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(71) Applicant(s)  
**Carna Biosciences, Inc.**

(72) Inventor(s)  
**Irie, Takayuki;Sawa, Ayako;Sawa, Masaaki;Asami, Tokiko;Funakoshi, Yoko;Tanaka, Chika**

(74) Agent / Attorney  
**Griffith Hack, GPO Box 4164, Sydney, NSW, 2001, AU**

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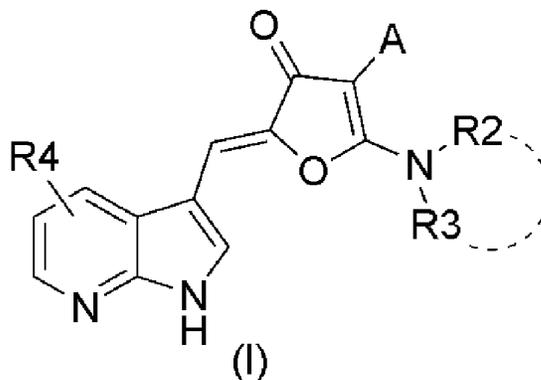
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- (72) 発明者; および  
(75) 発明者/出願人 (米国についてのみ): 入江 隆行 (IRIE Takayuki) [JP/JP]; 〒6550047 兵庫県神戸市垂水区東舞子町10-1-2208 Hyogo (JP). 澤綾子 (SAWA Ayako) [JP/JP]; 〒5400004 大阪府大阪市中央区玉造1丁目1-25-3105 Osaka (JP). 澤匡明 (SAWA Masaaki) [JP/JP]; 〒5670046 大阪府茨木市南春日丘3丁目3-8 Osaka (JP). 浅見 斉子 (ASAMI Tokiko) [JP/JP]; 〒6540154 兵庫県神戸市須磨区中落合2丁目3-2-1401 Hyogo (JP). 船越 陽子 (FUNAKOSHI Yoko) [JP/JP]; 〒1080071 東京都港区白金台4-7-4 白金台S Tビル S B I バイオテック株式会社内 Tokyo (JP). 田中 智香 (TANAKA Chika) [JP/JP]; 〒1080071 東京都港区白金台4-7-4 白金台S Tビル S B I バイオテック株式会社内 Tokyo (JP).
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(71) 出願人 (米国を除く全ての指定国について): S B I バイオテック株式会社 (SBI Biotech Co., Ltd.) [JP/JP]; 〒1080071 東京都港区白金台4-7-4 白金台S Tビル Tokyo (JP). カルナバイオサイエンス株式会社 (Carna Biosciences, Inc.) [JP/JP]; 〒6500047 兵庫県神戸市中央区港島南町1丁目5番5号 Hyogo (JP).  
(74) 代理人: 木島 智子 (KIJIMA Tomoko); 〒5610883 大阪府豊中市岡町南3-2-25-107 智特許事務所 Osaka (JP).  
(81) 指定国 (表示のない限り、全ての種類の国内保護が可能): 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,

[続葉有]

(54) Title: NOVEL FURANONE DERIVATIVE

(54) 発明の名称: 新規フラノン誘導体



(57) Abstract: [Problem] To provide a novel furanone derivative and a pharmaceutical product composed of the furanone derivative. [Solution] A compound represented by formula (I). (In the formula, A represents -COOR1 or a hydrogen atom; R1 represents a hydrogen atom, an optionally substituted hydrocarbon group or an optionally substituted heterocyclic ring; R2 and R3 may be the same or different and each represents a hydrogen atom, an optionally substituted hydrocarbon group, an optionally substituted phenyl group, an optionally substituted heterocyclic ring, an optionally substituted heterocyclic fused ring or an optionally substituted amino group, or alternatively, R2 and R3 may form an optionally substituted heterocyclic ring or an optionally substituted heterocyclic fused ring together with a nitrogen atom to which R2 and R3 are bonded; and R4 represents a hydrogen atom or a halogen atom. In this connection, when A represents -COOR1, R2 and R3 are not optionally substituted amino groups at the same time, and when A represents a hydrogen atom, R3 represents a hydrogen atom.)

(57) 要約:

[続葉有]



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- 国際調査報告 (条約第 21 条(3))

【課題】新規なフラノン誘導体およびそれからなる医薬の提供。【解決手段】式 (I) (式中、A は、 $-COOR1$  もしくは水素原子を表わし、R1 は、水素原子、置換基を有してもよい炭化水素基、置換基を有してもよい複素環を表し、R2 および R3 は同一または異なって、水素原子、置換基を有してもよい炭化水素基、置換基を有してもよいフェニル基、置換基を有してもよい複素環、置換基を有してもよい複素環式縮合環または置換基を有してもよいアミノ基を表す。あるいは、R2 および R3 は、これらが結合している窒素原子と共に、置換基を有してもよい複素環あるいは置換基を有してもよい複素環式縮合環を形成してもよい。R4 は、水素原子またはハロゲン原子を表す。ただし、A が  $-COOR1$  を表す場合は、R2、R3 は同時に置換基を有してもよいアミノ基にならず、A が水素原子を表す場合は、R3 は水素原子を表す。)

[DESCRIPTION]

[TITLE OF THE INVENTION]

NOVEL FURANONE DERIVATIVES

5 [Technical Field]

[0001]

The present invention relates to a medicine,  
particularly a novel furanone derivative having an inhibitory  
effect on Cdc7 or a pharmaceutically acceptable salt thereof.

10 [Background Art]

[0002]

Cancer is a group of diseases caused by uncontrolled,  
unlimited growth of cells within a living body. Since cancer  
cells usually grow faster than normal cells, cancers would be  
15 capable of being treated by controlling the replication of  
DNA during the cell division, particularly during the  
division of chromosomes. Actually, gemcitabine, which has  
the effect of inhibiting DNA replication, is widely used in  
the treatment of non-small cell lung cancer, pancreatic  
20 cancer, biliary tract cancer, bladder cancer, breast cancer,  
ovarian cancer, or others.

[0003]

Cdc7 is a serine-threonine protein kinase and is an  
enzyme which is essential for the initiation of DNA  
25 replication in the cell cycle. Specifically, Cdc7 forms a

complex with cofactors such as Dbf4 (ASK), and phosphorylates its substrate, MCM (mini-chromosome maintenance) proteins. It is supposed that this phosphorylation results in assembly of Cdc45 and a DNA polymerase on the DNA to form an MCM complex, thereby initiating the DNA replication (see Non Patent Literature 1). Furthermore, it has been shown in a recent study that Cdc7 plays an important role not only in the replication of DNA, but also in DNA damaging pathways (see Non Patent Literature 2).

