl, triazolylcarbamoyl, pyrrolylcarbamoyl, pyridylcarbamoyl, pyrimidinylcarbamoyl, pyrazinylcarbamoyl, furylcarbamoyl, thienylcarbamoyl, isoxazolylcarbamoyl, 10 thiazolidinylcarbamoyl, oxazolidinylcarbamoyl, imidazolidinylcarbamoyl, pyrrolidinylcarbamoyl, piperidylcarbamoyl, tetrahydrofurylcarbamoyl and tetrahydropyranylcarbamoyl.

As preferred groups for R^{4c} there may be 15 specifically mentioned, for example, phenethyl, α -hydroxybenzyl, 1-(acetyloxy)ethyl and (3,5-dioxo-2,4-thiazolidinyl)methyl.

Thus, as specific preferred combinations for R^1 , R^2 , R^3 , and R^4 there may be mentioned those in which, for 20 example, R^1 is methyl, ethyl, or isopropyl, R^2 is an acetyl or propionyl group substituted with a substituent selected from the group consisting of phenyl, phenoxy, amino, t-butoxycarbonylamino, benzyloxycarbonylamino, (benzyloxycarbonyl)-N-methylamino, acetylamino, and 25 morpholinylcarbonyl; or hydrogen, acetyl, propionyl, isobutyryl, benzoyl, pyridylcarbonyl, pyrrolidinylcarbonyl, furylcarbonyl, methanesulfonyl, or trifluoromethanesulfonyl, R^3 is methyl, ethyl, isopropyl, n-pentyl, cyclopentylmethyl or benzyl, and R^4 is 30 hydrogen, nitro, cyano, bromine, thienyl, piperazinyl, trifluoromethanesulfonyloxy, phenylsulfonyloxy, acetyloxy, dimethylamino, dibenzylamino, N-methyl-N-methanesulfonylamino, N-methyl-N-phenylsulfonylamino, N-methyl-N-acetylamino, N-methyl-N-isobutyrylamino, N- 35 methyl-N-benzoylamino, N-methyl-N-phenylacetylamino, N-methyl-N-imidazolylcarbonylamino, N-methyl-N-thiazolylcarbonylamino, N-methyl-N-pyridylcarbonylamino,

N-methyl-N-pyrimidinylcarbonylamino, N-methyl-N-pyrazinylcarbonylamino, N-methyl-N-thienylcarbonylamino, N-methyl-N-oxazolylcarbonylamino, N-methyl-N-(t-butoxycarbonyl)amino, thiazolylcarbonyl,
5 methoxycarbonyl, isopropoxycarbonyl, (3,5-dioxo-2,4-thiazolidinylidene)methyl, methoxy, 2-propynyloxy, benzyloxy, aminobenzyloxy, chlorobenzyloxy, fluorobenzyloxy, (trifluoromethyl)benzyloxy, dichlorobenzyloxy, dimethylbenzyloxy, methoxybenzyloxy,
10 sulfamoylbenzyloxy, (methylenedioxy)benzyloxy, carboxybenzyloxy, (methoxycarbonyl)benzyloxy, n-butoxybenzyloxy, thienylmethoxy, 2-(morpholinesulfonyl)thienylmethoxy, pyridylmethoxy, (2-methoxypyridyl)methoxy, 2-(pyridyl)ethoxy,
15 pyrazinylmethoxy, pyrimidinylmethoxy, N-tosylimidazolylmethoxy, oxazolylmethoxy, 2-phenyloxazolylmethoxy, thiazolylmethoxy, 2-(morpholinesulfonyl)thiazolylmethoxy, (3,5-dioxo-2,4-thiazolidinyl)methoxy, N-methylpiperidylmethoxy,
20 methoxymethyl, phenethyl, α -hydroxybenzyl, 1-(acetyloxy)ethyl or (3,5-dioxo-2,4-thiazolidinyl)methyl.

As specific compounds represented by structural formula (I) above there may be mentioned those compounds mentioned in the examples of the present specification,
25 but additional compounds that may be mentioned included the following:

6-(benzofuran-2-yl)-3-ethyl-4-hydroxy-5-methyl-2H-pyran-2-one;
6-(benzofuran-2-yl)-4-hydroxy-5-methyl-3-n-propyl-
30 2H-pyran-2-one;
4-acetyloxy-6-(benzofuran-2-yl)-5-ethyl-3-methyl-2H-pyran-2-one;
4-acetyloxy-6-(benzofuran-2-yl)-5-isopropyl-3-methyl-2H-pyran-2-one;
35 6-(benzofuran-2-yl)-4-(2-(t-butoxycarbonylamino)acetyloxy)-5-ethyl-3-methyl-2H-pyran-2-one;

- 6-(benzofuran-2-yl)-5-ethyl-3-methyl-4-(2-pyrrolidon-5-ylcarboxy)-2H-pyran-2-one;
4-(2-aminoacetyloxy)-6-(benzofuran-2-yl)-5-ethyl-3-methyl-2H-pyran-2-one;
5 4-(3-acetyl-amino-4-morpholinyl-4-oxobutyryloxy)-6-(benzofuran-2-yl)-5-ethyl-3-methyl-2H-pyran-2-one;
6-(benzofuran-2-yl)-3,5-dimethyl-4-propionyloxy-2H-pyran-2-one;
6-(benzofuran-2-yl)-5-ethyl-4-isobutyryloxy-3-methyl-2H-pyran-2-one;
10 6-(benzofuran-2-yl)-3,5-dimethyl-4-isovaleryloxy-2H-pyran-2-one;
6-(benzofuran-2-yl)-3,5-dimethyl-4-(2,2,2-trimethylacetyloxy)-2H-pyran-2-one;
15 6-(benzofuran-2-yl)-4-cyclohexylcarboxy-3,5-dimethyl-2H-pyran-2-one;
6-(benzofuran-2-yl)-4-(2-cyclopropylacetyloxy)-3,5-dimethyl-2H-pyran-2-one;
6-(benzofuran-2-yl)-4-(2-cyclopentylacetyloxy)-3,5-dimethyl-2H-pyran-2-one;
20 6-(benzofuran-2-yl)-4-benzoyloxy-5-ethyl-3-methyl-2H-pyran-2-one;
6-(benzofuran-2-yl)-4-benzoyloxy-5-isopropyl-3-methyl-2H-pyran-2-one;
25 6-(benzofuran-2-yl)-3,5-dimethyl-4-naphthylcarboxy-2H-pyran-2-one;
6-(benzofuran-2-yl)-3,5-dimethyl-4-imidazolylcarboxy-2H-pyran-2-one;
6-(benzofuran-2-yl)-3,5-dimethyl-4-thiazolylcarboxy-2H-pyran-2-one;
30 6-(benzofuran-2-yl)-3,5-dimethyl-4-triazolylcarboxy-2H-pyran-2-one;
6-(benzofuran-2-yl)-5-ethyl-3-methyl-4-pyridylcarboxy-2H-pyran-2-one;
35 6-(benzofuran-2-yl)-3,5-dimethyl-4-pyrimidinylcarboxy-2H-pyran-2-one;
6-(benzofuran-2-yl)-3,5-dimethyl-4-pyrazinylcarboxy-

- 2H-pyran-2-one;
6-(benzofuran-2-yl)-3,5-dimethyl-4-thienylcarboxy-
2H-pyran-2-one;
6-(benzofuran-2-yl)-3,5-dimethyl-4-
5 isoxazolylcarboxy-2H-pyran-2-one;
6-(benzofuran-2-yl)-3,5-dimethyl-4-(2-
imidazolylacetyloxy)-2H-pyran-2-one;
6-(benzofuran-2-yl)-3,5-dimethyl-4-(2-
pyridylacetyloxy)-2H-pyran-2-one;
10 6-(benzofuran-2-yl)-3,5-dimethyl-4-(2-
methoxyacetyloxy)-2H-pyran-2-one;
6-(benzofuran-2-yl)-3,5-dimethyl-4-(2-t-
butoxyacetyloxy)-2H-pyran-2-one;
6-(benzofuran-2-yl)-4-hydroxy-3-methyl-5-n-propyl-
15 2H-pyran-2-one;
6-(benzofuran-2-yl)-5-cyclopentyl-4-hydroxy-3-
methyl-2H-pyran-2-one;
6-(benzofuran-2-yl)-5-cyclopropylmethyl-4-hydroxy-3-
methyl-2H-pyran-2-one;
20 6-(benzofuran-2-yl)-5-cyclohexylmethyl-4-hydroxy-3-
methyl-2H-pyran-2-one;
6-(benzofuran-2-yl)-4-hydroxy-3-methyl-5-
naphthylmethyl-2H-pyran-2-one;
6-(benzofuran-2-yl)-5-ethoxy-4-hydroxy-3-methyl-2H-
25 pyran-2-one;
6-(benzofuran-2-yl)-4-hydroxy-5-isopropoxy-3-methyl-
2H-pyran-2-one;
4-acetyloxy-3,5-dimethyl-6-(5-(2-thienyl)benzofuran-
2-yl)-2H-pyran-2-one;
30 3,5-dimethyl-6-(5-((3,5-dioxo-2,4-oxazolidinylidene)
methyl)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one;
3,5-dimethyl-6-(5-((2,5-dioxoimidazolidin-4-
ylidene)methyl)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(5-((5-oxo-3-thioxo-2,4-
35 thiazolidinylidene)methyl)benzofuran-2-yl)-2H-pyran-2-
one;
3,5-dimethyl-4-hydroxy-6-(5-((2,4,6-trioxo-3,5-

- diazaperhydroinylidene)methyl)benzofuran-2-yl)-2H-pyran-2-one;
- 3,5-dimethyl-6-(5-((3,5-dimethyl-2,4,6-trioxo-3,5-diazaperhydroinylidene)methyl)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one;
- 5 3,5-dimethyl-6-(5-(2-(3,5-dioxo-2,4-thiazolidinylidene)ethoxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one;
- 3,5-dimethyl-6-(5-(2-(3,5-dioxo-2,4-oxazolidinylidene)ethoxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one;
- 10 3,5-dimethyl-6-(5-(2-(2,5-dioxoimidazolidin-4-ylidene)ethoxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one;
- 3,5-dimethyl-4-hydroxy-6-(5-(2-(5-oxo-3-thioxo-2,4-thiazolidinylidene)ethoxy)benzofuran-2-yl)-2H-pyran-2-one;
- 15 one;
- 3,5-dimethyl-4-hydroxy-6-(5-(2-(2,4,6-trioxo-3,5-diazaperhydroinylidene)ethoxy)benzofuran-2-yl)-2H-pyran-2-one;
- 20 3,5-dimethyl-6-(5-(2-(3,5-dimethyl-2,4,6-trioxo-3,5-diazaperhydroinylidene)ethoxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one;
- 3,5-dimethyl-6-(5-((3,5-dioxo-2,4-thiazolidinyl)sulfonylmethyl)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one;
- 25 3,5-dimethyl-6-(5-((3,5-dioxo-2,4-oxazolidinyl)sulfonylmethyl)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one;
- 3,5-dimethyl-6-(5-((2,5-dioxoimidazolidin-4-yl)sulfonylmethyl)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one;
- 30 3,5-dimethyl-4-hydroxy-6-(5-((5-oxo-3-thioxo-2,4-thiazolidinyl)sulfonylmethyl)benzofuran-2-yl)-2H-pyran-2-one;
- 3,5-dimethyl-6-(5-((3,5-dioxo-2,4-thiazolidinyl)methoxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one;
- 35 pyran-2-one;
- 3,5-dimethyl-6-(5-((3,5-dioxo-2,4-oxazolidinyl)methoxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-

2-one;

3,5-dimethyl-6-(5-((2,5-dioxoimidazolidin-4-yl)methoxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one;

3,5-dimethyl-4-hydroxy-6-(5-((5-oxo-3-thioxo-2,4-thiazolidinyl)methoxy)benzofuran-2-yl)-2H-pyran-2-one;

3,5-dimethyl-4-hydroxy-6-(5-((2,4,6-trioxo-3,5-diazaperhydroinyl)methoxy)benzofuran-2-yl)-2H-pyran-2-one;

3,5-dimethyl-6-(5-((3,5-dimethyl-2,4,6-trioxo-3,5-diazaperhydroinyl)methoxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one;

3,5-dimethyl-4-hydroxy-6-(5-(N-methyl-N-phenylcarbamoyl) benzofuran-2-yl)-2H-pyran-2-one;

6-(5-(N-benzyl-N-methylcarbamoyl)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one;

3,5-dimethyl-4-hydroxy-6-(5-(N-methyl-N-pyridylcarbamoyl) benzofuran-2-yl)-2H-pyran-2-one;

3,5-dimethyl-4-hydroxy-6-(5-(N-methyl-N-thiazolylcarbamoyl) benzofuran-2-yl)-2H-pyran-2-one;

3,5-dimethyl-4-hydroxy-6-(5-(N-methyl-N-(pyridylmethyl) carbamoyl)benzofuran-2-yl)-2H-pyran-2-one;

3,5-dimethyl-4-hydroxy-6-(5-(2-(2-hydroxy-2-phenethylamino) ethoxy)benzofuran-2-yl)-2H-pyran-2-one;

3,5-dimethyl-4-hydroxy-6-(5-(2-(2-hydroxy-3-phenoxypropylamino)ethoxy)benzofuran-2-yl)-2H-pyran-2-one;

3,5-dimethyl-4-hydroxy-6-(5-(2-hydroxy-3-aminopropoxy)benzofuran-2-yl)-2H-pyran-2-one;

3,5-dimethyl-4-hydroxy-6-(5-(2-hydroxy-3-phenylaminopropoxy)benzofuran-2-yl)-2H-pyran-2-one;

3,5-dimethyl-4-hydroxy-6-(5-(3-(2-hydroxy-2-phenethylamino) propyl)benzofuran-2-yl)-2H-pyran-2-one;

3,5-dimethyl-4-hydroxy-6-(5-(3-(2-hydroxy-3-phenoxypropylamino)propyl)benzofuran-2-yl)-2H-pyran-2-one;

3,5-dimethyl-4-hydroxy-6-(5-(2-(2-hydroxy-2-

- phenethylamino)ethyl)benzofuran-2-yl)-2H-pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(5-(2-(2-hydroxy-3-
phenoxypropylamino)ethyl)benzofuran-2-yl)-2H-pyran-2-one;
3,5-dimethyl-6-(5-(3,5-dioxopyrazolidin-4-ylmethyl)
5 benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one;
3,5-dimethyl-6-(5-(3,5-dioxooxazolidin-4-ylmethyl)
benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(5-(2-
oxoimidazolidinylmethyl) benzofuran-2-yl)-2H-pyran-2-one;
10 3,5-dimethyl-6-(5-(2,5-
dioxopiperazinylmethyl)benzofuran-2-yl)-4-hydroxy-2H-
pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(5-
(imidazolylmethyl)benzofuran-2-yl)-2H-pyran-2-one;
15 6-(5-(N-benzothiazolyl-N-methylcarbamoyl)benzofuran-
2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(5-(6-oxo-4,5-benzoxazin-2-
yl)benzofuran-2-yl)-2H-pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(5-(3-pyridylaminomethyl)
20 benzofuran-2-yl)-2H-pyran-2-one;
6-(5-(4-bromo-2-cyanophenylcarbamoyl)benzofuran-2-
yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(5-(N-methyl-N-(3-pyridyl)
aminomethyl)benzofuran-2-yl)-2H-pyran-2-one;
25 3,5-dimethyl-4-hydroxy-6-(5-(N-methyl-N-(3-pyridyl)
carbamoyl)benzofuran-2-yl)-2H-pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(5-(4-(2-pyridyl)
piperazinylcarbonyl)benzofuran-2-yl)-2H-pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(5-(4-(2-pyrimidinyl)
30 piperazinylcarbonyl)benzofuran-2-yl)-2H-pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(5-(N-methyl-N-(2-pyridyl)
carbamoyl)benzofuran-2-yl)-2H-pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(5-(N-(2-
pyrimidinyl)carbamoyl)benzofuran-2-yl)-2H-pyran-2-one;
35 3,5-dimethyl-4-hydroxy-6-(5-(2-
pyridylmethyl)carbamoyl)benzofuran-2-yl)-2H-pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(5-

- (triazolylcarbamoyle)benzofuran-2-yl)-2H-pyran-2-one;
3,5-dimethyl-6-(5-(2,5-dioxopyrrolidinyl)benzofuran-
2-yl)-4-hydroxy-2H-pyran-2-one;
3,5-dimethyl-6-(5-(2,6-dioxopiperidinyl)benzofuran-
5 2-yl)-4-hydroxy-2H-pyran-2-one;
3,5-dimethyl-6-(5-(2,3-dioxopiperazinyl)benzofuran-
2-yl)-4-hydroxy-2H-pyran-2-one;
6-(5-(2-(4-chlorobenzoylamino)ethyl)benzofuran-2-
yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one;
10 6-(5-(3-(acetylaminopropoxy)benzofuran-2-yl)-3,5-
dimethyl-4-hydroxy-2H-pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(5-(3-(2-
pyrazinylcarbonylamino)propoxy)benzofuran-2-yl)-2H-pyran-
2-one;
15 3,5-dimethyl-4-hydroxy-6-(5-(3-(2-
pyridylcarbonylamino)propoxy)benzofuran-2-yl)-2H-pyran-2-
one;
3,5-dimethyl-4-hydroxy-6-(5-(3-(5-
isoxazolylcarbonylamino)propoxy)benzofuran-2-yl)-2H-
20 pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(5-(3-
(morpholinylcarbonylamino)propoxy)benzofuran-2-yl)-2H-
pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(5-(3-
25 (methanesulfonylamino)propoxy)benzofuran-2-yl)-2H-pyran-
2-one;
3,5-dimethyl-6-(5-(3-(dimethylaminosulfonylamino)
propoxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(5-(3-
30 (isoxazolylsulfonylamino)propoxy)benzofuran-2-yl)-2H-
pyran-2-one;
6-(5-(N-acetylpiperidin-3-ylmethoxy)benzofuran-2-
yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(5-(N-(2-pyridylcarbonyl)
35 piperidin-3-ylmethoxy)benzofuran-2-yl)-2H-pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(5-(N-(2-pyrazinylcarbonyl)
piperidin-3-ylmethoxy)benzofuran-2-yl)-2H-pyran-2-one;

3,5-dimethyl-4-hydroxy-6-(5-(N-(5-isoxazolylcarbonyl)piperidin-3-ylmethoxy)benzofuran-2-yl)-2H-pyran-2-one;

3,5-dimethyl-4-hydroxy-6-(5-(N-(morpholinylcarbonyl)piperidin-3-ylmethoxy)benzofuran-2-yl)-2H-pyran-2-one;

3,5-dimethyl-4-hydroxy-6-(5-(N-methanesulfonylpiperidin-3-ylmethoxy)benzofuran-2-yl)-2H-pyran-2-one;

3,5-dimethyl-6-(5-(N-(dimethylaminosulfonyl)piperidin-3-ylmethoxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one;

3,5-dimethyl-4-hydroxy-6-(5-(N-(5-thiazolylsulfonyl)piperidin-3-ylmethoxy)benzofuran-2-yl)-2H-pyran-2-one; and

3,5-dimethyl-4-hydroxy-6-(5-(N-(5-isoxazolylsulfonyl)piperidin-3-ylmethoxy)benzofuran-2-yl)-2H-pyran-2-one.

As preferred specific compounds represented by structural formula (I) above there may be mentioned, for example, the following:

4-acetyloxy-6-(benzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one;

6-(benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one;

6-(benzofuran-2-yl)-4-benzoyloxy-3,5-dimethyl-2H-pyran-2-one;

6-(benzofuran-2-yl)-3,5-dimethyl-4-methanesulfonyloxy-2H-pyran-2-one;

6-(benzofuran-2-yl)-3,5-dimethyl-4-(2-pyridylcarboxy)-2H-pyran-2-one;

3,5-dimethyl-6-(5-((3,5-dioxo-2,4-thiazolidinylidene)methyl)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one;

3,5-dimethyl-6-(5-((3,5-dioxo-2,4-thiazolidinyl)methyl)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one;

6-(benzofuran-2-yl)-4-hydroxy-3-methyl-5-n-pentyl-

- 2H-pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(5-methoxybenzofuran-2-yl)-
2H-pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(7-methoxybenzofuran-2-yl)-
5 2H-pyran-2-one;
4-acetyloxy-3,5-dimethyl-6-(6-
(trifluoromethanesulfonyloxy)benzofuran-2-yl)-2H-pyran-2-
one;
4-acetyloxy-3,5-dimethyl-6-(6-(2-thienyl)benzofuran-
10 2-yl)-2H-pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(6-methoxybenzofuran-2-yl)-
2H-pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(5-(5-pyrimidinylmethoxy)
benzofuran-2-yl)-2H-pyran-2-one;
15 6-(benzofuran-2-yl)-3,5-dimethyl-4-(4-
hydroxymethylbenzoyloxy)-2H-pyran-2-one;
6-(benzofuran-2-yl)-4-(2-(N-carbobenzyloxy-N-
methylamino) acetyloxy)-3,5-dimethyl-2H-pyran-2-one;
6-(benzofuran-2-yl)-3,5-dimethyl-4-(4-
20 methoxybenzoyloxy)-2H-pyran-2-one;
6-(benzofuran-2-yl)-3,5-dimethyl-4-(2-
phenylacetyloxy)-2H-pyran-2-one;
6-(benzofuran-2-yl)-5-ethyl-4-hydroxy-3-methyl-2H-
pyran-2-one;
25 6-(benzofuran-2-yl)-4-hydroxy-5-isopropyl-3-methyl-
2H-pyran-2-one;
6-(benzofuran-2-yl)-5-benzyl-4-hydroxy-3-methyl-2H-
pyran-2-one;
6-(benzofuran-2-yl)-3,5-dimethyl-4-isobutyryloxy-2H-
30 pyran-2-one;
4-acetyloxy-3,5-dimethyl-6-(5-nitrobenzofuran-2-yl)-
2H-pyran-2-one;
6-(benzofuran-2-yl)-3,5-dimethyl-4-(2-
phenoxyacetyloxy)-2H-pyran-2-one;
35 3,5-dimethyl-4-hydroxy-6-(5-nitrobenzofuran-2-yl)-
2H-pyran-2-one;
3,5-dimethyl-6-(5-(dimethylamino)benzofuran-2-yl)-4-

- hydroxy-2H-pyran-2-one;
6-(5-(dibenzylamino)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(5-(N-methyl-N-(2-thienylcarbonyl)amino)benzofuran-2-yl)-2H-pyran-2-one;
5 3,5-dimethyl-4-hydroxy-6-(5-(N-methyl-N-(3-pyridylcarbonyl)amino)benzofuran-2-yl)-2H-pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(5-(N-isobutyryl-N-methylamino)benzofuran-2-yl)-2H-pyran-2-one;
10 3,5-dimethyl-4-hydroxy-6-(5-(N-methyl-N-(phenylacetyl)amino)benzofuran-2-yl)-2H-pyran-2-one;
6-(5-(N-benzoyl-N-methylamino)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one;
6-(5-(N-t-butoxycarbonyl-N-methylamino)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one;
15 6-(5-(benzothiazolylcarbamoyl)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one;
6-(5-(benzimidazolylcarbamoyl)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one;
20 3,5-dimethyl-4-hydroxy-6-(5-(N-methyl-N-phenylcarbamoyl)benzofuran-2-yl)-2H-pyran-2-one;
6-(5-(N-(4-chlorophenylsulfonyl)-N-methylamino)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one;
25 3,5-dimethyl-4-hydroxy-6-(5-(1,3,4-trihydroisoquinolin-2-ylcarbonyl)benzofuran-2-yl)-2H-pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(5-morpholinylbenzofuran-2-yl)-2H-pyran-2-one;
30 6-(benzofuran-2-yl)-3,5-dimethyl-4-isonicotinoyloxy-2H-pyran-2-one;
4-(2-aminoacetyloxy)-6-(benzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one;
6-(5-benzyloxybenzofuran-2-yl)-4-(2-(t-butoxycarbonylamino) acetyloxy)-3,5-dimethyl-2H-pyran-2-one;
35 4-(2-aminoacetyloxy)-6-(5-benzyloxybenzofuran-2-yl)-

- 3,5-dimethyl-2H-pyran-2-one;
4-(4-(acetylamino)benzoyloxy)-6-(5-benzyloxybenzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one;
6-(5-benzyloxybenzofuran-2-yl)-3,5-dimethyl-4-nicotinoyloxy-2H-pyran-2-one;
5 6-(5-benzyloxybenzofuran-2-yl)-3,5-dimethyl-4-isonicotinoyloxy-2H-pyran-2-one;
6-(5-benzyloxybenzofuran-2-yl)-5-ethyl-4-hydroxy-3-methyl-2H-pyran-2-one;
10 5-ethyl-4-hydroxy-3-methyl-6-(5-(3-pyridylmethoxy)benzofuran-2-yl)-2H-pyran-2-one;
4-acetyloxy-3,5-dimethyl-6-(5-(2-thiazolylmethoxy)benzofuran-2-yl)-2H-pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(5-(5-thiazolylmethoxy)benzofuran-2-yl)-2H-pyran-2-one;
15 4-acetyloxy-6-(5-(2,4-dichloro-5-thiazolylmethoxy)benzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(5-(2-(4-methyl-5-thiazolyl)ethoxy)benzofuran-2-yl)-2H-pyran-2-one;
20 4-acetyloxy-3,5-dimethyl-6-(5-(2-(4-methyl-5-thiazolyl)ethoxy)benzofuran-2-yl)-2H-pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(5-(4-methyl-5-thiazolylmethoxy)benzofuran-2-yl)-2H-pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(5-(2-(morpholinesulfonyl)-5-thiazolylmethoxy)benzofuran-2-yl)-2H-pyran-2-one;
25 4-acetyloxy-3,5-dimethyl-6-(5-(4-methyl-1-tosyl-5-imidazolylmethoxy)benzofuran-2-yl)-2H-pyran-2-one;
6-(benzofuran-2-yl)-3,5-dimethyl-4-(3-phenylpropionyloxy)-2H-pyran-2-one;
30 6-(benzofuran-2-yl)-3,5-dimethyl-4-(2-furoyloxy)-2H-pyran-2-one;
6-(benzofuran-2-yl)-3,5-dimethyl-4-nicotinoyloxy-2H-pyran-2-one;
6-(benzofuran-2-yl)-3,5-dimethyl-4-(2-acetylamino-4-(morpholin-4-yl)-4-oxobutyryloxy)-2H-pyran-2-one;
35 4-acetyloxy-6-(5-bromobenzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one;

