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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
4 March 2010 (04.03.2010)

PCT

(10) International Publication Number
WO 2010/024365 A1

(51) International Patent Classification:
C07D 277/82 (2006.01) *A01N 43/78* (2006.01)
A01P 3/00 (2006.01)

(21) International Application Number:
PCT/JP2009/065022

(22) International Filing Date:
21 August 2009 (21.08.2009)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

2008-216359	26 August 2008 (26.08.2008)	JP
2008-216360	26 August 2008 (26.08.2008)	JP
2008-216361	26 August 2008 (26.08.2008)	JP

(71) Applicant *(for all designated States except US)*: **SUMITOMO CHEMICAL COMPANY, LIMITED** [JP/JP]; 27-1, Shinkawa 2-chome, Chuo-ku, Tokyo, 1048260 (JP).

(72) Inventor; and

(75) Inventor/Applicant *(for US only)*: **SAKAGUCHI, Hiroshi** [JP/JP]; 2-10-5-103, Sonehigashino-cho, Toyonaka-shi, Osaka, 5610802 (JP).

(74) Agents: **NAKAYAMA, Tohru** et al.; c/o Sumitomo Chemical Intellectual Property Service, Limited, 5-33, Kitahama 4-chome, Chuo-ku, Osaka-shi, Osaka, 5418550 (JP).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

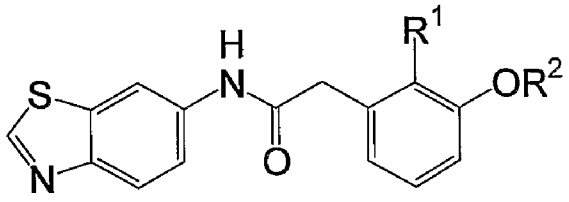
Published:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

WO 2010/024365 A1

(54) **Title**: AMIDE COMPOUNDS AND USE THEREOF



(I)

(57) **Abstract**: An amide compound of the formula (I): wherein R1 represents a hydrogen atom or a fluorine atom and R2 represents a C1-C6 linear alkyl group or a linear (C1-C2 alkoxy)C2-C5 alkyl group, has an excellent controlling effect on a plant disease.

DESCRIPTION

AMIDE COMPOUNDS AND USE THEREOF

TECHNICAL FIELD

The present invention relates to an amide compound and a plant disease controlling use thereof.

BACKGROUND ART

A lot of compounds have been developed as active ingredients of a plant disease controlling composition, and put into practical use. However, these compounds do not necessarily show a sufficient plant disease controlling effect in some cases.

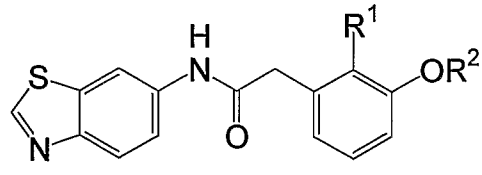
The present invention provides a compound having an excellent controlling effect on plant diseases.

The present invention also provides an amide compound used for the compound of the present invention.

DISCLOSURE OF THE INVENTION

The present inventions are as follows.

[1] An amide compound of the formula (I):



(I)

wherein R^1 represents a hydrogen atom or a fluorine atom and R^2 represents a C1-C6 linear alkyl group or a linear (C1-C2 alkoxy)C2-C5 alkyl group.

[2] The amide compound according to [1], wherein R^1 is a fluorine atom and R^2 is a C1-C6 linear alkyl group.

[3] The amide compound according to [2], wherein R^2 is a methyl group or an ethyl group.

[4] The amide compound according to [1], wherein R^1 is a hydrogen atom and R^2 is a C1-C6 linear alkyl group.

[5] The amide compound according to [4], wherein R^2 is a methyl group, an ethyl group or a butyl group.

[6] The amide compound according to [1], wherein R^1 is a hydrogen atom or a fluorine atom and R^2 is a linear (C1-C2 alkoxy)C2-C5 alkyl group.

[7] The amide compound according to [5], wherein R^1 is a hydrogen atom.

[8] The amide compound according to [5], wherein R^1 is a fluorine atom.

[9] The amide compound according to any one of [6] to [8], wherein R^2 is a linear (C1-C2 alkoxy)C3-C4 alkyl group.

[10] N-benzothiazol-6-yl-2-(2-fluoro-3-methoxyphenyl)acetamide

[11] N-benzothiazol-6-yl-2-(2-fluoro-3-ethoxyphenyl)acetamide

[12] N-benzothiazol-6-yl-2-(2-fluoro-3-propoxyphenyl)acetamide

[13] N-benzothiazol-6-yl-2-(2-fluoro-3-butoxyphenyl)acetamide

[14] N-benzothiazol-6-yl-2-(2-fluoro-3-pentyloxyphenyl)acetamide

[15] N-benzothiazol-6-yl-2-(2-fluoro-3-hexyloxyphenyl)acetamide

[16] N-(benzothiazol-6-yl-)-2-(3-methoxyphenyl)acetamide

[17] N-benzothiazol-6-yl-2-(3-ethoxyphenyl)acetamide

[18] N-benzothiazol-6-yl-2-(3-propoxyphenyl)acetamide

[19] N-benzothiazol-6-yl-2-(3-butoxyphenyl)acetamide

[20] N-benzothiazol-6-yl-2-(3-pentyloxyphenyl)acetamide

[21] N-benzothiazol-6-yl-2-(3-hexyloxyphenyl)acetamide

[22] N-benzothiazol-6-yl-2-(3-(3-methoxypropoxy)phenyl)acetamide

[23] N-benzothiazol-6-yl-2-(3-(4-methoxybutoxy)phenyl)acetamide

[24] N-benzothiazol-6-yl-2-(3-(3-ethoxypropoxy)phenyl)acetamide

[25] N-benzothiazol-6-yl-2-(3-(4-ethoxybutoxy)phenyl)acetamide

[26] N-benzothiazol-6-yl-2-(2-fluoro-3-(3-methoxypropoxy)phenyl)-acetamide

[27] N-benzothiazol-6-yl-2-(2-fluoro-3-(3-ethoxypropoxy)phenyl)acetamide

[28] N-benzothiazol-6-yl-2-(2-fluoro-3-(4-methoxybutoxy)phenyl)acetamide

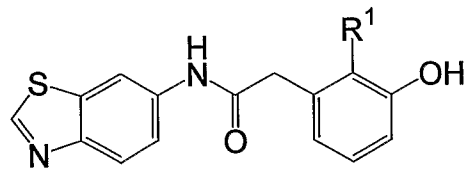
[29] N-benzothiazol-6-yl-2-(2-ethoxyethoxyphenyl)acetamide

[30] A plant disease controlling composition comprising the amide compound according to any one of [1] to [29] and an inert carrier.

[31] A plant disease controlling method having a step of applying a plant or soil with an effective amount of the amide compound according to any one of [1] to [29].

[32] Use of the amide compound according to any one of [1] to [29] for controlling a plant disease.

[33] An amide compound of the formula (II):



(II)

wherein R^1 represents a hydrogen atom or a fluorine atom.

The compound of the present invention includes, for example, the following embodiments.

An amide compound in which R^1 represents a hydrogen atom in the formula (I);

An amide compound in which R^1 represents a fluorine atom in the formula (I);

An amide compound in which R^2 represents a C1-C6 linear alkyl group in the formula (I);

An amide compound in which R^2 represents a methyl group, an ethyl group or a butyl group in the formula (I);

An amide compound in which R^2 represents a methyl group or an ethyl group in the formula (I);

An amide compound in which R^2 represents a linear (C1-C2 alkoxy)C2-C5 alkyl group in the formula (I);

An amide compound in which R^2 represents a linear methoxy C2-C5 alkyl group in the formula (I);

An amide compound in which R^2 represents a linear ethoxy C2-C5 alkyl group in the formula (I);

An amide compound in which R^1 represents a hydrogen atom and R^2 represents a C1-C6 linear alkyl group in the formula (I);

An amide compound in which R^1 represents a fluorine atom and R^2 represents a C1-C6 linear alkyl group in the formula (I);

An amide compound in which R^1 represents a hydrogen atom and R^2 represents a methyl group, an ethyl group or a butyl group in the formula (I);

An amide compound in which R^1 represents a fluorine atom and R^2 represents a methyl group or an ethyl group in the formula (I);

An amide compound in which R^1 represents a hydrogen atom and R^2 represents a linear (C1-C2 alkoxy)C2-C5 alkyl group in the formula (I);

An amide compound in which R^1 represents a fluorine atom and R^2 represents a linear (C1-C2 alkoxy)C2-C5 alkyl group in the formula (I);

An amide compound in which R^1 represents a hydrogen atom and R^2 represents a linear methoxy C2-C3 alkyl group in the formula (I);

An amide compound in which R^1 represents a fluorine atom and R^2 represents a linear methoxy C2-C3 alkyl group in the formula (I);

An amide compound in which R^1 represents a hydrogen atom and R^2 represents a linear ethoxy C2-C3 alkyl group in the formula (I);

An amide compound in which R^1 represents a fluorine atom and R^2 represents a linear ethoxy C2-C3 alkyl group in the formula (I).

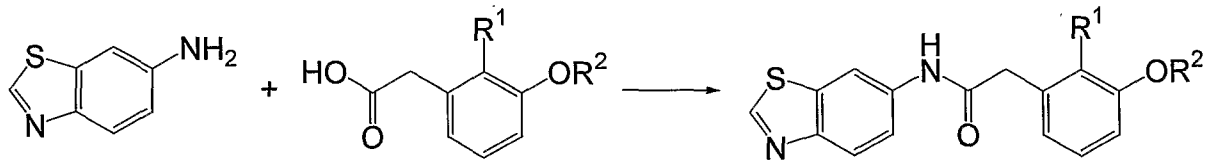
BEST MODE FOR CARRYING OUT THE INVENTION

The production method for the compound of the present invention will be described.

The compound of the present invention can be produced, for example, by the following (Production Method 1) to (Production Method 3).

(Production Method 1)

The compound of the present invention can be produced by reacting a compound (IV) and a compound (III) or its salt (for example, hydrochloride and hydrobromide are listed) in the presence of a condensing agent.



(III) (IV) (I)

wherein R^1 and R^2 have the same meaning as defined above.

The reaction is carried out usually in the presence of a solvent.

Examples of the solvent used in the reaction include ethers such as tetrahydrofuran (hereinafter, referred to as THF), ethylene glycol dimethyl ether and tert-butyl methyl ether (hereinafter, referred to as MTBE); aliphatic hydrocarbons such as hexane, heptane and octane; aromatic hydrocarbons such as toluene and xylene; halogenated hydrocarbons such as chlorobenzene; esters such as butyl acetate and ethyl acetate; nitriles such as acetonitrile; acid amides such as N,N-dimethylformamide (hereinafter, referred to as DMF); sulfoxides such as dimethyl sulfoxide (hereinafter, referred to as DMSO); nitrogen-containing aromatic compounds such as pyridine; and mixtures thereof.

Examples of the condensing agent used in the reaction include carbodiimides such as 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (hereinafter, referred to as WSC) and 1,3-dicyclohexyl-

carbodiimide, and (benzotriazol-1-yloxy)tris(dimethylamino)phosphonium hexafluorophosphate (hereinafter, referred to as BOP reagent).

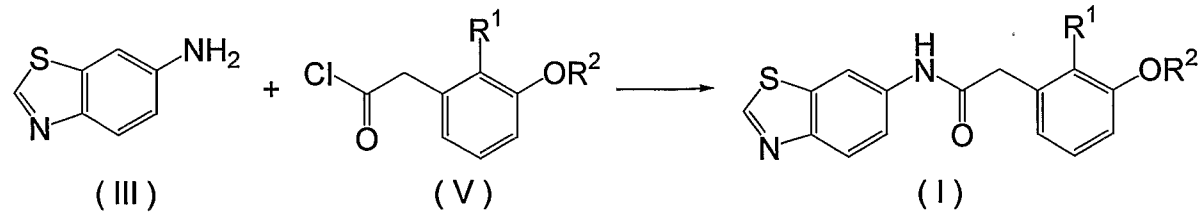
In the reaction, the compound (IV) is used usually in a proportion of 0.5 to 3 mol based on 1 mol of the compound (III), and the condensing agent is used usually in a proportion of 1 to 5 mol based on 1 mol of the compound (III).

The reaction temperature of the reaction is usually in the range of from -20°C to 140°C. The reaction time of the reaction is usually in the range of from 1 to 24 hours.

After completion of the reaction, if a solid deposits by adding water to the reaction mixture, the compound of the present invention can be isolated by filtration. If no deposition of a solid occurs by adding water to the reaction mixture, the compound of the present invention can be isolated by extracting a mixture of the reaction mixture and water with an organic solvent and drying and concentrating the organic layer. The isolated compound of the present invention can also be further purified by chromatography, re-crystallization and so on.

(Production method 2)

The compound of the present invention can be produced by reacting a compound (V) or its hydrochloride, and a compound (III) or its salt (for example, hydrochloride and hydrobromide are mentioned) in the presence of a base.