10 [0004]

Recently, Cdc7 has drawn attention as a target of anti-cancer agents, and active researches on Cdc7 have been made. For example, it was found that CDC7 is overexpressed not only in common established cell lines derived from human tumors, but also in cells taken from live tissues, such as breast cancer, colon cancer, and lung cancer (see Non Patent Literature 3). Particularly, it was shown, in more recent days, that CDC7 is overexpressed in p53-mutated triple negative (ER-/PR-/Her2-) breast cancer cells (see Non Patent Literature 4), and thus it has been expected that Cdc7 will be a promising target molecule against a triple negative type of breast cancer, which has been considered to be difficult to treat. Actually, it was observed that in experiments for suppressing the expression of Cdc7 using RNA interference techniques, the arresting of the cell cycle was induced when

the expression of Cdc7 was inhibited. More importantly, the Cdc7 inhibition using RNA interference techniques suppressed the growth of human tumor cells, such as HeLa and HCT116 cells, and exhibited only limited effects on normal cells (normal human skin fibroblasts) (see Non Patent Literature 5).

[0005]

Therefore, selective inhibitors of Cdc7 can be expected to have an effective therapeutic effect against various types of cancer. Although various compounds having an inhibitory effect on Cdc7 have been reported in the past, there are no reports in which novel furanone derivatives of the present invention or pharmaceutically acceptable salts thereof have an inhibitory effect on Cdc7.

[Citation List]

[Non Patent Literature]

[0006]

[Non Patent Literature 1]

H. Masai et al., *Journal of Cellular Physiology*, 190, 2002, 287-296

[Non Patent Literature 2]

JM. Kim et al., *Oncogene*, 27, 2008, 3475-3482

[Non Patent Literature 3]

D Bonte et al., *Neoplasia*, 10, 2008, 920-931

[Non Patent Literature 4]

S. Rodriguez-Acebes et al., *The American Journal of*

Pathology, 177, 2010, 2034-2045

[Non Patent Literature 5]

A. Montagnoli et al., Cancer Research, 64, 2004, 7110-7116

[Summary of Invention]

[0007]

It would be advantageous if at least preferred embodiments of the present invention were to provide a medicine, particularly a novel furanone derivative having an inhibitory effect on Cdc7 or a pharmaceutically acceptable salt thereof.

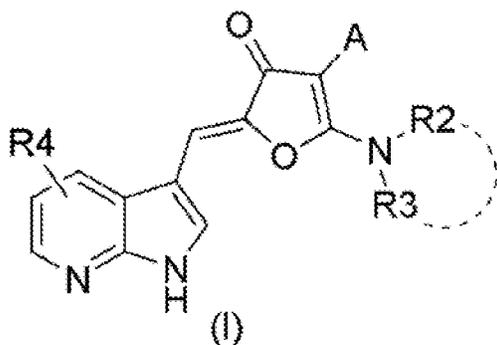
[0008]

The present invention is achieved by the following (1) to (3):

(1) A furanone derivative or a pharmaceutically acceptable salt thereof, represented by the formula (I):

[0009]

[Chemical Formula 1]



[0010]

wherein A represents -COOR<sub>1</sub> or a hydrogen atom; R<sub>1</sub> represents a hydrogen atom, an optionally substituted hydrocarbon group, or an optionally substituted heterocycle; R<sub>2</sub> and R<sub>3</sub> are the same or different and each independently represent a hydrogen atom, an optionally substituted hydrocarbon group, an optionally substituted phenyl group, an optionally substituted heterocycle, an optionally substituted heterocyclic fused ring, or an optionally substituted amino group; or alternatively, R<sub>2</sub> and R<sub>3</sub>, taken together with the nitrogen atom to which they are attached, may form an optionally substituted heterocycle or an optionally substituted heterocyclic fused ring; and R<sub>4</sub> represents a hydrogen atom

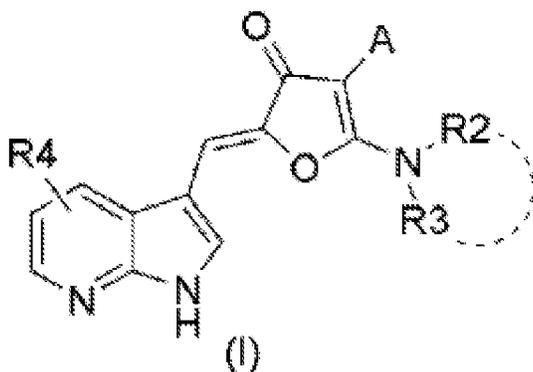
or a halogen atom; with the proviso that when A represents -COOR1, R2 and R3 are not optionally substituted amino groups at the same time, and when A represents a hydrogen atom, R3 represents a hydrogen atom;

(2) The furanone derivative or a pharmaceutically acceptable salt thereof according to (1), wherein A is -COOR1; and

(3) The furanone derivative or a pharmaceutically acceptable salt thereof according to (1), wherein A is a hydrogen atom.

The present invention as claimed herein is described in the following items 1 to 13:

1. A furanone derivative or a pharmaceutically acceptable salt thereof, represented



by the formula (I):

wherein

A represents -COOR1 or a hydrogen atom;

R1 represents a hydrogen atom, an optionally substituted hydrocarbon group selected from a linear or branched alkyl group having 1 to 6 carbon atoms, a linear or branched alkenyl group having 2 to 6 carbon atoms, an alkynyl group having 2 to 6 carbon atoms, a cycloalkyl group having 3 to 8 carbon atoms, a cycloalkenyl group having 3 to 8 carbon atoms, or an aralkyl group the aryl moiety of which is an aryl group having 6 to 14 carbon atoms and the alkyl moiety of which having 1 to 6 carbon atoms; or an optionally substituted heterocycle wherein the heterocycle is selected from a 3-8 membered alicyclic heterocycle containing at least one heteroatom selected from N, S, and O, or a 5- or 6- membered monocyclic aromatic heterocycle containing at least one heteroatom selected from N, S, and O;