- 6-(benzofuran-2-yl)-5-cyclopentylmethyl-4-hydroxy-3-methyl-2H-pyran-2-one;
- 6-(benzofuran-2-yl)-4-(1-carbobenzyloxy-2-pyrrolidon-5-ylcarboxy)-3,5-dimethyl-2H-pyran-2-one;
- 5 6-(benzofuran-2-yl)-3,5-dimethyl-4-(2-pyrrolidon-5-ylcarboxy)-2H-pyran-2-one;
- 6-(benzofuran-2-yl)-4-(2-(t-butoxycarbonylamino)acetyloxy)-3,5-dimethyl-2H-pyran-2-one;
- 10 6-(benzofuran-2-yl)-4-(2,4-dimethoxybenzoyloxy)-3,5-dimethyl-2H-pyran-2-one;
- 6-(benzofuran-2-yl)-3,5-dimethyl-4-(3-dimethylaminobenzoyloxy)-2H-pyran-2-one;
- 4-(4-(acetylamino)benzoyloxy)-6-(benzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one;
- 15 3,5-dimethyl-6-(5-(2-fluorobenzyloxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one;
- 3,5-dimethyl-4-hydroxy-6-(5-(3,4-(methylenedioxy)benzyloxy)benzofuran-2-yl)-2H-pyran-2-one;
- 20 3,5-dimethyl-4-hydroxy-6-(5-(3-pyridylmethoxy)benzofuran-2-yl)-2H-pyran-2-one;
- 3,5-dimethyl-4-hydroxy-6-(5-(5-hydroxy-3-pyridylmethoxy)benzofuran-2-yl)-2H-pyran-2-one;
- 25 4-acetyloxy-3,5-dimethyl-6-(5-(2-methoxy-5-pyridylmethoxy)benzofuran-2-yl)-2H-pyran-2-one;
- 3,5-dimethyl-4-hydroxy-6-(5-(1-methylpiperidin-3-ylmethoxy)benzofuran-2-yl)-2H-pyran-2-one;
- 6-(5-(4-carboxybenzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one;
- 30 3,5-dimethyl-4-hydroxy-6-(5-(2-(trifluoromethyl)benzyloxy)benzofuran-2-yl)-2H-pyran-2-one;
- 3,5-dimethyl-4-hydroxy-6-(5-(3-(trifluoromethyl)benzyloxy)benzofuran-2-yl)-2H-pyran-2-one;
- 35 6-(5-(3,4-dimethylbenzyloxy)benzofuran-2-yl)-3,5-

- dimethyl-4-hydroxy-2H-pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(5-(2-thienylmethoxy)benzofuran-2-yl)-2H-pyran-2-one;
4-acetyloxy-3,5-dimethyl-6-(5-(2-thienylmethoxy)benzofuran-2-yl)-2H-pyran-2-one;
5 3,5-dimethyl-4-hydroxy-6-(5-(3-thienylmethoxy)benzofuran-2-yl)-2H-pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(5-(2-(morpholinesulfonyl)-5-thienylmethoxy)benzofuran-2-yl)-2H-pyran-2-one;
10 4-acetyloxy-3,5-dimethyl-6-(5-(2-(morpholinesulfonyl)-5-thienylmethoxy)benzofuran-2-yl)-2H-pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(5-(4-oxazolylmethoxy)benzofuran-2-yl)-2H-pyran-2-one;
15 3,5-dimethyl-4-hydroxy-6-(5-(2-phenyl-4-oxazolylmethoxy)benzofuran-2-yl)-2H-pyran-2-one;
6-(5-(2,4-dichlorobenzoyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one;
6-(5-(3,4-dichlorobenzoyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one;
20 6-(5-(4-n-butoxybenzoyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(6-(1,2,3,4-tetrahydronaphthalen-1-yl)oxy)benzofuran-2-yl)-2H-pyran-2-one;
25 one;
3,5-dimethyl-4-hydroxy-6-(5-(2-propyn-1-yl)oxy)benzofuran-2-yl)-2H-pyran-2-one;
3,5-dimethyl-6-(5-(3-fluorobenzoyloxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one;
30 3,5-dimethyl-6-(5-(4-fluorobenzoyloxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one;
3,5-dimethyl-4-hydroxy-6-(5-(3-methoxybenzoyloxy)benzofuran-2-yl)-2H-pyran-2-one;
6-(5-(3-chlorobenzoyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one;
35 6-(5-(3-aminobenzoyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one;

6-(5-(3-(t-butoxycarbonylamino)benzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one;

4-acetyloxy-6-(5-(3-(t-butoxycarbonylamino)benzyloxy)benzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one;

4-acetyloxy-3,5-dimethyl-6-(5-trifluoromethanesulfonyloxy-benzofuran-2-yl)-2H-pyran-2-one;

4-acetyloxy-3,5-dimethyl-6-(5-(methoxycarbonyl)benzofuran-2-yl)-2H-pyran-2-one;

4-acetyloxy-6-(4-benzyloxybenzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one;

4-acetyloxy-6-(4-acetyloxybenzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one;

4-acetyloxy-3,5-dimethyl-6-(5-methoxybenzofuran-2-yl)-2H-pyran-2-one;

4-acetyloxy-6-(5-benzyloxybenzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one;

6-(5-benzyloxybenzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one;

4-acetyloxy-3,5-dimethyl-6-(5-p-toluenesulfonyloxybenzofuran-2-yl)-2H-pyran-2-one;

4-acetyloxy-6-(7-benzyloxybenzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one;

3,5-dimethyl-4-hydroxy-6-(5-(methoxycarbonyl)benzofuran-2-yl)-2H-pyran-2-one;

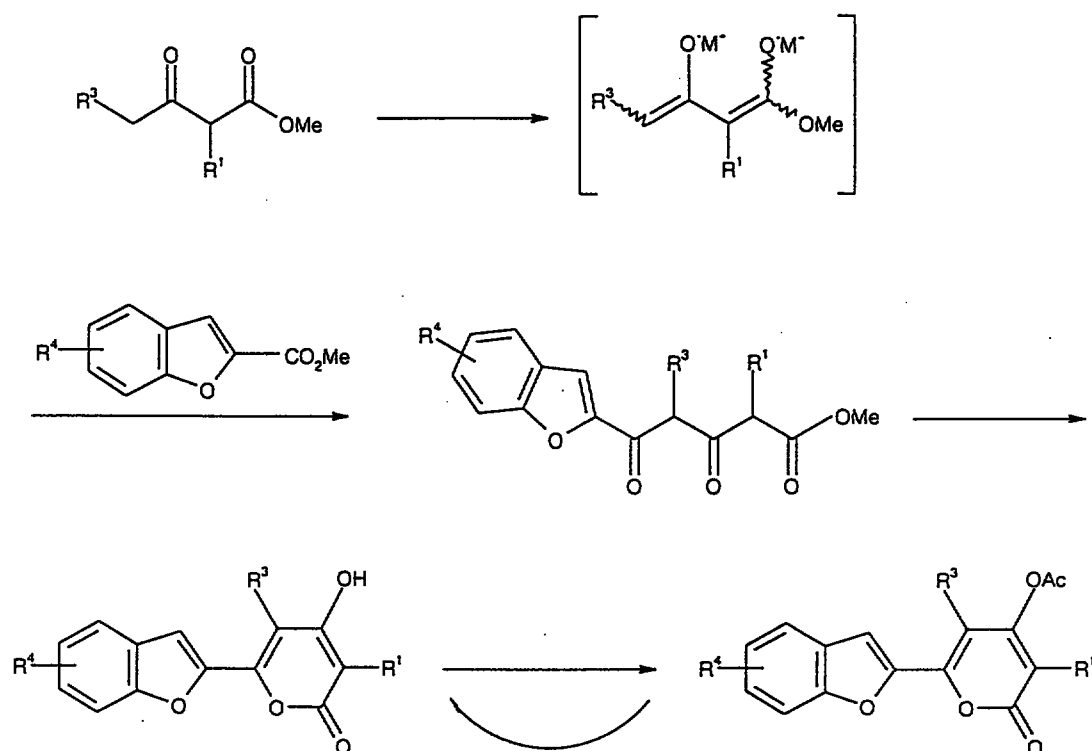
3,5-dimethyl-4-hydroxy-6-(6-methoxymethoxybenzofuran-2-yl)-2H-pyran-2-one.

The compounds represented by structural formula (I) above will sometimes form acid addition salts or base addition salts. As specific examples of acid addition salts there may be mentioned addition salts of mineral acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid and phosphoric acid; organic acids such as formic acid, acetic acid, trifluoroacetic acid, propionic acid, oxalic acid, malonic acid, succinic acid, fumaric acid, maleic acid, lactic acid, malic acid,

tartaric acid, citric acid, methanesulfonic acid and ethanesulfonic acid; and acidic amino acids such as aspartic acid and glutamic acid; as specific examples of base addition salts there may be mentioned salts of
5 metals such as lithium, sodium and potassium; salts of divalent or trivalent metals such as magnesium, calcium, zinc and aluminum; addition salts of basic amino acids such as lysine and arginine; as well as salts of ammonium and organic ammonium such as methylammonium,
10 dimethylammonium, trimethylammonium, benzylammonium and monoethanolammonium. The present invention also encompasses hydrates of the compounds represented by structural formula (I), as well as their various solvates and crystal polymorphs.

15 The compounds of the invention may generally be produced by the processes outlined below in Production Processes 1 to 5, with modifications if necessary, using readily available starting substances, reagents and common synthesis methods.

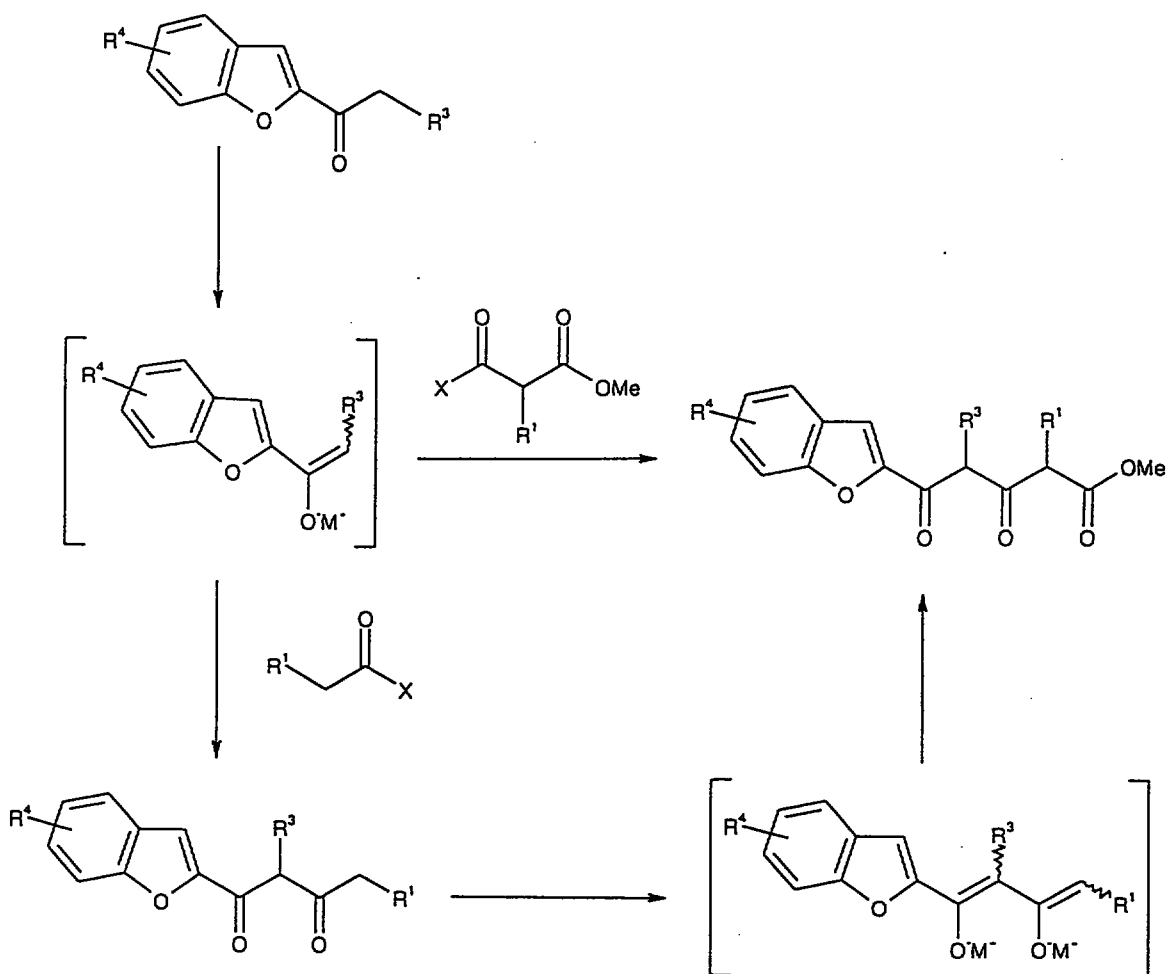
Production Process 1



5 Specifically, for example, a benzofuryl- α -pyrone
 derivative of the invention may be produced by the method
 shown as Production Process 1. A solution, such as a THF
 solution, of a 2,4-disubstituted- β -keto ester is treated
 with 2 equivalents of a base, for example, 1 equivalent
 10 of NaH and 1 equivalent of n-BuLi, or 2 equivalents of
 LDA, to prepare a dienolate, and then a
 benzofurancarboxylic acid ester derivative is allowed to
 act thereon for Claisen condensation to obtain a diketo
 ester intermediate. The diketo ester intermediate is
 15 subjected to alkali hydrolysis and then acid treatment to
 obtain an α -pyrone. The diketo ester intermediate can
 be subjected to alkali hydrolysis followed by acid
 treatment and then treatment with acetic anhydride and
 pyridine to obtain 4-acetyloxy- α -pyrone, and this may be
 20 again subjected to alkali hydrolysis to yield 4-hydroxy-

α -pyrone. Alternatively, the diketo ester intermediate may be treated with an acid such as sulfuric acid, polyphosphoric acid or p-TsOH or heat treated under reduced pressure, to obtain 4-hydroxy- α -pyrone.

5 Production Process 2

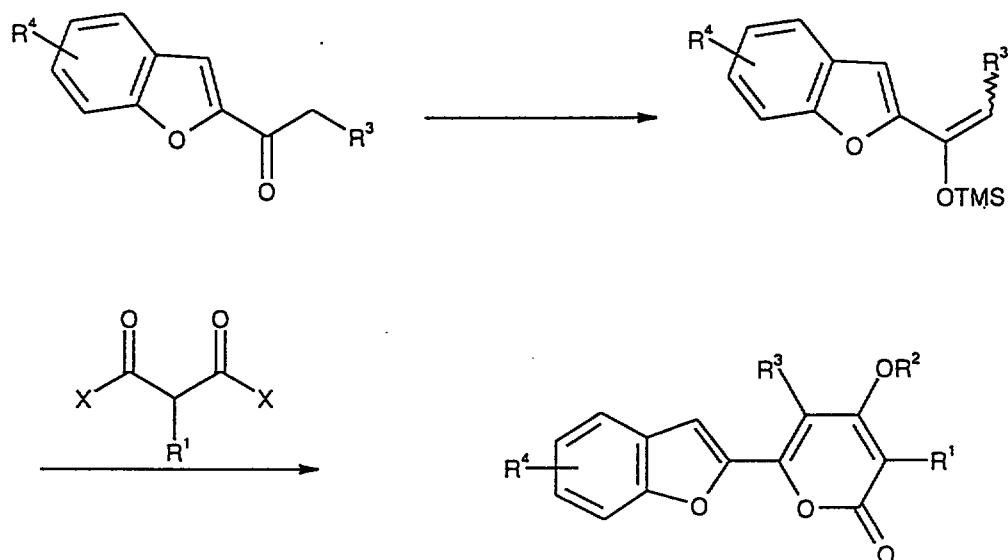


10 The diketo ester intermediate of Production Process 1 can also be produced by another method outlined as Production Process 2. A benzofurylketone is treated with a base such as LDA to prepare an enolate, and this is reacted with a malonic acid ester, such as malonic monomethyl ester-monochloride, to obtain a diketo ester intermediate. Alternatively, a diketo ester intermediate may be obtained by a process wherein a diketone obtained by reacting an acid chloride or ester with a

15

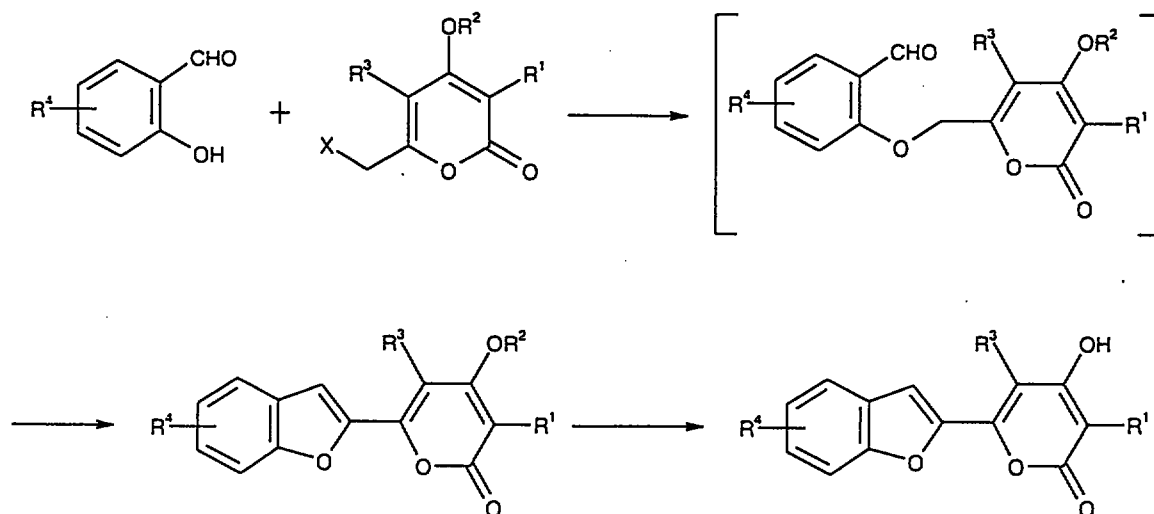
benzofurylketone enolate is treated with 2 equivalents of a base such as LDA to prepare a dienolate, which is then reacted with a CO₂-related compound such as carbon dioxide gas or dimethyl carbonate.

5 Production Process 3



10 A benzofuryl- α -pyrone derivative of the invention may also be produced by the method shown as Production Process 3. A benzofuryl- α -pyrone derivative can be obtained by a method in which a benzofurylketone is converted to a silylenol ether with TMSCl-Et₃ or TMSOTf-Et₃, for example, and this is reacted with malonic
15 dichloride or a malonic diester.

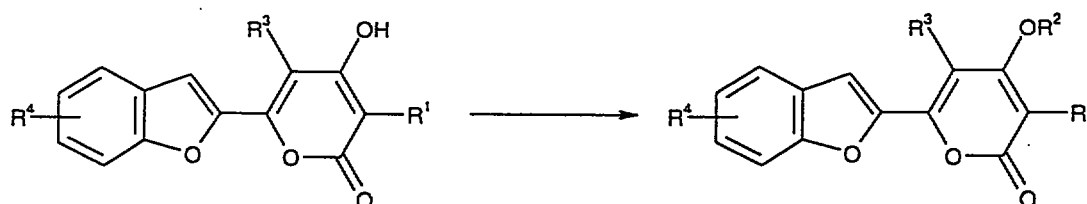
Production Process 4



5 A benzofuryl- α -pyrone derivative of the invention may also be produced by the method shown as Production Process 4. A benzofuryl- α -pyrone derivative can be obtained by a method in which an α -pyrone derivative with a $-CH_2X$ substituent at the 6-carbon (wherein X represents a leaving group such as Cl, Br, I, OMs or OTf)

10 is reacted with a substituted salicyl aldehyde in the presence of a base such as K_2CO_3 and/or DBU.

Production Process 5



15

 Benzofuryl- α -pyrone derivatives of the invention wherein R^2 (wherein R^2 represents a group as defined above) is COR^5 or SO_2R^6 (wherein R^5 and R^6 represent groups as defined above) can be produced by the method shown as

20 Production Process 5. Of the benzofuryl- α -pyrone

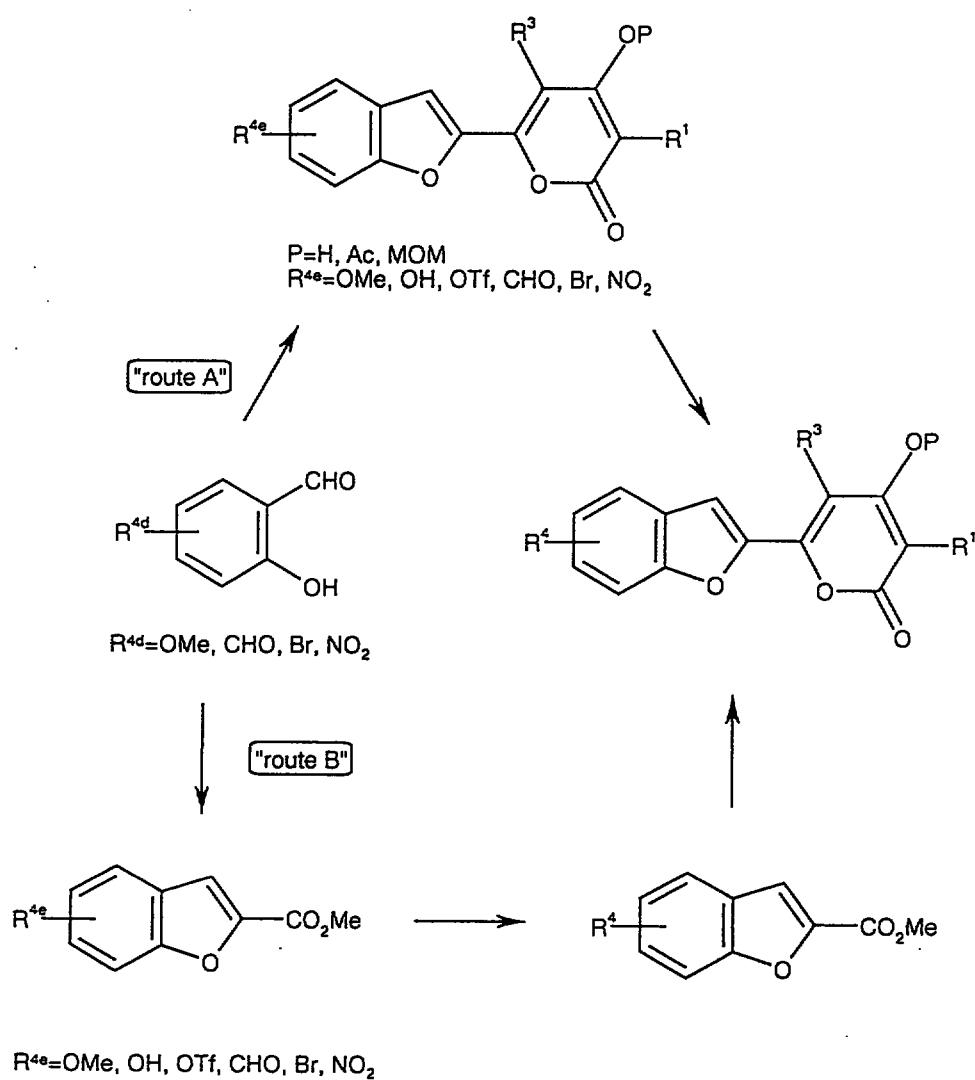
derivatives according to the invention, a benzofuryl- α -pyrone derivative wherein R^2 is $-\text{COR}^5$ may be produced by a method wherein a starting material, 6-benzofuryl-4-hydroxy- α -pyrone derivative obtained by any of

5 Production Processes 1 to 4 above, with modifications if necessary, is reacted with an acid chloride or acid anhydride in the presence of a base, for example, a tertiary amine such as Et_3N or a nitrogen-containing aromatic heterocycle such as pyridine or imidazole, or
10 alternatively, a method wherein the starting material is reacted with a carboxylic acid in the presence of a condensation agent such as WSC-HOBt, DCC-HOBt, CDI, diethyl cyanophosphate or diphenylphosphoryl azide, or by a method using the "Mitsunobu reaction" wherein the
15 starting material is reacted with a carboxylic acid in the presence of $\text{Ph}_3\text{P-DEAD}$. Similarly, a benzofuryl- α -pyrone derivative wherein R^2 is SO_2R^6 may be produced by reacting a starting material, 6-benzofuryl-4-hydroxy- α -pyrone derivative, with a sulfonyl chloride derivative
20 represented by RSO_2Cl , in the presence of a base, for example, a tertiary amine such as Et_3N or a nitrogen-containing aromatic heterocycle such as pyridine or imidazole.

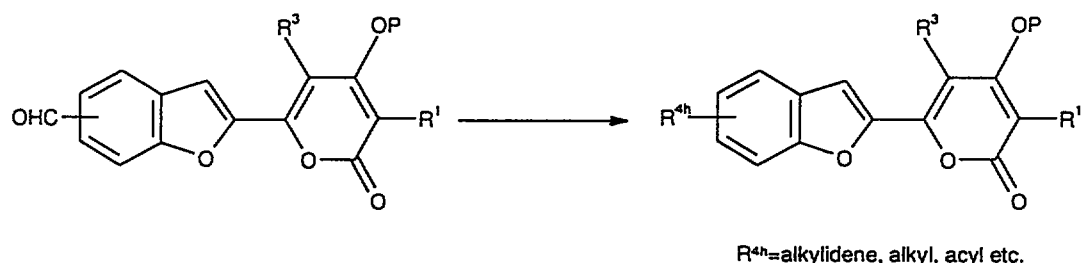
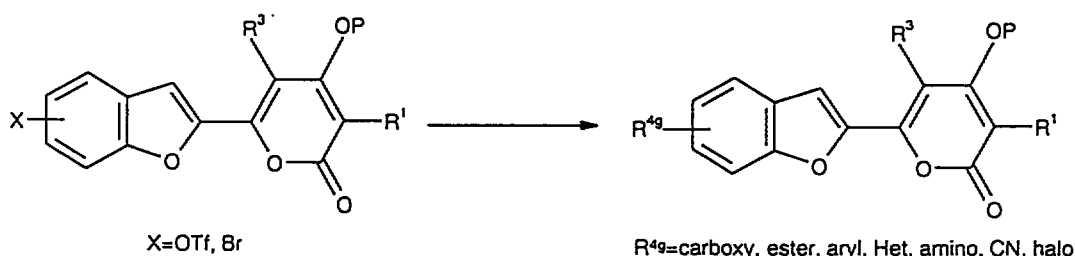
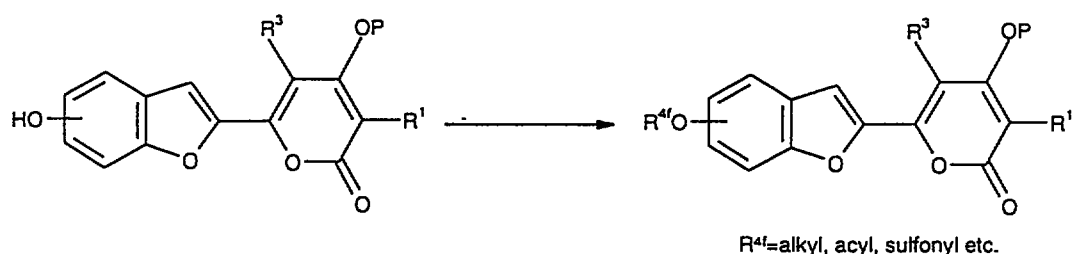
Benzofuryl- α -pyrone derivatives of the present
25 invention wherein R^4 is a substituent as defined above other than hydrogen can be produced by the method shown as Production Process 6 or 7. As shown in Production Process 6, a readily available substituted salicyl aldehyde derivative is used as the starting material for
30 any of Production Processes 1 to 5 above, with modifications if necessary, to obtain a benzofuryl- α -pyrone (route A) or a 2-benzofurancarboxylic acid ester intermediate (route B) substituted with hydroxy, methoxy, formyl, bromo, nitro, etc. Route A is a method involving
35 functional group conversion from the hydroxy, methoxy,

formyl, bromo or nitro substituent at the benzofuryl- α -pyrone stage, while route B is a method wherein the α -pyrone ring is constructed after functional group conversion of R^4 at the 2-benzofurancarboxylic acid ester intermediate stage.