(III) (V) (I)

wherein R^1 and R^2 have the same meaning as defined above.

The reaction is carried out usually in the presence of a solvent.

Examples of the solvent used in the reaction include ethers such as THF,

ethylene glycol dimethyl ether and MTBE; aliphatic hydrocarbons such as hexane, heptane and octane; aromatic hydrocarbons such as toluene and xylene; halogenated hydrocarbons such as chlorobenzene; esters such as butyl acetate and ethyl acetate; nitriles such as acetonitrile; and mixtures thereof.

Examples of the base used in the reaction include alkali metal carbonates such as sodium carbonate and potassium carbonate; tertiary amines such as triethylamine and diisopropylethylamine; and nitrogen-containing aromatic compounds such as pyridine and 4-dimethylaminopyridine.

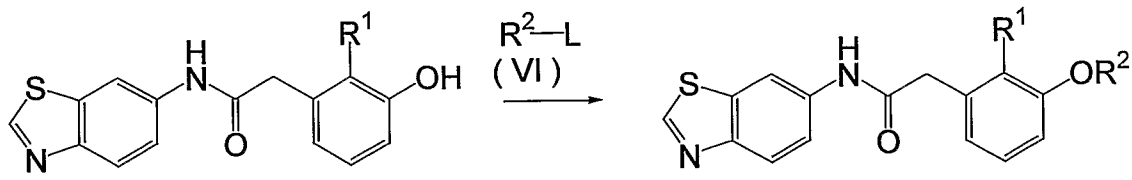
In the reaction, the compound (III) is used usually in a proportion of 0.5 to 3 mol based on 1 mol of the compound (V), and the base is used usually in a proportion of 1 to 5 mol based on 1 mol of the compound (V).

The reaction temperature of the reaction is usually in the range of from -20°C to 100°C. The reaction time of the reaction is usually in the range of from 0.1 to 24 hours.

After completion of the reaction, if a solid deposits by adding water to the reaction mixture, the compound of the present invention can be isolated by filtration. If no deposition of a solid occurs by adding water to the reaction mixture, the compound of the present invention can be isolated by extracting a mixture of the reaction mixture and water with an organic solvent and drying and concentrating the organic layer. The isolated compound of the present invention can also be further purified by chromatography, re-crystallization and so on.

(Production Method 3)

The compound of the present invention can be produced by reacting an amide compound (II) and a compound (VI) in the presence of a base.



(II) (I)

wherein R^1 and R^2 have the same meaning as defined above, and L represents a chlorine atom, a bromine atom, an iodine atom, a methanesulfonyloxy group, a trifluoromethanesulfonyloxy group or a p-toluenesulfonyloxy group.

The reaction is carried out usually in the presence of a solvent.

Examples of the solvent used in the reaction include ethers such as THF, ethylene glycol dimethyl ether and MTBE; aromatic hydrocarbons such as toluene and xylene; halogenated hydrocarbons such as chlorobenzene; nitriles such as acetonitrile; acid amides such as DMF; sulfoxides such as DMSO; ketones such as acetone, methyl ethyl ketone and methyl isobutyl ketone; water; and mixtures thereof.

Examples of the base used in the reaction include alkali metal carbonates such as sodium carbonate, potassium carbonate and cesium carbonate; alkali metal hydroxides such as sodium hydroxide, and alkali metal hydrides such as sodium hydride.

In the reaction, the compound (VI) is used usually in a proportion of 1 to 10 mol based on 1 mol of the compound (II), and the base is used usually in a proportion of 1 to 5 mol based on 1 mol of the compound (II).

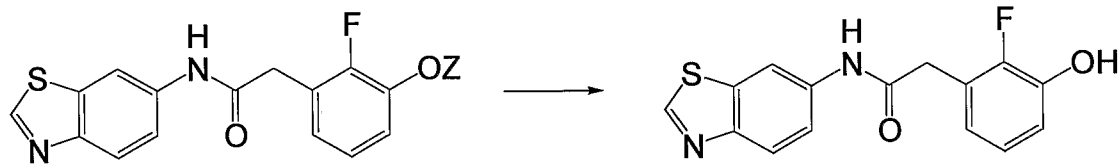
The reaction temperature of the reaction is usually in the range of from -20°C to 100°C. The reaction time of the reaction is usually in the range of from 0.1 to 24 hours.

After completion of the reaction, if a solid deposits by adding water to the reaction mixture, the compound of the present invention can be isolated by filtration. If no deposition of a solid occurs by adding water to the reaction mixture, the compound of the present invention can be isolated by extracting a

mixture of the reaction mixture and water with an organic solvent and drying and concentrating the organic layer. The isolated compound of the present invention can also be further purified by chromatography, re-crystallization and so on.

(Synthesis Example)

The amide compound of the present invention can be produced by de-protecting a protective group of the compound (VII).



(VII) (II)

wherein Z represents a protective group such as a tert-butyldimethylsilyl group, methyl group, methoxymethyl group, benzyl group and acetyl group.

When Z is a tert-butyldimethylsilyl group, said reaction is usually carried out in the presence of a solvent.

Examples of the solvent used in the reaction include ethers such as THF, ethylene glycol dimethyl ether and MTBE, aromatic hydrocarbons such as toluene and xylene, halogenated hydrocarbons such as chlorobenzene, nitriles such as acetonitrile, acid amides such as DMF, sulfoxides such as dimethyl sulfoxide, ketones such as acetone, methyl ethyl ketone and methyl isobutyl ketone, water, and mixtures thereof.

The base and fluoride used in the de-protecting reaction include alkali metal hydroxides such as lithium hydroxide, sodium hydroxide and potassium hydroxide, and fluorine compounds such as sodium fluoride, tetrabutylammonium hydrofluoride and hydrofluoric acid.

The base and fluorine compound are used usually in a proportion of 1 to 10

mol with respect to 1 mol of the compound (VII).

The reaction temperature of this reaction is usually in the range of from -20 to 100°C and the reaction time is usually in the range of from 0.1 to 24 hours.

After completion of the reaction, water is added to the reaction mixture, this is washed with an organic solvent such as MTBE and hexane to obtain an aqueous layer. After an acid such as hydrochloric acid, acetic acid and the like is added to the aqueous layer to make it acidic, post-treatments such as extraction with an organic solvent, concentration and the like are carried out, thus, the compound (V) can be isolated. The isolated compound (V) can also be further purified by chromatography and recrystallization.

The "linear (C1-C2 alkoxy)C2-C5 alkyl group" represented by R^2 in the present invention means a (C1-C2 alkoxy)C2-C5 alkyl group having no branch in the carbon chain.

Examples of the compound of the present invention includes, specifically,
N-benzothiazol-6-yl-2-(2-fluoro-3-methoxyphenyl)acetamide,
N-benzothiazol-6-yl-2-(3-ethoxy-2-fluorophenyl)acetamide,
N-benzothiazol-6-yl-2-(2-fluoro-3-propoxyphenyl)acetamide,
N-benzothiazol-6-yl-2-(3-butoxy-2-fluorophenyl)acetamide,
N-benzothiazol-6-yl-2-(2-fluoro-3-pentyloxyphenyl)acetamide,
N-benzothiazol-6-yl-2-(2-fluoro-3-hexyloxyphenyl)acetamide,
N-benzothiazol-6-yl-2-(3-methoxyphenyl)acetamide,
N-benzothiazol-6-yl-2-(3-ethoxyphenyl)acetamide,
N-benzothiazol-6-yl-2-(3-propoxyphenyl)acetamide,
N-benzothiazol-6-yl-2-(3-butoxyphenyl)acetamide,
N-benzothiazol-6-yl-2-(3-pentyloxyphenyl)acetamide,
N-benzothiazol-6-yl-2-(3-hexyloxyphenyl)acetamide,
N-benzothiazol-6-yl-2-(3-(2-methoxyethoxy)phenyl)acetamide,

N-benzothiazol-6-yl-2-(3-(2-ethoxyethoxy)phenyl)acetamide,
N-benzothiazol-6-yl-2-(3-(3-methoxypropoxy)phenyl)acetamide,
N-benzothiazol-6-yl-2-(3-(3-ethoxypropoxy)phenyl)acetamide,
N-benzothiazol-6-yl-2-(3-(4-methoxybutoxy)phenyl)acetamide,
N-benzothiazol-6-yl-2-(3-(4-ethoxybutoxy)phenyl)acetamide,
N-benzothiazol-6-yl-2-(3-(5-methoxypentyloxy)phenyl)acetamide,
N-benzothiazol-6-yl-2-(3-(5-ethoxypentyloxy)phenyl)acetamide,
N-benzothiazol-6-yl-2-(2-fluoro-3-(2-methoxyethoxy)phenyl)acetamide,
N-benzothiazol-6-yl-2-(3-(2-ethoxyethoxy)-2-fluorophenyl)acetamide,
N-benzothiazol-6-yl-2-(2-fluoro-3-(3-methoxypropoxy)phenyl)acetamide,
N-benzothiazol-6-yl-2-(3-(3-ethoxypropoxy)-2-fluorophenyl)acetamide,
N-benzothiazol-6-yl-2-(2-fluoro-3-(4-methoxybutoxy)phenyl)acetamide,
N-benzothiazol-6-yl-2-(3-(4-ethoxybutoxy)-2-fluoro-phenyl)acetamide,
N-benzothiazol-6-yl-2-(2-fluoro-3-(5-methoxypentyloxy)phenyl)acetamide and
N-benzothiazol-6-yl-2-(3-(5-ethoxypentyloxy)-2-fluoro-phenyl)acetamide.

The plant disease controlling composition of the present invention contains a compound of the present invention and an inert carrier. The inert carrier includes solid carriers, liquid carriers and gas carriers. The plant disease controlling composition of the.present invention is usually formulated into a wettable powder, dust, water dispersible granule, flowable, granule, dry flowable, emulsifiable concentrate, aqueous liquid agent, oil solution, smoking agent, aerosol, microcapsules and so on by further addition of auxiliary agents for formulation such as a surfactant, a sticking agent, a dispersing agent and a stabilizing agent. The plant disease controlling composition of the present invention contains the compound of the present invention in a weight ratio of usually 0.1 to 99%, preferably 0.2 to 90%.

Examples of the solid carrier include fine powders and granules of clays (for

example, kaolin, diatomaceous earth, synthetic hydrated silicon oxide, Fubasami clay, bentonite and acid clay), talc, other inorganic minerals (for example, sericite, quart powder, sulfur power, activated carbon, calcium carbonate and hydrated silica) and so on, and examples of the liquid carrier include water; alcohols (for example, methanol and ethanol), ketones (for example, acetone and methyl ethyl ketone), aromatic hydrocarbons (for example, benzene, toluene, xylene, ethylbenzene and methylnaphthalene), aliphatic hydrocarbons (for example, n-hexane, cyclohexane and kerosene), esters (for example, ethyl acetate and butyl acetate), nitriles (for example, acetonitrile and isobutyronitrile), ethers (for example, dioxane and diisopropyl ether), acid amides (for example, DMF and dimethylacetamide), halogenated hydrocarbons (for example, dichloroethane and trichloroethylene, carbon tetrachloride) and so on.

Examples of the surfactant include alkyl sulfates, alkyl sulfonates, alkyl aryl sulfonates, alkyl aryl ethers and their polyoxyethylenate, polyoxyethylene glycol ethers, poly-valent alcohol esters, sugar alcohol derivatives, and so on.

Examples of other auxiliary agents for formulation include sticking agents and dispersing agents, specifically, casein, gelatin, polysaccharides (for example, starch, gum Arabic, cellulose derivatives and alginic acid), lignin derivatives, bentonite, sugars, synthetic water-soluble polymers (for example, polyvinyl alcohol, polyvinylpyrrolidone and polyacrylic acids), PAP (acidic isopropyl phosphate), BHT (2,6-di-tert-butyl-4-methyl-phenol), BHA (a mixture of 2-tert-butyl-4-methoxyphenol and 3-tert-butyl-4-methoxyphenol), vegetable oils, mineral oils, fatty acids or esters thereof, and so on.

The use method of the plant disease controlling composition of the present invention for controlling a plant disease includes, for example, treatment on plants such as spraying on stem and leaves, treatment on cultivation ground for plant such as soil treatment, and treatment on seed such as seed disinfection.

The plant disease controlling composition of the present invention can also be used in admixture with other fungicides, insecticides, acaricides, nematocides, herbicides, plant growth regulating agents, fertilizers or soil improvement agents, or used simultaneously with them without mixing.