R2 and R3 are the same or different and each independently represent a hydrogen atom, a an optionally substituted hydrocarbon group selected from a linear or branched alkyl group having 1 to 6 carbon atoms, a linear or branched alkenyl group having 2 to 6 carbon atoms, an alkynyl group having 2 to 6 carbon atoms, a cycloalkyl group having 3 to 8 carbon atoms, a cycloalkenyl group having 3 to 8 carbon atoms, or an aralkyl group the aryl moiety of which is an aryl group having 6 to 14 carbon atoms and the alkyl moiety of which having 1 to 6 carbon atoms; an optionally substituted phenyl group; an optionally substituted heterocycle wherein the heterocycle is selected from a 3-8 membered alicyclic heterocycle containing at least one heteroatom selected from N, S, and O, or a 5- or 6- membered monocyclic aromatic heterocycle containing at least one heteroatom selected from N, S, and O; an optionally substituted heterocyclic fused ring wherein the heterocyclic fused ring moiety is bicyclic, formed by fusing 3-8 membered rings, and contains at least one heteroatom selected from N, S, and O; or an optionally substituted amino group in which the optional substituent group is selected from linear, branched, or cyclic alkyl, aryl, or heteroaryl having 1 to 6 carbon atoms, each of which may be optionally substituted with one or more groups selected from halogen, alkyl, alkenyl, alkynyl, alkoxy, amino, nitro, cyano, hydroxy, alkylamino, carbamoyl, carboxyl, formyl, acetyl, and benzoyl;

or alternatively, R2 and R3, taken together with the nitrogen atom to which they are attached, form an optionally substituted heterocycle wherein the heterocycle is selected from a 3-8 membered alicyclic heterocycle containing at least one heteroatom selected from N, S, and O, or a 5- or 6- membered monocyclic aromatic heterocycle containing at least one heteroatom selected from N, S, and O; or an optionally substituted heterocyclic fused ring wherein the heterocyclic fused ring moiety is bicyclic, formed by fusing 3-8 membered rings, and contains at least one heteroatom selected from N, S, and O; and

R4 represents a hydrogen atom or a halogen atom;

wherein the optional substituent(s) on the hydrocarbon group, heterocycle, phenyl, or heterocyclic fused ring is one or more groups selected from halogen, alkyl,

alkoxy, amino, nitro, cyano, hydroxy, alkylamino, carbamoyl, carboxyl, formyl, acetyl, and benzoyl;

with the proviso that when A represents –COOR1, R2 and R3 are not optionally substituted amino groups at the same time, and when A represents a hydrogen atom, R3 represents a hydrogen atom;

or the furanone derivative is selected from any one of examples 1-359 or pharmaceutically acceptable salts thereof.

2. The furanone derivative or a pharmaceutically acceptable salt thereof according to item 1, wherein A is –COOR1.
3. The furanone derivative or a pharmaceutically acceptable salt thereof according to item 1, wherein A is a hydrogen atom.
4. The furanone derivative or a pharmaceutically acceptable salt thereof according to item 1, wherein:

R1 is selected from a hydrogen atom, an optionally substituted hydrocarbon group having 1 to 6 carbon atoms, and an optionally substituted heterocycle wherein the heterocycle is selected from a 3-8 membered alicyclic heterocycle containing at least one heteroatom selected from N, S, and O;

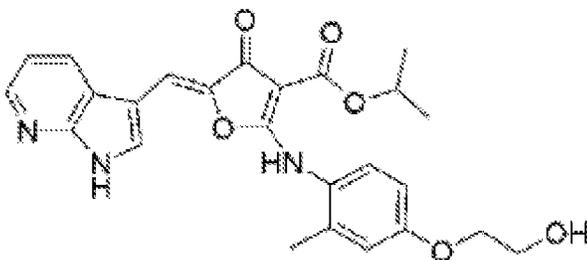
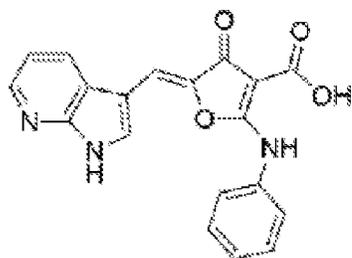
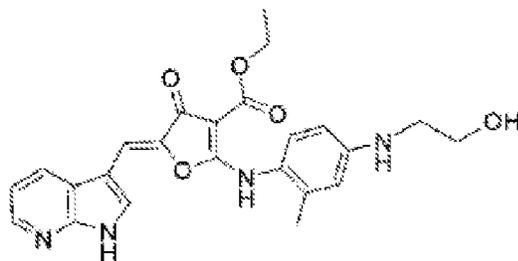
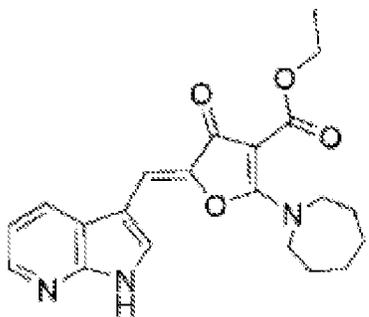
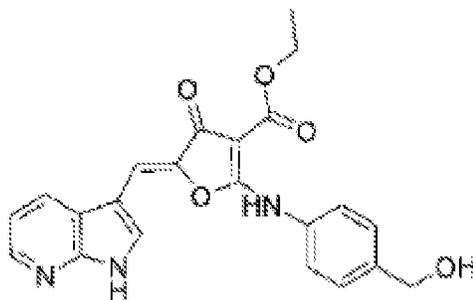
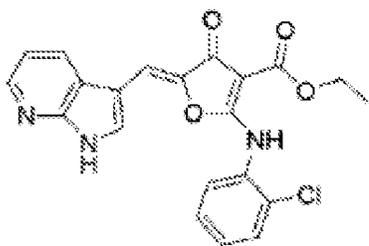
R2 and R3 taken together with the nitrogen atom to which they are attached, form an optionally substituted heterocycle wherein the heterocycle is selected from a 3-8 membered alicyclic heterocycle containing at least one heteroatom selected from N, S, and O; or an optionally substituted heterocyclic fused ring wherein the heterocyclic fused ring moiety is bicyclic, formed by fusing 3-8 membered rings, and contains at least one heteroatom selected from N, S, and O

wherein the optional substituents are as defined in item 1.

5. The furanone derivative or a pharmaceutically acceptable salt thereof according to item 4, wherein A and R4 are both a hydrogen atom, and R2 and R3 taken together with the nitrogen atom to which they are attached, form an optionally substituted heterocycle wherein the heterocycle is selected from a 3-8 membered alicyclic heterocycle containing at least one heteroatom selected from N, S, and O.