Production Process 6



Production Process 7



- 5 The functional group conversion of R⁴ from hydroxy, methoxy, formyl, bromo, nitro, etc. can be accomplished by the method shown in Production Process 7. For the benzofuran- α -pyrone intermediate obtained by route A in
- 10 hydroxyl may be accomplished by acylation with an acid chloride or acid anhydride, sulfonylation with sulfonyl chloride or sulfonic anhydride, alkylation by the Mitsunobu reaction, etc.; functional group conversion
- 15 from bromo or trifluoromethanesulfonyloxy may be accomplished by carbonylation, allylation, cyanation, halogenation, amination, etc. with a transition metal catalyst such as a palladium catalyst, for example; and functional group conversion from formyl may be accomplished by alkylation or acylation with a

nucleophilic agent such as an organometallic reagent or an enolate.

Functional group conversion of R⁴ from a 2-benzofurancarboxylic acid ester intermediate obtained by route B of Production Process 6 can also be accomplished using the same method of Production Process 7.

Production Processes 1 to 7 shown above are not intended to restrict the synthesis processes for the compounds of the invention, and any other processes known in the art may also be used.

Benzofuryl- α -pyrone derivatives of the invention and their salts that are obtained in the manner described above have a triglyceride biosynthesis inhibiting effect, a blood triglyceride lowering effect and a blood HDL elevating effect, as demonstrated by Examples given below, and can therefore be used as active ingredients, in combination with the carriers, etc. described below if necessary, to provide pharmaceutical compositions, and to provide triglyceride biosynthesis inhibitors, blood triglyceride lowering agents or blood HDL elevating agents according to the invention.

For clinical application of a benzofuryl- α -pyrone derivative of the invention or its salt as a prophylactic or therapeutic agent for hypertriglyceridemia, arteriosclerosis or the like, it may be administered orally or parenterally such as intrarectally, subcutaneously, intramuscularly, intravenously or percutaneously, but oral or intravenous administration is preferred.

For oral administration, it may be in the form of a solid or liquid preparation. Solid preparations include tablets, pills, powders and granules. The active substances in such solid preparations are blended with pharmacologically acceptable carriers such as sodium bicarbonate, calcium carbonate, potato starch, sucrose, mannitol and carboxymethyl cellulose. The formulation

may be carried out by a common method, and other additives, for example, lubricants such as calcium stearate and magnesium stearate, may also be included for formulation in addition to the carrier. Enteric coated
5 preparations may also be prepared having an enteric coating formed by spraying the above-mentioned solid preparations with, for example, an aqueous solution or an organic solvent solution of an enteric coating substance such as cellulose acetate phthalate, hydroxypropylmethyl
10 cellulose phthalate, polyvinyl alcohol phthalate or styrene-maleic anhydride copolymer, or a methacrylic acid or methyl methacrylate copolymer. Solid preparations such as powders or granules may also be encapsulated by enteric coated capsules.

15 A liquid preparation for oral administration contains, for example, an emulsifier, solution, suspension, syrup or elixir. These preparations contain conventionally used pharmacologically acceptable carriers such as water or liquid paraffin. Oily bases such as
20 coconut oil, fractionated coconut oil, soybean oil or corn oil are also used as carriers. Pharmacologically acceptable carriers also contain, when necessary, commonly used adjuvants, aromatics, stabilizers or preservatives. A liquid preparation may be administered
25 in the form of a capsule formed from an absorbable substance such as gelatin. Solid preparations for intrarectal administration include suppositories that are produced by known methods to contain the active ingredient.

30 A preparation for parenteral administration is administered as a sterile aqueous or non-aqueous solution, suspension or emulsion. A non-aqueous solution or suspension may contain propyl glycol, polyethylene glycol, a vegetable oil such as olive oil or soybean oil
35 or an injectable organic ester such as ethyl oleate, as pharmacologically acceptable carriers. Such preparations may also contain adjuvants such as preservatives,

humectants, emulsifiers, dispersers and stabilizers. These solutions, suspensions and emulsions may be sterilized by appropriate means such as, for example, filtration through a bacteria-retaining filter, heating, inclusion of a sterilizing agent or treatment with ultraviolet irradiation. After production and just prior to use of the sterile solid preparation, it may be dissolved in sterile water or a sterile injection solvent for use. Fatty emulsions prepared by adding water to a uniform solution of the active ingredients with a vegetable oil such as soybean oil and a phospholipid such as lecithin, may be homogenized with a homogenizer such as a pressure jet homogenizer or an ultrasonic homogenizer to be used as injections.

Percutaneous administration dosage forms include ointments, creams and the like. These may be produced by common methods.

When an active ingredient according to the invention is used as a treatment agent for hypertriglyceridemia or as a prophylactic agent for arteriosclerosis, it may usually be administered at about 1 to 1000 mg per day for adults, though this will depend on the patient's condition, age, gender and body weight and the route of administration. The dosage may be administered either at one time, or over a few times, such as 2 to 6 times, per day.

The various routes of administration are preferably selected based on the absorption efficiency in the body for the particular physiologically active benzofuryl- α -pyrone derivative, as determined by well-known pharmacological methods.

Examples

The abbreviations used for the derivatives used throughout the present specification including the examples, and for the groups within their structures and the reagents used, are those commonly used in the field

of organic chemistry; the meanings of the abbreviations are given below.

THF: tetrahydrofuran, Et₂O: diethyl ether, DMF: N,N-dimethylformamide, AcOEt: ethyl acetate, MeOH: methanol, EtOH: ethanol, DBU: 1,8-diazabicyclo[5.4.0]-7-undecene, DEAD: diethyl azodicarboxylate, TMAD: azodicarboxylic acid bis(dimethylamide), DMSO: dimethylsulfoxide, Et₃N: triethylamine, Py: pyridine, n-BuLi: normal-butyllithium, LDA: lithium diisopropylamide, Ac₂O: acetic anhydride, WSC: 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride, DCC: 1,3-dicyclohexylcarbodiimide, CDI: carbonyldiimidazole, HOBt: 1-hydroxybenzotriazole, PPTS: pyridinium para-toluenesulfonate, TMSOTf: trimethylsilyl trifluoromethanesulfonate, TfOH: trifluoromethanesulfonic acid, Ms: methanesulfonyl, Tf: trifluoromethanesulfonyl, p-Ts: para-toluenesulfonyl, Ph: phenyl, Bu: butyl, Bzl: benzyl, Ac: acetyl, TMS: trimethylsilyl

Production Examples

Synthesis of intermediates

Synthesis of methyl 2-benzofurancarboxylate

After adding thionyl chloride (3.80 ml) to a solution of 2-benzofurancarboxylic acid (2.00 g) in MeOH (60 ml) at -40°C, the mixture was stirred for 19 hours while the temperature gradually increased to room temperature. The reaction solution was concentrated under reduced pressure and the residue was purified by silica gel column chromatography (n-hexane/AcOEt = 6/1) to obtain methyl 2-benzofurancarboxylate.

Yield: 2.16 g (y. 99.2%)

¹H NMR(δppm, CDCl₃): 3.99(s, 3H), 7.28 to 7.50(m, 2H), 7.54(s, 1H), 7.60(d, J=8.9Hz, 1H), 7.69(d, J=7.6Hz, 1H)

Synthesis of methyl 2-methyl-3-oxopentanoate

Methyl iodide (57 ml) and K₂CO₃ (127 g) were added to a solution of methyl propionylacetate (100 g) in acetone (800 ml) while cooling on ice. The reaction

solution was stirred for 96 hours at room temperature and celite filtered, and then the mother liquor was slowly concentrated under reduced pressure and distilled under reduced pressure to obtain methyl 2-methyl-3-

5 oxopentanoate.

Yield: 105 g (y. 94.8%)

^1H NMR(δ ppm, CDCl_3): 1.08(t, $J=7.3\text{Hz}$, 3H), 1.35(d, $J=7.3\text{Hz}$, 3H), 2.45 to 2.72(m, 2H), 3.54(q, $J=7.3\text{Hz}$, 1H), 3.73(s, 3H)

10 Synthesis of methyl 3-oxononanoate

Pyridine (11.2 ml) and n-heptanoyl chloride (11.8 ml) were added to a solution of merudoramu acid (10.0 g) in CHCl_3 (150 ml) at 0°C , and the mixture was stirred at 0°C for 30 minutes and then at room temperature for 2
15 hours. The reaction solution was cooled to 0°C , diluted hydrochloric acid was added and extraction was performed with CH_2Cl_2 . The organic layer was rinsed with water and saturated saline, dried with Na_2SO_4 and then filtered and concentrated. MeOH (150 ml) was added to the residue
20 prior to heated reflux for 3 hours. After cooling, the reaction solution was concentrated under reduced pressure and the residue was purified by silica gel column chromatography (n-hexane/AcOEt = 13/1) to obtain methyl 3-oxononanoate.

25 Yield: 8.51 g (y. 65.9%)

^1H NMR(δ ppm, CDCl_3): 0.88(t, $J=6.9\text{Hz}$, 3H), 1.22 to 1.40(m, 6H), 1.51 to 1.69(m, 2H), 2.53(t, $J=7.3\text{Hz}$, 2H), 3.45(s, 2H), 3.74(s, 3H)

Synthesis of methyl 2-methyl-3-oxononanoate

30 K_2CO_3 (2.67 g) was added to a solution of methyl 3-oxononanoate (3.01 g) and methyl iodide (2.77 g) in acetone (100 ml) and the mixture was stirred at room temperature for 24 hours. The reaction solution was celite filtered, and then the mother liquor was
35 concentrated under reduced pressure and the residue was purified by silica gel column chromatography (n-

hexane/AcOEt = 13/1) to obtain methyl 2-methyl-3-oxononanoate.

Yield: 3.06 g (y. 94.6%)

¹H NMR(δppm, CDCl₃): 0.90(t, J=6.9Hz, 3H), 1.21 to 1.39(m, 9H), 1.51 to 1.65(m, 2H), 2.47 to 2.56(m, 2H), 3.53(q, J=7.3Hz, 1H), 3.73(s, 3H)

Synthesis of ethyl 2-(benzyloxy)acetate

Benzyl alcohol (27.5 ml) was added to a suspension of NaH (1.1 g) in Et₂O (250 ml) at 0°C, and after stirring at 0°C for 10 minutes and at room temperature for 5 minutes, the reaction solution was cooled to -10 to 0°C and trichloroacetonitrile (27 ml) was added dropwise over 15 minutes. The reaction solution was stirred for one hour while the temperature slowly increased to room temperature, and was then concentrated under reduced pressure. A solution of MeOH (1.0 ml) in n-pentane (100 ml) was added to the residue, and the mixture was vigorously stirred, filtered and concentrated. After then adding n-pentane to the residue and refiltering, the mother liquor was concentrated. Et₂O (80 ml), n-pentane (80 ml) and ethyl glycolate (25 g) were added to the residue, and then TfOH (1.5 ml) was added at 0°C and the mixture was stirred at 0°C for 10 minutes and at room temperature for 2 hours. The reaction solution was filtered, the mother liquor was poured into a saturated NaHCO₃ aqueous solution and extraction was performed with Et₂O. The organic layer was rinsed with water and dried with MgSO₄, and then filtered and concentrated. The residue was purified by silica gel column chromatography (n-hexane/AcOEt = 10/1 → 6/1) to obtain ethyl 2-(benzyloxy)acetate.

Yield: 38.76 g (y. 83.2%)

¹H NMR(δppm, CDCl₃): 1.29(t, J=7.26Hz, 3H), 4.09(s, 2H), 4.23(q, J=7.26Hz, 2H), 4.63(s, 2H), 7.21 to 7.45(m, 5H)

Synthesis of methyl 6-benzyloxy-2,4-dimethyl-3,5-dioxohexanoate

A solution of methyl 2-methyl-3-oxopentanoate (13.05 g) in THF (100 ml) was added to a suspension of NaH (3.80 g) in THF (100 ml) at 0°C, and after stirring at 0°C for 15 minutes, 1.63 M n-BuLi (58 ml) was added and the mixture was stirred at 0°C for 20 minutes to prepare a light yellow dienolate. The reaction solution was cooled to -78°C, a solution of ethyl 2-(benzyloxy) acetate (17.56 g) in THF (30 ml) was added, and the mixture was stirred at -78°C for 5 minutes and then at 0°C for one hour. Diluted hydrochloric acid was poured into the reaction solution for quenching, and extraction was performed with AcOEt at near neutral. The organic layer was rinsed with saturated saline and dried with MgSO₄, and then filtered and concentrated. The residue was purified by silica gel column chromatography (n-hexane/AcOEt = 5/1 → 3/1) to obtain methyl 6-benzyloxy-2,4-dimethyl-3,5-dioxohexanoate.

Yield: 9.78 g (y. 37%)

¹H NMR(δppm, CDCl₃): 1.17 to 1.42(m, 6H), 3.62 to 3.80(m, 4H), 3.98 to 4.28(m, 3H), 4.48 to 4.65(m, 2H), 7.12 to 7.42(m, 5H)

Synthesis of 4-acetyloxy-6-(benzyloxy)methyl-3,5-dimethyl-2H-pyran-2-one

An aqueous solution (6 ml) of LiOH-hydrate (64 mg) was added to a solution of methyl 6-benzyloxy-2,4-dimethyl-3,5-dioxohexanoate (430 mg) in THF (10 ml), and the mixture was stirred at room temperature for 1.5 hours. The reaction solution was neutralized with diluted hydrochloric acid, and after distilling off the volatile components under reduced pressure, extraction was performed with AcOEt at pH 3. The organic layer was dried with MgSO₄ and then filtered and concentrated. Ac₂O (6 ml) was added to the residue, and after stirring at room temperature for 30 minutes, pyridine (4 ml) was added and the mixture was stirred at room temperature for one hour. The reaction solution was concentrated under

reduced pressure, and the residue was purified by silica gel column chromatography (n-hexane/AcOEt = 3/1 → 12/5) to obtain 4-acetyloxy-6-(benzyloxy)methyl-3,5-dimethyl-2H-pyran-2-one.

5 Yield: 212 mg (y. 47.7%)

¹H NMR(δppm, CDCl₃): 1.88(s, 3H), 1.93(s, 3H), 2.34(s, 3H), 4.35(s, 2H), 4.58(s, 2H), 7.23 to 7.41(m, 5H)

Synthesis of 6-(benzyloxy)methyl-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

10 K₂CO₃ (3.0 g) and water (10 ml) were added to a solution of 4-acetyloxy-6-(benzyloxy)methyl-3,5-dimethyl-2H-pyran-2-one (6.08 g) in MeOH (100 ml), and after stirring at room temperature overnight, the reaction solution was celite filtered and the mother liquor was
15 concentrated under reduced pressure. Water was added to the residue, extraction was performed with AcOEt, and the organic layer was dried with Na₂SO₄ and then filtered and concentrated. The residue was purified by silica gel column chromatography (n-hexane/AcOEt = 5/1 → 1/1) to
20 obtain 6-(benzyloxy)methyl-3,5-dimethyl-4-hydroxy-2H-pyran-2-one.

Yield: 4.82 g (y. 86%)

(TLC R_f=0.3; n-hexane/AcOEt=1/1)

Synthesis of 6-(benzyloxy)methyl-3,5-dimethyl-4-methoxymethoxy-2H-pyran-2-one

25 Diisopropylethylamine (2.1 ml) was added to a solution of 6-(benzyloxy)methyl-3,5-dimethyl-4-hydroxy-2H-pyran-2-one (2.60 g) in THF (50 ml), and after stirring the mixture at room temperature for one hour,
30 chloromethyl methyl ether (921 μl) was added at 0°C and the mixture was stirred at room temperature for one hour. After concentrating the reaction solution under reduced pressure, water was added to the residue, extraction was performed with AcOEt, and the organic layer was dried
35 with Na₂SO₄ and then filtered and concentrated. The residue was purified by silica gel column chromatography

(n-hexane/AcOEt = 5/1 → 1/1) to obtain 6-(benzyloxy)methyl-3,5-dimethyl-4-methoxymethoxy-2H-pyran-2-one.

Yield: 1.80 g (y. 60%)

5 (TLC Rf = 0.6; n-hexane/AcOEt = 1/1)

Synthesis of 3,5-dimethyl-6-hydroxymethyl-4-methoxymethoxy-2H-pyran-2-one

20% Pd(OH)₂/C (360 mg) was added to a solution of 6-(benzyloxy)methyl-3,5-dimethyl-4-methoxymethoxy-2H-pyran-2-one (1.80 g) in EtOH (50 ml), and the mixture was vigorously stirred at room temperature for 3 hours under a hydrogen gas atmosphere. The reaction solution was celite filtered and the mother liquor was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane/AcOEt = 1/1) to obtain 3,5-dimethyl-6-hydroxymethyl-4-methoxymethoxy-2H-pyran-2-one.

Yield: 1.26 g (y. 99%)

(TLC Rf = 0.15; n-hexane/AcOEt = 1/1)

20 Synthesis of 3,5-dimethyl-4-methoxymethoxy-6-(methylsulfonyloxy)methyl-2H-pyran-2-one

Triethylamine (606 mg) was added to a solution of 3,5-dimethyl-6-hydroxymethyl-4-methoxymethoxy-2H-pyran-2-one (1.26 g) in THF (50 ml), and after stirring the mixture at room temperature for one hour, methanesulfonyl chloride (1.05 g) was added and the mixture was stirred at room temperature overnight. Water was added to the reaction solution, extraction was performed with AcOEt, and the organic layer was dried with Na₂SO₄ and then filtered and concentrated. The residue was purified by silica gel column chromatography (n-hexane/AcOEt = 1/1) to obtain 3,5-dimethyl-4-methoxymethoxy-6-(methylsulfonyloxy)methyl-2H-pyran-2-one.

Yield: 1.35 g (y. 73%)

35 (TLC Rf = 0.5; n-hexane/AcOEt = 1/1)

Synthesis of 6-bromomethyl-3,5-dimethyl-4-methoxymethoxy-2H-pyran-2-one

Sodium bromide (500 mg) was added to a solution of 3,5-dimethyl-4-methoxymethoxy-6-(methylsulfonyloxy)methyl-2H-pyran-2-one (1.35 g) in DMF (20 ml), and after the stirring the mixture at room temperature for one hour, the reaction solution was concentrated under reduced pressure. Water was added to the residue, extraction was performed with AcOEt, and the organic layer was dried with Na₂SO₄ and then filtered and concentrated. The residue was purified by silica gel column chromatography (n-hexane/AcOEt = 1/1) to obtain 6-bromomethyl-3,5-dimethyl-4-methoxymethoxy-2H-pyran-2-one. Yield: 1.21 g (y. 99%)

(TLC R_f = 0.7; n-hexane/AcOEt = 1/1)

Synthesis of methyl 6-hydroxybenzofuran-2-carboxylate

A suspension of 4-methoxysalicyl aldehyde (50 g), K₂CO₃ (65 g) and methyl bromoacetate (65 g) in DMF (500 ml) was stirred at 60°C for one hour, and after cooling, the reaction solution was concentrated under reduced pressure. Water was added to the residue, extraction was performed with AcOEt, and the organic layer was dried with MgSO₄ and then filtered and concentrated. Toluene (500 ml) was added to the residue to make a suspension, and upon addition of DBU (70 g), the mixture was stirred at 130°C overnight. After cooling, the reaction solution was concentrated under reduced pressure, water was added to the residue and extraction was performed with AcOEt. The organic layer was dried with MgSO₄ and then filtered and concentrated. The residue was dissolved in MeOH (500 ml), concentrated hydrochloric acid (50 ml) was added and the mixture was stirred at 60°C overnight. After cooling, the reaction solution was concentrated under reduced pressure, AcOEt (500 ml) was added to the residue, a saturated NaHCO₃ aqueous solution (500 ml) was slowly added to separate the organic layer and aqueous layer, and the aqueous layer was extracted with AcOEt. The organic layer was dried with MgSO₄ and then filtered

and concentrated. The residue was dissolved in CH_2Cl_2 (1000 ml), boron tribromide (125 g) was slowly added at 0°C , and then the mixture was stirred at room temperature for 24 hours. The reaction solution was concentrated under reduced pressure, the resulting brown oil was dissolved in MeOH (500 ml), concentrated hydrochloric acid (50 ml) was further added and the mixture was stirred at 60°C overnight. After cooling, the reaction solution was concentrated under reduced pressure, AcOEt (500 ml) was added to the residue, a saturated NaHCO_3 aqueous solution (500 ml) was slowly added to separate the organic layer and aqueous layer, and the aqueous layer was extracted with AcOEt. The organic layer was dried with MgSO_4 and then filtered and concentrated.

The residue was purified by silica gel column chromatography (n-hexane/AcOEt = 3/1) to obtain methyl 6-hydroxybenzofuran-2-carboxylate.

Yield: 37.9 g (y. 60%)

^1H NMR(δ ppm, CDCl_3): 3.88(s, 3H), 5.50 to 6.50(brs, 1H), 6.80 to 7.80(m, 4H)

Synthesis of methyl 6-(benzyloxy)benzofuran-2-carboxylate

A solution of methyl 6-hydroxybenzofuran-2-carboxylate (3.58 g) in THF (30 ml) was slowly added to a suspension of NaH (800 mg) in THF (100 ml) at room temperature, and after stirring for one hour, DMF (35 ml) was added, benzyl bromide (3.77 g) was slowly added and the mixture was stirred for one hour. Water was added to the reaction solution, extraction was performed with AcOEt, and the organic layer was dried with MgSO_4 and then filtered and concentrated. The residue was purified by silica gel column chromatography (n-hexane/AcOEt = 10/1) to obtain methyl 6-(benzyloxy)benzofuran-2-carboxylate.

Yield: 4.85 g (y. 95%)

^1H NMR(δ ppm, CDCl_3): 3.95(s, 3H), 5.19(s, 2H), 6.85(dd,

J=8.1Hz, 2.0Hz, 1H), 7.05(d, J=2.0Hz, 1H), 7.43(s, 1H), 7.51(d, J=8.1Hz, 1H)

Synthesis of 2-hydroxy-4-morpholinobenzaldehyde

After slowly adding a solution of 3-morpholinophenol
5 (5.0 g) in THF (100 ml) to a 3 M diethyl ether solution
(10 ml) of ethylmagnesium bromide, the mixture was
stirred at 30°C for 1.5 hours. Paraformaldehyde (3.0 g)
and Et₃N (3.0 g) were added to the reaction solution and
the mixture was stirred at 80°C for 4 hours. After
10 cooling, a 6 N hydrochloric acid aqueous solution (20 ml)
was added, the mixture was stirred for an hour, and then
the organic layer and aqueous layer were separated and
the aqueous layer was rendered weakly alkaline prior to
extraction with AcOEt. The organic layers were combined
15 and dried with MgSO₄, and then filtered and concentrated.
The residue was purified by silica gel column
chromatography (n-hexane/AcOEt = 3/1) to obtain 2-
hydroxy-4-morpholinobenzaldehyde.

Yield: 3.57 g (y. 62%)

20 ¹H NMR(δppm, CDCl₃): 3.30(t, J=4.8Hz, 4H), 3.84(t,
J=4.8Hz, 4H), 6.18(d, J=2.1Hz, 1H), 6.55(dd, J=8.9Hz,
2.1Hz, 1H), 7.78(d, J=8.9Hz, 1H), 10.30(s, 1H)

Synthesis of methyl 6-morpholinobenzofuran-2-
carboxylate

25 Methyl bromoacetate (3.0 g) and K₂CO₃ (3.0 g) were
added to a solution of 2-hydroxy-4-morpholinobenzaldehyde
(3.5 g) in acetonitrile (100 ml), and after heated reflux
for 16 hours, the reaction solution was filtered and the
mother liquor was concentrated under reduced pressure.
30 MeOH (100 ml) and concentrated hydrochloric acid (10 ml)
were added to the residue, and after reflux for 5 hours,
the reaction solution was concentrated under reduced
pressure. A saturated NaHCO₃ aqueous solution (100 ml)
was added to the residue prior to extraction with AcOEt,
35 and the organic layer was dried with MgSO₄ and then
filtered and concentrated. The residue was purified by
silica gel column chromatography (n-hexane/AcOEt = 5/1)

to obtain methyl 6-morpholinobenzofuran-2-carboxylate.

Yield: 3.1 g (y. 71%)

¹H NMR(δppm, CDCl₃): 3.22(t, J=4.8Hz, 4H), 3.80(t, J=4.8Hz, 4H), 3.95(s, 3H), 6.96 to 7.00(m, 2H), 7.44(s, 1H), 7.53(d, J=8.6Hz, 1H)

Synthesis of methyl 5-formylbenzofuran-2-carboxylate

K₂CO₃ (30 g) was added to a solution of 5-formylsalicyl aldehyde (25 g) and methyl bromoacetate (30 g) in acetonitrile (500 ml), and after heated reflux for 24 hours followed by cooling, the reaction solution was filtered and the mother liquor was concentrated under reduced pressure. A saturated ammonium chloride aqueous solution (100 ml) was added to the residue prior to extraction with AcOEt, and the organic layer was dried with MgSO₄ and then filtered and concentrated. The residue was purified by silica gel column chromatography (n-hexane/AcOEt = 5/1) to obtain methyl 5-formylbenzofuran-2-carboxylate.