Examples of active ingredients of such other fungicides include: azole fungicidal compounds such as propiconazole, prothioconazole, triadimenol, prochloraz, penconazole, tebuconazole, flusilazole, diniconazole, bromuconazole, epoxiconazole, difenoconazole, cyproconazole, metconazole, triflumizole, tetraconazole, microbutanil, fenbuconazole, hexaconazole, fluquinconazole, triticonazole, bitertanol, imazalil, flutriafol, simeconazole and ipconazole; cyclic amine fungicidal compounds such as fenpropimorph, tridemorph and fenpropidin; benzimidazole fungicidal compounds such as carbendazim, benomyl, thiabendazole and thiophanate-methyl; procymidone; cyprodinil; pyrimethanil; diethofencarb; thiuram; fluazinam, mancozeb; iprodione; vinclozolin, chlorothalonil; captan; mepanipyrim, fenpiclonil; fludioxonil; dichlofluanid; folpet; kresoxim-methyl; azoxystrobin; trifloxystrobin; fluoxastrobin; picoxystrobin; pyraclostrobin; dimoxystrobin; pyribencarb; metominostrobin; enestroburin; spiroxamine; quinoxyfen; fenhexamid; famoxadone; fenamidone; zoxamide; etaboxam; amisulbrom; iprovalicarb; benthiavalicarb; cyazofamid; mandipropamid; boscalid; penthiopyrad; metrafenone; fluopyram; bixafen; cyflufenamid; proquinazid; orysastrobin; furametpyr; thifluzamide; mepronil; flutolanil; flusulfamide; fluopicolide; metalaxyl M; kiralaxyl; fosetyl; cymoxanil; pencycuron; tolclofos-methyl; carpropamid; diclocymet; fenoxanil; tricyclazole; pyroquilon; probenazole; isotianil; tiadinil; tebufroquin; diclomezine; kasugamycin; ferimzone; fthalide; validamycin; hydroxyisoxazole; iminoctadin-acetate; isoprothiolane; oxolinic acid; oxytetracycline; streptomycin; sedaxane; isopyrazam; BYF-14182; flutianil; basic copper chloride; cupric hydroxide; basic copper sulfate; organic

copper; and sulfur.

Examples of active ingredients of insecticides include the following compounds:

(1) Organophosphorus compounds

acephate, Aluminium phosphide, butathiofos, cadusafos, chlorethoxyfos, chlorfenvinphos, chlorpyrifos, chlorpyrifos-methyl, cyanophos: CYAP, diazinon, DCIP(dichlorodiisopropyl ether), dichlofenthion: ECP, dichlorvos: DDVP, dimethoate, dimethylvinphos, disulfoton, EPN, ethion, ethoprophos, etrimfos, fenthion: MPP, fenitrothion: MEP, fosthiazate, formothion, Hydrogen phosphide, isofenphos, isoxathion, malathion, mesulfenfos, methidathion: DMTP, monocrotophos, naled: BRP, oxydeprofos: ESP, parathion, phosalone, phosmet: PMP, pirimiphos-methyl, pyridafenthion, quinalphos, phenthoate: PAP, profenofos, propaphos, prothiofos, pyraclorfos, salithion, sulprofos, tebupirimfos, temephos, tetrachlorvinphos, terbufos, thiometon, trichlorphon: DEP, vamidothion, phorate, cadusafos, etc.;

(2) Carbamate compounds

alanycarb, bendiocarb, benfuracarb, BPMC, carbaryl, carbofuran, carbosulfan, cloethocarb, ethiofencarb, fenobucarb, fenothiocarb, fenoxycarb, furathiocarb, isoprocarb: MIPC, metolcarb, methomyl, methiocarb, NAC, oxamyl, pirimicarb, propoxur: PHC, XMC, thiodicarb, xylylcarb, aldicarb, etc.;

(3) Synthetic pyrethroid compounds

acrinathrin, allethrin, benfluthrin, beta-cyfluthrin, bifenthrin, cycloprothrin, cyfluthrin, cyhalothrin, cypermethrin, deltamethrin, esfenvalerate, ethofenprox, fenpropathrin, fenvalerate, flucythrinate, flufenoprox, flumethrin, fluvalinate, halfenprox, imiprothrin, permethrin, prallethrin, pyrethrins, resmethrin, sigma-cypermethrin, silafluofen, tefluthrin, tralomethrin, transfluthrin, tetramethrin, phenothrin, cyphenothrin, alpha-cypermethrin, zeta-cypermethrin,

lambda-cyhalothrin, furamethrin, tau-fluvalinate,
2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl(EZ)-(1RS, 3RS; 1RS, 3SR)-2,2-dimethyl-3-prop-1-enyl cyclopropane carboxylate,
2,3,5,6-tetrafluoro-4-methylbenzyl(EZ)-(1RS, 3RS; 1RS, 3SR)-2,2-dimethyl-3-prop-1-enyl cyclopropane carboxylate,
2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl(1RS, 3RS; 1RS, 3SR)-2,2-dimethyl-3-(2-methyl-1-propenyl) cyclopropane carboxylate, etc.;

(4) Nereistoxin compounds
cartap, bensultap, thiocyclam, monosultap, bisultap, etc.;

(5) Neonicotinoid compounds
imidacloprid, nitenpyram, acetamiprid, thiamethoxam, thiacloprid, dinotefuran, clothianidin, etc.;

(6) Benzoylurea compounds
chlorfluazuron, bistrifluron, diafenthiuron, diflubenzuron, fluazuron, flucycloxuron, flufenoxuron, hexaflumuron, lufenuron, novaluron, noviflumuron, teflubenzuron, triflumuron, triazlon, etc.;

(7) Phenylpyrazole compounds
acetoprole, ethiprole, fipronil, vaniliprole, pyriprole, pyrafluprole, etc.;

(8) Bt toxin insecticides
Fresh spores derived from *Bacillus thuringiensis*, crystalline toxins generated from *Bacillus thuringiensis*, and the mixtures thereof;

(9) Hydrazine compounds
chromafenozide, halofenozide, methoxyfenozide, tebufenozide, etc.;

(10) Organochlorine compounds
aldrin, dieldrin, dienochlor, endosulfan, methoxychlor, etc.;

(11) Natural insecticides
machine oil and nicotine-sulfate; and

(12) Other insecticides

avermectin-B, bromopropylate, buprofezin, chlorphenapyr, cyromazine, D-D(1, 3-Dichloropropene), emamectin-benzoate, fenazaquin, flupyrazofos, hydroprene, methoprene, indoxacarb, metoxadiazone, milbemycin-A, pymetrozine, pyridalyl, pyriproxyfen, spinosad, sulfluramid, tolfenpyrad, triazamate, flubendiamide, lepimectin, Arsenic acid, benclothiaz, Calcium cyanamide, Calcium polysulfide, chlordane, DDT, DSP, flufenerim, flonicamid, flurimfen, formetanate, metam-ammonium, metam-sodium, Methyl bromide, nidinotefuran, Potassium oleate, protrifenbute, spiromesifen, Sulfur, metaflumizone, spirotetramat, pyrifluquinazone, spinetoram, chlorantraniliprole and cyantraniliprole.

Examples of active ingredients of acaricides include acequinocyl, amitraz, benzoximate, bifenaate, bromopropylate, chinomethionat, chlorobenzilate, CPCBS (chlorfenson), clofentezine, cyflumetofen, kelthane (dicofol), etoxazole, fenbutatin oxide, fenothiocarb, fenpyroximate, fluacrypyrim, fluproxyfen, hexythiazox, propargite: BPPS, polynactins, pyridaben, Pyrimidifen, tebufenpyrad, tetradifon, spirodiclofen, spiromesifen, spirotetramat, amidoflumet, and cyenopyrafen.

Examples of active ingredients of nematicides include DCIP, fosthiazate, levamisol hydrochloride, methylisothiocyanate; moraltel tartarate, and imicyafos.

The plant disease controlling method of the present invention has a step of applying a plant or soil with an effective amount of the compound of the present invention. The controlling method of the present invention is usually carried out by applying a plant or soil with the plant disease controlling composition of the present invention.

The amount of the plant disease controlling composition of the present invention when used in the plant disease controlling method of the present

invention varies depending on weather conditions, formulation form, application period, application method, application site, subject disease, subject crop and so on, and the amount of the compound of the present invention in the plant disease controlling composition of the present invention is usually 1 to 500 g, preferably 2 to 200 g per 1000 m^2. The emulsifiable concentrate, wettable powder, flowable and so on are usually diluted with water before application, and in this case, the concentration of the compound of the present invention after dilution is usually 0.0005 to 2 wt%, preferably 0.005 to 1 wt%, and the dust, granule and so on are usually used as they are without dilution. In treatment on seed, the amount of the compound of the present invention in the plant disease controlling composition of the present invention is usually 0.001 to 100 g, preferably 0.01 to 50 g based on 1 kg of the seed.

The plant disease controlling composition of the present invention can be used as a controlling composition for plant diseases in agricultural grounds such as field, paddy field, turf and orchard. The plant disease controlling composition of the present invention is able to control or prevent plant diseases caused by plant diseases in crop lands for cultivating the following "crops."

Agricultural crops: corn, rice, wheat, barley, rye, oat, sorghum, cotton, soybean, peanut, buckwheat, beet, rapeseed, sunflower, sugar cane, tobacco, etc.; vegetables: solanaceous vegetables (eggplant, tomato, bell pepper, pepper, potato, etc.), cucurbitaceous vegetables (cucumber, pumpkin, zucchini, water melon, melon, etc.), cruciferous vegetables (Japanese radish, white turnip, horseradish, kohlrabi, Chinese cabbage, cabbage, leaf mustard, broccoli, cauliflower, etc.), asteraceous vegetables (burdock, crown daisy, artichoke, lettuce, etc.), liliaceous vegetables (green onion, onion, garlic, and asparagus), ammiaceous vegetables (carrot, parsley, celery, parsnip, etc.), chenopodiaceous vegetables (spinach, Swiss chard, etc.), lamiaceous vegetables (Perilla frutescens, mint, basil, etc.),

strawberry, sweet potato, Dioscorea japonica, colocasia, etc.,

flowers;

foliage plants;

fruits: pomaceous fruits (apple, pear, Japanese pear, Chinese quince, quince, etc.), stone fleshy fruits (peach, plum, nectarine, Prunus mume, cherry fruit, apricot, prune, etc.), citrus fruits (Citrus unshiu, orange, lemon, rime, grapefruit, etc.), nuts (chestnuts, walnuts, hazelnuts, almond, pistachio, cashew nuts, macadamia nuts, etc.), berries (blueberry, cranberry, blackberry, raspberry, etc.), grape, persimon, olive, Japanese medlar, banana, coffee, date palm, coconuts, etc.,

trees other than fruit trees; tea, mulberry, flowering plant, roadside trees (ash, birch, dogwood, Eucalyptus, Ginkgo biloba, lilac, maple, Quercus, poplar, Judas tree, Liquidambar formosana, plane tree, zelkova, Japanese arborvitae, fir wood, hemlock, juniper, Pinus, Picea, and Taxus cuspidate), etc.

The aforementioned "crops" include crops, to which resistance to HPPD inhibitors such as isoxaflutole, ALS inhibitors such as imazethapyr and thifensulfuron-methyl, EPSP synthetase inhibitors, glutamine synthetase inhibitors, and herbicides such as bromoxynil, has been imparted by a classical breeding method or genetically engineering technology.

Examples of "crops" to which resistance is imparted by a classical breeding method include Clearfield (registered trademark) canola that is resistant to imidazolinone herbicides such as imazethapyr, and STS soybean that is resistant to sulfonylurea ALS inhibitory herbicides such as thifensulfuron-methyl. In addition, examples of "crops" to which resistance is imparted by genetic recombination include corn varieties resistant to glyphosate or glufosinate. Such corn varieties have already been on the market with product names such as "RoundupReady (registered trademark)" and "LibertyLink (registered

trademark)."

The aforementioned "crops" include genetically engineered crops produced using such genetic recombination techniques, which, for example, are able to synthesize selective toxins as known in genus Bacillus.

Examples of toxins expressed in such genetically engineered crops include: insecticidal proteins derived from *Bacillus cereus* or *Bacillus popilliae*; δ-endotoxins such as Cry1Ab, Cry1Ac, Cry1F, Cry1Fa2, Cry2Ab, Cry3A, Cry3Bb1 or Cry9C, derived from *Bacillus thuringiensis*; insecticidal proteins such as VIP1, VIP2, VIP3, or VIP3A; insecticidal proteins derived from nematodes; toxins generated by animals, such as scorpion toxin, spider toxin, bee toxin, or insect-specific neurotoxins; mold fungi toxins; plant lectin; agglutinin; protease inhibitors such as a trypsin inhibitor, a serine protease inhibitor, patatin, cystatin, or a papain inhibitor; ribosome-inactivating proteins (RIP) such as lycine, corn-RIP, abrin, luffin, saporin, or briodin; steroid-metabolizing enzymes such as 3-hydroxysteroid oxidase, ecdysteroid-UDP-glucosyl transferase, or cholesterol oxidase; an ecdysone inhibitor; HMG-COA reductase; ion channel inhibitors such as a sodium channel inhibitor or calcium channel inhibitor; juvenile hormone esterase; a diuretic hormone receptor; stilbene synthase; bibenzyl synthase; chitinase; and glucanase.