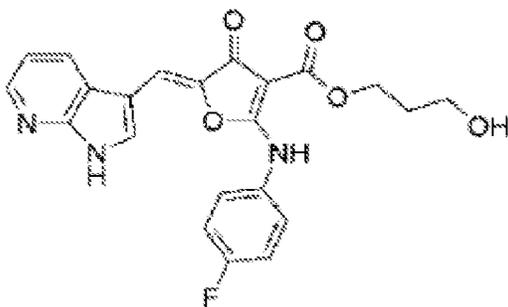
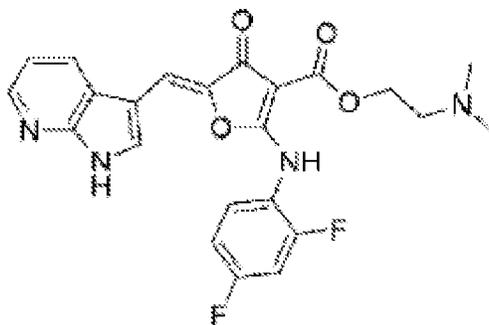
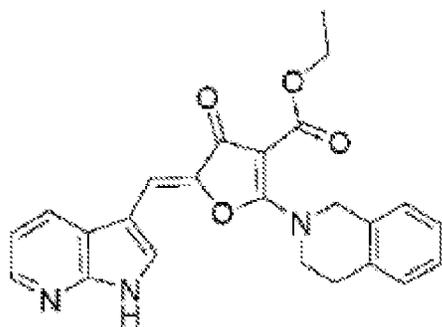
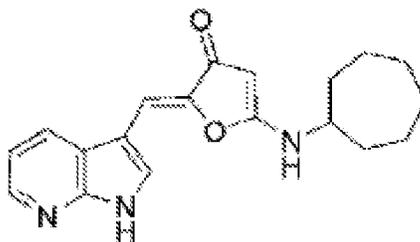
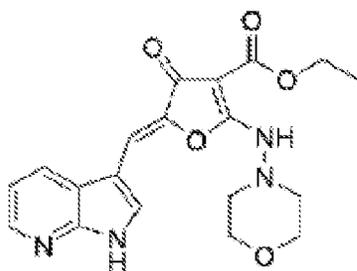


7. The furanone derivative or a pharmaceutically acceptable salt thereof according to item 1, wherein the furanone derivative or pharmaceutically acceptable salt thereof is selected from:

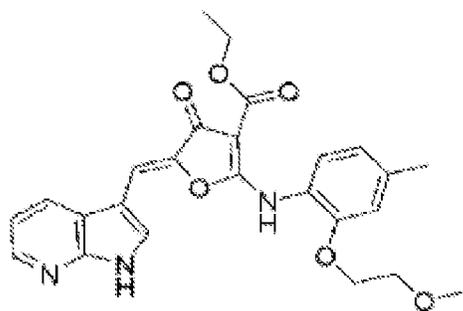


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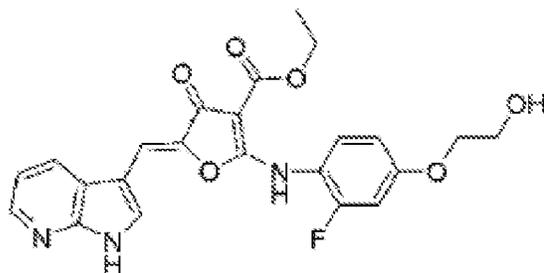
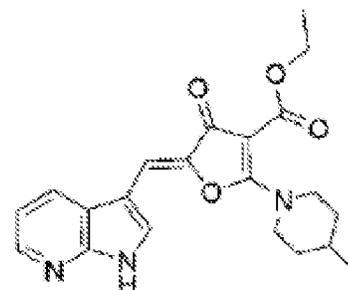
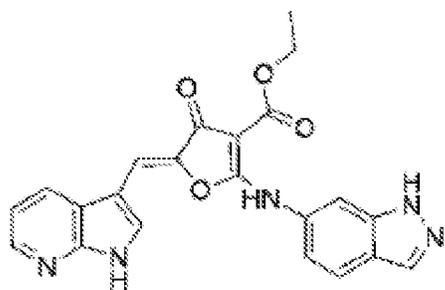
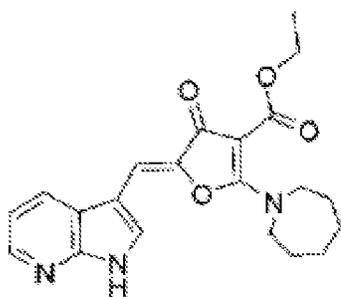
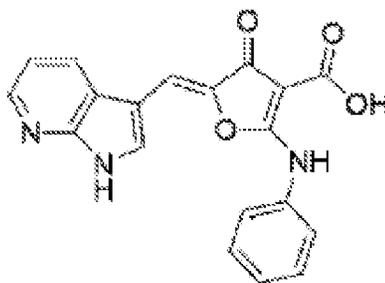
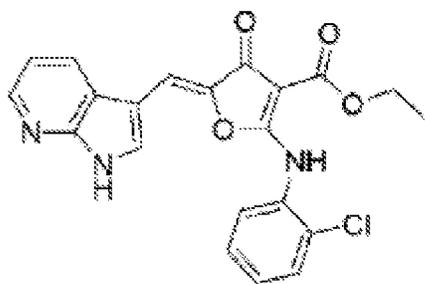
8. The furanone derivative or a pharmaceutically acceptable salt thereof according to item 1, wherein the furanone derivative or pharmaceutically acceptable salt thereof is selected from:

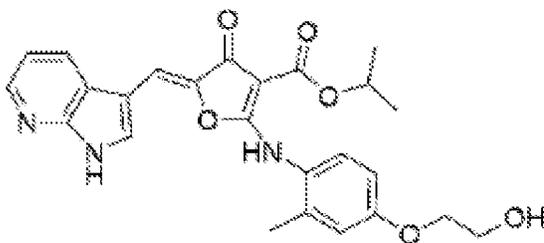
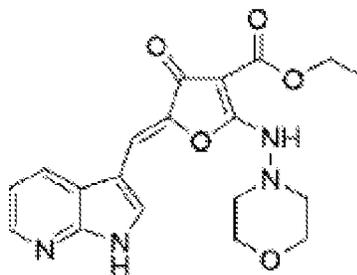
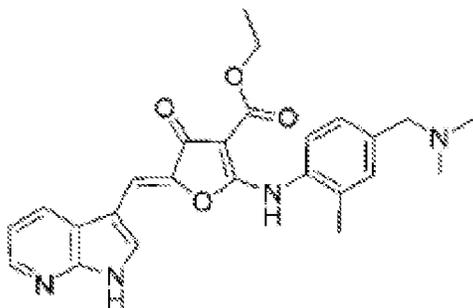
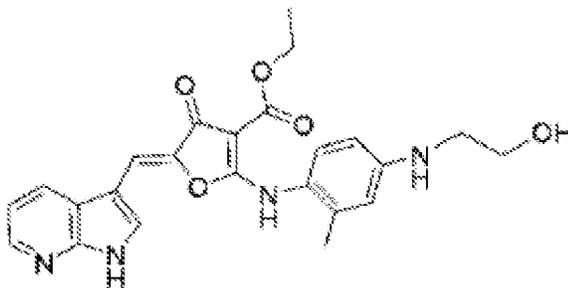
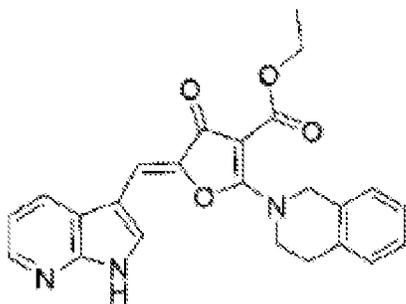
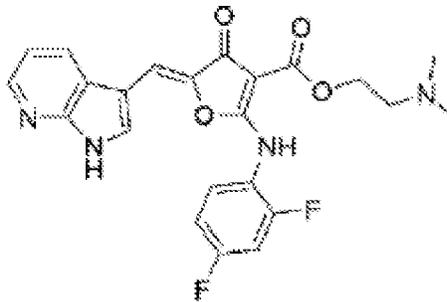
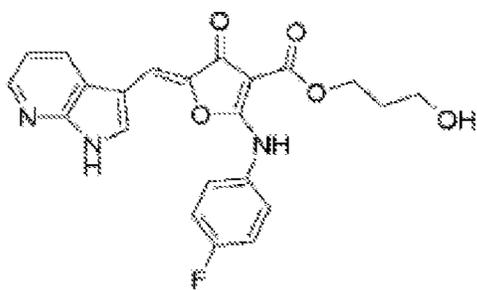