Yield: 15 g (y. 44%)

Mass analysis: [M⁺ + H] = 205.2

Synthesis of methyl 5-(dimethoxymethyl)benzofuran-2-carboxylate

Methyl orthoformate (1.0 g) and polymer-bound PPTS (1.0 g) were added to a solution of methyl 5-formylbenzofuran-2-carboxylate (15 g) in MeOH (100 ml), and after allowing the mixture to stand at room temperature for 8 hours, the reaction solution was filtered and the mother liquor was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane/AcOEt = 9/1) to obtain methyl 5-(dimethoxymethyl)benzofuran-2-carboxylate.

Yield: 10 g (y. 54%)

¹H NMR(δppm, CDCl₃): 3.35(s, 3H), 3.98(s, 3H), 5.49(s, 1H), 7.53 to 7.61(m, 3H), 7.81(s, 1H)

The following compound was produced by a process similar to the preceding production example, using

organic chemical techniques well-known to those skilled in the art.

Ethyl 5-bromobenzofuran-2-carboxylate

¹H NMR(δppm, CDCl₃): 1.43(t, J=7.3Hz, 3H), 4.45(q, J=7.3Hz, 2H), 7.45(s, 1H), 7.47(d, J=8.4Hz, 1H), 7.54(dd, J=8.4Hz, 2.2Hz, 1H), 7.82(d, J=2.2Hz, 1H)

Example 1. Synthesis of 4-acetyloxy-6-(benzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one

After adding 60% NaH (220 mg) to a solution of methyl 2-methyl-3-oxopentanoate (750 mg) in THF (5 ml) at 0°C and stirring at 0°C for 5 minutes, the mixture was cooled to -78°C. To this reaction solution there was added 1.63 M n-BuLi (3.3 ml), and the mixture was stirred at -78°C for 30 minutes to prepare a dienolate. A solution of methyl 2-benzofurancarboxylate (300 mg) in THF (10 ml) was added to the dienolate, and the mixture was stirred at -78°C for 20 minutes. The reaction solution was allowed to return to 0°C, aqueous KHSO₄ was added for quenching, and extraction was performed with AcOEt. The organic layer was rinsed with saturated saline and dried with MgSO₄, and then filtered and concentrated. The residue was crudely purified by silica gel column chromatography (n-hexane/AcOEt = 3/1 → 2/1) to obtain methyl 5-(benzofuran-2-yl)-2,4-dimethyl-3,5-dioxopentanoate.

Yield: 433 mg (mixture)

An aqueous solution (30 ml) of LiOH-hydrate (2.62 g) was added to a solution of 5-(benzofuran-2-yl)-2,4-dimethyl-3,5-dioxopentanoate (14.98 g) in MeOH (50 ml), and after stirring at room temperature for 20 minutes, the MeOH was distilled off under reduced pressure. The aqueous solution of the residue was rinsed with Et₂O and then cooled on ice, and a KHSO₄ aqueous solution was added for adjustment to pH 2.0 to 2.5. The precipitated crystals were filtered off and rinsed with water. The mother liquor was saturated with saline and extracted

with AcOEt, and the organic layer was concentrated. The residue was combined with the filtered off crystals, and after adding pyridine (40 ml) and Ac₂O (40 ml), the mixture was stirred at room temperature for 3.5 hours.

5 The reaction solution was concentrated under reduced pressure and the residue was recrystallized from n-hexane/AcOEt = 3/1 to obtain 4-acetyloxy-6-(benzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one.

Yield: 6.11 g (y. 47.3%)

10 ¹H NMR(δppm, CDCl₃): 2.00(s, 3H), 2.31(s, 3H), 2.40(s, 3H), 7.23 to 7.42(m, 2H), 7.36(s, 1H), 7.53(d, J=8.2Hz, 1H), 7.65(d, J=7.6Hz, 1H)

Example 2. Synthesis of 6-(benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

15 An aqueous solution (30 ml) of LiOH-hydrate (465 mg) was added to a solution of 4-acetyloxy-6-(benzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one (3.00 g) in MeOH (100 ml) at 0°C, and after stirring at room temperature for 2 hours, the MeOH was distilled off under reduced pressure.

20 The residue was rinsed with Et₂O, and then a KHSO₄ aqueous solution was added at 0°C for adjustment to pH 2.0. The precipitated crystals were filtered off and thoroughly rinsed with water and Et₂O in that order and then dried to obtain 6-(benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one.

25 Yield: 2.54 g (y. 98.5%)

¹H NMR(δppm, DMSO-d₆): 1.93(s, 3H), 2.28(s, 3H), 7.28 to 7.47(m, 2H), 7.39(s, 1H), 7.68(d, J=8.3Hz, 1H), 7.74(d, J=7.3Hz, 1H), 10.91(brs, 1H)

30 Example 3. Synthesis of 6-(benzofuran-2-yl)-4-benzoyloxy-3,5-dimethyl-2H-pyran-2-one

Pyridine (64 μl) and benzoyl chloride (45 μl) were added to a suspension of 6-(benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one (40 mg) in CH₂Cl₂ (5 ml), and the mixture was stirred at room temperature for 50 minutes. The reaction solution was poured into a

KHSO₄ aqueous solution and extracted with AcOEt, and the organic layer was rinsed with saturated saline and dried with MgSO₄, and then filtered and concentrated. The residue was purified by silica gel column chromatography (n-hexane/AcOEt = 5/1 → 4/1) to obtain 6-(benzofuran-2-yl)-4-benzoyloxy-3,5-dimethyl-2H-pyran-2-one.

Yield: 48 mg (y. 71.2%) Light yellow crystals.

¹H NMR(δppm, CDCl₃): 2.04(s, 3H), 2.35(s, 3H), 7.24 to 7.42(m, 3H), 7.49 to 7.77(m, 5H), 8.23(d, J=7.3Hz, 2H)

10 Example 4. Synthesis of 6-(benzofuran-2-yl)-3,5-dimethyl-4-methanesulfonyloxy-2H-pyran-2-one

Et₃N (130 μl) and methanesulfonyl chloride (24 μl) were added to a suspension of 6-(benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one (40 mg) in THF (5 ml), and the mixture was stirred at room temperature for one hour. The reaction solution was poured into aqueous KHSO₄ and extracted with AcOEt, and the organic layer was rinsed with saturated saline and dried with MgSO₄, and then filtered and concentrated. The residue was purified by silica gel column chromatography (n-hexane/AcOEt = 2/1) to obtain 6-(benzofuran-2-yl)-3,5-dimethyl-4-methanesulfonyloxy-2H-pyran-2-one.

Yield: 46 mg (y. 88.2%) Yellow crystals.

25 ¹H NMR(δppm, CDCl₃): 2.22(s, 3H), 2.50(s, 3H), 3.39(s, 3H), 7.26 to 7.44(m, 3H), 7.54(d, J=8.2Hz, 1H), 7.66(d, J=7.6Hz, 1H)

Example 5. Synthesis of 6-(benzofuran-2-yl)-3,5-dimethyl-4-(2-pyridylcarboxy)-2H-pyran-2-one

WSC (43 mg) was added to a solution of 6-(benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one (40 mg), picolinic acid (23 mg) and HOBt (21 mg) in DMF (3 ml), and the mixture was stirred at room temperature for 21.5 hours. The reaction solution was concentrated under reduced pressure, and the residue was purified by silica gel column chromatography (n-hexane/AcOEt = 2/1 →

3/2) to obtain 6-(benzofuran-2-yl)-3,5-dimethyl-4-(2-pyridylcarboxy)-2H-pyran-2-one.

Yield: 30 mg (y. 53.2%) Light yellow crystals.

¹H NMR(δppm, CDCl₃): 2.07(s, 3H), 2.38(s, 3H), 7.25 to 7.42(m, 3H), 7.53(d, J=8.2Hz, 1H), 7.61 to 7.69(m, 2H), 7.99(dd, J=1.6Hz, 7.9Hz, 1H), 8.32(d, J=7.9Hz, 1H), 8.90(d, J=4.6Hz, 1H)

Example 6. Synthesis of 3,5-dimethyl-4-hydroxy-6-(6-morpholinylbenzofuran-2-yl)-2H-pyran-2-one

10 A solution of methyl 2-methyl-3-oxopentanoate (865 mg) in THF (30 ml) was slowly added to a suspension of NaH (240 mg) in THF (50 ml), and after stirring for 10 minutes, the mixture was cooled to -78°C and 1.58 M n-BuLi (3.8 ml) was slowly added dropwise. After stirring 15 the reaction solution at -78°C for 30 minutes, a solution of methyl 6-morpholinylbenzofuran-2-carboxylate (1.3 g) in THF (15 ml) was slowly added and the mixture was stirred at -78°C for 4 hours. A saturated ammonium chloride aqueous solution (30 ml) was added to the 20 reaction solution, and after bringing it to room temperature, extraction was performed with AcOEt and the organic layer was dried with MgSO₄ and then filtered and concentrated. The residue was dissolved in MeOH (30 ml) and THF (30 ml), a 4 N lithium hydroxide aqueous solution 25 (10 ml) was added, and after stirring at room temperature for 4 hours, a saturated KHSO₄ aqueous solution (50 ml) was slowly added. The deposited yellow precipitate was filtered off and rinsed with AcOEt to obtain 3,5-dimethyl-4-hydroxy-6-(6-morpholinylbenzofuran-2-yl)-2H-pyran-2-one. 30

Yield: 1.40 g (y. 82%)

¹H NMR(δppm, DMSO-d₆): 1.92(s, 3H), 2.26(s, 3H), 3.19(t, J=4.8Hz, 4H), 3.75(t, J=4.8Hz, 4H), 7.05(d, J=8.4Hz, 1H), 7.16(s, 1H), 7.25(s, 1H), 7.54(d, J=8.4Hz, 1H), 10.8(s, 1H) 35

Example 7. Synthesis of 3,5-dimethyl-6-(5-formylbenzofuran-2-yl)-4-hydroxy 2H-pyran-2-one

A solution of methyl 2-methyl-3-oxopentanoate (7.5 g) in THF (50 ml) was slowly added to a suspension of NaH (2.1 g) in THF (200 ml), and after stirring for 10 minutes, the mixture was cooled to -78°C and 1.58 M n-BuLi (32 ml) was slowly added dropwise. After stirring the reaction solution at -78°C for 30 minutes, a solution of methyl 5-(dimethoxymethyl)benzofuran-2-carboxylate (10 g) in THF (50 ml) was slowly added and the mixture was stirred at -78°C for 4 hours. A saturated ammonium chloride aqueous solution (30 ml) was added to the reaction solution, and after bringing it to room temperature, extraction was performed with AcOEt and the organic layer was dried with MgSO_4 and then filtered and concentrated. The residue was dissolved in MeOH (100 ml) and THF (100 ml), a 4 N lithium hydroxide aqueous solution (25 ml) was added, and after stirring at room temperature for 4 hours, a saturated KHSO_4 aqueous solution (50 ml) was slowly added. The deposited yellow precipitate was filtered off and rinsed with AcOEt to obtain 3,5-dimethyl-6-(5-formylbenzofuran-2-yl)-4-hydroxy-2H-pyran-2-one

Yield: 10.8 g (y. 95%)

^1H NMR(δ ppm, DMSO- d_6): 1.87(s, 3H), 2.23(s, 3H), 7.51(s, 1H), 7.78 to 7.92(m, 2H), 8.28(s, 1H), 10.0(s, 1H)

Example 8. Synthesis of 4-acetyloxy-3,5-dimethyl-6-(5-formylbenzofuran-2-yl)-2H-pyran-2-one

After adding Et_3N (1.7 g) to a suspension of 3,5-dimethyl-6-(5-formylbenzofuran-2-yl)-4-hydroxy-2H-pyran-2-one (5.0 g) in CH_2Cl_2 (100 ml), the mixture was cooled on ice, acetyl chloride (1.32 g) was added and the mixture was stirred at room temperature for one hour. Water (100 ml) was added to the reaction solution, extraction was performed with AcOEt, and the organic layer was dried with MgSO_4 and then filtered and

concentrated. The residue was purified by silica gel column chromatography (n-hexane/AcOEt = 3/1) to obtain 4-acetyloxy-3,5-dimethyl-6-(5-formylbenzofuran-2-yl)-2H-pyran-2-one.

5 Yield: 5.1 g (y. 88%)

¹H NMR(δppm, CDCl₃): 2.02(s, 3H), 2.32(s, 3H), 2.41(s, 3H), 7.46(s, 1H), 7.66(d, J=8.4Hz, 1H), 7.96(d, J=8.4Hz, 1H), 8.20(s, 1H), 10.1(s, 1H)

10 Example 9. Synthesis of 3,5-dimethyl-6-(5-((3,5-dioxo-2,4-thiazolidinylidene)methyl)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one

Piperidine (100 mg) was added to a solution of 4-acetyloxy-3,5-dimethyl-6-(5-formylbenzofuran-2-yl)-2H-pyran-2-one (374 mg) and 1,3-thiazolidine-2,4-dione (135
15 mg) in THF (50 ml), and the mixture was subjected to heated reflux for 4 hours. After cooling, a 15% sodium hydroxide aqueous solution (10 ml) was added to the reaction solution, and then after stirring for one hour it was concentrated under reduced pressure. The residue
20 was purified by silica gel column chromatography (CH₂Cl₂/MeOH = 5/1) to obtain 3,5-dimethyl-6-(5-((3,5-dioxo-2,4-thiazolidinylidene)methyl)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one.

Yield: 400 mg (y. 91%)

25 ¹H NMR(δppm, DMSO-d₆): 1.96(s, 3H), 2.22(s, 3H), 7.32(s, 1H), 7.45(d, J=8.4Hz, 1H), 7.75(d, J=8.4Hz, 1H), 8.12(s, 1H), 8.24(s, 1H), 10.91(s, 1H), 12.90(s, 1H)

30 Example 10. Synthesis of 3,5-dimethyl-6-(5-((3,5-dioxo-2,4-thiazolidinyl)methyl)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one

To 3,5-dimethyl-6-(5-((3,5-dioxo-2,4-thiazolidinylidene) methyl)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one (350 mg) in a mixed solvent of EtOH (10 ml) and 1,4-dioxane (10 ml) there was added 10% Pd/C (70 mg),
35 and the mixture was stirred for one day in a hydrogen gas atmosphere. The reaction solution was filtered, the

mother liquor was concentrated under reduced pressure, and then the residue was purified by silica gel column chromatography ($\text{CH}_2\text{Cl}_2/\text{MeOH} = 5/1$) to obtain 3,5-dimethyl-6-(5-((3,5-dioxo-2,4-

5 thiazolidinyl)methyl)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one.

Yield: 352 mg (y. quant.)

^1H NMR(δ ppm, DMSO- d_6): 1.97(s, 3H), 2.24(s, 3H), 3.34 to 3.55(m, 1H), 3.67 to 3.82(m, 1H), 4.98 to 5.01(m, 1H), 10 7.24(s, 1H), 7.39(d, $J=8.4\text{Hz}$, 1H), 7.61(d, $J=8.4\text{Hz}$, 1H), 8.12(s, 1H), 10.93(s, 1H), 12.20(s, 1H)

Example 11. Synthesis of 6-(benzofuran-2-yl)-4-hydroxy-3-methyl-5-n-pentyl-2H-pyran-2-one

A solution of methyl 2-methyl-3-oxononanoate (3.06 g) in THF (5 ml) was added to a suspension of 60% NaH (608 mg) in THF (30 ml) while cooling on ice, and the mixture was stirred at 0°C for 10 minutes and then at room temperature for 30 minutes. The reaction solution was cooled to -78°C , 1.66 M n-BuLi (9.2 ml) was added, 20 and the mixture was stirred at -78°C for 30 minutes to prepare a dienolate. A solution of methyl 2-benzofurancarboxylate (1.25 g) in THF (5 ml) was added to the dienolate, and the mixture was stirred at -78°C for 30 minutes. The reaction solution was brought to 0°C , an 25 NH_4Cl aqueous solution was added for quenching, and extraction was performed with AcOEt. The organic layer was rinsed with water and saturated saline in that order, and then dried with Na_2SO_4 , filtered and concentrated. The residue was dissolved in MeOH (50 ml), and after 30 adding 2N-LiOH (30 ml) and stirring at room temperature for 2 hours, 1N-HCl was added at 0°C to acidity of approximately pH 3, and extraction was performed with AcOEt. The organic layer was rinsed with water and saturated saline in that order, and then dried with 35 Na_2SO_4 , filtered and concentrated. Pyridine (20 ml) and Ac_2O (20 ml) were added to the residue, and after stirring the mixture at room temperature for 5 hours it

was concentrated under reduced pressure. The residue was dissolved in MeOH (20 ml), imidazole (483 mg) was added at 0°C, and after stirring the mixture at 0°C for 10 minutes and then at room temperature for 30 minutes, it was concentrated under reduced pressure. AcOEt was added to the residue, and the precipitated crystals were filtered off. The crystals were recrystallized from EtOH to obtain 6-(benzofuran-2-yl)-4-hydroxy-3-methyl-5-n-pentyl-2H-pyran-2-one.

Yield: 357.9 mg (y. 16.1%)

¹H NMR(δppm, DMSO-d₆): 0.87(t, J=6.9Hz, 3H), 1.28 to 1.60(m, 6H), 1.93(s, 3H), 2.74 to 2.85(m, 2H), 7.28 to 7.46(m, 3H), 7.63(d, J=8.3Hz, 1H), 7.75(d, J=7.3Hz, 1H), 10.86(brs, 1H)

Example 12. Synthesis of 3,5-dimethyl-4-hydroxy-6-(5-methoxybenzofuran-2-yl)-2H-pyran-2-one

K₂CO₃ (138 mg) was added to a solution of 5-methoxysalicyl aldehyde (152 mg) and 6-bromomethyl-3,5-dimethyl-4-methoxymethoxy-2H-pyran-2-one (277 mg) in DMF (5 ml), and the mixture was stirred at room temperature for 16 hours. A 6 N hydrochloric acid aqueous solution was slowly added to the reaction solution, and after stirring for one hour, extraction was performed with AcOEt and the organic layer was dried with MgSO₄ and then filtered and concentrated. The residue was purified by silica gel column chromatography (n-hexane/AcOEt = 1/1) to obtain 3,5-dimethyl-4-hydroxy-6-(5-methoxybenzofuran-2-yl)-2H-pyran-2-one.

Yield: 229 mg (y. 80%)

¹H NMR(δppm, CDCl₃): 2.01(s, 3H), 2.25(s, 3H), 4.00(s, 3H), 5.50 to 6.50(brs, 1H), 6.80 to 7.80(m, 4H)

Example 13. Synthesis of 3,5-dimethyl-4-hydroxy-6-(7-methoxybenzofuran-2-yl)-2H-pyran-2-one

3,5-dimethyl-4-hydroxy-6-(7-methoxybenzofuran-2-yl)-2H-pyran-2-one was obtained in the same manner as the preceding example.

Yield: 78%

^1H NMR(δ ppm, CDCl_3): 2.10(s, 3H), 2.26(s, 3H), 4.00(s, 3H), 5.50 to 6.50(brs, 1H), 6.80 to 7.80(m, 4H)

5 Example 14. Synthesis of 6-(5-aminobenzofuran-2-yl)-3,5-dimethyl-4-methoxymethoxy-2H-pyran-2-one and 3,5-dimethyl-6-(5-(ethylamino)benzofuran-2-yl)-4-methoxymethoxy-2H-pyran-2-one

10 To a solution of 3,5-dimethyl-4-methoxymethoxy-6-(5-nitrobenzofuran-2-yl)-2H-pyran-2-one (100 mg) in dioxane (20 ml) and EtOH (20 ml) there was added 5% Pd/C (5 mg), and after displacing the reaction vessel atmosphere with hydrogen, the mixture was stirred at room temperature overnight. The reaction solution was filtered and concentrated, and then purified by silica gel thin-layer chromatography (n-hexane/AcOEt = 1/1) to obtain 6-(5-aminobenzofuran-2-yl)-3,5-dimethyl-4-methoxymethoxy-2H-pyran-2-one and 3,5-dimethyl-6-(5-(ethylamino)benzofuran-2-yl)-4-methoxymethoxy-2H-pyran-2-one.

20 6-(5-aminobenzofuran-2-yl)-3,5-dimethyl-4-methoxymethoxy-2H-pyran-2-one;

Yield: 45 mg (y. 49%)

25 ^1H NMR(δ ppm, CDCl_3): 2.12(s, 3H), 2.42(s, 3H), 3.64(s, 3H), 5.16(s, 2H), 6.83(dd, $J=2.3\text{Hz}$, 8.9Hz , 1H), 6.96(d, $J=2.3\text{Hz}$, 1H), 7.20(s, 1H), 7.33(d, $J=8.9\text{Hz}$, 1H), 7.42(s, 2H)

3,5-dimethyl-6-(5-(ethylamino)benzofuran-2-yl)-4-methoxymethoxy-2H-pyran-2-one;

Yield: 33 mg (y. 33%)

30 ^1H NMR(δ ppm, CDCl_3): 1.30(t, $J=7.3\text{Hz}$, 3H), 2.11(s, 3H), 2.39(s, 3H), 3.19(q, $J=7.3\text{Hz}$, 2H), 3.62(s, 3H), 5.11(s, 2H), 6.69(dd, $J=2.3\text{Hz}$, 8.9Hz , 1H), 6.75(d, $J=2.3\text{Hz}$, 1H), 7.20(s, 1H), 7.31(d, $J=8.9\text{Hz}$, 1H)

35 Example 15. Synthesis of 6-(5-(acetylamino)benzofuran-2-yl)-3,5-dimethyl-4-methoxymethoxy-2H-pyran-2-one

Pyridine (400 μ l) and Ac_2O (15 μ l) were added to 6-(5-aminobenzofuran-2-yl)-3,5-dimethyl-4-methoxymethoxy-2H-pyran-2-one (45 mg), and after stirring the mixture at room temperature for 6 hours, an NH_4Cl aqueous solution was added and extraction was performed with CH_2Cl_2 . The organic layer was dried, filtered and concentrated, and the residue was purified by silica gel thin-layer chromatography (CH_2Cl_2) to obtain 6-(5-acetylamino)benzofuran-2-yl)-3,5-dimethyl-4-methoxymethoxy-2H-pyran-2-one.

Yield: 20 mg (y. 39%)

^1H NMR(δ ppm, CDCl_3): 2.10(s, 3H), 2.17(s, 3H), 2.43(s, 3H), 3.64(s, 3H), 5.20(s, 2H), 7.32(s, 1H), 7.45(d, $J=8.9\text{Hz}$, 1H), 7.50(d, $J=8.9\text{Hz}$, 1H), 7.97(d, $J=0.7\text{Hz}$, 1H)

Example 16. Synthesis of 6-(5-aminobenzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

THF (20 ml) was added to and stirred with 6-(5-aminobenzofuran-2-yl)-3,5-dimethyl-4-methoxymethoxy-2H-pyran-2-one (58 mg), one drop of concentrated hydrochloric acid was added and the mixture was stirred at room temperature for one hour. The reaction solution was concentrated under reduced pressure and the residue was purified by thin-layer chromatography (n-hexane/ AcOEt = 1/1) to obtain 6-(5-aminobenzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one.

Yield: 13 mg (y. 27%)

^1H NMR(δ ppm, $\text{DMSO}-d_6$): 1.93(s, 3H), 2.27(s, 3H), 6.71(dd, $J=2.0\text{Hz}$, 8.9Hz, 1H), 6.79(d, $J=2.0\text{Hz}$, 1H), 7.16(s, 1H), 7.33(d, $J=8.9\text{Hz}$, 1H)

Example 17. Synthesis of 6-(6-(benzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one and 4-acetyloxy-6-(6-(benzyloxy)benzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one

A solution of methyl 2-methyl-3-oxopentanoate (3.24 g) in THF (30 ml) was slowly added to a suspension of NaH (900 mg) in THF (50 ml) at 0°C , and after stirring for 10

minutes, the mixture was cooled to -78°C and 1.58 M n-BuLi (14.2 ml) was slowly added dropwise. After stirring the reaction solution at -78°C for 30 minutes, a solution of methyl 6-(benzyloxy)benzofuran-2-carboxylate (4.26 g) in THF (15 ml) was slowly added and the mixture was stirred at -78°C for 4 hours. A saturated ammonium chloride aqueous solution was added to the reaction solution, and after bringing it to room temperature, extraction was performed with AcOEt and the organic layer was dried with MgSO_4 and then filtered and concentrated. The residue was dissolved in MeOH (30 ml) and THF (10 ml), a 4 N lithium hydroxide aqueous solution (5 ml) and water (50 ml) were added, and after stirring at room temperature for 4 hours, a saturated KHSO_4 aqueous solution (30 ml) was slowly added. The deposited yellow precipitate was filtered off and rinsed with AcOEt to obtain 6-(6-(benzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one.

Yield: 964 mg (y. 25%)

^1H NMR(δ ppm, DMSO- d_6): 2.00(s, 3H), 2.24(s, 3H), 5.27(s, 2H), 7.11(d, $J=8.4\text{Hz}$, 1H), 7.30 to 7.70(m, 8H), 10.8(brs, 1H)

The filtrate was further concentrated under reduced pressure, water (30 ml) and AcOEt (30 ml) were added, the organic layer and aqueous layer were separated, and the aqueous layer was extracted with AcOEt. The organic layers were combined, dried with MgSO_4 , filtered and concentrated. Acetic anhydride (10 ml) and pyridine (3 ml) were added to the residue, and after stirring overnight, the reaction solution was concentrated under reduced pressure and purified by silica gel column chromatography (n-hexane/AcOEt = 5/1 $\rightarrow$ 1/1) to obtain 4-acetyloxy-6-(6-(benzyloxy)benzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one.

Yield: 904 mg (y. 21%)

^1H NMR(δ ppm, CDCl_3): 1.92(s, 3H), 1.97(s, 3H), 2.37(s,

3H), 5.09(s, 2H), 6.80 to 7.80(m, 9H)

Example 18. Synthesis of 4-acetyloxy-3,5-dimethyl-6-(6-hydroxybenzofuran-2-yl)-2H-pyran-2-one

To a solution of 4-acetyloxy-6-(6-(benzyloxy)benzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one (500 mg) in EtOH (50 ml) and 1,4-dioxane (50 ml) there was added 10% Pd/C (100 mg), and the mixture was vigorously stirred at room temperature for 3 hours under a hydrogen gas atmosphere. The reaction solution was celite filtered, and then the filtrate was concentrated under reduced pressure and the residue was purified by silica gel column chromatography (n-hexane/AcOEt = 1/1) to obtain 4-acetyloxy-3,5-dimethyl-6-(6-hydroxybenzofuran-2-yl)-2H-pyran-2-one.