Moreover, toxins expressed in such genetically recombinant crops also include: hybrid toxins of δ-endotoxin proteins such as Cry1Ab, Cry1Ac, Cry1F, Cry1Fa2, Cry2Ab, Cry3A, Cry3Bb1 or Cry9C, and insecticidal proteins such as VIP1, VIP2, VIP3 or VIP3A; partially deleted toxins; and modified toxins. Such hybrid toxins are produced from a new combination of the different domains of such proteins, using a genetic recombination technique. As a partially deleted toxin, Cry1Ab comprising a deletion of a portion of an amino

acid sequence has been known. A modified toxin is produced by substitution of one or multiple amino acids of natural toxins.

Examples of such toxins and recombinant plants capable of synthesizing such toxins are described in EP-A-0 374 753, WO 93/07278, WO 95/34656, EP-A-0 427 529, EP-A-451 878, WO 03/052073, etc.

Toxins contained in such recombinant plants are able to impart resistance particularly to insect pests belonging to Coleoptera, Diptera and Lepidoptera, to the plants.

Furthermore, genetically recombinant plants, which comprise one or multiple insecticidal pest-resistant genes and which express one or multiple toxins, have already been known, and some of such genetically recombinant plants have already been on the market. Examples of such genetically recombinant plants include YieldGard (registered trademark) (a corn variety for expressing Cry1Ab toxin), YieldGard Rootworm (registered trademark) (a corn variety for expressing Cry3Bb1 toxin), YieldGard Plus (registered trademark) (a corn variety for expressing Cry1Ab and Cry3Bb1 toxins), Herculex I (registered trademark) (a corn variety for expressing phosphinotricine N-acetyl transferase (PAT) so as to impart resistance to Cry1Fa2 toxin and gluphosinate), NuCOTN33B (a cotton variety for expressing Cry1Ac toxin), Bollgard I (registered trademark) (a cotton variety for expressing Cry1Ac toxin), Bollgard II (registered trademark) (a cotton variety for expressing Cry1Ac and Cry2Ab toxins), VIPCOT (registered trademark) (a cotton variety for expressing VIP toxin), NewLeaf (registered trademark) (a potato variety for expressing Cry3A toxin), NatureGard (registered trademark) Agrisure (registered trademark) GT Advantage (GA21 glyphosate-resistant trait), Agrisure (registered trademark) CB Advantage (Bt11 corn borer (CB) trait), and Protecta (registered trademark).

The aforementioned "crops" also include crops produced using a genetic engineered technique, which have ability to generate antipathogenic substances having selective action.

A PR protein and the like have been known as such antipathogenic substances (PRPs, EP-A-0 392 225). Such antipathogenic substances and genetically recombinant crops that generate them are described in EP-A-0 392 225, WO 95/33818, EP-A-0 353 191, etc.

Examples of such antipathogenic substances expressed in genetically recombinant crops include: ion channel inhibitors such as a sodium channel inhibitor or a calcium channel inhibitor (KP1, KP4 and KP6 toxins, etc., which are produced by viruses, have been known); stilbene synthase; bibenzyl synthase; chitinase; glucanase; a PR protein; and antipathogenic substances generated by microorganisms, such as a peptide antibiotic, an antibiotic having a hetero ring, a protein factor associated with resistance to plant diseases (which is called a plant disease-resistant gene and is described in WO 03/000906).

As the plant diseases which can be controlled by the compound of the present invention, for example, plant diseases caused by mold fungi are mentioned. More specific examples include, but not limited to, the following diseases.

The plant disease controlling method of the present invention is carried out usually by using a plant disease controlling composition of the present invention according to the above-described method for application of the plant disease controlling composition of the present invention.

Rice plant: Magnaporthe grisea, Cochliobolus miyabeanus, Rhizoctonia solani, Gibberella fujikuroi, Sclerophthora macrospora; Wheats, barleys and oats: Erysiphe graminis, Fusarium graminearum, F. avenacerum, F. culmorum, Microdochium nivale, Puccinia striiformis, P. graminis, P. recondita, P. hordei,

Typhula sp.,Micronectriella nivalis, Ustilago tritici, U. nuda, Tilletia caries, Pseudocercosporella herpotrichoides, Rhynchosporium secalis, Septoria tritici, Leptosphaeria nodorum, Pyrenophora teres Drechsler, Gaeumannomyces graminis, Pyrenophora tritici-repentis; Citruses: Diaporthe citri, Elsinoe fawcetti, Penicillium digitatum, P. italicum; Apple: Monilinia mali, Valsa ceratosperma, Podosphaera leucotricha, Alternaria alternata apple pathotype, Venturia inaequalis, Glomerella cingulata; Pear: Venturia nashicola, V. pirina, Alternaria alternata Japanese pear pathotype, Gymnosporangium haraeanum; Peach: Monilinia fructicola, Cladosporium carpophilum, Phomopsis sp.; Grape: Elsinoe ampelina, Glomerella cingulata, Uncinula necator, Phakopsora ampelopsidis, Guignardia bidwellii, Plasmopara viticola; Persimmon: Gloeosporium kaki, Cercospora kaki, Mycosphaerella nawae; Gourds Colletotrichum lagenarium, Sphaerotheca fuliginea, Mycosphaerella melonis, Fusarium oxysporum, Pseudoperonospora cubensis, Phytophthora sp., Pythium sp.; Tomato: Alternaria solani, Cladosporium fulvum, Phytophthora infestans; Eggplant: Phomopsis vexans, Erysiphe cichoracearum; Brassica family Alternaria japonica, Cercosporella brassicae, Plasmodiophora parasitica, Peronospora parasitica; Welsh onion: Puccinia allii; Soya: Cercospora kikuchii, Elsinoe glycines, Diaporthe phaseolorum var. sojae, Phakopsora pachyrhizi; Kidney bean: Colletotrichum lindemthianum; Peanut: Cercospora personata, Cercospora arachidicola, Sclerotium rolfsii; Pea: Erysiphe pisi; Potato: Alternaria solani, Phytophthora infestans, Verticillium albo-atrum, V. dahliae, V. nigrescens; Strawberry: Sphaerotheca humuli; Tea crop: Exobasidium reticulatum, Elsinoe leucospila, Pestalotiopsis sp., Colletotrichum theae-sinensis; Tobacco: Alternaria longipes, Erysiphe cichoracearum, Colletotrichum tabacum, Peronospora tabacina, Phytophthora nicotianae; Suger beet: Cercospora beticola, Thanatephorus cucumeris, Thanatephorus cucumeris, Aphanomyces sochlioides; Rose: Diplocarpon rosae, Sphaerotheca pannosa; Crysanthemum: Septoria

chrysanthemi-indici, Puccinia horiana; Onion: Botrytis cinerea, B. byssoidea, B. squamosa, Botrytis alli; Various crops: Botrytis cinerea, Sclerotinia sclerotiorum; Radish: Alternaria brassicicola; Lawns: Sclerotinia homeocarpa, Rhizoctonia solani; and, Banana: Mycosphaerella fijiensis, Mycosphaerella musicola.

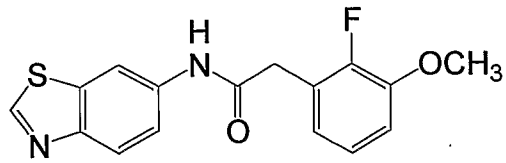
(Examples)

Production Examples, Preparation Examples and Test Examples of the present invention will be shown below.

Production Example 1

0.18 g of 6-aminobenzothiazol, 0.20 g of 2-fluoro-3-methoxyphenylacetic acid, 0.20 g of 1-hydroxybenzotriazole, 0.30 g of WSC and 0.30 g of pyridine were added to 2 ml of DMF, and the mixture was stirred at 140°C for 5 minutes, and at room temperature for 8 hours. To the reaction mixture was added water. The mixture was extracted with ethyl acetate. The organic layer obtained was washed sequentially with water and saturated saline solution, then, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue obtained was subjected to silica gel column chromatography, and 0.27 g of N-benzothiazol-6-yl-2-(2-fluoro-3-methoxyphenyl)acetamide (hereinafter, referred to as compound of the present invention (1)) was obtained.

Compound of the present invention (1)

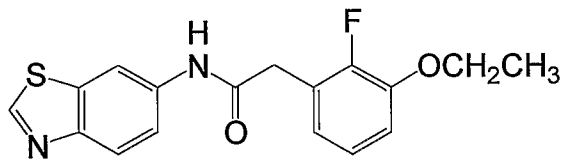


^{1}H-NMR ($CDCl_3$) δ: 3.80 (2H, d, J = 1.4 Hz), 3.91 (3H, s), 6.93-6.98 (2H, m), 7.09-7.14 (1H, m), 7.23-7.27 (1H, m), 7.47 (1H, br s), 8.00 (1H, d, J = 8.7 Hz), 8.50 (1H, d, J = 2.2 Hz), 8.91 (1H, s).

Production Example 2

To a mixture of 0.20 g of N-benzothiazol-6-yl-2-(2-fluoro-3-hydroxyphenyl)acetamide, 0.18 g of iodoethane and 7 ml of DMF was added 0.34 g of cesium carbonate. The mixture was stirred at room temperature for 4 hours. Ice water was added to the reaction mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated saline solution, then, dried over magnesium sulfate and concentrated under reduced pressure. 0.16 g of N-benzothiazol-6-yl-2-(2-fluoro-3-ethoxyphenyl)acetamide (hereinafter, referred to as compound of the present invention (2)) was obtained.

Compound of the present invention (2)

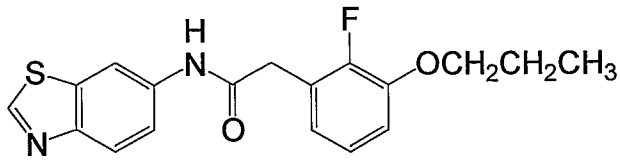


^{1}H-NMR (DMSO-D_6)δ: 1.34 (3H, t, J = 7.0 Hz), 3.76 (2H, s), 4.09 (2H, q, J = 7.0 Hz), 6.91-6.95 (1H, m), 7.05-7.07 (2H, m), 7.61 (1H, dd, J = 8.9, 2.1 Hz), 7.95 (1H, s), 8.02 (1H, d, J = 8.8 Hz), 8.52 (1H, d, J = 2.0 Hz), 9.26 (1H, s), 10.49 (1H, s).

Production Example 3

To a mixture of 0.20 g of N-benzothiazol-6-yl-2-(2-fluoro-3-hydroxyphenyl)acetamide, 0.15 g of iodopropane and 5 ml of DMF was added 0.26 g of cesium carbonate. The mixture was stirred at room temperature for 4 hours. Ice water was added to the reaction mixture, and the deposited solid was agglomerated, and 0.18 g of N-benzothiazol-6-yl-2-(2-fluoro-3-propoxyphenyl)acetamide (hereinafter, referred to as compound of the present invention (3)) was obtained.

Compound of the present invention (3)

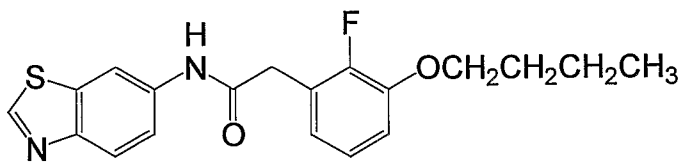


^{1}H-NMR (DMSO-D_6) δ: 0.98 (3H, t, J = 7.4 Hz), 1.70-1.79 (2H, m), 3.76 (2H, s), 3.99 (2H, t, J = 6.5 Hz), 6.90-6.96 (1H, m), 7.04-7.09 (2H, m), 7.60 (1H, dd, J = 8.8, 2.0 Hz), 8.02 (1H, d, J = 8.8 Hz), 8.52 (1H, d, J = 2.2 Hz), 9.26 (1H, s), 10.49 (1H, s).

Production Example 4

To a mixture of 0.20 g of N-benzothiazol-6-yl-2-(2-fluoro-3-hydroxyphenyl)acetamide, 0.22 g of iodobutane and 7 ml of DMF was added 0.37 g of cesium carbonate. The mixture was stirred at room temperature for 4 hours. Ice water was added to the reaction mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated saline solution, then, dried over magnesium sulfate and concentrated under reduced pressure. The resultant residue was washed with hexane, and 0.15 g of N-benzothiazol-6-yl-2-(2-fluoro-3-butoxyphenyl)acetamide (hereinafter, referred to as compound of the present invention (4)) was obtained.

Compound of the present invention (4)

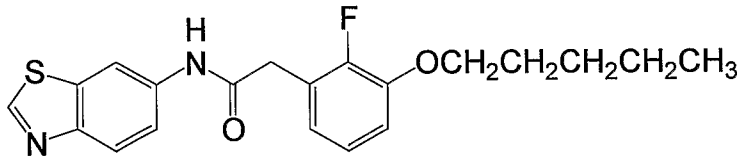


^{1}H-NMR (DMSO-D_6) δ: 0.93 (3H, t, J = 7.5 Hz), 1.39-1.49 (2H, m), 1.67-1.74 (2H, m), 3.76 (2H, s), 4.03 (2H, t, J = 6.3 Hz), 6.90-6.95 (1H, m), 7.03-7.09 (2H, m), 7.60 (1H, dd, J = 9.2, 1.7 Hz), 8.02 (1H, d, J = 8.7 Hz), 8.52 (1H, d, J = 1.7 Hz), 9.26 (1H, s), 10.48 (1H, s).