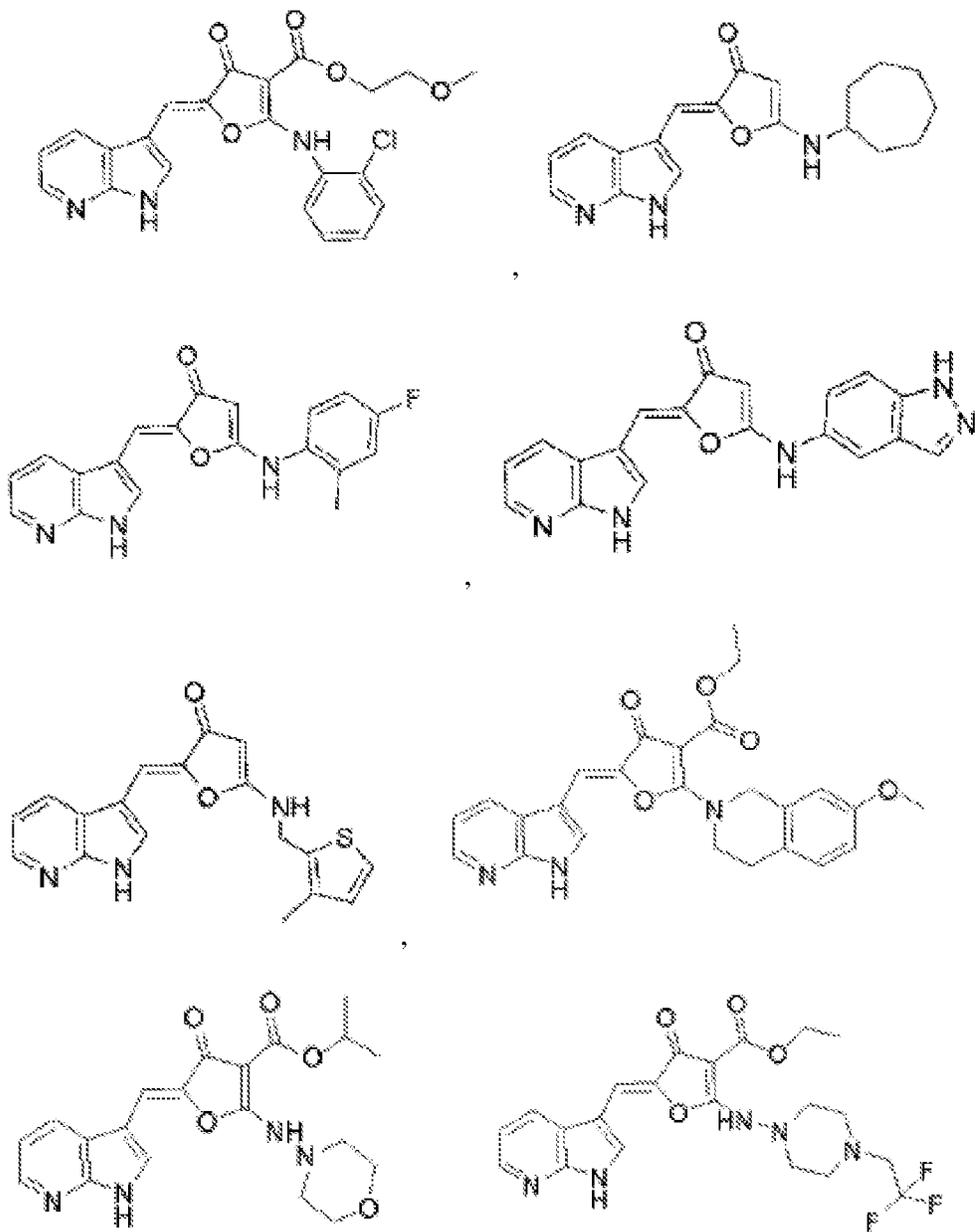
, and



9. The furanone derivative or a pharmaceutically acceptable salt thereof according to item 1 selected from:







, and

10. The furanone derivative or a pharmaceutically acceptable salt thereof according to any one of the preceding items, wherein the pharmaceutically acceptable salt is the hydrochloride or p-toluenesulfonate salt.
11. The furanone derivative or a pharmaceutically acceptable salt thereof according to any one of items 1 to 10 for use in therapy.

12. The furanone derivative or a pharmaceutically acceptable salt thereof according to any one of items 1 to 10 for use as an anti-tumour agent.
13. A pharmaceutical composition comprising the furanone derivative or a pharmaceutically acceptable salt thereof according to any one of items 1 to 10.

[Advantageous Effects of Invention]

[0011]

The present inventors have made various studies, and found that

novel furanone derivatives represented by the formula (I) and pharmaceutically acceptable salts thereof had excellent inhibitory effect on Cdc7, resulting in completion of the present invention. The compounds provided by the present invention are capable of controlling the growth of cells. Therefore, the compounds of the present invention having an inhibitory effect on Cdc7 will be useful as a medicine, particularly an agent for the treatment of diseases derived from abnormal growth of cells, such as cancers.