Yield: 388 mg (y. 95%)

^1H NMR(δ ppm, CDCl_3): 1.92(s, 3H), 1.97(s, 3H), 2.37(s, 3H), 5.50 to 6.50(brs, 1H), 6.80 to 7.80(m, 4H)

Example 19. Synthesis of 4-acetyloxy-3,5-dimethyl-6-(6-(trifluoromethanesulfonyloxy)benzofuran-2-yl)-2H-pyran-2-one

Pyridine (100 mg) was added to a solution of 4-acetyloxy-3,5-dimethyl-6-(6-hydroxybenzofuran-2-yl)-2H-pyran-2-one (385 mg) in CH_2Cl_2 (10 ml), and after stirring at room temperature for one hour, trifluoromethanesulfonic anhydride (415 mg) was slowly added while cooling on ice and the mixture was stirred at room temperature for 2 hours. A saturated NaHCO_3 aqueous solution (10 ml) was added to the reaction solution, extraction was performed with AcOEt, and the organic layer was dried with Na_2SO_4 and then filtered and concentrated. The residue was purified by silica gel column chromatography (n-hexane/AcOEt = 2/1) to obtain 4-acetyloxy-3,5-dimethyl-6-(6-(trifluoromethanesulfonyloxy)benzofuran-2-yl)-2H-pyran-2-one.

Yield: 392 mg (y. 72%)

Mass analysis: $[\text{M}^+ + \text{H}] = 447.3$

Example 20. Synthesis of 4-acetyloxy-3,5-dimethyl-6-(6-(methoxycarbonyl)benzofuran-2-yl)-2H-pyran-2-one

After adding a solution of 4-acetyloxy-3,5-dimethyl-
5 6-(6-(trifluoromethanesulfonyloxy)benzofuran-2-yl)-2H-pyran-2-one (350 mg) in THF (5 ml) and Et₃N (80 mg) to a mixed solution of palladium acetate (3.5 mg) and diphenylphosphinopropane (6.5 mg) in DMSO (5 ml) and MeOH (5 ml), the mixture was stirred at room temperature for
10 one hour under a carbon monoxide atmosphere, and then further stirred at 80°C for 2 hours. The reaction solution was concentrated under reduced pressure and the residue was purified by silica gel column chromatography (n-hexane/AcOEt = 1/1) to obtain 4-acetyloxy-3,5-
15 dimethyl-6-(6-(methoxycarbonyl) benzofuran-2-yl)-2H-pyran-2-one.

Yield: 92 mg (y. 33%)

Mass analysis: [M⁺ + H] = 357.3

Example 21. Synthesis of 6-(6-carboxybenzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

A mixed solution of 4-acetyloxy-3,5-dimethyl-6-(6-(methoxycarbonyl)benzofuran-2-yl)-2H-pyran-2-one (85 mg) and K₂CO₃ (45 mg) in MeOH (5 ml) and H₂O (1 ml) was stirred at room temperature for one hour, and then the
25 reaction solution was rendered acidic with a 1 N hydrochloric acid aqueous solution and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (AcOEt/MeOH = 5/1) to obtain 6-(6-carboxybenzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-
30 2-one.

Yield: 71 mg (y. quant.)

Mass analysis: [M⁺ + H] = 301.2

Example 22. Synthesis of 3,5-dimethyl-4-hydroxy-6-(6-(methoxycarbonyl)benzofuran-2-yl)-2H-pyran-2-one

Trimethylsilyldiazomethane (2 M hexane solution, 85
μl) was added to a mixed solution of 6-(6-

carboxybenzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one (50 mg) in MeOH (5 ml) and toluene (1 ml), and the mixture was stirred at room temperature for 10 minutes. After adding acetic acid to the reaction solution for

5 quenching of the excess trimethylsilyldiazomethane, it was concentrated under reduced pressure. The residue was purified by silica gel column chromatography ($\text{CH}_2\text{Cl}_2/\text{MeOH} = 9/1$) to obtain 3,5-dimethyl-4-hydroxy-6-(6-(methoxycarbonyl) benzofuran-2-yl)-2H-pyran-2-one.

10 Yield: 50 mg (y. 96%)

Mass analysis: $[\text{M}^+ + \text{H}] = 315.3$

Example 23. Synthesis of 4-acetyloxy-3,5-dimethyl-6-(6-dimethylaminobenzofuran-2-yl)-2H-pyran-2-one

Tetrakis(triphenylphosphine)palladium (3 mg) and

15 dimethylaminotrimethyltin (34 mg) were added to a solution of 4-acetyloxy-3,5-dimethyl-6-(6-(trifluoromethanesulfonyloxy) benzofuran-2-yl)-2H-pyran-2-one (45 mg) in toluene (5 ml), and the mixture was stirred at 50°C overnight. After cooling, the reaction

20 solution was concentrated under reduced pressure and the residue was purified by silica gel column chromatography ($n\text{-hexane}/\text{AcOEt} = 5/1$) to obtain 4-acetyloxy-3,5-dimethyl-6-(6-dimethylaminobenzofuran-2-yl)-2H-pyran-2-one.

25 Yield: 9.6 mg (y. 28%)

Mass analysis: $[\text{M}^+ + \text{H}] = 342.3$

Example 24. Synthesis of 4-acetyloxy-3,5-dimethyl-6-(6-(2-furyl)benzofuran-2-yl)-2H-pyran-2-one

4-acetyloxy-3,5-dimethyl-6-(6-(2-furyl)benzofuran-2-yl)-2H-pyran-2-one was obtained in the same manner as the

30 preceding example, using 2-(tributylstannyl)furan.

Yield: 31 mg (y. 87%)

Mass analysis: $[\text{M}^+ + \text{H}] = 365.3$

Example 25. Synthesis of 4-acetyloxy-3,5-dimethyl-6-(6-(2-thienyl)benzofuran-2-yl)-2H-pyran-2-one

4-acetyloxy-3,5-dimethyl-6-(6-(2-thienyl)benzofuran-2-yl)-2H-pyran-2-one was obtained in the same manner as

the preceding example, using 2-(tributylstannyl)thiophene.

Yield: 31 mg (y. 85%)

Mass analysis: $[M^+ + H] = 381.4$

5 Example 26. Synthesis of 3,5-dimethyl-4-hydroxy-6-(6-methoxybenzofuran-2-yl)-2H-pyran-2-one

K_2CO_3 (1.38 g) was added to a solution of 4-methoxysalicyl aldehyde (1.52 g) and 6-bromo-3,5-dimethyl-4-methoxymethoxy-2H-pyran-2-one (2.77 g) in DMF
10 (50 ml), and after stirring at room temperature overnight, the reaction solution was concentrated under reduced pressure. Water (50 ml) was added to the residue, extraction was performed with AcOEt, and the organic layer was dried with $MgSO_4$ and then filtered and
15 concentrated. The residue was purified by silica gel column chromatography (n-hexane/AcOEt = 1/1) to obtain 3.46 g of a yellow oil. Diisopropylethylamine (1.29 g) and DMF (20 ml) were added to 1.74 g of the yellow oil, prior to heated reflux overnight. After cooling, a 6 N
20 hydrochloric acid aqueous solution (10 ml) was slowly added to the reaction solution, and the mixture was stirred at room temperature for one hour and then concentrated under reduced pressure. Water (50 ml) was added to the residue, extraction was performed with
25 AcOEt, and the organic layer was dried with $MgSO_4$ and then filtered and concentrated. The residue was purified by silica gel column chromatography (n-hexane/AcOEt = 1/1) to obtain 3,5-dimethyl-4-hydroxy-6-(6-methoxybenzofuran-2-yl)-2H-pyran-2-one.

30 Yield: 20 mg (y. 1.3%)

1H NMR(δ ppm, $CDCl_3$): 2.12(s, 3H), 2.27(s, 3H), 4.00(s, 3H), 5.50 to 6.50(brs, 1H), 6.80 to 7.80(m, 4H)

Example 27. Synthesis of 3,5-dimethyl-4-hydroxy-6-(5-(5-pyrimidinylmethoxy)benzofuran-2-yl)-2H-pyran-2-one

35 A solution of tributylphosphine in 2 N THF (0.94 ml) and a solution of TMAD (323 mg) in CH_2Cl_2 (3 ml) were

added dropwise to a solution of 4-acetyloxy-3,5-dimethyl-6-(5-hydroxybenzofuran-2-yl)-2H-pyran-2-one (118 mg) and 5-hydroxymethylpyrimidine (202 mg) in THF (30 ml) at 0°C, and the mixture was stirred at room temperature overnight. The reaction solution was cooled on ice, a 1 N lithium hydroxide aqueous solution (5 ml) was added and the mixture was stirred at room temperature for one hour, after which the reaction solution was again cooled on ice, a 1 N hydrochloric acid aqueous solution (5 ml) and AcOEt were added, the organic layer and aqueous layer were separated, and the aqueous layer was further extracted with AcOEt. The organic layers were combined and dried with MgSO₄, and then filtered and concentrated. The residue was purified by silica gel column chromatography (AcOEt/MeOH = 10/1) to obtain 3,5-dimethyl-4-hydroxy-6-(5-(5-pyrimidinylmethoxy)benzofuran-2-yl)-2H-pyran-2-one.

Yield: 35 mg (y. 26%)

¹H NMR(δppm, DMSO-d₆): 1.95(s, 3H), 2.29(s, 3H), 5.24(s, 2H), 7.12 to 7.14(m, 1H), 7.33 to 7.38(m, 2H), 7.61 to 7.63(m, 1H), 8.95(s, 2H), 9.18(s, 1H), 10.91(brs, 1H)

The following compounds were produced by processes similar to those described in the preceding examples and production examples, using organic chemical techniques well-known to those skilled in the art.

Example 28. 6-(benzofuran-2-yl)-3,5-dimethyl-4-(4-hydroxymethylbenzoyloxy)-2H-pyran-2-one

¹H NMR(δppm, CDCl₃): 2.04(s, 3H), 2.34(s, 3H), 4.86(s, 2H), 7.24 to 7.42(m, 3H), 7.53(d, J=8.2Hz, 1H), 7.58(d, J=8.3Hz, 1H), 7.66(d, J=7.9Hz, 1H), 8.22(d, J=8.3Hz, 1H)

Example 29. 6-(benzofuran-2-yl)-4-(2-(N-carbobenzyloxy-N-methylamino)acetyloxy)-3,5-dimethyl-2H-pyran-2-one

¹H NMR(δppm, CDCl₃): 1.84, 2.00(s, 3H), 2.14, 2.32(s, 3H), 3.13, 3.14(s, 3H), 4.33, 4.36(s, 2H), 5.18, 5.20(s, 2H), 7.25 to 7.43(m, 8H), 7.53(d, J=8.6Hz, 1H), 7.66(d,

J=6.9Hz, 1H)

Example 30. 6-(benzofuran-2-yl)-3,5-dimethyl-4-(4-methoxybenzoyloxy)-2H-pyran-2-one

¹H NMR(δppm, CDCl₃): 2.03(s, 3H), 2.34(s, 3H), 3.93(s, 3H), 7.04(d, J=8.9Hz, 2H), 7.24 to 7.42(m, 3H), 7.52(d, J=8.2Hz, 1H), 7.66(d, J=7.9Hz, 1H), 8.17(d, J=9.2Hz, 1H)

Example 31. 6-(benzofuran-2-yl)-3,5-dimethyl-4-phenylacetyloxy-2H-pyran-2-one

¹H NMR(δppm, CDCl₃): 1.86(s, 3H), 2.14(s, 3H), 3.93(s, 2H), 7.21 to 7.45(m, 8H), 7.50(d, J=7.9Hz, 1H), 7.63(d, J=7.9Hz, 1H)

Example 32. 6-(benzofuran-2-yl)-4-hydroxy-3-methyl-2H-pyran-2-one

¹H NMR(δppm, DMSO-d₆): 1.85(s, 3H), 6.73(s, 1H), 7.29 to 7.46(m, 3H), 7.67(d, J=7.9Hz, 1H), 7.73(d, J=7.3Hz, 1H), 11.58(brs, 1H)

Example 33. 6-(benzofuran-2-yl)-5-ethyl-4-hydroxy-3-methyl-2H-pyran-2-one

¹H NMR(δppm, DMSO-d₆): 1.18(t, J=7.3Hz, 3H), 1.93(s, 3H), 2.79(q, J=7.3Hz, 2H), 7.29 to 7.44(m, 3H), 7.67(d, J=8.3Hz, 1H), 7.74(d, J=8.3Hz, 1H), 10.89(brs, 1H)

Example 34. 6-(benzofuran-2-yl)-4-hydroxy-5-isopropyl-3-methyl-2H-pyran-2-one

¹H NMR(δppm, DMSO-d₆): 1.33(d, J=6.9Hz, 6H), 1.93(s, 3H), 3.40 to 3.56(m, 1H), 7.29 to 7.46(m, 3H), 7.67(d, J=8.6Hz, 1H), 7.74(d, J=7.6Hz, 1H), 10.85(s, 1H)

Example 35. 6-(benzofuran-2-yl)-4-hydroxy-3-methyl-5-phenyl-2H-pyran-2-one

¹H NMR(δppm, DMSO-d₆): 2.06(s, 3H), 6.32(s, 1H), 7.27 to 7.63(m, 9H), 10.79(brs, 1H)

Example 36. 6-(benzofuran-2-yl)-5-benzyl-4-hydroxy-3-methyl-2H-pyran-2-one

¹H NMR(δppm, DMSO-d₆): 1.93(s, 3H), 4.23(s, 2H), 7.13 to 7.37(m, 8H), 7.62(d, J=8.3Hz, 1H), 7.71(d, J=7.6Hz, 1H), 11.01(brs, 1H)

Example 37. 6-(benzofuran-2-yl)-4-hydroxy-5-methoxy-3-methyl-2H-pyran-2-one

¹H NMR(δppm, DMSO-d₆): 1.92(s, 3H), 3.82(s, 3H), 7.32 to 7.51(m, 3H), 7.72(d, J=7.9Hz, 1H), 7.78(d, J=7.3Hz, 1H),
5 11.40(brs, 1H)

Example 38. 6-(benzofuran-2-yl)-4-hydroxy-3-isopropyl-5-methyl-2H-pyran-2-one

¹H NMR(δppm, DMSO-d₆): 1.22(d, J=6.9Hz, 6H), 2.29(s, 3H),
3.20 to 3.30(m, 1H), 7.30 to 7.45(m, 3H), 7.68(d,
10 J=7.9Hz, 1H), 7.74(d, J=7.6Hz, 1H), 10.68(s, 1H)

Example 39. 6-(benzofuran-2-yl)-3,5-dimethyl-4-isobutyryloxy-2H-pyran-2-one

¹H NMR(δppm, CDCl₃): 1.39(d, J=6.9Hz, 6H), 1.98(s, 3H),
2.29(s, 3H), 2.83 to 3.01(m, 1H), 7.25 to 7.42(m, 2H),
15 7.36(s, 1H), 7.52(d, J=8.3Hz, 1H), 7.65(d, J=7.6Hz, 1H)

Example 40. 4-acetyloxy-3,5-dimethyl-6-(5-nitrobenzofuran-2-yl)-2H-pyran-2-one

¹H NMR(δppm, CDCl₃): 2.02(s, 3H), 2.32(s, 3H), 2.42(s,
3H), 7.46(s, 1H), 7.64(d, J=8.9Hz, 1H), 8.30(dd, J=2.3Hz,
20 8.9Hz, 1H), 8.59(d, J=2.3Hz, 1H)

Example 41. 3,5-dimethyl-4-methoxymethoxy-6-(5-nitrobenzofuran-2-yl)-2H-pyran-2-one

¹H NMR(δppm, CDCl₃): 2.14(s, 3H), 2.43(s, 3H), 3.64(s,
3H), 5.14(s, 2H), 7.43(s, 1H), 7.63(d, J=9.0Hz, 1H),
25 8.30(dd, J=2.1Hz, 9.0Hz, 1H), 8.58(d, J=2.1Hz, 1H)

Example 42. 6-(benzofuran-2-yl)-3,5-dimethyl-4-phenoxyacetyloxy-2H-pyran-2-one

¹H NMR(δppm, CDCl₃): 1.97(s, 3H), 2.28(s, 3H), 4.98(s,
2H), 6.95 to 7.12(m, 3H), 7.23 to 7.44(m, 5H), 7.52(d,
30 J=7.9Hz, 1H), 7.65(d, J=7.6Hz, 1H)

Example 43. 6-(benzofuran-2-yl)-3,5-dimethyl-4-trifluoromethanesulfonyloxy-2H-pyran-2-one

¹H NMR(δppm, CDCl₃): 2.23(s, 3H), 2.50(s, 3H), 7.28 to 7.46(m, 3H), 7.55(d, J=8.2Hz, 1H), 7.68(d, J=7.6Hz, 1H)

Example 44. 6-(benzofuran-2-yl)-3,5-dimethyl-4-paratoluenesulfonyloxy-2H-pyran-2-one

¹H NMR(δppm, CDCl₃): 1.81(s, 3H), 2.33(s, 3H), 2.51(s, 3H), 7.28 to 7.48(m, 5H), 7.53(d, J=8.2Hz, 1H), 7.66(d, J=7.6Hz, 1H), 7.90(d, J=8.3Hz, 2H)

Example 45. 3,5-dimethyl-4-hydroxy-6-(5-nitrobenzofuran-2-yl)-2H-pyran-2-one

¹H NMR(δppm, CD₃OD): 1.96(s, 3H), 2.32(s, 3H), 7.61(s, 1H), 7.95(d, J=9.2Hz, 1H), 8.30(dd, J=2.3Hz, 9.2Hz, 1H), 8.71(d, J=2.3Hz, 1H), 11.00(brs, 1H)

Example 46. 3,5-dimethyl-6-(5-(ethylamino)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one

¹H NMR(δppm, CD₃OD): 1.42(t, J=7.3Hz, 3H), 2.04(s, 3H), 2.43(s, 3H), 3.44(q, J=7.3Hz, 2H), 7.37(s, 1H), 7.50(dd, J=2.0Hz, 8.9Hz, 1H), 7.68(d, J=8.9Hz, 1H), 7.79(d, J=2.0Hz, 1H)

Example 47. 3,5-dimethyl-4-hydroxy-6-(5-(p-toluenesulfonylamino) benzofuran-2-yl)-2H-pyran-2-one

¹H NMR(δppm, CD₃OD): 2.00(s, 3H), 2.36(s, 6H), 7.07 to 7.11(m, 1H), 7.21 to 7.26(m, 2H), 7.34 to 7.41(m, 2H), 7.57 to 7.61(m, 2H), 7.70 to 7.77(m, 1H)

Example 48. 3,5-dimethyl-6-(5-(dimethylamino)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one

¹H NMR(δppm, CD₃OD): 1.95(s, 3H), 2.30(s, 3H), 3.12(s, 6H), 7.41 to 7.75(m, 4H)

Example 49. 6-(5-(dibenzylamino)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

¹H NMR(δppm, CD₃OD): 1.94(s, 3H), 2.31(s, 3H), 4.65(s, 4H), 6.89 to 6.94(m, 2H), 7.07(s, 1H), 7.13 to 7.88(m, 11H)

Example 50. 6-(benzofuran-2-yl)-3,5-dimethyl-4-isonicotinoyloxy-2H-pyran-2-one

¹H NMR(δppm, CDCl₃): 2.04(s, 3H), 2.34(s, 3H), 7.26 to 7.42(m, 3H), 7.53(d, J=7.9Hz, 1H), 7.67(d, J=7.3Hz, 1H),

8.03, 8.95(ABq, J=6.3Hz, 4H)

Example 51. 4-(2-aminoacetyloxy)-6-(benzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one hydrochloride

¹H NMR(δppm, DMSO-d₆): 1.96(s, 3H), 2.27(s, 3H), 4.41(s, 2H), 7.31 to 7.50(m, 2H), 7.55(s, 1H), 7.71(d, J=8.3Hz, 1H), 7.78(d, J=7.9Hz, 1H), 8.61(brs, 3H)

Example 52. 6-(5-benzyloxybenzofuran-2-yl)-4-(2-(t-butoxy carbonylamino)acetyloxy)-3,5-dimethyl-2H-pyran-2-one

¹H NMR(δppm, CDCl₃): 1.48(s, 9H), 2.00(s, 3H), 2.30(s, 3H), 4.23(d, J=5.9Hz, 2H), 5.06 to 5.14(m, 1H), 5.11(s, 2H), 7.06(dd, J=2.6Hz, 8.9Hz, 1H), 7.14(d, J=2.6Hz, 1H), 7.27 to 7.50(m, 7H)

Example 53. 4-(2-aminoacetyloxy)-6-(5-benzyloxybenzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one hydrochloride

¹H NMR(δppm, DMSO-d₆): 1.95(s, 3H), 2.24(s, 3H), 4.41(s, 2H), 5.16(s, 2H), 7.13(d, J=9.2Hz, 1H), 7.29 to 7.51(m, 7H), 7.62(d, J=9.6Hz, 1H), 8.57(brs, 2H)

Example 54. 4-(4-(acetyl amino)benzoyloxy)-6-(5-benzyloxy benzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one

¹H NMR(δppm, CDCl₃): 2.02(s, 3H), 2.26(s, 3H), 2.31(s, 3H), 5.12(s, 2H), 7.06(dd, J=2.6Hz, 8.9Hz, 1H), 7.15(d, J=2.6Hz, 1H), 7.21 to 7.50(m, 8H), 7.72(d, J=8.9Hz, 1H), 8.18(d, J=8.9Hz, 1H)

Example 55. 6-(5-benzyloxybenzofuran-2-yl)-3,5-dimethyl-4-nicotinoyloxy-2H-pyran-2-one

¹H NMR(δppm, CDCl₃): 2.04(s, 3H), 2.33(s, 3H), 5.12(s, 2H), 7.07(dd, J=2.6Hz, 8.9Hz, 1H), 7.16(d, J=2.6Hz, 1H), 7.31 to 7.60(m, 8H), 8.48(d, J=7.9Hz, 1H), 8.94(brs, 1H), 9.43(s, 1H)

Example 56. 6-(5-benzyloxybenzofuran-2-yl)-3,5-dimethyl-4-isonicotinoyloxy-2H-pyran-2-one

¹H NMR(δppm, CDCl₃): 2.03(s, 3H), 2.32(s, 3H), 5.12(s, 2H), 7.07(dd, J=2.3Hz, 8.9Hz, 1H), 7.16(d, J=2.3Hz, 1H),

7.30 to 7.50(m, 7H), 8.03(d, J=5.9Hz, 2H), 8.94(d, J=5.9Hz, 2H)

Example 57. 6-(5-benzyloxybenzofuran-2-yl)-5-ethyl-4-hydroxy-3-methyl-2H-pyran-2-one

5 ^1H NMR(δ ppm, DMSO- d_6): 1.17(t, J=7.3Hz, 3H), 1.93(s, 3H), 2.78(q, J=7.3Hz, 2H), 5.14(s, 2H), 7.07(dd, J=2.6Hz, 8.9Hz, 1H), 7.29 to 7.48(m, 7H), 7.57(d, J=9.2Hz, 1H), 10.87(brs, 1H)

Example 58. 5-ethyl-4-hydroxy-3-methyl-6-(5-(3-pyrimidinyl methoxy)benzofuran-2-yl)-2H-pyran-2-one

10 ^1H NMR(δ ppm, DMSO- d_6): 1.24(t, J=7.3Hz, 3H), 1.99(s, 3H), 2.93(q, J=7.3Hz, 2H), 5.20(s, 2H), 7.07 to 7.10(m, 1H), 7.27 to 7.28(m, 2H), 7.45 to 7.49(m, 2H), 7.97(d, J=7.6Hz, 1H), 8.51(m, 1H), 8.67(s, 1H)

Example 59. 4-acetyloxy-3,5-dimethyl-6-(5-(2-thiazolylmethoxy)benzofuran-2-yl)-2H-pyran-2-one

20 ^1H NMR(δ ppm, CDCl_3): 2.13(s, 3H), 2.34(s, 3H), 2.41(s, 3H), 5.30(s, 2H), 7.09(dd, J=8.6Hz, 2.4Hz, 1H), 7.32(s, 1H), 7.36(d, J=1.9Hz, 1H), 7.47(d, J=1.9Hz, 1H), 7.51(d, J=8.6Hz, 1H), 7.86(d, J=2.4Hz, 1H)

Example 60. 4-hydroxy-3,5-dimethyl-6-(5-(2-thiazolylmethoxy)benzofuran-2-yl)-2H-pyran-2-one

25 ^1H NMR(δ ppm, CD_3OD): 1.98(s, 3H), 2.29(s, 3H), 5.41(s, 2H), 6.87(dd, J=8.9Hz, 2.4Hz, 1H), 7.03(d, J=2.4Hz, 1H), 7.48(d, J=8.9Hz, 1H), 7.87(d, J=3.2Hz, 1H), 7.91(d, J=3.2Hz, 1H), 9.40(s, 1H)

Example 61. 6-(benzofuran-2-yl)-3,5-dimethyl-4-(3-phenylpropionyloxy)-2H-pyran-2-one

30 ^1H NMR(δ ppm, CDCl_3): 1.86(s, 3H), 2.16(s, 3H), 2.94 to 3.18(m, 4H), 7.20 to 7.41(m, 8H), 7.52(d, J=7.9Hz, 1H), 7.64(d, J=7.6Hz, 1H)

Example 62. 6-(benzofuran-2-yl)-3,5-dimethyl-4-(2-furoyloxy)-2H-pyran-2-one

¹H NMR(δppm, CDCl₃): 2.04(s, 3H), 2.35(s, 3H), 6.67(dd, J=1.7Hz, 3.6Hz, 1H), 7.25 to 7.42(m, 2H), 7.38(s, 1H),
5 7.50(d, J=3.6Hz, 1H), 7.53(d, J=8.6Hz, 1H), 7.66(d, J=7.6Hz, 1H), 7.76(d, J=1.7Hz, 1H)

Example 63. 6-(benzofuran-2-yl)-3,5-dimethyl-4-nicotinoyloxy-2H-pyran-2-one

¹H NMR(δppm, CDCl₃): 2.05(s, 3H), 2.36(s, 3H), 7.26 to
10 7.43(m, 3H), 7.50 to 7.60(m, 2H), 7.67(d, J=7.6Hz, 1H), 8.49(d, J=7.9Hz, 1H), 8.95(d, J=4.3Hz, 1H), 9.44(s, 1H)

Example 64. 6-(benzofuran-2-yl)-3,5-dimethyl-4-(2-acetylamino-4-(morpholin-4-yl)-4-oxobutyryloxy)-2H-pyran-2-one

¹H NMR(δppm, CDCl₃): 2.01(s, 3H), 2.05(s, 3H), 2.33(s, 3H), 3.00(dd, J=4.4Hz, 16.8Hz, 1H), 3.16(dd, J=7.6Hz, 16.8Hz, 1H), 3.60 to 3.73(m, 8H), 5.37 to 5.44(m, 1H),
15 6.44(d, J=9.3Hz, 1H), 7.27 to 7.40(m, 3H), 7.52(d, J=8.3Hz, 1H), 7.65(d, J=7.3Hz, 1H)