Production Example 5

To a mixture of 0.20 g of N-benzothiazol-6-yl-2-(2-fluoro-3-hydroxy-phenyl)acetamide, 0.17 g of iodopentane and 5 ml of DMF was added 0.26 g of cesium carbonate. The mixture was stirred at room temperature for 4 hours. Ice water was added to the reaction mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated saline solution, then, dried over magnesium sulfate and concentrated under reduced pressure. The resultant residue was washed with hexane, and 0.15 g of N-benzothiazol-6-yl-2-(2-fluoro-3-pentyloxyphenyl)acetamide (hereinafter, referred to as compound of the present invention (5)) was obtained.

Compound of the present invention (5)

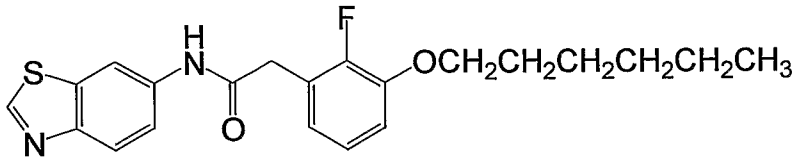


^{1}H-NMR (DMSO-D_6) δ: 0.89 (3H, t, J = 6.8 Hz), 1.30-1.45 (4H, m), 1.69-1.77 (2H, m), 3.76 (2H, s), 4.03 (2H, t, J = 6.4 Hz), 6.90-6.97 (1H, m), 7.04-7.10 (2H, m), 7.61 (1H, d, J = 8.7 Hz), 8.02 (1H, d, J = 8.9 Hz), 8.53 (1H, s), 9.26 (1H, s), 10.48 (1H, s).

Production Example 6

To a mixture of 0.20 g of N-benzothiazol-6-yl-2-(2-fluoro-3-hydroxy-phenyl)acetamide, 0.22 g of 1-bromohexane and 5 ml of DMF was added 0.43 g of cesium carbonate. The mixture was stirred at room temperature for 4 hours. Ice water was added to the reaction mixture was added, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated saline, then, dried over magnesium sulfate and concentrated under reduced pressure. The resultant residue was washed with hexane, and 0.14 g of N-benzothiazol-6-yl-2-(2-fluoro-3-hexyloxyphenyl)acetamide (hereinafter, referred to as compound of the present invention (6)) was obtained.

Compound of the present invention (6)

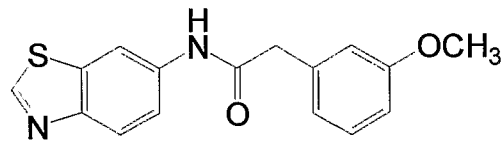


^{1}H-NMR (DMSO-D_6)δ: 0.87 (3H, t, J = 7.0 Hz), 1.26-1.34 (4H, m), 1.37-1.46 (2H, m), 1.67-1.76 (2H, m), 3.76 (2H, s), 4.02 (2H, t, J = 6.5 Hz), 6.89-6.96 (1H, m), 7.03-7.09 (2H, m), 7.60 (1H, dd, J = 8.8, 2.1 Hz), 8.02 (1H, d, J = 8.7 Hz), 8.52 (1H, d, J = 2.2 Hz), 9.26 (1H, s), 10.48 (1H, s).

Production Example 7

To 2 ml of DMF, 0.15 g of 6-aminobenzothiazol, 0.20 g of 3-methoxyphenylacetic acid, 0.15 g of 1-hydroxybenzotriazole, 0.25 g of WSC and 0.35 g of pyridine were added, and the mixture was stirred at 140°C for 5 minutes, and at room temperature for 8 hours. To the reaction mixture was added water. The generated solid was agglomerated. The resultant solid was washed sequentially with water, sodium bicarbonate aqueous solution, MTBE and hexane, and 0.25 g of N-(benzothiazol-6-yl-)-2-(3-methoxyphenyl)acetamide (hereinafter, referred to as compound of the present invention (7)) was obtained.

Compound of the present invention (7)



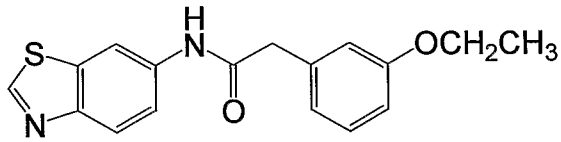
^{1}H-NMR ($CDCl_3$) δ: 3.77 (2H, s), 3.84 (3H, s), 6.88-6.96 (3H, m), 7.19 (1H, dd, J = 8.9, 2.1 Hz), 7.27-7.38 (2H, m), 7.99 (1H, d, J = 8.9 Hz), 8.49 (1H, d, J = 2.1 Hz), 8.90 (1H, s).

Production Example 8

To a mixture of 0.20 g of

N-benzothiazol-6-yl-2-(3-hydroxyphenyl)acetamide, 0.14 g of 1-iodoethane and 5 ml of DMF was added 0.28 g of cesium carbonate. The mixture was stirred at room temperature for 2.5 hours. To the reaction mixture was added water. The deposited solid was agglomerated, and washed sequentially with a sodium hydroxide aqueous solution, water and hexane, and 0.17 g of N-benzothiazol-6-yl-2-(3-ethoxyphenyl)acetamide (hereinafter, referred to as compound of the present invention (8)) was obtained.

Compound of the present invention (8)

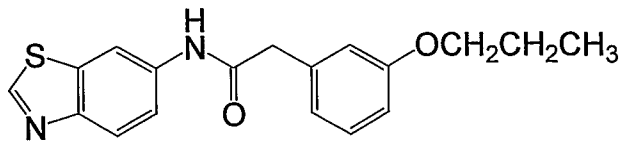


^{1}H-NMR ($CDCl_3$) δ: 1.43 (3H, t, J = 7.0 Hz), 3.75 (2H, s), 4.05 (2H, q, J = 7.0 Hz), 6.88-6.93 (3H, m), 7.18 (1H, dd, J = 8.8, 2.1 Hz), 7.23 (1H, s), 7.33 (1H, dd, J = 8.9, 7.5 Hz), 7.98 (1H, d, J = 8.7 Hz), 8.50 (1H, d, J = 2.2 Hz), 8.90 (1H, s).

Production Example 9

To a mixture of 0.20 g of N-benzothiazol-6-yl-2-(3-hydroxyphenyl)acetamide, 0.11 g of 1-bromopropane and 5 ml of DMF was added 0.28 g of cesium carbonate. The mixture was stirred at room temperature for 4 hours. To the reaction mixture was added water. The deposited solid was agglomerated, and washed sequentially with a sodium hydroxide aqueous solution, water and hexane, and 0.13 g of N-benzothiazol-6-yl-2-(3-propoxyphenyl)acetamide (hereinafter, referred to as compound of the present invention (9)) was obtained.

Compound of the present invention (9)

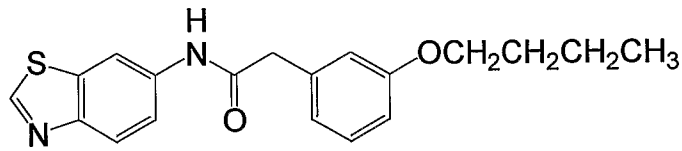


^{1}H-NMR ($CDCl_3$) δ: 1.05 (3H, t, J = 7.5 Hz), 1.78-1.87 (2H, m), 3.76 (2H, s), 3.94 (2H, t, J = 6.5 Hz), 6.89-6.93 (3H, m), 7.18 (1H, dd, J = 8.8, 2.1 Hz), 7.28 (1H, s), 7.31-7.35 (1H, m), 7.99 (1H, d, J = 8.9 Hz), 8.49 (1H, d, J = 2.2 Hz), 8.90 (1H, s).

Production Example 10

To a mixture of 0.20 g of N-benzothiazol-6-yl-2-(3-hydroxyphenyl)-acetamide, 0.13 g of 1-bromobutane and 5 ml of DMF was added 0.28 g of cesium carbonate. The mixture was stirred at room temperature for 5 hours. To the reaction mixture was added water. The deposited solid was agglomerated, and washed sequentially with a sodium hydroxide aqueous solution, water and hexane, and 0.15 g of N-benzothiazol-6-yl-2-(3-butoxy-phenyl)acetamide (hereinafter, referred to as compound of the present invention (10)) was obtained.

Compound of the present invention (10)



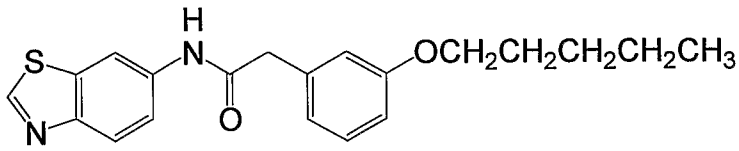
^{1}H-NMR ($CDCl_3$) δ: 0.98 (3H, t, J = 7.3 Hz), 1.45-1.55 (2H, m), 1.74-1.81 (2H, m), 3.76 (2H, s), 3.98 (2H, t, J = 6.5 Hz), 6.88-6.93 (3H, m), 7.18 (1H, dd, J = 8.8, 2.2 Hz), 7.23 (1H, s), 7.33 (1H, dd, J = 9.0, 7.6 Hz), 7.99 (1H, d, J = 8.8 Hz), 8.50 (1H, d, J = 2.0 Hz), 8.90 (1H, s).

Production Example 11

To a mixture of 0.20 g of N-benzothiazol-6-yl-2-(3-hydroxyphenyl)-acetamide, 0.18 g of 1-iodopentane and 5 ml of DMF was added 0.28 g of cesium carbonate. The mixture was stirred at room temperature for 4 hours. To the reaction mixture was added water. The deposited solid was

agglomerated, and washed sequentially with a sodium hydroxide aqueous solution, water and hexane, and 0.18 g of N-benzothiazol-6-yl-2-(3-pentyloxy-phenyl)acetamide (hereinafter, referred to as compound of the present invention (11)) was obtained.

Compound of the present invention (11)

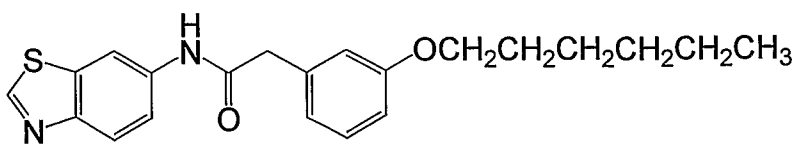


^{1}H-NMR ($CDCl_3$) δ: 0.93 (3H, t, J = 7.0 Hz), 1.34-1.48 (4H, m), 1.76-1.83 (2H, m), 3.75 (2H, s), 3.97 (2H, t, J = 6.6 Hz), 6.88-6.92 (3H, m), 7.17-7.20 (1H, m), 7.23 (1H, s), 7.31-7.35 (1H, m), 7.98 (1H, d, J = 8.7 Hz), 8.50 (1H, s), 8.90 (1H, s).

Production Example 12

To a mixture of 0.20 g of N-benzothiazol-6-yl-2-(3-hydroxyphenyl)acetamide, 0.15 g of 1-bromohexane and 5 ml of DMF was added 0.28 g of cesium carbonate. The mixture was stirred at room temperature for 4 hours. To the reaction mixture was added water. The deposited solid was agglomerated, and washed sequentially with a sodium hydroxide aqueous solution, water and hexane, and 0.17 g of N-benzothiazol-6-yl-2-(3-hexyloxyphenyl)acetamide (hereinafter, referred to as compound of the present invention (12)) was obtained.

Compound of the present invention (12)



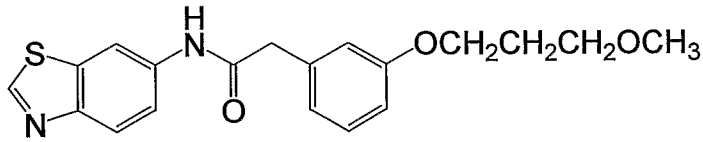
^{1}H-NMR ($CDCl_3$) δ: 0.89-0.92 (3H, m), 1.32-1.36 (4H, m), 1.43-1.50 (2H, m), 1.75-1.82 (2H, m), 3.76 (2H, s), 3.97 (2H, t, J = 6.6 Hz), 6.88-6.93 (3H, m), 7.18

(1H, dd, J = 8.8, 2.1 Hz), 7.29 (1H, s), 7.33 (1H, dd, J = 8.9, 7.5 Hz), 7.99 (1H, d, J = 8.7 Hz), 8.49 (1H, d, J = 1.9 Hz), 8.90 (1H, s).

Production Example 13

To a mixture of 0.20 g of N-benzothiazol-6-yl-2-(3-hydroxyphenyl)-acetamide, 0.14 g of 1-bromo-3-methoxypropane and 5 ml of DMF was added 0.28 g of cesium carbonate. The mixture was stirred at room temperature for 5.5 hours. To the reaction mixture was added water. The deposited solid was agglomerated, and washed sequentially with a sodium hydroxide aqueous solution, water and hexane, and 0.17 g of N-benzothiazol-6-yl-2-(3-(3-methoxy-propoxy)phenyl)acetamide (hereinafter, referred to as compound of the present invention (13)) was obtained.