[Description of Embodiments]

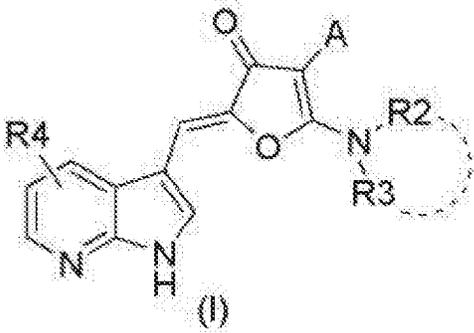
[0012]

The present invention will be described in detail below.

A novel furanone derivative of the present invention is a compound represented by the formula (I):

[0013]

[Chemical Formula 2]



[0014]

wherein A represents -COOR1 or a hydrogen atom; R1 represents

a hydrogen atom, an optionally substituted hydrocarbon group,  
or an optionally substituted heterocycle; R2 and R3 are the  
same or different and each independently represent a hydrogen  
atom, an optionally substituted hydrocarbon group, an  
5 optionally substituted phenyl group, an optionally  
substituted heterocycle, an optionally substituted  
heterocyclic fused ring, or an optionally substituted amino  
group; or alternatively, R2 and R3, taken together with the  
nitrogen atom to which they are attached, may form an  
10 optionally substituted heterocycle or an optionally  
substituted heterocyclic fused ring; and R4 represents a  
hydrogen atom or a halogen atom; with the proviso that when A  
represents -COOR1, R2 and R3 are not optionally substituted  
amino groups at the same time, and when A represents a  
15 hydrogen atom, R3 represents a hydrogen atom.

In the formula (I), an optionally substituted hydrocarbon  
group includes, for example, a) a linear or branched alkyl  
group having 1 to 6 carbons (for example, methyl, ethyl,  
isopropyl, tert-butyl, hexyl, etc.);  
20 b) a linear or branched alkenyl group having 1 to 6 carbons  
(for example, vinyl, allyl, isopropenyl, 2-butenyl, etc.);  
c) an alkynyl group having 2 to 6 carbons (for example,  
ethynyl, propargyl, 2-butyne, etc.);  
d) a cycloalkyl group having 3 to 8 carbons (for example,  
25 cyclopropyl, cyclopentyl, cyclohexyl, cycloheptyl, etc.);

e) a cycloalkenyl group having 3 to 8 carbons (for example, cyclohexenyl, cycloheptenyl, etc.);

[0015]

f) an aralkyl group, the aryl moiety of which is an aryl  
5 having 6 to 14 carbons (for example, phenyl, naphthyl, indenyl, etc.) and the alkylene moiety of which has the same meaning as a group where one hydrogen atom has removed from the above-mentioned alkyl group; and others.

[0016]

10 The heterocyclic moiety of an optionally substituted heterocycle includes an alicyclic heterocyclic group and an aromatic heterocyclic group. An alicyclic heterocyclic group is, for example, a 3- to 8-membered heterocyclic group containing at least one heteroatom selected from a nitrogen  
15 atom, a sulfur atom, and an oxygen atom. Specific examples of the alicyclic heterocyclic group include pyrrolidinyl, piperidyl, piperazinyl, morpholinyl, thiomorpholinyl, etc. An aromatic heterocyclic group is, for example, a 5- or 6-membered monocyclic aromatic heterocyclic group containing at  
20 least one heteroatom selected from a nitrogen atom, a sulfur atom, and an oxygen atom. Specific examples of the aromatic heterocyclic group include imidazolyl, pyrazolyl, thienyl, thiazolyl, pyridyl, etc.

[0017]

25 The heterocyclic fused ring moiety of an optionally

substituted heterocyclic fused ring is, for example, a fused heterocyclic group which is bicyclic by fusing 3- to 8-membered rings and which contains at least one heteroatom selected from a nitrogen atom, a sulfur atom, and an oxygen atom. Specific examples of the fused heterocyclic group include benzothiophenyl, benzimidazolyl, indazolyl, benzoxazolyl, benzothiazolyl, indolyl, isoquinolyl, phthalimide, etc.

[0018]

10 An optionally substituted amino group is, for example, an amino group having a linear, branched, or cyclic alkyl, aryl, or heteroaryl group which is substituted or unsubstituted and containing 1 to 6 carbons, for example, an amino group to which an alkyl group, an alkylamino group, an aryl group, a heteroaryl group, a heterocyclic group, a  
15 heterocyclic fused ring group, or the like which is unsubstituted or substituted with one or more substituents may be attached. The "one or more substituents" in these groups attached to an amino group may be any one or more  
20 substituents which are the same or different, unless otherwise specified, and include, for example, a halogen atom, a substituted or unsubstituted alkyl group, a substituted or unsubstituted alkenyl group, a substituted or unsubstituted alkynyl group, a substituted or unsubstituted alkoxy group,  
25 an amino group, a nitro group, a cyano group, a hydroxy group,

a substituted or unsubstituted alkylamino group, a carbamoyl group, a carboxyl group, a formyl group, an acetyl group, a benzoyl group, etc.

[0019]

5           The "substituent(s)" in an optionally substituted hydrocarbon group, an optionally substituted heterocycle, an optionally substituted phenyl group, or an optionally substituted heterocyclic fused ring is/are be one or more substituents of any type which are allowed to be located at  
10 any chemically acceptable positions, unless otherwise specified. When two or more substituents are present, these substituents may be the same or different and include, for example, a halogen atom, a substituted or unsubstituted alkyl group, a substituted or unsubstituted alkoxy group, a  
15 substituted or unsubstituted amino group, a nitro group, a cyano group, a hydroxy group, a substituted or unsubstituted alkylamino group, a carbamoyl group, a carboxyl group, a formyl group, an acetyl group, a benzoyl group, etc.

[0020]

20           The heterocyclic group in the case where R2 and R3, taken together with the nitrogen atom to which they are attached, form an optionally substituted heterocycle or an optionally substituted heterocyclic fused ring is, for example, a 3- to 8-membered heterocyclic group containing at  
25 least one heteroatom selected from a nitrogen atom, a sulfur

atom, and an oxygen atom, or a fused alicyclic heterocyclic group which is bicyclic by fusing 3- to 8-membered rings and which contains at least one heteroatom selected from a nitrogen atom, a sulfur atom, and an oxygen atom. Specific  
5 examples of such heterocyclic groups include pyrrolidinyl, piperidyl, morpholinyl, thiomorpholinyl, azepinyl, diazepinyl, dihydroisoquinolyl, tetrahydroisoquinolyl, tetrahydroquinolyl, isoindolinyl, indolinyl, tetrahydrobenzazepinyl, benzazepinyl, benzodiazepinyl, benzoxyazepinyl, benzothiazepinyl, etc.