Example 65. 4-acetyloxy-6-(5-bromobenzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one

¹H NMR(δppm, CDCl₃): 2.00(s, 3H), 2.30(s, 3H), 2.40(s, 3H), 7.29(s, 1H), 7.40(d, J=8.9Hz, 1H), 7.47(dd, J=8.9Hz, 2.2Hz, 1H), 7.78(d, J=2.2Hz, 1H)

Example 66. 6-(benzofuran-2-yl)-5-cyclopentylmethyl-4-hydroxy-3-methyl-2H-pyran-2-one

¹H NMR(δppm, DMSO-d₆): 1.16 to 1.27(m, 2H), 1.40 to 1.69(m, 6H), 1.94(s, 3H), 2.02 to 2.17(m, 1H), 2.90(d, J=7.3Hz, 2H), 7.29 to 7.44(m, 3H), 7.65(d, J=8.2Hz, 1H),
25 7.74(d, J=7.3Hz, 1H), 10.85(s, 1H)

Example 67. 6-(benzofuran-2-yl)-4-hydroxy-3-methyl-5-phenoxy-2H-pyran-2-one

¹H NMR(δppm, DMSO-d₆): 2.03(s, 3H), 7.11 to 7.22(m, 3H), 7.32 to 7.49(m, 5H), 7.69(d, J=8.3Hz, 1H), 7.76(d, J=7.6Hz, 1H), 11.56(brs, 1H)
35

Example 68. 6-(benzofuran-2-yl)-5-(2-butenyl)-4-hydroxy-3-methyl-2H-pyran-2-one

¹H NMR(δppm, DMSO-d₆): 1.70 to 1.78(m, 3H), 2.03(s, 3H),
3.57 to 3.64(m, 2H), 5.61 to 5.67(m, 2H), 7.39 to 7.54(m,
5 3H), 7.78(d, J=8.3Hz, 1H), 7.84(d, J=7.6Hz, 1H),
11.00(brs, 1H)

Example 69. 6-(benzofuran-2-yl)-4-(1-carbobenzyloxy-2-pyrrolidon-5-ylcarboxy)-3,5-dimethyl-2H-pyran-2-one

10 ¹H NMR(δppm, CDCl₃): 1.94(s, 3H), 2.25(s, 3H), 2.30 to
2.40(m, 1H), 2.51 to 2.88(m, 3H), 5.03(dd, J=2.6Hz,
8.9Hz, 1H), 5.33, 5.38(ABq, J=2.2Hz, 2H), 7.28 to 7.48(m,
8H), 7.52(d, J=8.6Hz, 1H), 7.66(d, J=7.9Hz, 1H)

Example 70. 6-(benzofuran-2-yl)-3,5-dimethyl-4-(2-pyrrolidon-5-ylcarboxy)-2H-pyran-2-one

15 ¹H NMR(δppm, DMSO-d₆): 1.91(s, 3H), 2.23(s, 3H), 2.19 to
2.38(m, 3H), 2.47 to 2.66(m, 1H), 4.65 to 4.73(m, 1H),
7.31 to 7.40(m, 1H), 7.41 to 7.50(m, 1H), 7.53(s, 1H),
7.71(d, J=8.3Hz, 1H), 7.77(d, J=7.6Hz, 1H), 8.34(s, 1H)

20 Example 71. 6-(benzofuran-2-yl)-4-(2-(t-butoxycarbonylamino) acetyloxy)-3,5-dimethyl-2H-pyran-2-one

¹H NMR(δppm, CDCl₃): 1.48(s, 9H), 2.00(s, 3H), 2.32(s,
3H), 4.23(d, J=6.3Hz, 2H), 5.10(brs, 1H), 7.25 to 7.42(m,
25 3H), 7.53(d, J=7.9Hz, 1H), 7.65(d, J=7.9Hz, 1H)

Example 72. 6-(benzofuran-2-yl)-4-(2,4-dimethoxybenzoyloxy)-3,5-dimethyl-2H-pyran-2-one

30 ¹H NMR(δppm, CDCl₃): 2.05(s, 3H), 2.35(s, 3H), 3.92(s,
3H), 3.95(s, 3H), 6.54 to 6.66(m, 2H), 7.25 to 7.41(m,
3H), 7.52(d, J=8.2Hz, 1H), 7.65(d, J=7.6Hz, 1H), 8.08(d,
J=8.6Hz, 1H)

Example 73. 6-(benzofuran-2-yl)-4-(2,6-dimethoxybenzoyloxy)-3,5-dimethyl-2H-pyran-2-one

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¹H NMR(δppm, CDCl₃): 2.17(s, 3H), 2.48(s, 3H), 3.91(s, 6H), 6.65(d, J=8.3Hz, 2H), 7.25 to 7.45(m, 4H), 7.54(d, J=8.2Hz, 1H), 7.66(d, J=7.9Hz, 1H)

5 Example 74. 6-(benzofuran-2-yl)-3,5-dimethyl-4-(6-hydroxynicotinoyloxy)-2H-pyran-2-one

¹H NMR(δppm, DMSO-d₆): 1.91(s, 3H), 2.24(s, 3H), 6.48(d, J=9.9Hz, 1H), 7.31 to 7.50(m, 2H), 7.54(s, 1H), 7.71(d, J=8.3Hz, 1H), 7.78(d, J=7.9Hz, 1H), 7.95(d, J=9.9Hz, 1H), 8.43(s, 1H), 12.51(brs, 1H)

10 Example 75. 6-(benzofuran-2-yl)-3,5-dimethyl-4-(3-dimethylaminobenzoyloxy)-2H-pyran-2-one

¹H NMR(δppm, CDCl₃): 2.04(s, 3H), 2.35(s, 3H), 3.05(s, 6H), 7.04(dd, J=2.6Hz, 8.6Hz, 1H), 7.25 to 7.44(m, 4H), 7.48 to 7.59(m, 3H), 7.66(d, J=7.6Hz, 1H)

15 Example 76. 4-(4-(acetylamino)benzoyloxy)-6-(benzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one

¹H NMR(δppm, CDCl₃): 2.03(s, 3H), 2.26(s, 3H), 2.33(s, 3H), 7.24 to 7.41(m, 3H), 7.49(s, 1H), 7.52(d, J=8.2Hz, 1H), 7.66(d, J=7.6Hz, 1H), 7.73(d, J=8.6Hz, 2H), 8.18(d, J=8.6Hz, 2H)

20 Example 77. 3,5-dimethyl-6-(6-(2-fluorobenzoyloxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one

Mass analysis: [M⁺ + H] = 381.0

25 Example 78. 3,5-dimethyl-6-(5-(2-fluorobenzoyloxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one

Mass analysis: [M⁺ + H] = 381.0

30 Example 79. 6-(5-(4-chlorobenzoyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: [M⁺ + H] = 397.0

Example 80. 6-(6-(2-bromobenzoyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: [M⁺ + H] = 442.0

Example 81. 6-(5-(2-bromobenzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 442.0$

5 Example 82. 6-(6-(3-bromobenzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 442.0$

Example 83. 6-(5-(3-bromobenzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 442.0$

10 Example 84. 3,5-dimethyl-4-hydroxy-6-(6-(3,4-(methylenedioxy) benzyloxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 407.0$

15 Example 85. 3,5-dimethyl-4-hydroxy-6-(5-(3,4-(methylenedioxy) benzyloxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 407.0$

20 Example 86. 3,5-dimethyl-4-hydroxy-6-(6-(2-pyridylmethoxy) benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 364.0$

Example 87. 3,5-dimethyl-4-hydroxy-6-(5-(2-pyridylmethoxy) benzofuran-2-yl)-2H-pyran-2-one

25 Mass analysis: $[M^+ + H] = 364.0$

Example 88. 3,5-dimethyl-4-hydroxy-6-(6-(3-pyridylmethoxy) benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 364.0$

30 Example 89. 3,5-dimethyl-4-hydroxy-6-(5-(3-pyridylmethoxy) benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 364.0$

35 Example 90. 3,5-dimethyl-4-hydroxy-6-(6-(4-pyridylmethoxy) benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 364.0$

Example 91. 3,5-dimethyl-4-hydroxy-6-(5-(4-pyridylmethoxy) benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 364.0$

5 Example 92. 3,5-dimethyl-4-hydroxy-6-(6-(tetrahydrofuran-3-ylmethoxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 357.0$

Example 93. 3,5-dimethyl-4-hydroxy-6-(5-(tetrahydrofuran-3-ylmethoxy)benzofuran-2-yl)-2H-pyran-2-one

10 Mass analysis: $[M^+ + H] = 357.0$

Example 94. 3,5-dimethyl-4-hydroxy-6-(6-(1-methylpiperidin-2-ylmethoxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 384.0$

15 Example 95. 3,5-dimethyl-4-hydroxy-6-(5-(1-methylpiperidin-2-ylmethoxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 384.0$

Example 96. 3,5-dimethyl-4-hydroxy-6-(6-(1-methylpiperidin-3-ylmethoxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 384.0$

Example 97. 3,5-dimethyl-4-hydroxy-6-(5-(1-methylpiperidin-3-ylmethoxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 384.0$

Example 98. 3,5-dimethyl-4-hydroxy-6-(6-(1-methyl-3-piperidyl oxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 370.0$

30 Example 99. 3,5-dimethyl-4-hydroxy-6-(5-(1-methyl-3-piperidyl oxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 370.0$

Example 100. 3,5-dimethyl-4-hydroxy-6-(6-(1-methyl-3-pyrrolidyl oxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 356.0$

Example 101. 3,5-dimethyl-4-hydroxy-6-(5-(1-methyl-3-pyrrolidyl oxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 356.0$

5 Example 102. 3,5-dimethyl-4-hydroxy-6-(6-(2-pyrrolidinylethoxy) benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 370.0$

10 Example 103. 3,5-dimethyl-4-hydroxy-6-(5-(2-pyrrolidinylethoxy) benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 370.0$

15 Example 104. 6-(6-(4-(diethylamino)-1-methylbutoxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 414.0$

Example 105. 6-(5-(4-(diethylamino)-1-methylbutoxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

20 Mass analysis: $[M^+ + H] = 414.0$

Example 106. 6-(6-(1,3-bis(dimethylamino)-2-propoxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 401.0$

25 Example 107. 6-(5-(1,3-bis(dimethylamino)-2-propoxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 401.0$

30 Example 108. 3,5-dimethyl-4-hydroxy-6-(6-(2-pyrrolidon-5-ylmethoxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 370.0$

Example 109. 3,5-dimethyl-4-hydroxy-6-(5-(2-pyrrolidon-5-ylmethoxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 370.0$

35 Example 110. 6-(6-(chroman-4-yloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 405.0$

Example 111. 6-(5-(chroman-4-yloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 405.0$

Example 112. 6-(6-(1-(n-butoxycarbonyl)ethoxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 401.0$

Example 113. 6-(5-(1-(n-butoxycarbonyl)ethoxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 401.0$

Example 114. 3,5-dimethyl-4-hydroxy-6-(6-(2-(morpholin-4-yl)ethoxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 386.0$

Example 115. 3,5-dimethyl-4-hydroxy-6-(5-(2-(morpholin-4-yl)ethoxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 386.0$

Example 116. 6-(6-(4-carboxybenzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 407.0$

Example 117. 6-(5-(4-carboxybenzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 407.0$

Example 118. 6-(6-(4-chlorobenzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 397.0$

Example 119. 3,5-dimethyl-4-hydroxy-6-(6-(2-(trifluoromethyl) benzyloxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 431.0$

Example 120. 3,5-dimethyl-4-hydroxy-6-(5-(2-(trifluoromethyl) benzyloxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 431.0$

Example 121. 3,5-dimethyl-4-hydroxy-6-(6-(3-(trifluoromethyl) benzyloxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 431.0$

Example 122. 3,5-dimethyl-4-hydroxy-6-(5-(3-(trifluoromethyl) benzyloxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 431.0$

5 Example 123. 3,5-dimethyl-4-hydroxy-6-(6-(4-(trifluoromethyl) benzyloxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 431.0$

10 Example 124. 3,5-dimethyl-4-hydroxy-6-(5-(4-(trifluoromethyl) benzyloxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 431.0$

Example 125. 6-(6-(cyclopentylmethoxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

15 Mass analysis: $[M^+ + H] = 355.0$

Example 126. 6-(5-(cyclopentylmethoxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 355.0$

20 Example 127. 6-(6-(cyclopropylmethoxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 327.0$

Example 128. 6-(5-(cyclopropylmethoxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 327.0$

25 Example 129. 6-(6-(2,4-dimethylbenzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 391.0$

Example 130. 6-(5-(2,4-dimethylbenzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

30 Mass analysis: $[M^+ + H] = 391.0$

Example 131. 6-(6-(2,5-dimethylbenzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 391.0$

35 Example 132. 6-(5-(2,5-dimethylbenzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 391.0$

Example 133. 6-(6-(3,4-dimethylbenzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 391.0$

Example 134. 6-(5-(3,4-dimethylbenzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 391.0$

Example 135. 6-(6-(3,5-dimethylbenzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 391.0$

Example 136. 6-(5-(3,5-dimethylbenzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 391.0$

Example 137. 3,5-dimethyl-4-hydroxy-6-(6-((2-thienyl)methoxy) benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 369.0$

Example 138. 3,5-dimethyl-4-hydroxy-6-(5-((2-thienyl)methoxy) benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 369.0$

Example 139. 3,5-dimethyl-6-(6-((2-furyl)methoxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 353.0$

Example 140. 3,5-dimethyl-6-(5-((2-furyl)methoxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 353.0$

Example 141. 3,5-dimethyl-4-hydroxy-6-(6-(2-phenoxyethoxy) benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 392.0$

Example 142. 3,5-dimethyl-4-hydroxy-6-(5-(2-phenoxyethoxy) benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 392.0$

Example 143. 3,5-dimethyl-4-hydroxy-6-(6-(1-(2-(trifluoromethyl) phenyl)ethoxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 445.0$

5 Example 144. 3,5-dimethyl-4-hydroxy-6-(5-(1-(2-(trifluoromethyl) phenyl)ethoxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 445.0$

10 Example 145. 6-(6-(2-chloro-5-nitrobenzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 442.0$

Example 146. 6-(6-(3-chloro-6-nitrobenzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 442.0$

15 Example 147. 6-(5-(3-chloro-6-nitrobenzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 442.0$

Example 148. 6-(6-(2-cyclohexylethoxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

20 Mass analysis: $[M^+ + H] = 383.0$

Example 149. 6-(5-(2-cyclohexylethoxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 383.0$

25 Example 150. 3,5-dimethyl-4-hydroxy-6-(6-(1,4-pentadien-3-yloxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 339.0$

Example 151. 3,5-dimethyl-4-hydroxy-6-(5-(1,4-pentadien-3-yloxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 339.0$

30 Example 152. 6-(6-(2,4-dichlorobenzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 432.0$

Example 153. 6-(5-(2,4-dichlorobenzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

35 Mass analysis: $[M^+ + H] = 432.0$

Example 154. 6-(6-(2,5-dichlorobenzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 432.0$

Example 155. 6-(5-(2,5-dichlorobenzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 432.0$

Example 156. 6-(6-(2,6-dichlorobenzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 432.0$

Example 157. 6-(5-(2,6-dichlorobenzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 432.0$

Example 158. 6-(6-(3,4-dichlorobenzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 432.0$

Example 159. 6-(5-(3,4-dichlorobenzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 432.0$

Example 160. 6-(6-(3,5-dichlorobenzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 432.0$

Example 161. 6-(5-(3,5-dichlorobenzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 432.0$

Example 162. 6-(6-(4-n-butoxybenzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 435.0$

Example 163. 6-(5-(4-n-butoxybenzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 435.0$

Example 164. 3,5-dimethyl-4-hydroxy-6-(6-(3-methyl-2-nitrobenzyloxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 422.0$

Example 165. 3,5-dimethyl-4-hydroxy-6-(5-(3-methyl-2-nitrobenzyloxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 422.0$

5 Example 166. 3,5-dimethyl-6-(6-(2,3-dimethyl-4-methoxybenzyloxy) benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 421.0$

10 Example 167. 3,5-dimethyl-6-(5-(2,3-dimethyl-4-methoxybenzyloxy) benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 421.0$

15 Example 168. 3,5-dimethyl-6-(6-(3,5-dinitrobenzyloxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 453.0$

Example 169. 3,5-dimethyl-6-(5-(3,5-dinitrobenzyloxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one

20 Mass analysis: $[M^+ + H] = 453.0$

Example 170. 3,5-dimethyl-4-hydroxy-6-(6-(1,2,3,4-tetrahydro naphthalen-1-yloxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 403.0$

25 Example 171. 3,5-dimethyl-4-hydroxy-6-(5-(1,2,3,4-tetrahydro naphthalen-1-yloxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 403.0$

30 Example 172. 3,5-dimethyl-4-hydroxy-6-(6-(1-naphthylmethoxy) benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 413.0$

35 Example 173. 3,5-dimethyl-4-hydroxy-6-(5-(1-naphthylmethoxy) benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 413.0$

Example 174. 3,5-dimethyl-4-hydroxy-6-(6-(2-naphthylmethoxy) benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 413.0$

5 Example 175. 3,5-dimethyl-4-hydroxy-6-(5-(2-naphthylmethoxy) benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 413.0$

10 Example 176. 6-(6-(1,4-benzodioxan-2-ylmethoxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 421.0$

15 Example 177. 6-(5-(1,4-benzodioxan-2-ylmethoxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 421.0$

Example 178. 3,5-dimethyl-6-(6-(3-hexen-1-yloxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one

20 Mass analysis: $[M^+ + H] = 355.0$

Example 179. 3,5-dimethyl-6-(5-(3-hexen-1-yloxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 355.0$

25 Example 180. 6-(6-(2-butyn-1-yloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 325.0$

Example 181. 6-(5-(2-butyn-1-yloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

30 Mass analysis: $[M^+ + H] = 325.0$

Example 182. 3,5-dimethyl-6-(6-(2,2-dimethyl-1,3-dioxolan-4-ylmethoxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 387.0$

Example 183. 3,5-dimethyl-6-(5-(2,2-dimethyl-1,3-dioxolan-4-ylmethoxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 387.0$

5 Example 184. 3,5-dimethyl-6-(6-(2-ethoxyethoxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 345.0$

10 Example 185. 3,5-dimethyl-6-(5-(2-ethoxyethoxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 345.0$

Example 186. 3,5-dimethyl-4-hydroxy-6-(6-(3-methyloxetan-3-ylmethoxy)benzofuran-2-yl)-2H-pyran-2-one

15 Mass analysis: $[M^+ + H] = 357.0$

Example 187. 3,5-dimethyl-4-hydroxy-6-(5-(3-methyloxetan-3-ylmethoxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 357.0$

20 Example 188. 3,5-dimethyl-6-(6-(5-hexyn-1-yloxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 353.0$

25 Example 189. 3,5-dimethyl-6-(5-(5-hexyn-1-yloxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 353.0$

Example 190. 3,5-dimethyl-6-(6-(5-hexen-1-yloxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one

30 Mass analysis: $[M^+ + H] = 355.0$

Example 191. 3,5-dimethyl-6-(5-(5-hexen-1-yloxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 355.0$

Example 192. 3,5-dimethyl-6-(6-(2,2-
dimethylpropoxy)benzofuran-2-yl)-4-hydroxy-
2H-pyran-2-one

Mass analysis: $[M^+ + H] = 343.0$

5 Example 193. 3,5-dimethyl-6-(5-(2,2-
dimethylpropoxy)benzofuran-2-yl)-4-hydroxy-
2H-pyran-2-one

Mass analysis: $[M^+ + H] = 343.0$

10 Example 194. 3,5-dimethyl-6-(6-(2,2-
diphenylethoxy)benzofuran-2-yl)-4-hydroxy-
2H-pyran-2-one

Mass analysis: $[M^+ + H] = 453.0$

15 Example 195. 3,5-dimethyl-6-(5-(2,2-
diphenylethoxy)benzofuran-2-yl)-4-hydroxy-
2H-pyran-2-one

Mass analysis: $[M^+ + H] = 453.0$

Example 196. 3,5-dimethyl-4-hydroxy-6-(6-(2-phenyl-2-
propoxy) benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 391.0$

20 Example 197. 3,5-dimethyl-4-hydroxy-6-(5-(2-phenyl-2-
propoxy) benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 391.0$

25 Example 198. 3,5-dimethyl-4-hydroxy-6-(6-(2-(1-
naphthyl)ethoxy) benzofuran-2-yl)-2H-pyran-
2-one

Mass analysis: $[M^+ + H] = 427.0$

Example 199. 3,5-dimethyl-4-hydroxy-6-(5-(2-(1-
naphthyl)ethoxy) benzofuran-2-yl)-2H-pyran-
2-one

30 Mass analysis: $[M^+ + H] = 427.0$

Example 200. 6-(6-(bis(4-
methoxyphenyl)methoxy)benzofuran-2-yl)-3,5-
dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 499.0$

Example 201. 6-(5-(bis(4-methoxyphenyl)methoxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 499.0$

5 Example 202. 3,5-dimethyl-4-hydroxy-6-(6-(3-phenylpropoxy) benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 391.0$

10 Example 203. 3,5-dimethyl-4-hydroxy-6-(5-(3-phenylpropoxy) benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 391.0$

Example 204. 3,5-dimethyl-4-hydroxy-6-(6-(4-phenylbutoxy) benzofuran-2-yl)-2H-pyran-2-one

15 Mass analysis: $[M^+ + H] = 405.0$

Example 205. 3,5-dimethyl-4-hydroxy-6-(5-(4-phenylbutoxy) benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 405.0$

20 Example 206. 6-(6-(cyclohexylmethoxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 369.0$

Example 207. 6-(5-(cyclohexylmethoxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 369.0$

25 Example 208. 6-(6-(3-cyclohexylpropoxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 397.0$

Example 209. 6-(5-(3-cyclohexylpropoxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

30 Mass analysis: $[M^+ + H] = 397.0$

Example 210. 6-(6-(3-buten-1-yloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 327.0$

35 Example 211. 6-(5-(3-buten-1-yloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 327.0$

Example 212. 6-(6-(2-(benzyloxy)ethoxy)benzofuran-2-yl)-
3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 407.0$

Example 213. 6-(5-(2-(benzyloxy)ethoxy)benzofuran-2-yl)-
3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 407.0$

Example 214. 3,5-dimethyl-4-hydroxy-6-(6-(2-propyn-1-
yloxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 311.0$

Example 215. 3,5-dimethyl-4-hydroxy-6-(5-(2-propyn-1-
yloxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 311.0$

Example 216. 3,5-dimethyl-6-(6-(5-
(ethoxycarbonyl)pentyl)oxy) benzofuran-2-yl)-
4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 415.0$

Example 217. 3,5-dimethyl-6-(5-(5-
(ethoxycarbonyl)pentyl)oxy) benzofuran-2-yl)-
4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 415.0$

Example 218. 3,5-dimethyl-6-(6-ethoxybenzofuran-2-yl)-4-
hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 301.0$

Example 219. 3,5-dimethyl-4-hydroxy-6-(6-
isopropoxybenzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 329.0$

Example 220. 6-(5-(1-t-butoxycarbonylpiperidin-2-
ylmethoxy) benzofuran-2-yl)-3,5-dimethyl-4-
hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 470.0$

Example 221. 6-(5-(1-t-butoxycarbonylpiperidin-4-
ylmethoxy) benzofuran-2-yl)-3,5-dimethyl-4-
hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 470.0$

Example 222. 6-(5-(1-t-butoxycarbonylpiperidin-4-yloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 456.0$

5 Example 223. 6-(5-(1-t-butoxycarbonylpyrrolidin-3-yloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 442.0$

10 Example 224. 6-(5-(4-(t-butoxycarbonylamino)butoxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 444.0$

15 Example 225. 3,5-dimethyl-6-(6-(3-fluorobenzyloxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 381.0$

Example 226. 3,5-dimethyl-6-(5-(3-fluorobenzyloxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one

20 Mass analysis: $[M^+ + H] = 381.0$

Example 227. 3,5-dimethyl-6-(6-(4-fluorobenzyloxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 381.0$

25 Example 228. 3,5-dimethyl-6-(5-(4-fluorobenzyloxy)benzofuran-2-yl)-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 381.0$

30 Example 229. 3,5-dimethyl-4-hydroxy-6-(6-(2-nitrobenzyloxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 408.0$

35 Example 230. 3,5-dimethyl-4-hydroxy-6-(5-(2-nitrobenzyloxy)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 408.0$

Example 231. 3,5-dimethyl-4-hydroxy-6-(6-(3-nitrobenzyloxy) benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 408.0$

5 Example 232. 3,5-dimethyl-4-hydroxy-6-(5-(3-nitrobenzyloxy) benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 408.0$

10 Example 233. 3,5-dimethyl-4-hydroxy-6-(6-(4-nitrobenzyloxy) benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 408.0$

15 Example 234. 3,5-dimethyl-4-hydroxy-6-(5-(4-nitrobenzyloxy) benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 408.0$

20 Example 235. 3,5-dimethyl-4-hydroxy-6-(6-(3-methoxybenzyloxy) benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 393.0$

25 Example 236. 3,5-dimethyl-4-hydroxy-6-(5-(3-methoxybenzyloxy) benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 393.0$

30 Example 237. 3,5-dimethyl-4-hydroxy-6-(6-(4-methoxybenzyloxy) benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 393.0$

35 Example 238. 3,5-dimethyl-4-hydroxy-6-(5-(4-methoxybenzyloxy) benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 393.0$

Example 239. 6-(6-(2-chlorobenzyloxy)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 397.0$

Example 240. 6-(5-(2-chlorobenzoyloxy)benzofuran-2-yl)-
3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 397.0$

Example 241. 6-(6-(3-chlorobenzoyloxy)benzofuran-2-yl)-
3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 397.0$

Example 242. 6-(5-(3-chlorobenzoyloxy)benzofuran-2-yl)-
3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 397.0$

10 Example 243. 3,5-dimethyl-4-hydroxy-6-(5-(5-
thiazolylmethoxy) benzofuran-2-yl)-2H-pyran-
2-one

$^1\text{H NMR}(\delta\text{ppm, DMSO-d}_6\text{): 1.93(s, 3H), 2.28(s, 3H), 5.44(s,$
2H), 7.08(dd, $J=8.9\text{Hz}, 2.7\text{Hz}, 1\text{H}), 7.31(s, 1\text{H}), 7.37(d,$
15 $J=2.7\text{Hz}, 1\text{H}), 7.59(d, J=8.9\text{Hz}, 1\text{H}), 8.02(s, 1\text{H}), 9.11(s,$
1H)