Compound of the present invention (13)



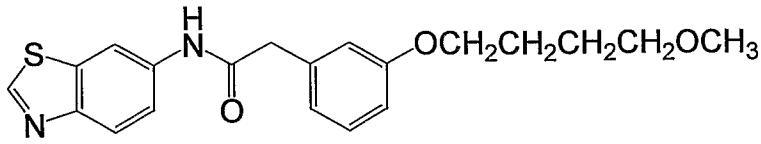
^{1}H-NMR ($CDCl_3$) δ: 2.03-2.09 (2H, m), 3.35 (3H, s), 3.56 (2H, t, J = 6.1 Hz), 3.75 (2H, s), 4.08 (2H, t, J = 6.3 Hz), 6.89-6.94 (3H, m), 7.19 (1H, dd, J = 8.8, 2.2 Hz), 7.29 (1H, s), 7.33 (1H, dd, J = 9.0, 7.6 Hz), 7.99 (1H, d, J = 8.5 Hz), 8.49 (1H, d, J = 2.0 Hz), 8.90 (1H, s).

Production Example 14

To a mixture of 0.20 g of N-benzothiazol-6-yl-2-(3-hydroxyphenyl)-acetamide, 0.17 g of 4-methoxybutyl methanesulfonate and 5 ml of DMF was added 0.28 g of cesium carbonate. The mixture was stirred at room temperature for 7.5 hours. To the reaction mixture was added water. The deposited solid was agglomerated, and washed sequentially with a sodium hydroxide aqueous solution, water and hexane, and 0.091 g of N-benzothiazol-6-yl-2-(3-(4-methoxy-

butoxy)phenyl)acetamide (hereinafter, referred to as compound of the present invention (14)) was obtained.

Compound of the present invention (14)

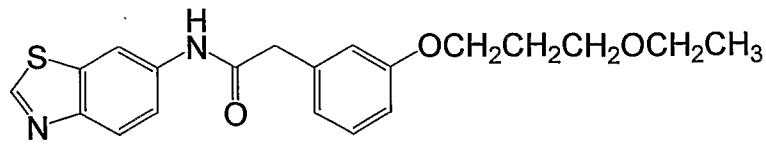


^{1}H-NMR ($CDCl_3$) δ: 1.73-1.79 (2H, m), 1.84-1.91 (2H, m), 3.35 (3H, s), 3.45 (2H, t, J = 6.3 Hz), 3.75 (2H, s), 4.01 (2H, t, J = 6.2 Hz), 6.88-6.93 (3H, m), 7.19 (1H, dd, J = 8.8, 2.0 Hz), 7.28 (1H, s), 7.31-7.35 (1H, m), 7.99 (1H, d, J = 8.8 Hz), 8.49 (1H, d, J = 1.5 Hz), 8.90 (1H, s).

Production Example 15

To a mixture of 0.20 g of N-benzothiazol-6-yl-2-(3-hydroxyphenyl)-acetamide, 0.17 g of 3-ethoxypropyl methanesulfonate and 5 ml of DMF was added 0.28 g of cesium carbonate. The mixture was stirred at room temperature for 7.5 hours. To the reaction mixture was added water. The deposited solid was agglomerated, and washed sequentially with a sodium hydroxide aqueous solution, water and hexane, and 0.087 g of N-benzothiazol-6-yl-2-(3-(3-ethoxypropoxy)phenyl)acetamide (hereinafter, referred to as compound of the present invention (15)) was obtained.

Compound of the present invention (15)

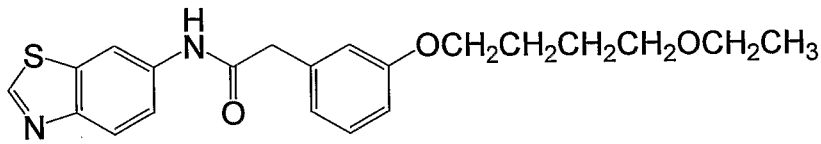


^{1}H-NMR ($CDCl_3$) δ: 1.20 (3H, t, J = 7.0 Hz), 2.03-2.09 (2H, m), 3.50 (2H, q, J = 7.0 Hz), 3.60 (2H, t, J = 6.1 Hz), 3.75 (2H, s), 4.09 (2H, t, J = 6.2 Hz), 6.90-6.93 (3H, m), 7.18 (1H, d, J = 9.0 Hz), 7.27 (1H, s), 7.33 (1H, t, J = 8.0 Hz), 7.99 (1H, d, J = 8.5 Hz), 8.49 (1H, s), 8.90 (1H, s).

Production Example 16

To a mixture of 0.20 g of N-benzothiazol-6-yl-2-(3-hydroxyphenyl)-acetamide, 0.25 g of 4-ethoxybutyl p-toluenesulfonate and 5 ml DMF was added 0.28 g of cesium carbonate. The mixture was stirred at room temperature for 4 hours. To the reaction mixture was added water. The deposited solid was agglomerated, and washed sequentially with a sodium hydroxide aqueous solution, water and hexane, and 0.080 g N-benzothiazol-6-yl-2-(3-(4-ethoxybutoxy)phenyl)acetamide (hereinafter, referred to as compound of the present invention (16)) was obtained.

Compound of the present invention (16)



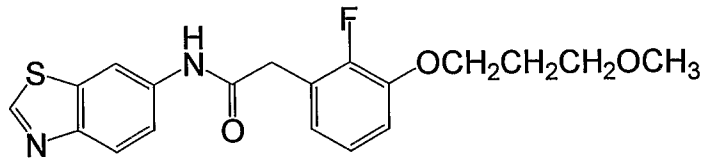
^{1}H-NMR ($CDCl_3$) δ: 1.20 (3H, t, J = 7.0 Hz), 1.73-1.80 (2H, m), 1.85-1.91 (2H, m), 3.46-3.51 (4H, m), 3.76 (2H, s), 4.01 (2H, t, J = 6.4 Hz), 6.88-6.93 (3H, m), 7.18 (1H, dd, J = 8.9, 2.2 Hz), 7.27 (1H, s), 7.33 (1H, dd, J = 9.1, 7.6 Hz), 7.99 (1H, d, J = 8.9 Hz), 8.49 (1H, d, J = 1.9 Hz), 8.90 (1H, s).

Production Example 17

To a mixture of 0.20 g of N-benzothiazol-6-yl-2-(2-fluoro-3-hydroxy-phenyl)acetamide, 0.20 g of 1-bromo-3-methoxypropane and 5 ml of DMF was added 0.43 g of cesium carbonate. The mixture was stirred at room temperature for 4 hours. Ice water was added to the reaction mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated saline solution, then, dried over magnesium sulfate and concentrated under reduced pressure. The resultant residue was subjected to silica gel column chromatography, 0.10 g of N-benzothiazol-6-yl-2-(2-fluoro-3-(3-methoxy-

propoxy)phenyl)acetamide (hereinafter, referred to as compound of the present invention (17)).

Compound of the present invention (17)

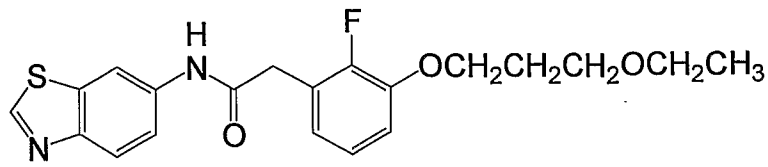


^{1}H-NMR (DMSO-D_6) δ: 1.92-1.99 (2H, m), 3.25 (3H, s), 3.47 (2H, t, J = 6.3 Hz), 3.76 (2H, s), 4.08 (2H, t, J = 6.3 Hz), 6.91-6.97 (1H, m), 7.04-7.10 (2H, m), 7.61 (1H, dd, J = 8.8, 2.1 Hz), 8.02 (1H, d, J = 8.9 Hz), 8.53 (1H, d, J = 1.9 Hz), 9.26 (1H, s), 10.49 (1H, s).

Production Example 18

To a mixture of 0.20 g of N-benzothiazol-6-yl-2-(2-fluoro-3-hydroxy-phenyl)acetamide, 0.22 g of 3-ethoxypropyl methanesulfonate and 7 ml of DMF was added 0.37 g of cesium carbonate. The mixture was stirred at room temperature for 4 hours. Ice water was added to the reaction mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated saline solution, then, dried over magnesium sulfate and concentrated under reduced pressure. The resultant residue was subjected to silica gel column chromatography and concentrated to obtain a residue which was washed with MTBE, and 0.09 g of N-benzothiazol-6-yl-2-(2-fluoro-3-(3-ethoxy-propoxy)phenyl)acetamide (hereinafter, referred to as compound of the present invention (18)) was obtained.

Compound of the present invention (18)



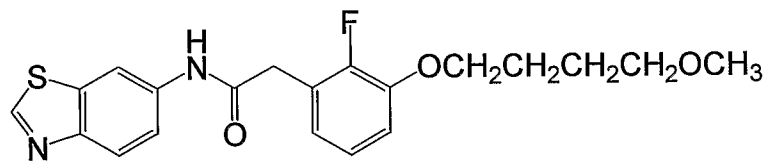
^{1}H-NMR (DMSO-D_6) δ: 1.10 (3H, t, J = 6.5 Hz), 1.91-1.99 (2H, m), 3.42 (2H, q,

J = 7.0 Hz), 3.51 (2H, t, J = 6.3 Hz), 3.76 (2H, s), 4.09 (2H, t, J = 6.2 Hz), 6.91-6.96 (1H, m), 7.04-7.10 (2H, m), 7.60 (1H, d, J = 8.9 Hz), 8.02 (1H, d, J = 8.7 Hz), 8.53 (1H, s), 9.26 (1H, s), 10.48 (1H, s).

Production Example 19

To a mixture of 0.20 g of N-benzothiazol-6-yl-2-(2-fluoro-3-hydroxyphenyl)acetamide, 0.22 g of 4-methoxybutyl methanesulfonate and 7 ml of DMF was added 0.37 g of cesium carbonate. The mixture was stirred at room temperature for 4 hours. Ice water was added to the reaction mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated saline solution, then, dried over magnesium sulfate and concentrated under reduced pressure. The resultant residue was washed with hexane, and 0.16 g of N-benzothiazol-6-yl-2-(2-fluoro-3-(4-methoxybutoxy)phenyl)acetamide (hereinafter, referred to as compound of the present invention (19)) was obtained.

Compound of the present invention (19)



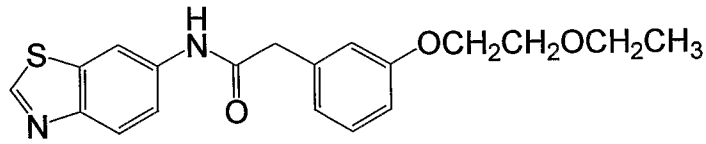
1H-NMR (DMSO-D_6) δ: 1.60-1.70 (2H, m), 1.72-1.80 (2H, m), 3.23 (3H, s), 3.37 (2H, t, J = 6.3 Hz), 3.76 (2H, s), 4.04 (2H, t, J = 6.3 Hz), 6.90-6.97 (1H, m), 7.04-7.10 (2H, m), 7.60 (1H, dd, J = 8.7, 1.9 Hz), 8.02 (1H, d, J = 8.9 Hz), 8.53 (1H, s), 9.26 (1H, s), 10.47 (1H, s).

Production Example 20

To a mixture of 0.20 g of N-benzothiazol-6-yl-2-(3-hydroxyphenyl)acetamide, 0.25 g of 1-bromo-2-ethoxyethane and 5 ml of DMF was added 0.52 g of cesium carbonate. The

mixture was stirred at 60°C for 2 hours. The reaction mixture was cooled down to room temperature, then, ice water was added and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated saline solution, then, dried over magnesium sulfate and concentrated under reduced pressure. The resultant residue was subjected to silica gel column chromatography, and 0.12 g of N-benzothiazol-6-yl-2-(2-ethoxyethoxyphenyl)acetamide (hereinafter, referred to as compound of the present invention (20)) was obtained.

Compound of the present invention (20)



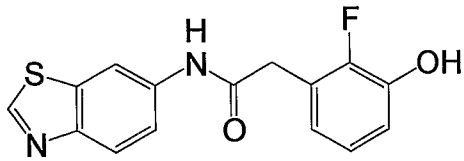
1H-NMR (CDCl3) δ: 1.23 (3H, t, J = 6.9 Hz), 3.60 (2H, q, J = 7.0 Hz), 3.71 (2H, s), 3.79 (2H, t, J = 4.8 Hz), 4.11 (2H, t, J = 4.8 Hz), 6.86-6.92 (3H, m), 7.23 (1H, dd, J = 8.7, 1.9 Hz), 7.26-7.31 (1H, m), 7.73 (1H, s), 7.96 (1H, d, J = 8.7 Hz), 8.47 (1H, d, J = 2.2 Hz), 8.88 (1H, s).