10 A halogen atom includes, for example, fluorine, chlorine, bromine, and the like.

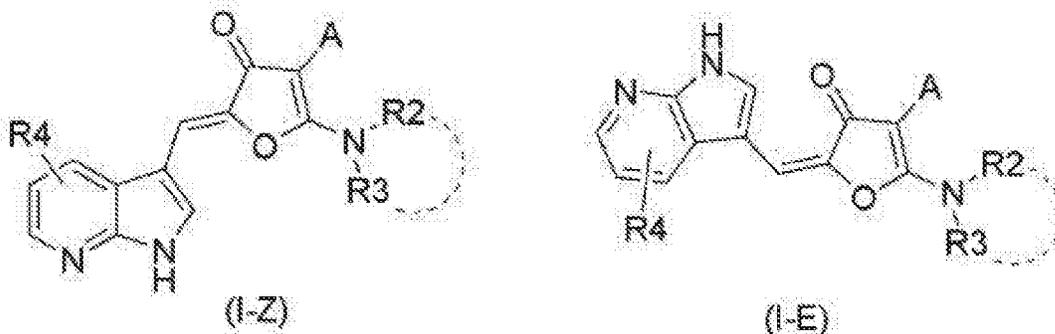
[0021]

A compound (I) of the present invention may have isomers, for example, depending on the type of its  
15 substituents. In the specification, such a compound is sometimes described by the chemical structure of only one of its isomeric forms. However, the present invention includes all of the structurally possible isomers of such a compound (geometrical isomers, optical isomers, tautomers, etc.), and  
20 also include its individual isomers or mixtures thereof.

Also, the present invention encompasses stereoisomers of a compound of the present invention represented specifically by the formulae (I-2) and (I-E), and mixtures thereof.

25 [0022]

[Chemical Formula 3]



[0023]

A pharmaceutically acceptable salt of a compound (I) of the present invention includes a salt with an inorganic acid, such as hydrochloric acid, sulfuric acid, carbonic acid, and phosphoric acid, and a salt with an organic acid, such as formic acid, acetic acid, fumaric acid, maleic acid, methanesulfonic acid, and p-toluenesulfonic acid. Also included in the present invention are, for example, a salt with an alkali metal, such as sodium and potassium, a salt with an alkaline earth metal, such as magnesium and calcium, a salt with an organic amine, such as a lower alkyl amine and a lower alcohol amine, and a salt with a basic amino acid, such as lysine, arginine, and ornithine, and in addition, an ammonium salt.

[0024]

Compounds (I) of the present invention and pharmaceutically acceptable salts thereof can be produced, for example, by the methods mentioned below. In the

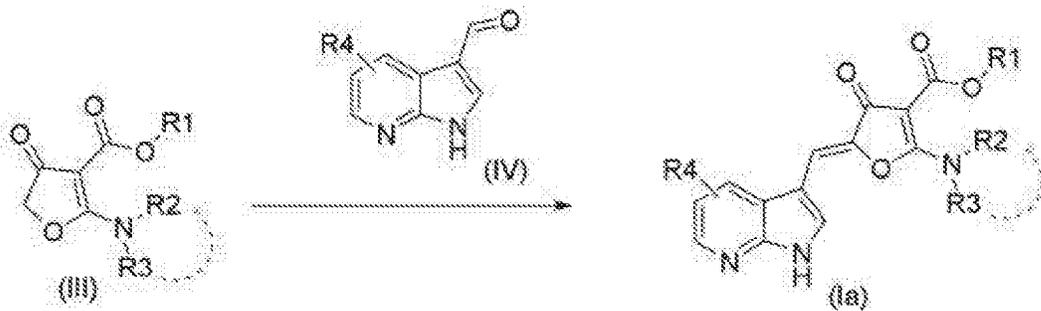
production methods mentioned below, when a defined group is changed under conditions where the method is performed, or when a defined group is not suitable for performing the method, the production can be easily achieved by applying methods usually used in organic synthetic chemistry, such as procedures for protection and deprotection of functional groups [T. W. Greene, Protective Groups in Organic Synthesis, 3rd Edition, John Wiley & Sons, Inc., 1999]. In addition, the order of reaction steps, for example, those for introducing a substituent or substituents, may be changed as needed.

A compound (Ia) wherein A is -COOR1 can be produced, for example, by scheme 1:

[Scheme 1]

15 [0025]

[Chemical Formula 4]



wherein R1, R2, R3 and R4 have the same meaning as mentioned above.

20 [0026]

A compound (Ia) of the present invention can be obtained by heating and reacting a compound (III) and 1 to 5, preferably 1 to 1.5, molar equivalents of a compound (IV) in a solvent under conditions for a Knoevenagel condensation reaction, that is, in the presence of a catalytic base such as piperidine. The solvent can be any solvent which is inert in the reaction, and is not limited in particular. For example, a lower alcohol, preferably ethanol, can be used as the solvent. As the base, piperidine or proline, for example, can be used in an amount of from a catalytic amount to an equivalent amount relative to the compound (III). The reaction can be carried out in the range of from room temperature to reflux temperature and for a period of 3 hours to 2 weeks. Preferably, the reaction can be carried out for 1 to 3 days under conditions of reflux in ethanol, thereby to synthesize the compound. In addition, this reaction can also be performed under other usual conditions used in the Knoevenagel condensation reaction, for example, under acidic conditions using hydrochloric acid, acetic acid, or the like, to produce the compound.

[0027]

The compound (IV) which can be used as one starting material in scheme 1 is commercially available (for example, from SIGMA-ALDRICH) or can be obtained by known methods (see, for example, Rajesh H. Bahekar et al., Bioorganic & Medicinal

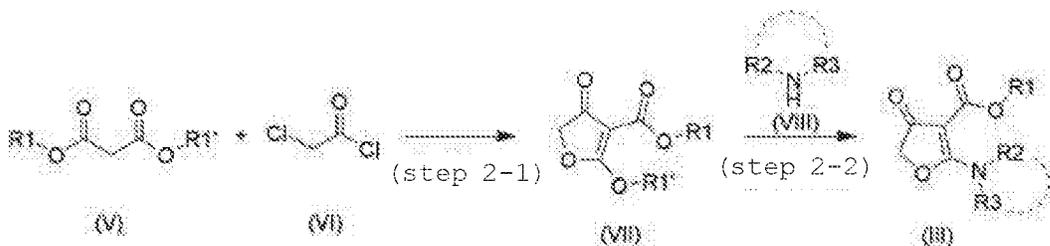
Chemistry, 15 (21), 6782-6795 (2007); and Seung-Jun Oh et al.,  
Bioorganic & Medicinal Chemistry, 12 (21), 5505-5513 (2004)).