Example 244. 4-acetyloxy-6-(5-(2,4-dichloro-5-
thiazolylmethoxy) benzofuran-2-yl)-3,5-
dimethyl-2H-pyran-2-one

20 $^1\text{H NMR}(\delta\text{ppm, CDCl}_3\text{): 2.00(s, 3H), 2.30(s, 3H), 2.39(s,$
3H), 5.21(s, 2H), 7.01(dd, $J=8.9\text{Hz}, 2.4\text{Hz}, 1\text{H}), 7.04(d,$
 $J=8.9\text{Hz}, 1\text{H}), 7.27(d, J=2.4\text{Hz}, 1\text{H}), 7.44(d, J=8.9\text{Hz}, 1\text{H})$

Example 245. 3,5-dimethyl-4-hydroxy-6-(5-(2-
(morpholinesulfonyl) -5-
25 thiazolylmethoxy)benzofuran-2-yl)-2H-pyran-
2-one

$^1\text{H NMR}(\delta\text{ppm, DMSO-d}_6\text{): 1.94(s, 3H), 2.29(s, 3H), 3.15-$
3.18(m, 4H), 3.64 to 3.67(m, 4H), 5.53(s, 2H), 7.12(dd,
 $J=8.8\text{Hz}, 2.7\text{Hz}, 1\text{H}), 7.34(s, 1\text{H}), 7.39(d, J=2.7\text{Hz}, 1\text{H}),$
30 7.63(d, $J=8.8\text{Hz}, 1\text{H}), 8.26(s, 1\text{H})$

Example 246. 3,5-dimethyl-4-hydroxy-6-(5-(3-
thienylmethoxy) benzofuran-2-yl)-2H-pyran-2-
one

$^1\text{H NMR}(\delta\text{ppm, CD}_3\text{OD}): 1.93(s, 3H), 2.33(s, 3H), 5.13(s,$
35 2H), 7.02(dd, $J=8.9\text{Hz}, 2.7\text{Hz}, 1\text{H}), 7.18(d, J=2.7\text{Hz}, 1\text{H}),$
7.20(s, 1H), 7.24(d, $J=2.7\text{Hz}, 1\text{H}), 7.39 \text{ to } 7.45(\text{m}, 3\text{H})$

Example 247. 3,5-dimethyl-4-hydroxy-6-(5-(2-(morpholinesulfonyl)-5-thienylmethoxy)benzofuran-2-yl)-2H-pyran-2-one

5 ^1H NMR(δ ppm, CDCl_3): 1.91(s, 3H), 2.31(s, 3H), 2.98 to 3.03(m, 4H), 3.71 to 3.75(m, 4H), 5.38(s, 2H), 7.03(dd, $J=8.9\text{Hz}$, 2.7Hz , 1H), 7.19(s, 1H), 7.27 to 7.29(m, 2H), 7.51(d, $J=2.7\text{Hz}$, 1H)

10 Example 248. 4-acetyloxy-3,5-dimethyl-6-(5-(2-(morpholine sulfonyl)-5-thienylmethoxy)benzofuran-2-yl)-2H-pyran-2-one

^1H NMR(δ ppm, CDCl_3): 2.00(s, 3H), 2.30(s, 3H), 2.40(s, 3H), 3.06 to 3.10(m, 4H), 3.74 to 3.81(m, 4H), 5.29(s, 2H), 7.04(dd, $J=9.2\text{Hz}$, 2.7Hz , 1H), 7.15(d, $J=2.7\text{Hz}$, 1H),
15 7.31(s, 1H), 7.43 to 7.47(m, 2H)

Example 249. 3,5-dimethyl-4-hydroxy-6-(5-(4-oxazolylmethoxy) benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[\text{M}^+ + \text{H}] = 354.0$

20 Example 250. 6-(5-(N-benzoyl-N-methylamino)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[\text{M}^+ + \text{H}] = 390.0$

Example 251. 3,5-dimethyl-4-hydroxy-6-(5-(N-methyl-N-(phenylacetyl)amino)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[\text{M}^+ + \text{H}] = 404.5$

Example 252. 3,5-dimethyl-4-hydroxy-6-(5-(N-methyl-N-(2-thienylcarbonyl)amino)benzofuran-2-yl)-2H-pyran-2-one

30 Mass analysis: $[\text{M}^+ + \text{H}] = 396.0$

Example 253. 3,5-dimethyl-4-hydroxy-6-(5-(N-methyl-N-(3-pyridylcarbonyl)amino)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[\text{M}^+ + \text{H}] = 391.0$

Example 254. 3,5-dimethyl-4-hydroxy-6-(5-(N-isobutyryl-N-methylamino)benzofuran-2-yl)-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 356.0$

Example 255. 6-(5-(N-(t-butoxycarbonyl)-N-methylamino)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Mass analysis: $[M^+ + H] = 386.0$

The following compounds were also produced by processes similar to those described in the preceding examples and production examples, using organic chemical techniques well-known to those skilled in the art.

Example 256. 6-(5-benzoylaminobenzofuran-2-yl)-4-benzoyloxy-3,5-dimethyl-2H-pyran-2-one

Example 257. 4-acetyloxy-3,5-dimethyl-6-(5-trifluoromethane sulfonyloxybenzofuran-2-yl)-2H-pyran-2-one

Example 258. 6-(4-benzyloxybenzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Example 259. 4-acetyloxy-3,5-dimethyl-6-(5-(methoxycarbonyl) benzofuran-2-yl)-2H-pyran-2-one

Example 260. 4-acetyloxy-6-(4-benzyloxybenzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one

Example 261. 4-acetyloxy-3,5-dimethyl-6-(5-hydroxybenzofuran-2-yl)-2H-pyran-2-one

Example 262. 3,5-dimethyl-4-hydroxy-6-(5-hydroxybenzofuran-2-yl)-2H-pyran-2-one

Example 263. 4-acetyloxy-3,5-dimethyl-6-(5-(4-methoxybenzoyloxy) benzofuran-2-yl)-2H-pyran-2-one

Example 264. 4-acetyloxy-6-(5-carboxybenzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one

Example 265. 4-acetyloxy-6-(4-acetyloxybenzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one

Example 266. 4-acetyloxy-3,5-dimethyl-6-(4-methoxybenzofuran-2-yl)-2H-pyran-2-one

- Example 267. 3,5-dimethyl-4-hydroxy-6-(4-methoxybenzofuran-2-yl)-2H-pyran-2-one
- Example 268. 4-acetyloxy-3,5-dimethyl-6-(5-methoxybenzofuran-2-yl)-2H-pyran-2-one
- 5 Example 269. 4-acetyloxy-6-(5-acetyloxybenzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one
- Example 270. 4-acetyloxy-6-(5-benzyloxybenzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one
- Example 271. 6-(5-benzyloxybenzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one
- 10 Example 272. 3,5-dimethyl-4-hydroxy-6-(6-hydroxybenzofuran-2-yl)-2H-pyran-2-one
- Example 273. 4-acetyloxy-3,5-dimethyl-6-(6-methoxybenzofuran-2-yl)-2H-pyran-2-one
- 15 Example 274. 4-acetyloxy-3,5-dimethyl-6-(5-p-toluenesulfonyloxy benzofuran-2-yl)-2H-pyran-2-one
- Example 275. 4-acetyloxy-6-(6-acetyloxybenzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one
- 20 Example 276. 6-(6-cyclohexyloxybenzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one
- Example 277. 3,5-dimethyl-4-hydroxy-6-(6-trifluoromethanesulfonyloxybenzofuran-2-yl)-2H-pyran-2-one
- Example 278. 4-acetyloxy-3,5-dimethyl-6-(6-(2-(methoxycarbonyl) ethoxy)benzofuran-2-yl)-2H-pyran-2-one
- 25 Example 279. 3,5-dimethyl-4-hydroxy-6-(6-(2-(methoxycarbonyl) ethoxy)benzofuran-2-yl)-2H-pyran-2-one
- 30 Example 280. 4-acetyloxy-6-(6-(2-(acetyloxy)ethoxy)benzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one
- Example 281. 3,5-dimethyl-4-hydroxy-6-(7-hydroxybenzofuran-2-yl)-2H-pyran-2-one
- 35 Example 282. 4-acetyloxy-3,5-dimethyl-6-(7-methoxybenzofuran-2-yl)-2H-pyran-2-one

- Example 283. 3,5-dimethyl-4-hydroxy-6-(4-hydroxybenzofuran-2-yl)-2H-pyran-2-one
- Example 284. 4-acetyloxy-6-(7-acetyloxybenzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one
- 5 Example 285. 4-acetyloxy-6-(7-benzyloxybenzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one
- Example 286. 6-(7-benzyloxybenzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one
- Example 287. 4-acetyloxy-6-(benzofuran-2-yl)-3-isopropyl-5-methyl-2H-pyran-2-one
- 10 Example 288. 6-(4,6-dimethoxybenzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one
- Example 289. 4-acetyloxy-6-(4,6-dimethoxybenzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one
- 15 Example 290. 3,5-dimethyl-4-hydroxy-6-(5-(methoxycarbonyl) benzofuran-2-yl)-2H-pyran-2-one
- Example 291. 3,5-dimethyl-4-hydroxy-6-(6-methoxymethoxy benzofuran-2-yl)-2H-pyran-2-one
- 20 Example 292. 4-acetyloxy-3,5-dimethyl-6-(6-methoxymethoxy benzofuran-2-yl)-2H-pyran-2-one
- Example 293. 6-(5-carboxybenzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one
- Example 294. 4-acetyloxy-3,5-dimethyl-6-(5-(phenoxycarbonyl) benzofuran-2-yl)-2H-pyran-2-one
- 25 Example 295. 4-acetyloxy-3,5-dimethyl-6-(5-(phenylcarbamoyl) benzofuran-2-yl)-2H-pyran-2-one
- 30 Example 296. 4-acetyloxy-6-(5-benzoyloxybenzofuran-2-yl)-3,5-dimethyl-2H-pyran-2-one
- Example 297. 6-(5-(N-(4-chlorophenylsulfonyl)-N-methylamino) benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one
- 35 Example 298. 3,5-dimethyl-4-hydroxy-6-(5-(N-methyl-N-phenylsulfonyl)benzofuran-2-yl)-2H-pyran-2-one

Example 299. 3,5-dimethyl-4-hydroxy-6-(5-(N-methyl-N-phenylcarbamoyl)benzofuran-2-yl)-2H-pyran-2-one

Example 300. 6-(5-(benzimidazolylcarbamoyl)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Example 301. 6-(5-(benzothiazolylcarbamoyl)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Example 302. 3,5-dimethyl-4-hydroxy-6-(5-(1,3,4-trihydroisoquinolin-2-ylcarbonyl)benzofuran-2-yl)-2H-pyran-2-one

Example 303. 3,5-dimethyl-4-hydroxy-6-(5-morpholinylbenzofuran-2-yl)-2H-pyran-2-one

Example 304. 3,5-dimethyl-4-hydroxy-6-(5-(5-hydroxy-3-pyridylmethoxy)benzofuran-2-yl)-2H-pyran-2-one

Example 305. 3,5-dimethyl-4-hydroxy-6-(5-(4-(sulfamoyl)phenylcarbamoyl)benzofuran-2-yl)-2H-pyran-2-one

Example 306. 3,5-dimethyl-4-hydroxy-6-(5-(4-pyridylmethylcarbamoyl)benzofuran-2-yl)-2H-pyran-2-one

Example 307. 3,5-dimethyl-4-hydroxy-6-(5-(4-piperidinyl)benzofuran-2-yl)-2H-pyran-2-one

Example 308. 6-(5-(N-benzyl-N-methylcarbamoyl)benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one

Example 309. 3,5-dimethyl-4-hydroxy-6-(5-(N-methyl-N-(4-pyridyl)carbamoyl)benzofuran-2-yl)-2H-pyran-2-one

Example 310.

Preparation of cells

Human hepatic cancer cells HepG2 were inoculated into a 24-well plate (Costar No. 3524) at 4×10^4 cells/well, and 1 ml of medium (eRDF medium containing 10% bovine serum (Kyokuto Chemical Co.)) was used for 6 day culturing with 5% CO₂ at 37°C. After drawing off the supernatant medium, the cells were freshly rinsed with 1 ml of PBS(-) buffer solution (Takara Shuzo) and drawn off. This procedure was repeated twice and then 1 ml of

fresh medium (eRDF medium) was added.

Preparation of sample

6-(benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one (Example 2) was dissolved in dimethylsulfoxide (DMSO) to prepare a 20 mM sample stock solution. A diluted solution was obtained by diluting the sample solution with DMSO.

TG production

To the cells prepared above there were added the sample stock solution or its diluted solution at 5 μ l per well and 10 μ l of 14 C-acetic acid solution (a solution of Amersham Code No. CFA13 diluted 4.4-fold with PBS(-) buffer), and culturing was carried out for one day with 5% CO₂ at 37°C.

TG quantification

After the culturing was completed, the culture solution was removed, and 1 ml of extraction solution (a mixture of n-hexane and isopropyl alcohol at 2:1) was added for extraction treatment on the lipid components in the cells. After the treatment, the extract containing the obtained lipid components was air-dried, the residue was redissolved in 20 μ l of a mixed solution of n-hexane and ethyl acetate at 9:1, and the solution was spotted on a thin-layer chromatography plate (S319, Tokyo Kasei) and developed by thin-layer chromatography with the mixed solution mentioned above. After air-drying, the lipid components were colored with iodine vapor, the portion corresponding to TG was cut out, and the amount of TG biosynthesized was measured with a liquid scintillation counter. The results are shown in Table 1. It was demonstrated that 6-(benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-2-one exhibits triglyceride biosynthesis inhibiting activity.

Table 1

Sample concentration. (Example 2)	TG production inhibiting activity
1 μ M	22%
10 μ M	70%
100 μ M	98%

Example 311

5 The TG production inhibiting activity of the
invention compounds was evaluated in the same manner as
the above example. According to the results of the
evaluation, the compounds of the following example
10 numbers exhibited an IC_{50} value of less than 10 μ M, at
least 30% TG production inhibiting activity at a
concentration of 1 μ M, or at least 50% TG production
inhibiting activity at a concentration of 10 μ M: 1, 2, 3,
4, 5, 9, 10, 11, 12, 13, 19, 25, 26, 27, 28, 29, 30, 31,
33, 34, 36, 39, 40, 42, 45, 48, 49, 50, 51, 52, 53, 54,
15 55, 56, 57, 58, 59, 61, 62, 63, 64, 65, 66, 69, 70, 71,
72, 75, 76, 78, 85, 89, 97, 117, 120, 122, 134, 138, 153,
159, 163, 170, 215, 226, 228, 236, 242, 243, 244, 245,
246, 247, 248, 249, 250, 251, 252, 255, 257, 259, 260,
265, 268, 270, 271, 274, 285, 290, 291, 297, 298, 299,
20 300, 301, 302, 303, 304, 305, 306, 307, 308, 309.

 The compounds of the following example numbers
exhibited an IC_{50} value of at least 10 μ M and less than
100 μ M; at least 5% and less than 30% TG production
inhibiting activity at a concentration of 1 μ M; or at
25 least 30% and less than 50% TG production inhibiting
activity at a concentration of 10 μ M: 6, 7, 8, 14, 17,
18, 20, 22, 23, 24, 32, 35, 37, 38, 43, 46, 47, 60, 67,
68, 74, 79, 81, 83, 87, 95, 107, 115, 124, 126, 144, 155,
157, 175, 177, 179, 181, 183, 185, 187, 191, 193, 195,
30 197, 201, 203, 207, 213, 217, 220, 222, 224, 230, 240,
253, 254, 258, 261, 262, 263, 264, 266, 267, 269, 272,

273, 275, 278, 280, 281, 282, 283, 284, 286, 287, 292, 295, 296.

Example 312. Drug effect evaluation test

5 6-(benzofuran-2-yl)-3,5-dimethyl-4-hydroxy-2H-pyran-
2-one (Example 2) was suspended in a 0.5% carboxymethyl
cellulose Na aqueous solution (vehicle) to prepare 20
mg/ml and 60 mg/ml administration solutions, and these
were orally administered to 6-week-old SD male rats at a
dose of 5 ml/kg once a day, for 7 consecutive days. CE-2
10 by Nihon Crea Co. was used for the rat feed, and the rats
were allowed free access to food and water. The rats
were separated into a vehicle-administered group of 6
rats and a drug-administered group of 6 rats for a test.
At 4 hours after the final drug administration, the rats
15 were killed under ether anesthesia, blood was drawn from
the abdominal aorta, and the serum levels of TG, total
cholesterol (TC) and HDL were measured.

Triglyceride EII-HA Test Wako (product of Wako
Junyaku Kogyo) was used for the TG measurement, HA Test
20 Wako/Cholesterol E-HA Test Wako (product of Wako Junyaku
Kogyo) was used for the total cholesterol (TC)
measurement, and HDL-cholesterol Test Wako (product of
Wako Junyaku Kogyo) was used for the HDL measurement.

As shown in Table 2, the invention compound-
25 administered group had dose-dependent lower TG levels.
Also, as shown in Table 3, the TC and HDL levels
increased in a dose dependent manner. The increase in TC
was almost totally due to an increase in HDL. No cases
of rat death or inhibited body weight gain were found
30 during the administration period.

Table 2

Administered solution	Serum TG (mg/dl) (mean $\pm$ SE)
No sample administered	108.3 $\pm$ 8.9
Example 2 (100 mg/kg)	94.8 $\pm$ 6.5
Example 2 (300 mg/kg)	74.8 $\pm$ 10.7

Table 3

Administered solution	Serum HDL-C (mg/dl) (mean $\pm$ SE)
No sample administered	30.5 $\pm$ 1.7
Example 2 (100 mg/kg)	35.0 $\pm$ 3.1
Example 2 (300 mg/kg)	42.2 $\pm$ 3.8

The above data demonstrate that the compounds of the invention have TG-lowering effects and/or HDL-elevating effects, and are therefore useful as blood triglyceride lowering agents, lipid metabolism enhancers, arteriosclerosis prophylactic agents or arteriosclerosis treatment agents.

Example 313

Tablets were prepared with each tablet having the following composition.

Active ingredient	200 μ g
Lactose	180 mg
Potato starch	50 mg
Polyvinyl pyrrolidone	10 mg
Magnesium stearate	5 mg

The active ingredient, lactose and potato starch were combined, and the mixture was evenly moistened with a 20% ethanol solution of polyvinyl pyrrolidone. The moistened mixture was passed through a 20 mesh sieve, dried at 45°C and then passed through a 15 mesh sieve. The granules obtained in this manner were blended with magnesium stearate and compressed into tablets.

Example 314

Hard gelatin capsules were prepared with each capsule containing the following composition.

Active ingredient	100 μ g
Fine crystalline cellulose	195 mg
Amorphous silicic acid	5 mg

The active ingredient, fine crystalline cellulose and unpressed amorphous silicic acid were thoroughly blended and filled into hard gelatin capsules.

Example 315

5 The active ingredient was dissolved in fractionated coconut oil. This was heated and dissolved in a coating component having the following formula, and a soft capsule manufacturing machine was used to prepare soft capsules by a common procedure, with 100 µg of the active ingredient in each capsule.

Coating formula

	Gelatin	10 parts by weight
10	Glycerin	5 parts by weight
	Sorbic acid	0.08 parts by weight
	Purified water	14 parts by weight

Industrial Applicability

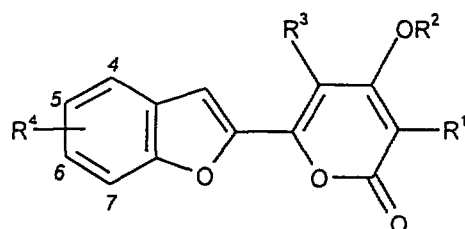
15 The pharmaceutical agents of the present invention exhibit triglyceride biosynthesis inhibiting action, blood triglyceride lowering effects or blood HDL level elevating effects, and they may therefore be used as therapeutic agents for hypertriglyceridemia, as lipid metabolism enhancers, or as prophylactic and/or
20 therapeutic agents for arteriosclerosis.



CLAIMS

1. A benzofuryl- α -pyrone derivative represented by the following structural formula (I)

5



(I)

10 wherein R^1 represents hydrogen or an alkyl group of 1 to 5 carbons;

R^2 represents hydrogen, $-\text{CO}-R^5$ (wherein R^5 represents hydrogen, an alkyl group of 1 to 5 carbons with optional substituents, a cycloalkyl group of 3 to 7 carbons, an aryl group of 6 to 10 carbons or a heterocycle), or $-\text{SO}_2R^6$ (wherein R^6 represents an optionally halogen-substituted alkyl group of 1 to 5 carbons or aryl group of 6 to 10 carbons);

20 R^3 represents hydrogen, an alkyl group of 1 to 5 carbons, an alkenyl group of 2 to 5 carbons, an alkynyl group of 2 to 5 carbons, a cycloalkyl group of 3 to 7 carbons, a cycloalkyl group of 3 to 7 carbons-alkyl group of 1 to 5 carbons, an aryl group of 6 to 10 carbons, an aralkyl group of 7 to 20 carbons, an alkoxy group of 1 to 5 carbons or an aryloxy group of 6 to 10 carbons;

25 R^4 is a substituent at the C-4 position, C-5 position, C-6 position or C-7 position of the benzofuran ring and represents:

30 R^{4a} which represents hydrogen, a nitro group, a cyano group, a halogen atom, a heterocycle, an alkenyl group of 2 to 5 carbons, an alkynyl group of 2 to 5 carbons, an aryl group of 6 to 10 carbons, $\text{A}=\text{CH}(\text{CH}_2)_n-$ (wherein A represents an alicyclic heterocycle, "=" represents a double bond and n represents 0, 1 or 2), $\text{A}=\text{CH}(\text{CH}_2)_m\text{O}-$ (wherein A represents an alicyclic heterocycle, "=" represents a double bond and m represents 1, 2 or 3), $\text{A}-\text{SO}_2-(\text{CH}_2)_m-$ (wherein A represents



an alicyclic heterocycle and m represents 1, 2 or 3),
-OR⁷ (wherein R⁷ represents hydrogen, a cycloalkyl group
of 3 to 7 carbons, an aryl group of 6 to 10 carbons, a
heterocycle or an optionally halogen-substituted
5 alkylsulfonyl group of 1 to 4 carbons or arylsulfonyl
group of 6 to 10 carbons), -O-CO-R⁸ (wherein R⁸
represents hydrogen, an alkyl group of 1 to 4 carbons, an
aryl group of 6 to 10 carbons, an aralkyl group of 7 to
20 carbons or a heterocycle), -NR⁹R¹⁰ (wherein R⁹ and R¹⁰
10 each independently represents hydrogen, an alkyl group of
1 to 4 carbons, an aralkyl group of 7 to 20 carbons, a
heterocycle, a phenyl group, -SO₂-R¹¹ (wherein R¹¹
represents an optionally halogen-substituted alkyl group
of 1 to 12 carbons, a heterocycle-substituted alkyl group
15 of 1 to 6 carbons, an aryl group of 6 to 10 carbons, a
heterocycle or an aralkyl group of 7 to 20 carbons) or
-CO-R¹² (wherein R¹² represents hydrogen, an alkyl group
of 1 to 12 carbons, an aryl group of 6 to 10 carbons, an
aralkyl group of 7 to 20 carbons, a heterocycle, an
20 alkoxy group of 1 to 10 carbons, a heterocycle-
substituted alkyl group of 1 to 6 carbons, an aryloxy
group of 6 to 10 carbons, a heteroaryloxy group or an
aralkyloxy group of 7 to 20 carbons)), -CO-R¹³ (wherein
R¹³ represents hydrogen, -OH, an alkyl group of 1 to 4
25 carbons, an aryl group of 6 to 10 carbons, a heterocycle,
an alkoxy group of 1 to 4 carbons, an aryloxy group of 6
to 10 carbons or an aralkyloxy group of 7 to 20 carbons)
or -CO-NR¹⁴R¹⁵ (wherein R¹⁴ and R¹⁵ each independently
represents hydrogen, an alkyl group of 1 to 4 carbons, a
30 cycloalkyl group of 3 to 7 carbons, an aryl group of 6 to
10 carbons, an aralkyl group of 7 to 20 carbons, a
heterocycle or a heterocycle-substituted alkyl group of 1
to 4 carbons);

R^{4b} which represents a saturated or unsaturated
35 alkoxy group of 1 to 6 carbons optionally substituted
with 1 to 3 groups selected from the group consisting of
halogens, cycloalkyl groups of 3 to 7 carbons, phenyl,



naphthyl, heterocycles, $-OR^{16}$ (wherein R^{16} represents hydrogen, an alkyl group of 1 to 4 carbons, a phenyl group, a naphthyl group, a benzyl group or a heterocycle), $-O-CO-R^{16}$ (wherein R^{16} represents hydrogen, an alkyl group of 1 to 4 carbons, a phenyl group, a naphthyl group, a benzyl group or a heterocycle), $-NR^{17}R^{18}$ (wherein R^{17} and R^{18} each independently represents hydrogen, an alkyl group of 1 to 4 carbons, a heterocycle, an alkylsulfonyl group of 1 to 4 carbons, a phenylsulfonyl group, $-SO_2-Het$ (wherein Het represents a heterocycle), an aminosulfonyl group, a methylaminosulfonyl group, a dimethylaminosulfonyl group, a diethylaminosulfonyl group, or an alkyl group of 1 to 4 carbons substituted with 1 or 2 groups selected from among phenyl, heterocycles, phenoxy, $-O-Het$ (wherein Het represents a heterocycle) and hydroxyl, $-NH-CO-R^{19}$ (wherein R^{19} represents hydrogen, an alkyl group of 1 to 4 carbons, a phenyl group, a naphthyl group, a benzyl group, a heterocycle, an alkoxy group of 1 to 4 carbons or a benzyloxy group), $-CO-R^{20}$ (wherein R^{20} represents hydrogen, a heterocycle, an alkoxy group of 1 to 4 carbons, a phenoxy group, a benzyloxy group or $-OR^{21}$ (wherein R^{21} represents hydrogen or a heterocycle)) and $-CO-NR^{22}R^{23}$ (wherein R^{22} and R^{23} each independently represents hydrogen, an alkyl group of 1 to 4 carbons, a benzyl group or a heterocycle); or

R^{4c} which represents an alkyl group of 1 to 4 carbons optionally substituted with 1 to 3 groups selected from the group consisting of halogens, cycloalkyl groups of 3 to 7 carbons, phenyl, naphthyl, heterocycles, $-SH$, $-OR^{16}$ (wherein R^{16} represents hydrogen, an alkyl group of 1 to 4 carbons, a phenyl group, a naphthyl group, a benzyl group or a heterocycle), $-O-CO-R^{16}$ (wherein R^{16} represents hydrogen, an alkyl group of 1 to 4 carbons, a phenyl group, a naphthyl group, a benzyl group or a heterocycle), $-NR^{17}R^{18}$ (wherein R^{17} and R^{18} each independently represents hydrogen, an alkyl



group of 1 to 4 carbons, a heterocycle, an alkylsulfonyl group of 1 to 4 carbons, a phenylsulfonyl group, $-\text{SO}_2\text{-Het}$ (wherein Het represents a heterocycle), an aminosulfonyl group, a methylaminosulfonyl group, a
5 dimethylaminosulfonyl group, a diethylaminosulfonyl group, or an alkyl group of 1 to 4 carbons substituted with 1 or 2 groups selected from among phenyl, heterocycles, phenoxy, $-\text{O-Het}$ (wherein Het represents a heterocycle) and hydroxyl, $-\text{NH-CO-R}^{19}$ (wherein R^{19}
10 represents hydrogen, an alkyl group of 1 to 4 carbons, a phenyl group, a naphthyl group, a benzyl group, a heterocycle, an alkoxy group of 1 to 4 carbons or a benzyloxy group), $-\text{CO-R}^{20}$ (wherein R^{20} represents hydrogen, a heterocycle, an alkoxy group of 1 to 4
15 carbons, a phenoxy group, a benzyloxy group or $-\text{OR}^{21}$ (wherein R^{21} represents hydrogen or a heterocycle)) and $-\text{CO-NR}^{22}\text{R}^{23}$ (wherein R^{22} and R^{23} each independently represents hydrogen, an alkyl group of 1 to 4 carbons, a benzyl group or a heterocycle); and
20 the numbers in italics represents the positions on the benzofuran ring;
or a salt thereof.