Next, synthesis examples are shown for production of the amide compound of the present invention.

Synthesis Example 1

A mixture of 5.8 g of N-benzothiazol-6-yl-2-(2-fluoro-3-(tert-butyldimethyl-silyloxy)phenyl)acetamide, 1.8 g of lithium hydroxide monohydrate and 60 ml of DMF was stirred at room temperature for 5 hours. To the reaction mixture was added ice water. The mixture was washed with MTBE. To the aqueous layer was added 2N hydrochloric acid to adjust pH to around 2, and extracted with ethyl acetate. The organic layer was washed with saturated saline solution, then, dried over magnesium sulfate and concentrated under reduced pressure. The resultant residue was washed with hexane, and 3.4 g of N-benzothiazol-6-yl-2-(2-fluoro-3-hydroxyphenyl)acetamide was obtained.

N-benzothiazol-6-yl-2-(2-fluoro-3-hydroxyphenyl)acetamide

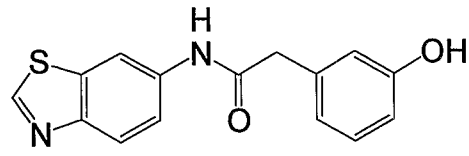


^{1}H-NMR (DMSO-D_6) δ: 3.73 (2H, s), 6.75-6.95 (3H, m), 7.61 (1H, dd, J = 8.8, 1.6 Hz), 8.02 (1H, d, J = 8.7 Hz), 8.53 (1H, d, J = 1.9 Hz), 9.26 (1H, s), 9.75 (1H, s), 10.46 (1H, s).

Synthesis Example 2

A mixture of 7.8 g of 3-tert-butyldimethylsilyloxyphenylacetic acid, 4.0 g of 6-aminobenzothiazol, 7.4 ml of triethylamine, 14 g of BOP reagent and 150 ml of DMF was stirred at room temperature for 3 hours. To the reaction mixture was added 3% hydrochloric acid, and the mixture was extracted with ethyl acetate. The obtained organic layer was washed with 3% hydrochloric acid, water, saturated sodium bicarbonate aqueous solution and saturated saline solution, then, dried over anhydrous magnesium sulfate and concentrated under reduced pressure. Next, a mixture of the obtained residue, 3.4 g of lithium hydroxide monohydrate and 100 ml of DMF was stirred at room temperature for 5 hours. To the reaction mixture was added water. The mixture was washed with MTBE. To the aqueous layer was added 2N hydrochloric acid to adjust pH to around 2, and extracted with ethyl acetate. The organic layer was washed with saturated saline solution, then, dried over magnesium sulfate and concentrated under reduced pressure. The resultant residue was washed with hexane, and 6.8g of N-benzothiazol-6-yl-2-(3-hydroxyphenyl)acetamide.

N-benzothiazol-6-yl-2-(3-hydroxyphenyl)acetamide



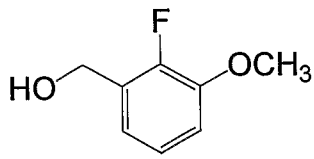
^{1}H-NMR (DMSO-D_6) δ: 3.58 (2H, s), 6.63-6.65 (1H, m), 6.75-6.77 (2H, m), 7.11 (1H, t, J = 7.9 Hz), 7.59-7.61 (1H, m), 8.01 (1H, d, J = 8.8 Hz), 8.54 (1H, s), 9.25 (1H, s), 9.34 (1H, s), 10.41 (1H, s).

Next, reference production examples are shown for production of a production intermediate of the compound of the present invention.

Reference Production Example 1

A mixture of 20 g of 2-fluoro-3-methoxybenzaldehyde, 2.4 g of sodium borohydride and 200 ml of methanol was stirred at room temperature for 30 minutes. To the reaction mixture was added water and 5% hydrochloric acid sequentially. The mixture was extracted with ethyl acetate. The organic layer was washed with saturated saline solution, then, dried over magnesium sulfate and concentrated under reduced pressure, and 20 g of (2-fluoro-3-methoxyphenyl)methanol was obtained.

(2-fluoro-3-methoxyphenyl)methanol



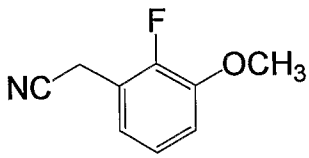
^{1}H-NMR ($CDCl_3$) δ: 3.89 (3H, s), 4.76 (2H, s), 6.92 (1H, td, J = 8.1, 1.6 Hz), 6.97-7.01 (1H, m), 7.08 (1H, td, J = 7.9, 1.4 Hz).

Reference Production Example 2

To a mixture of 20 g of (2-fluoro-3-methoxyphenyl)methanol, 16 g of methanesulfonyl chloride and 200 ml of THF was mixed 22 ml of triethylamine, and the mixture was stirred at 0°C for 30 minutes. To the reaction mixture was added water and 5% hydrochloric acid sequentially. The mixture was extracted with ethyl acetate. The organic layer was washed with saturated saline solution, then, dried over magnesium sulfate and concentrated under reduced pressure.

The obtained residue and 200 ml of DMF, 50 ml of water and 8.3 g of sodium cyanide were mixed, and heated under reflux for 8 hours. To the reaction mixture allowed to cool to around room temperature was added water. The mixture was extracted with ethyl acetate. The organic layer was washed with water twice and with 5% hydrochloric acid and saturated saline solution sequentially, then, dried over magnesium sulfate and concentrated under reduced pressure. The resultant residue was subjected to silica gel column chromatography, and 12g of (2-fluoro-3-methoxyphenyl)acetonitrile was obtained.

(2-fluoro-3-methoxyphenyl)acetonitrile

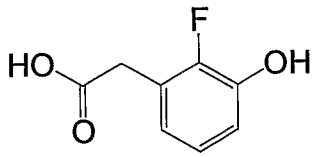


^{1}H-NMR ($CDCl_3$) δ: 3.77 (2H, s), 3.90 (3H, s), 6.94-7.03 (2H, m), 7.11 (1H, td, J = 8.0, 1.5 Hz).

Reference Production Example 3

To 10 g of (2-fluoro-3-methoxyphenyl)acetonitrile was added 100 ml of 48% hydrobromic acid. The mixture was heated under reflux for 4 hours. To the reaction mixture was added 20 ml of 48% hydrobromic acid. The mixture was heated under reflux for 4 hours. The reaction mixture allowed to cool to around room temperature was concentrated under reduced pressure, and ethyl acetate and hexane were added, and the mixed liquid was filtrated. The filtrate was concentrated under reduced pressure, and 9.3g of 2-fluoro-3-hydroxyphenyl-acetic acid was obtained.

2-fluoro-3-hydroxyphenylacetic acid

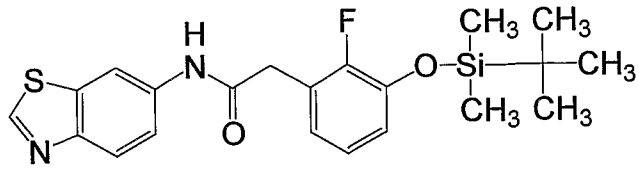


^{1}H-NMR (DMSO-D_6) δ: 3.56 (2H, s), 6.68-6.72 (1H, m), 6.82-6.92 (2H, m), 9.73 (1H, s), 12.40 (1H, s).

Reference Production Example 4

9.2 g of 2-fluoro-3-hydroxyphenylacetic acid, 19 g of tert-butyldimethylsilyl chloride, 11 g of imidazole and 150 ml of DMF were mixed, and the mixture was stirred at room temperature for 8 hours. To the reaction mixture was added water, and the mixture was extracted with ethyl acetate. The obtained organic layer was washed with a saturated ammonium chloride aqueous solution, saturated sodium bicarbonate aqueous solution and saturated saline solution, then, dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The resultant residue was subjected to silica gel column chromatography. Next, 8.8 g of the resultant residue, 6.0 g of 6-aminobenzothiazol, 13 ml of triethylamine, 18 g of BOP reagent and 100 ml of DMF were mixed, and the mixture was stirred at room temperature for 8 hours. To the reaction mixture was added water. The mixture was extracted with ethyl acetate. The resultant organic layer was washed sequentially with water and saturated saline, then, dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The resultant residue was subjected to silica gel column chromatography, and 5.8 g of N-benzothiazol-6-yl-2-(2-fluoro-3-(tert-butyldimethylsilyloxy)phenyl)acetamide.

N-benzothiazol-6-yl-2-(2-fluoro-3-(tert-butyldimethylsilyloxy)phenyl)-acetamide

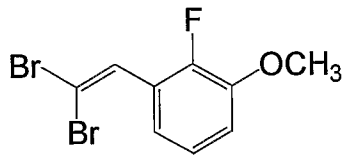


^{1}H-NMR ($CDCl_3$) δ: 0.21 (6H, s), 1.01 (9H, s), 3.78 (2H, d, J = 1.5 Hz), 6.89-6.97 (2H, m), 7.01-7.05 (1H, m), 7.22 (1H, dd, J = 8.8, 2.2 Hz), 7.42 (1H, s), 8.00 (1H, d, J = 8.8 Hz), 8.51 (1H, d, J = 2.0 Hz), 8.90 (1H, s).

Reference Production Example 5

Into a mixture of 3.0 g of 2-fluoro-3-methoxybenzaldehyde and 150 ml of chloroform, 9.7 g of carbon tetrabromide and a triphenylphosphine chloroform solution (solution composed of 15.3 g of triphenylphosphine and 150 ml of chloroform) were dropped at 0°C sequentially, and the mixture was stirred at room temperature for 1 day. The reaction mixture was filtrated through Celite (registered trademark), and the filtrate was concentrated under reduced pressure. The resultant residue was subjected to silica gel column chromatography, and 6.1 g of methyl (2-fluoro-3-(2,2-dibromoethenyl)phenyl) ether was obtained.

Methyl (2-fluoro-3-(2,2-dibromoethenyl)phenyl) ether



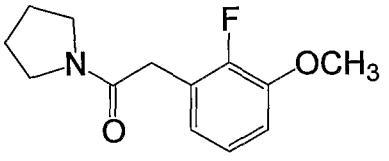
^{1}H-NMR ($CDCl_3$) δ: 3.89 (3H, s), 6.93-6.99 (1H, m), 7.04-7.10 (1H, m), 7.26-7.31 (1H, m), 7.53-7.55 (1H, m).

Reference Production Example 6

6.1 g of methyl (2-fluoro-3-(2,2-dibromoethenyl)phenyl) ether and 4 ml of water were added to 40 ml of pyrrolidine, and the mixture was stirred at room temperature for 1 day. The reaction mixture was concentrated under reduced pressure. To the residue was added dilute hydrochloric acid. The acid added

residue was extracted with ethyl acetate. The organic layer was washed sequentially with water and saturated saline solution, dried over anhydrous magnesium sulfate, then, concentrated under reduced pressure, and 4.5 g of N-(2-(2-fluoro-3-methoxyphenyl)acetyl)pyrrolidine was obtained.

N-(2-(2-fluoro-3-methoxyphenyl)acetyl)pyrrolidine

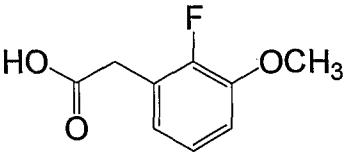


^{1}H-NMR ($CDCl_3$)δ: 1.41-1.62 (2H, m), 1.81-1.98 (2H, m), 3.37-3.59 (4H, m), 3.65-3.74 (2H, m), 3.88 (3H, s), 6.84-6.95 (2H, m), 6.99-7.05 (1H, m).

Reference Production Example 7

4.5 g of N-(2-(2-fluoro-3-methoxyphenyl)acetyl)pyrrolidine, 3.0 g of 10N hydrochloric acid and 12 g of water were added to 15 ml of 1,4-dioxane, and the mixture was heated under reflux for 18 hours. The reaction mixture allowed to cool to around room temperature was extracted with ethyl acetate, and the organic layer was extracted with a sodium hydroxide aqueous solution. To the resultant aqueous layer was added hydrochloric acid to make it acidic, and the mixture was extracted with chloroform. The obtained organic layer was dried over anhydrous magnesium sulfate and concentrated under reduced pressure, and the resultant residue was washed with hexane, and 1.8 g of 2-fluoro-3-methoxyphenylacetic acid was obtained.

2-fluoro-3-methoxyphenylacetic acid

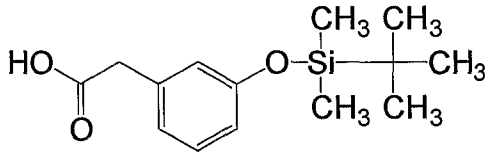


^{1}H-NMR ($CDCl_3$)δ: 3.71 (2H, d, J = 1.7 Hz), 3.88 (3H, s), 6.81-6.85 (1H, m), 6.88-6.93 (1H, m), 7.01-7.06 (1H, m).