2. A benzofuryl- α -pyrone derivative according to claim 1 wherein R^1 is hydrogen, methyl, ethyl or
25 isopropyl; or a salt thereof.

3. A benzofuryl- α -pyrone derivative according to claim 1 wherein R^1 is methyl; or a salt thereof.

4. A benzofuryl- α -pyrone derivative according to any one of claims 1 to 3, wherein R^5 is (1) an alkyl
30 group of 1 to 5 carbons optionally substituted with 1 to 4 substituents selected from the group consisting of halogens, $-\text{OR}^8$ (wherein R^8 represents hydrogen, an alkyl group of 1 to 4 carbons, an aryl group of 6 to 10 carbons, an aralkyl group of 7 to 20 carbons or a
35 heterocycle), $-\text{O-CO-R}^8$ (wherein R^8 represents hydrogen, an alkyl group of 1 to 4 carbons, an aryl group of 6 to



10 carbons, an aralkyl group of 7 to 20 carbons or a heterocycle), $-NR^9R^{10}$ (wherein R^9 and R^{10} each independently represents hydrogen, an alkyl group of 1 to 4 carbons, an aralkyl group of 7 to 20 carbons, a heterocycle, an optionally halogen-substituted alkylsulfonyl group of 1 to 4 carbons or an arylsulfonyl group of 6 to 10 carbons), $-NH-CO-R^{24}$ (wherein R^{24} represents hydrogen, an alkyl group of 1 to 4 carbons, an aryl group of 6 to 10 carbons, an aralkyl group of 7 to 20 carbons, a heterocycle, an alkoxy group of 1 to 4 carbons or an aralkyloxy group of 7 to 20 carbons), cycloalkyl groups of 3 to 7 carbons, aryl groups of 6 to 10 carbons, heterocycles and $-CO-R^{25}$ (wherein R^{25} represents hydrogen, an alkyl group of 1 to 4 carbons, a heterocycle, $-OR^8$ (wherein R^8 represents hydrogen, an alkyl group of 1 to 4 carbons, an aryl group of 6 to 10 carbons, an aralkyl group of 7 to 20 carbons or a heterocycle) or $-NR^{26}R^{27}$ (wherein R^{26} and R^{27} each independently represents hydrogen, an alkyl group of 1 to 4 carbons, an aralkyl group of 7 to 20 carbons or a heterocycle)), (2) a hydrogen atom, (3) a cycloalkyl group of 3 to 7 carbons, (4) an aryl group of 6 to 10 carbons, or (5) a heterocycle; or a salt thereof.

5. A benzofuryl- α -pyrone derivative according to any one of claims 1 to 3, wherein R^5 is (1) an alkyl group of 1 to 5 carbons optionally substituted with 1 to 3 substituents selected from the group consisting of $-OH$, alkoxy groups of 1 to 4 carbons, phenoxy, benzyloxy, $-O-CO-R^{28}$ (wherein R^{28} represents hydrogen, an alkyl group of 1 to 4 carbons, a phenyl group or a heterocycle), $-NR^{29}R^{30}$ (wherein R^{29} and R^{30} each independently represents hydrogen, an alkyl group of 1 to 4 carbons, a benzyl group, a heterocycle or an optionally halogen-substituted alkylsulfonyl group of 1 to 4 carbons), $-NH-CO-R^{31}$ (wherein R^{31} represents hydrogen, an alkyl group of 1 to 4 carbons, a heterocycle, an alkoxy group of 1 to 4



carbons or a benzyloxy group), aryl groups of 6 to 10 carbons, heterocycles and $-\text{CO}-\text{R}^{32}$ (wherein R^{32} represents hydrogen, $-\text{OR}^{32}$ (wherein R^{32} represents hydrogen, an alkyl group of 1 to 4 carbons, a benzyl group or a heterocycle), $-\text{NR}^{33}\text{R}^{34}$ (wherein R^{33} and R^{34} each independently represents hydrogen, methyl, ethyl, benzyl or a heterocycle) or a heterocycle), (2) a cycloalkyl group of 3 to 7 carbons, (3) an aryl group of 6 to 10 carbons, or (4) a heterocycle; or a salt thereof.

6. A benzofuryl- α -pyrone derivative according to any one of claims 1 to 3, wherein R^5 is (1) an alkyl group of 1 to 5 carbons optionally substituted with 1 to 3 substituents selected from the group consisting of phenoxy, $-\text{NR}^{29}\text{R}^{30}$ (wherein R^{29} and R^{30} each independently represents hydrogen, an alkyl group of 1 to 4 carbons, a benzyl group, a heterocycle or an optionally halogen-substituted alkylsulfonyl group of 1 to 4 carbons), $-\text{NH}-\text{CO}-\text{R}^{31}$ (wherein R^{31} represents hydrogen, an alkyl group of 1 to 4 carbons, a heterocycle, an alkoxy group of 1 to 4 carbons or a benzyloxy group), phenyl and $-\text{CO}-\text{R}^{35}$ (wherein R^{35} represents $-\text{OH}$, an alkoxy group of 1 to 4 carbons, a benzyloxy group, $-\text{NR}^{33}\text{R}^{34}$ (wherein R^{33} and R^{34} each independently represents hydrogen, methyl, ethyl, benzyl or a heterocycle) or a heterocycle), (2) an aryl group of 6 to 10 carbons, or (3) a heterocycle; or a salt thereof.

7. A benzofuryl- α -pyrone derivative according to any one of claims 1 to 3, wherein R^5 is (1) an alkyl group of 1 to 5 carbons optionally substituted with 1 or 2 substituents selected from the group consisting of phenoxy, $-\text{NR}^{36}\text{R}^{37}$ (wherein R^{36} and R^{37} each independently represents hydrogen or methyl), $-\text{NH}-\text{CO}-\text{R}^{38}$ (wherein R^{38} represents hydrogen, methyl, a heterocycle, t-butoxy or benzyloxy), phenyl and $-\text{CO}-\text{R}^{39}$ (wherein R^{39} represents a heterocycle), (2) a phenyl group, or (3) a heterocycle;



or a salt thereof.

8. A benzofuryl- α -pyrone derivative according to any one of claims 1 to 7, wherein R^2 is hydrogen or $-\text{CO}-R^5$; or a salt thereof.

5 9. A benzofuryl- α -pyrone derivative according to any one of claims 1 to 3, wherein R^2 is hydrogen, acetyl, isobutyryl, benzoyl, 4-methoxybenzoyl, 2,4-dimethoxybenzoyl, 4-hydroxymethylbenzoyl, 3-dimethylaminobenzoyl, 4-acetylaminobenzoyl, phenylacetyl,
10 3-phenylpropionyl, phenoxyacetyl, furan-2-carbonyl, pyridine-4-carbonyl, pyridine-3-carbonyl, pyridine-2-carbonyl, 6-hydroxypyridine-3-carbonyl, 2-aminoacetyl, 2-(*t*-butoxycarbonylamino)acetyl, 2-(*N*-carbobenzyloxy-*N*-methylamino)acetyl, 1-carbobenzyloxy-2-pyrrolidone-5-
15 carbonyl, 2-pyrrolidone-5-carbonyl, 3-acetylamino-4-morpholinyl-4-oxobutyryl, trifluoromethanesulfonyl or methanesulfonyl;
or a salt thereof.

10 10. A benzofuryl- α -pyrone derivative according to any one of claims 1 to 3, wherein R^2 is hydrogen or acetyl; or a salt thereof.

25 11. A benzofuryl- α -pyrone derivative according to any one of claims 1 to 10, wherein R^3 is hydrogen, an alkyl group of 1 to 5 carbons, an alkenyl group of 2 to 5
25 carbons, an alkynyl group of 2 to 5 carbons, 2-cycloalkylmethyl group of 4 to 8 carbons, a cycloalkylethyl group of 5 to 9 carbons, a phenyl group, a benzyl group, a phenethyl group, a methoxy group or a phenoxy group;
30 or a salt thereof.

35 12. A benzofuryl- α -pyrone derivative according to any one of claims 1 to 10, wherein R^3 is hydrogen, an alkyl group of 1 to 5 carbons, an alkenyl group of 2 to 4 carbons, a cycloalkylmethyl group of 6 to 7 carbons, 2-cycloalkylethyl group of 7 to 8 carbons, a phenyl group,



a benzyl group, a methoxy group or a phenoxy group;
or a salt thereof.

13. A benzofuryl- α -pyrone derivative according to
any one of claims 1 to 10 wherein R^3 is an alkyl group of
1 to 5 carbons; or a salt thereof.

14. A benzofuryl- α -pyrone derivative according to
any one of claims 1 to 10 wherein R^3 is methyl or ethyl;
or a salt thereof.

15. A benzofuryl- α -pyrone derivative according to
any one of claims 1 to 14, wherein R^{4c} is an alkyl group
of 1 to 3 carbons optionally substituted with 1 to 3
substituents selected from the group consisting of
heterocycles, -SH, -OH, alkoxy groups of 1 to 4 carbons,
acyloxy groups of 1 to 4 carbons, $-NR^{40}R^{41}$ (wherein R^{40} and
 R^{41} each independently represents hydrogen, an alkyl
group of 1 to 4 carbons, an optionally halogen-
substituted alkylsulfonyl group of 1 to 4 carbons, or an
alkyl group of 1 or 2 carbons substituted with 1 or 2
substituents selected from among phenyl, heterocycles,
phenoxy, -O-Het (wherein Het represents a heterocycle)
and hydroxyl), $-NH-CO-R^{42}$ (wherein R^{42} represents
hydrogen, phenyl, an alkyl group of 1 to 4 carbons or an
alkoxy group of 1 to 4 carbons), $-CO-R^{43}$ (wherein R^{43}
represents hydrogen, a heterocycle, an alkoxy group of 1
to 4 carbons or $-OR^{21}$ (wherein R^{21} represents hydrogen or
a heterocycle)) and $-CO-NR^{44}R^{45}$ (wherein R^{44} and R^{45} each
independently represents hydrogen, an alkyl group of 1 to
4 carbons or a heterocycle);
or a salt thereof.

16. A benzofuryl- α -pyrone derivative according to
any one of claims 1 to 14, wherein R^{4c} is an alkyl group
of 1 to 3 carbons substituted with a heterocycle, -SH,
benzoylamino, an acylamino group of 1 to 5 carbons or
 $-NR^{40}R^{41}$ (wherein R^{40} and R^{41} each independently represents
hydrogen, an alkyl group of 1 to 4 carbons, an optionally
halogen-substituted alkylsulfonyl group of 1 to 4



carbons, or an alkyl group of 1 or 2 carbons substituted with 1 or 2 substituents selected from among phenyl, heterocycles, phenoxy, -O-Het (wherein Het represents a heterocycle) and hydroxyl);

5 or a salt thereof.

17. A benzofuryl- α -pyrone derivative according to any one of claims 1 to 14, wherein R^{4c} is (3,5-dioxo-2,4-thiazolidinyl)methyl, (3,5-dioxo-2,4-oxazolidinyl)methyl, (2,5-dioxoimidazolidin-4-yl)methyl or (5-oxo-3-thioxo-
10 2,4-thiazolidinyl)methyl; or a salt thereof.

18. A benzofuryl- α -pyrone derivative according to any one of claims 1 to 14, wherein R^{4c} is (3,5-dioxo-2,4-thiazolidinyl)methyl; or a salt thereof.

19. A benzofuryl- α -pyrone derivative according to
15 any one of claims 1 to 18, wherein R^{4b} is an alkoxy group of 1 to 6 carbons optionally substituted with 1 to 3 substituents selected from the group consisting of halogens, cycloalkyl groups of 3 to 7 carbons, phenyl, naphthyl, heterocycles, acyloxy groups of 1 to 4 carbons,
20 -CHO, -CO₂H, alkoxycarbonyl groups of 2 to 5 carbons, -OR⁴⁶ (wherein R^{46} represents hydrogen, an alkyl group of 1 to 4 carbons, a phenyl group, a benzyl group or a heterocycle) and -NR⁴⁷R⁴⁸ (wherein R^{47} and R^{48} each independently represents hydrogen, an alkyl group of 1 to
25 4 carbons, an alkoxycarbonyl group of 2 to 5 carbons, a heterocycle, an alkylsulfonyl group of 1 to 4 carbons, a phenylsulfonyl group, -SO₂-Het (wherein Het represents a heterocycle), an aminosulfonyl group, a methylaminosulfonyl group, a dimethylaminosulfonyl group,
30 a diethylaminosulfonyl group, an acyl group of 1 to 5 carbons, a benzoyl group, -CO-Het (wherein Het represents a heterocycle), a benzyloxycarbonyl group, or an alkyl group of 1 to 4 carbons substituted with 1 or 2 groups selected from among phenyl, heterocycles, phenoxy, -O-Het
35 (wherein Het represents a heterocycle) and hydroxyl) or an unsaturated alkoxy group of 3 to 6 carbons;



or a salt thereof.

20. A benzofuryl- α -pyrone derivative according to any one of claims 1 to 18, wherein R^{4b} is methoxy, 2-propynyloxy, 2,2-dimethylpropoxy, cyclopentylmethoxy, 2-bromoethoxy, benzyloxy, chlorobenzyloxy, fluorobenzyloxy, (trifluoromethyl)benzyloxy, dichlorobenzyloxy, dimethylbenzyloxy, methoxybenzyloxy, sulfamoylbenzyloxy, (methylenedioxy)benzyloxy, carboxybenzyloxy, (methoxycarbonyl)benzyloxy, n-butoxybenzyloxy, aminobenzyloxy, (t-butoxycarbonylamino)benzyloxy, 3-phenylpropoxy, di(methoxyphenyl)methoxy, 1-methyl-1-phenylethoxy, naphthylmethoxy, thienylmethoxy, 2-(morpholinesulfonyl)thienylmethoxy, pyridylmethoxy, (2-methoxypyridyl)methoxy, 2-(pyridyl)ethoxy, pyrazinylmethoxy, pyrimidinylmethoxy, oxazolylmethoxy, 4-phenyloxazolylmethoxy, imidazolylmethoxy, 3-tosyl-5-methylimidazolylmethoxy, thiazolylmethoxy, 4-methylthiazolylmethoxy, 2-(morpholinesulfonyl)thiazolylmethoxy, 2,4-dichlorothiazolylmethoxy, 2-(5-thiazolyl)ethoxy, 2-(4-methyl-5-thiazolyl)ethoxy, (3,5-dioxo-2,4-thiazolidinyl)methoxy, N-methylpiperidylmethoxy, (4-oxachroman-2-yl)methoxy, (3,3-dimethyl-2,4-dioxolanyl)methoxy, methoxymethyl, 2-(acetyloxy)ethoxy, bis(dimethylaminomethyl)methoxy, 4-(t-butoxycarbonylamino)butoxy, ethoxycarbonylmethoxy, 2-(methoxycarbonyl)ethoxy, 5-(ethoxycarbonyl)pentyloxy or 2-(benzyloxy)ethoxy; or a salt thereof.

21. A benzofuryl- α -pyrone derivative according to any one of claims 1 to 18, wherein R^{4b} is methoxy, 2-propynyloxy, benzyloxy, chlorobenzyloxy, fluorobenzyloxy, (trifluoromethyl)benzyloxy, dichlorobenzyloxy, dimethylbenzyloxy, methoxybenzyloxy, sulfamoylbenzyloxy, (methylenedioxy)benzyloxy, carboxybenzyloxy, (methoxycarbonyl)benzyloxy, n-butoxybenzyloxy,



aminobenzyloxy, (t-butoxycarbonylamino)benzyloxy,
thienylmethoxy, 2-(morpholinesulfonyl)thienylmethoxy,
pyridylmethoxy, (2-methoxypyridyl)methoxy, 2-
(pyridyl)ethoxy, pyrazinylmethoxy, pyrimidinylmethoxy,
5 oxazolylmethoxy, 4-phenyloxazolylmethoxy,
imidazolylmethoxy, 3-tosyl-5-methylimidazolylmethoxy,
thiazolylmethoxy, 4-methylthiazolylmethoxy, 2-
(morpholinesulfonyl)thiazolylmethoxy, 2,4-
dichlorothiazolylmethoxy, 2-(5-thiazolyl)ethoxy, 2-(4-
10 methyl-5-thiazolyl)ethoxy, (3,5-dioxo-2,4-
thiazolidinyl)methoxy, N-methylpiperidylmethoxy or
methoxymethyl;
or a salt thereof.

22. A benzofuryl- α -pyrone derivative according to
15 any one of claims 1 to 21, wherein R^{4a} is hydrogen, a
nitro group, a cyano group, a halogen atom, a
heterocycle, $A=CH(CH_2)_n-$ (wherein A represents an
alicyclic heterocycle, "=" represents a double bond and n
represents 0, 1 or 2), $A=CH(CH_2)_mO-$ (wherein A represents
20 an alicyclic heterocycle, "=" represents a double bond
and m represents 1, 2 or 3), $A-SO_2-(CH_2)_m-$ (wherein A
represents an alicyclic heterocycle and m represents 1, 2
or 3), $-OR^{49}$ (wherein R^{49} represents hydrogen, a
heterocycle, an optionally halogen-substituted
25 alkylsulfonyl group of 1 to 4 carbons or a phenylsulfonyl
group), $-O-CO-R^{50}$ (wherein R^{50} represents hydrogen, an
alkyl group of 1 to 4 carbons or phenyl), $-NR^{51}R^{52}$
(wherein R^{51} and R^{52} each independently represents
hydrogen, an alkyl group of 1 to 4 carbons, phenyl,
30 benzyl, $-SO_2-R^{53}$ (wherein R^{53} represents phenyl, naphthyl,
a heterocycle or an alkyl group of 1 to 3 carbons
optionally substituted with 1 to 3 substituents selected
from the group consisting of halogen atoms, heterocycles
and phenyl), or $-CO-R^{54}$ (wherein R^{54} represents hydrogen,
35 phenyl, naphthyl, a heterocycle, an alkoxy group of 1 to
4 carbons, a phenoxy group, a naphthyloxy group, a
heteroaryloxy group, an aralkyloxy group of 7 to 11



carbons or an alkyl group of 1 to 3 carbons optionally substituted with phenyl or a heterocycle)), $-\text{CO}-\text{R}^{55}$ (wherein R^{55} represents hydrogen, $-\text{OH}$, a heterocycle, an alkoxy group of 1 to 4 carbons or a phenoxy group), or
5 $-\text{CO}-\text{NR}^{56}\text{R}^{57}$ (wherein R^{56} and R^{57} each independently represent hydrogen, an alkyl group of 1 to 4 carbons, a cycloalkyl group of 3 to 7 carbons, a phenyl group, a benzyl group, a phenethyl group, a heterocycle or a heterocycle-substituted alkyl group of 1 to 4 carbons);
10 or a salt thereof.

23. A benzofuryl- α -pyrone derivative according to any one of claims 1 to 21, wherein R^{4a} is hydrogen, a nitro group, a cyano group, a halogen atom, a heterocycle, $\text{A}=\text{CH}(\text{CH}_2)_n-$ (wherein A represents an
15 alicyclic heterocycle, "=" represents a double bond and n represents 0, 1 or 2), $\text{A}=\text{CH}(\text{CH}_2)_m\text{O}-$ (wherein A represents an alicyclic heterocycle, "=" represents a double bond and m represents 1, 2 or 3), $\text{A}-\text{SO}_2-(\text{CH}_2)_m-$ (wherein A represents an alicyclic heterocycle and m represents 1, 2
20 or 3), $-\text{OR}^{58}$ (wherein R^{58} represents hydrogen, an optionally halogen-substituted alkylsulfonyl group of 1 to 4 carbons or a phenylsulfonyl group), $-\text{O}-\text{CO}-\text{R}^{59}$ (wherein R^{59} represents an alkyl group of 1 to 4 carbons or phenyl), $-\text{NR}^{60}\text{R}^{61}$ (wherein R^{60} and R^{61} each independently
25 represents hydrogen, an alkyl group of 1 to 4 carbons, phenyl, benzyl, $-\text{SO}_2-\text{R}^{62}$ (wherein R^{62} represents an optionally halogen-substituted alkyl group of 1 to 3 carbons, a heterocycle-substituted alkyl group of 1 to 3 carbons, a phenyl group, a heterocycle, a benzyl group or
30 a phenethyl group) or $-\text{CO}-\text{R}^{63}$ (wherein R^{63} represents an alkyl group of 1 to 4 carbons, a phenyl group, an aralkyl group of 7 to 9 carbons, a heterocycle, an alkoxy group of 1 to 4 carbons, a heterocycle-substituted alkyl group of 1 to 3 carbons, a phenoxy group, a heteroaryloxy group
35 or a benzyloxy group)), $-\text{CO}-\text{R}^{64}$ (wherein R^{64} represents hydrogen, $-\text{OH}$ or an alkoxy group of 1 to 4 carbons), or $-\text{CO}-\text{NR}^{65}\text{R}^{66}$ (wherein R^{65} and R^{66} each independently



represents hydrogen, an alkyl group of 1 to 4 carbons, a cycloalkyl group of 3 to 7 carbons, a phenyl group, a benzyl group, a phenethyl group, a heterocycle or a heterocycle-substituted alkyl group of 1 to 4 carbons);
5 or a salt thereof.

24. A benzofuryl- α -pyrone derivative according to any one of claims 1 to 21 wherein R^{4a} is hydrogen, nitro, cyano, bromine, thiazolyl, furyl, thienyl, morpholinyl, piperazinyl, hydroxyl, methanesulfonyloxy,
10 trifluoromethanesulfonyloxy, phenylsulfonyloxy, acetyloxy, benzoyloxy, dimethylamino, dibenzylamino, phenylsulfonylamino, dimethylcarbamoyl, N-methyl-N-phenylcarbamoyl, N-benzyl-N-methylcarbamoyl, cyclohexylcarbamoyl, phenylcarbamoyl,
15 imidazolylcarbamoyl, benzimidazolylcarbamoyl, thiazolylcarbamoyl, benzothiazolylcarbamoyl, isothiazolylcarbamoyl, pyrazolylcarbamoyl, triazolylcarbamoyl, pyridylcarbamoyl, pyrimidinylcarbamoyl, pyrazinylcarbamoyl,
20 isoxazolylcarbamoyl, formyl, carboxyl, methoxycarbonyl, ethoxycarbonyl, n-propoxycarbonyl, isopropoxycarbonyl, t-butoxycarbonyl, acetyl, benzoyl, 1,3,4-trihydroisoquinolin-2-ylcarbonyl, (3,5-dioxo-2,4-thiazolidinylidene)methyl, (3,5-dioxo-2,4-oxazolidinylidene)methyl, (2,5-dioxoimidazolidin-4-ylidene)methyl, (5-oxo-3-thioxo-2,4-thiazolidinylidene)methyl, ((3,5-dioxo-2,4-thiazolidinyl)sulfonyl)methyl, ((3,5-dioxo-2,4-oxazolidinyl)sulfonyl)methyl, ((2,5-dioxoimidazolidin-4-yl)sulfonyl)methyl, ((5-oxo-3-thioxo-2,4-thiazolidinyl)sulfonyl)methyl or -NR⁶⁷-CO-R⁶⁸ (wherein R⁶⁷ represents an alkyl group of 1 to 4 carbons and R⁶⁸ represents an alkyl group of 1 to 3 carbons, a phenyl group, a heterocycle, an aralkyl group of 7 to 9 carbons
35 or an alkoxy group of 1 to 4 carbons);
or a salt thereof.



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25. A benzofuryl- α -pyrone derivative according to any one of claims 1 to 21, wherein R^{4a} is hydrogen, nitro, cyano, bromine, thienyl, piperazinyl, hydroxyl, trifluoromethanesulfonyloxy, phenylsulfonyloxy, acetyloxy, dimethylamino, dibenzylamino, tiazolylcarbamoyl, methoxycarbonyl, isopropoxycarbonyl, (3,5-dioxo-2,4-thiazolidinylidene)methyl, or -N(Me)-CO-R⁶⁹ (wherein R⁶⁹ represents an alkyl group of 1 to 3 carbons, a phenyl group, a heterocycle, a benzyl group or an alkoxy group of 1 to 4 carbons); or a salt thereof.

26. A pharmaceutical composition comprising a therapeutically effective dose of a benzofuryl- α -pyrone derivative according to any one of claims 1 to 25 or its salt, and a pharmaceutically acceptable carrier.

27. A lipid metabolism enhancer comprising as an active ingredient a benzofuryl- α -pyrone derivative according to any one of claims 1 to 25 or its salt.

28. A triglyceride biosynthesis inhibitor comprising as an active ingredient a benzofuryl- α -pyrone derivative according to any one of claims 1 to 25 or its salt.

29. A blood triglyceride lowering agent comprising as an active ingredient a benzofuryl- α -pyrone derivative according to any one of claims 1 to 25 or its salt.

30. A blood HDL elevating agent comprising as an active ingredient a benzofuryl- α -pyrone derivative according to any one of claims 1 to 25 or its salt.

31. An arteriosclerosis prophylactic agent comprising as an active ingredient a benzofuryl- α -pyrone derivative according to any one of claims 1 to 25 or its salt.

32. An arteriosclerosis treatment agent comprising as an active ingredient a benzofuryl- α -pyrone derivative according to any one of claims 1 to 25 or its salt.