Reference Production Example 8

A mixture of 10 g of 3-hydroxyphenylacetic acid, 26 g of tert-butyldimethylsilyl chloride, 27 g of potassium carbonate and 200 ml of DMF was stirred at room temperature for 2 hours, then, at 80°C for 4 hours. To the reaction mixture allowed to cool to around room temperature was added water. The mixture was washed with MTBE. Then, to the aqueous layer was added 5% hydrochloric acid to adjust pH to 3. The acid added aqueous layer was extracted with ethyl acetate. The organic layer was washed with saturated saline solution, then, dried over magnesium sulfate and concentrated under reduced pressure. The resultant residue was washed with hexane, and 15 g of 3-tert-butyldimethylsilyloxyphenylacetic acid.

3-tert-butyldimethylsilyloxyphenylacetic acid



^{1}H-NMR ($CDCl_3$) δ: 0.19 (6H, s), 0.98 (9H, s), 3.57 (2H, s), 6.72-6.75 (1H, m), 6.79-6.80 (1H, m), 6.88 (1H, d, J = 7.6 Hz), 7.17 (1H, t, J = 7.9 Hz).

Next, preparation examples are shown. Parts are by weight.

Preparation Example 1

Each of 50 parts of the compound (1) to (20) of the present invention, 3 parts of calcium ligninsulfonate, 2 parts of magnesium laurylsulfate and 45 parts of synthetic hydrated silicon oxide were ground and mixed thoroughly, to obtain a wettable powder.

Preparation Example 2

Each of 20 parts of the compound (1) to (20) of the present invention and 1.5

parts of sorbitan trioleate were mixed with 28.5 parts of an aqueous solution containing 2 parts of polyvinyl alcohol, and the mixture was finely ground by a wet grinding method, then, into this was added 40 parts of an aqueous solution containing 0.05 parts of xanthan gum and 0.1 part of aluminium magnesium silicate, and further, 10 parts of propylene glycol was added and mixed by stirring, to obtain a flowable.

Preparation Example 3

Each of 2 parts of the compound (1) to (20) of the present invention, 88 parts of kaolin clay and 10 parts of talc were ground and mixed thoroughly to obtain a dust.

Preparation Example 4

Each of 5 parts of the compound (1) to (20) of the present invention, 14 parts of polyoxyethylene styryl phenyl ether, 6 parts of calcium dodecylbenzenesulfonate and 75 parts of xylene were mixed thoroughly, to obtain an emulsifiable concentrate.

Preparation Example 5

Each of 2 parts of the compound (1) to (20) of the present invention, 1 part of synthetic hydrated silicon oxide, 2 parts of calcium ligninsulfonate, 30 parts of bentonite and 65 parts of kaolin clay were ground and mixed thoroughly, then, water was added to this and the mixture was kneaded thoroughly, and granulated and dried, to obtain a granule.

Preparation Example 6

Each of 10 parts of the compound (1) to (20) of the present invention, 50 parts of polyoxyethylene alkyl ether sulfate ammonium salt, 35 parts of white

carbon and 55 parts of water were mixed, and finely ground by a wet grinding method, to obtain a formulation.

Next, Test Examples will show that the compound of the present invention is useful for controlling a plant disease.

The controlling effect was evaluated by visually observing the area of a disease spot on a subject plant in investigation, and comparing the area of a disease spot of a plant treated with a compound of the present invention with the area of a disease spot of a none-treated plant.

Test Example 1

Plastic pots were stuffed with sand loam, cucumber (plant variety; Sagami Hanjiro) was sowed on this, and allowed to grow in a greenhouse for 12 days. The compounds (1) to (5), (7) to (13), (17), (18) and (19) of the present invention were formulated according to Preparation Example 6, and the formulations were diluted with water so that the concentration of active ingredients was 500 ppm. This dilute liquid was sprayed on stem and leaves so as to adhere sufficiently to the leaf surface of the cucumber. After spraying, the plant was air-dried, and PDA medium containing mycelia of Sclerotinia sclerotiorum was placed on the leaf surface of the cucumber. After inoculation, this was left for 4 days at 18°C under humid condition, then, the disease spot area was checked. As a result, the disease spot areas on the plants treated with the compounds (1) to (5), (7) to (13), (17), (18) and (19) of the present invention were 10% or less of the disease spot area on the none-treated plant.

Test Example 2

Plastic pots were stuffed with sand loam, cucumber (plant variety; Sagami

Hanjiro) was sowed on this, and allowed to grow in a greenhouse for 12 days. The compounds (14), (15) and (16) of the present invention were formulated according to Preparation Example 6, and the formulations were diluted with water so that the concentration of active ingredients was 200 ppm. This dilute liquid was sprayed on stem and leaves so as to adhere sufficiently to the leaf surface of the cucumber. After spraying, the plant was air-dried, and PDA medium containing mycelia of Sclerotinia sclerotiorum was placed on the leaf surface of the cucumber. After inoculation, this was left for 4 days at 18°C under humid condition, then, the disease spot area was checked. As a result, the disease spot areas on the plants treated with the compounds (14), (15) and (16) of the present invention were 10% or less of the disease spot area on the none-treated plant.

Test Example 3

Plastic pots were stuffed with sand loam, cucumber (plant variety; Sagami Hanjiro) was sowed on this, and allowed to grow in a greenhouse for 12 days. The compounds (1), (7), (10), (11) and (12) of the present invention were formulated according to Preparation Example 6, and the formulations were diluted with water so that the concentration of active ingredients was 500 ppm. This dilute liquid was sprayed on stem and leaves so as to adhere sufficiently to the leaf surface of the cucumber. After spraying, the plant was air-dried, and PDA medium containing spores of Botrytis cinerea was placed on the leaf surface of the cucumber. After inoculation, this was left for 5 days at 12°C under humid condition, then, the disease spot area was checked. As a result, the disease spot areas on the plants treated with the compounds (1), (7), (10), (11) and (12) of the present invention were 10% or less of the disease spot area on the none-treated plant.

Test Example 4

Plastic pots were stuffed with sand loam, cucumber (plant variety; Sagami Hanjiro) was sowed on this, and allowed to grow in a greenhouse for 12 days. The compounds (15), (16) and (20) of the present invention were formulated according to Preparation Example 6, and the formulations were diluted with water so that the concentration of active ingredients was 200 ppm. This dilute liquid was sprayed on stem and leaves so as to adhere sufficiently to the leaf surface of the cucumber. After spraying, the plant was air-dried, and PDA medium containing spores of Botrytis cinerea was placed on the leaf surface of the cucumber. After inoculation, this was left for 5 days at 12°C under humid condition, then, the disease spot area was checked. As a result, the disease spot areas on the plants treated with the compounds (15), (16) and (20) of the present invention were 30% or less of the disease spot area on the none-treated plant.

Test Example 5

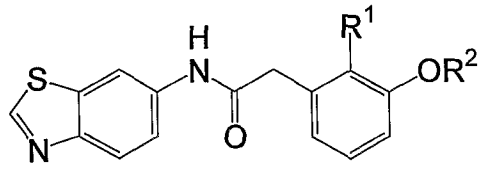
Plastic pots were stuffed with seedbed soil, rice plant (plant variety; Nihonbare) was sowed on this, and allowed to grow in a greenhouse for 12 days. The compounds (2) and (7) of the present invention were formulated according to Preparation Example 6, and the formulations were diluted with water so that the concentration of active ingredients was 500 ppm. This dilute liquid was sprayed on stem and leaves so as to adhere sufficiently to the leaf surface of the rice plant. After spraying, the plant was air-dried, and pots having leaves affected by Magnaporthe grisea were allowed to stand still around the sprayed plant. All rice plants were placed under humid condition only in night, and 5 days after inoculation, the disease spot area was checked. As a result, the disease spot areas on the plants treated with the compounds (2) and (7) of the present invention were 10% or less of the disease spot area on the none-treated plant.

Industrial Applicability

The compound of the present invention is useful as an active ingredient of a plant disease controlling composition since the compound has a plant disease controlling effect.

CLAIMS

1. An amide compound of the formula (I):



(I)

wherein R^1 represents a hydrogen atom or a fluorine atom and R^2 represents a C1-C6 linear alkyl group or a linear (C1-C2 alkoxy)C2-C5 alkyl group.

2. The amide compound according to Claim 1, wherein R^1 is a fluorine atom and R^2 is a C1-C6 linear alkyl group.

3. The amide compound according to Claim 2, wherein R^2 is a methyl group or an ethyl group.

4. The amide compound according to Claim 1, wherein R^1 is a hydrogen atom and R^2 is a C1-C6 linear alkyl group.

5. The amide compound according to Claim 4, wherein R^2 is a methyl group, an ethyl group or a butyl group.

6. The amide compound according to Claim 1, wherein R^1 is a hydrogen atom or a fluorine atom and R^2 is a linear (C1-C2 alkoxy)C2-C5 alkyl group.

7. The amide compound according to Claim 5, wherein R^1 is a hydrogen atom.

8. The amide compound according to Claim 5, wherein R^1 is a fluorine atom.

9. The amide compound according to any one of Claims 6 to 8, wherein R^2 is a linear (C1-C2 alkoxy)C3-C4 alkyl group.

10. N-benzothiazol-6-yl-2-(2-fluoro-3-methoxyphenyl)acetamide

11. N-benzothiazol-6-yl-2-(2-fluoro-3-ethoxyphenyl)acetamide

12. N-benzothiazol-6-yl-2-(2-fluoro-3-propoxyphenyl)acetamide

13. N-benzothiazol-6-yl-2-(2-fluoro-3-butoxyphenyl)acetamide

14. N-benzothiazol-6-yl-2-(2-fluoro-3-pentyloxyphenyl)acetamide

15. N-benzothiazol-6-yl-2-(2-fluoro-3-hexyloxyphenyl)acetamide

16. N-(benzothiazol-6-yl-)-2-(3-methoxyphenyl)acetamide

17. N-benzothiazol-6-yl-2-(3-ethoxyphenyl)acetamide

18. N-benzothiazol-6-yl-2-(3-propoxyphenyl)acetamide

19. N-benzothiazol-6-yl-2-(3-butoxyphenyl)acetamide

20. N-benzothiazol-6-yl-2-(3-pentyloxyphenyl)acetamide

21. N-benzothiazol-6-yl-2-(3-hexyloxyphenyl)acetamide

22. N-benzothiazol-6-yl-2-(3-(3-methoxypropoxy)phenyl)acetamide

23. N-benzothiazol-6-yl-2-(3-(4-methoxybutoxy)phenyl)acetamide

24. N-benzothiazol-6-yl-2-(3-(3-ethoxypropoxy)phenyl)acetamide

25. N-benzothiazol-6-yl-2-(3-(4-ethoxybutoxy)phenyl)acetamide

26. N-benzothiazol-6-yl-2-(2-fluoro-3-(3-methoxypropoxy)phenyl)-acetamide

27. N-benzothiazol-6-yl-2-(2-fluoro-3-(3-ethoxypropoxy)phenyl)acetamide

28. N-benzothiazol-6-yl-2-(2-fluoro-3-(4-methoxybutoxy)phenyl)acetamide

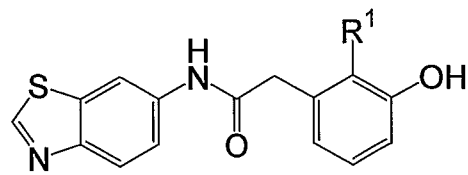
29. N-benzothiazol-6-yl-2-(2-ethoxyethoxyphenyl)acetamide

30. A plant disease controlling composition comprising the amide compound according to any one of Claims 1 to 29 and an inert carrier.

31. A plant disease controlling method having a step of applying a plant or soil with an effective amount of the amide compound according to any one of Claims 1 to 29.

32. Use of the amide compound according to any one of Claims 1 to 29 for controlling a plant disease.

33. An amide compound of the formula (II):



(II)

wherein R^1 represents a hydrogen atom or a fluorine atom.

INTERNATIONAL SEARCH REPORT

International application No
PCT/JP2009/065022

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D277/82 A01P3/00 A01N43/78

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07D A01P A01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 1 669 348 A (EISAI CO LTD [JP] EISAI R&D MAN CO LTD [JP]) 14 June 2006 (2006-06-14) page 216; claims 1,15,22; examples L-5	1-33
P,X	WO 2008/126684 A (SUMITOMO CHEMICAL CO [JP]; TAKAISHI MASANAO [JP]; KOMORI TAKASHI [JP]) 23 October 2008 (2008-10-23) examples 201,229,230	1

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
12 January 2010	18/01/2010

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Skulj, Primoz

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/JP2009/065022

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 1669348 A	14-06-2006	WO 2005033079 A1	14-04-2005
		US 2007105943 A1	10-05-2007
WO 2008126684 A	23-10-2008	AR 065788 A1	01-07-2009
		AU 2008239225 A1	23-10-2008
		CA 2681054 A1	23-10-2008
		CL 8162008 A1	22-08-2008
		DE 102008015267 A1	03-09-2009
		ES 2325523 A1	07-09-2009
		FR 2913852 A1	26-09-2008
		GB 2448056 A	01-10-2008
		JP 2009108021 A	21-05-2009