On the other hand, the compound (III) which can be  
used as the other starting material in scheme 1 can be  
5 produced, for example, by the procedures shown in scheme 2 or  
3.

[Scheme 2]

[0028]

[Chemical Formula 5]



10

wherein R1, R2, and R3 have the same meaning as mentioned  
above, and R1' represents a substituted or unsubstituted  
lower alkyl group.

Step 2-1

15 [0029]

A compound (VII) can be obtained by converting a  
malonic diester (V) to its enolate with a base, such as  
sodium hydride, in a solvent, such as anhydrous  
tetrahydrofuran, followed by reaction with chloroacetyl  
20 chloride (VI).

Step 2-2

[0030]

The compound (III) can be obtained by reacting the compound (VII) obtained in the previous step and an amine (VIII) in an amount of from an equivalent amount to an excess amount, preferably in an amount of 1.2 to 3 molar equivalents, in a solvent at room temperature or at heated temperature.

[0031]

The solvent can be any solvent which is inert in the reaction, and is not limited in particular. For example, tetrahydrofuran, dimethylformamide, ethanol, and the like can be used as the solvent.

[0032]

The reaction is dependent on the reactivity of the amine (VIII) used, and generally is completed in a period of 1 hour to 1 day at a temperature of from room temperature to the reflux temperature of the solvent. When the reaction progresses at a significantly slow rate, the desired product can be obtained by adding a base, such as sodium hydride, sodium hydroxide, triethylamine, or the like, in an amount of from an equivalent amount to an excess amount.

[0033]

Further, the compound (III) can also be produced by mean of a sequence of reactions without isolating the compound (VII), by known methods (see, for example, Sheng-Chu Kuo et al., Chem. Pharm. Bull., 36 (11), 4403-4407 (1988)) or

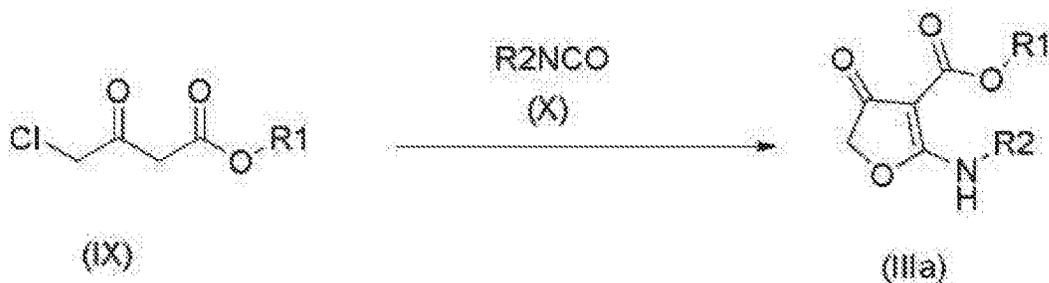
their modified methods. That is, the compound (III) can be obtained by adding the amine (VIII) in an amount of from an equivalent amount to an excess amount, preferably in an amount of 1.2 to 3 molar equivalents, to the solution after the reaction in step 2-1, and performing the reaction at room temperature or at heated temperature.

The malonic diester (V) and the amine (VIII) which can be used as the starting materials in scheme 2 are commercially available or can be obtained by known methods.

10 [Scheme 3]

[0034]

[Chemical Formula 6]



wherein R<sub>1</sub> and R<sub>2</sub> have the same meaning as mentioned above.

15 [0035]

Among the compounds (III), a compound (IIIa) wherein R<sub>3</sub> is a hydrogen atom can be produced by known methods (see, for example, Robert A. Mack et al., J. Med. Chem., 31 (10), 1910-1918 (1988)) or their modified methods. That is, the compound (IIIa) can be obtained by cyclocondensation of a compound (IX) with 1 to 5, preferably 1 to 1.5, molar

equivalents of isocyanate (X) in a solvent in the presence of a base, such as triethylamine.

[0036]

The solvent can be any solvent which is inert in the reaction, and is not limited in particular. For example, diethyl ether or ethyl acetate, or mixed solvents thereof can be used as the solvent.

[0037]

The reaction can be carried out in the range of from ice-cooled temperature to reflux temperature and for a period of 30 minutes to 1 day. Preferably, the reaction can be carried out at room temperature for 1 to 3 hours, thereby to synthesize the compound.

The compound (IX) and isocyanate (X) that are the starting materials in scheme 3 are commercially available or can be obtained by known methods.

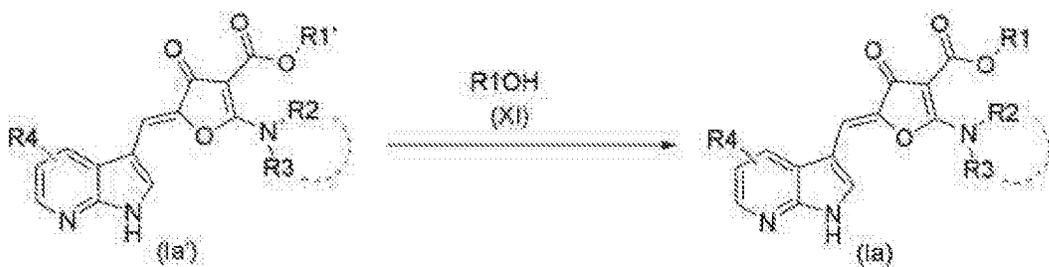
[0038]

Further, a compound (Ia) of the present invention can also be produced by a transesterification reaction of a compound (Ia'), which is a lower alkyl ester compound, as shown in scheme 4:

[Scheme 4]

[0039]

[Chemical Formula 7]



wherein R1, R2, R3, and R4 have the same meaning as mentioned above, and R1' represents a substituted or unsubstituted lower alkyl group.

5 [0040]

A compound (Ia) of the present invention can be produced by a transesterification reaction of the compound (Ia') by known methods (see, for example, Takanori Iwasaki et al., J. Org. Chem., 73 (13), 5147-5150 (2008)) or their modified methods. That is, the compound (Ia) can be obtained by heating and reacting the compound (Ia') and an excess amount, preferably more than 10 molar equivalents, of an alcohol (XI) in a solvent in the presence of a tetranuclear zinc cluster catalyst. The solvent can be any solvent which is inert in the reaction, and is not limited in particular. For example, dimethylacetamide, 1,4-dioxane, diisopropyl ether, or the like can be used as the solvent. Alternatively, the alcohol (XI) may be used as the solvent. As the tetranuclear zinc cluster catalyst, catalysts which are commercially available (for example, under a product name of ZnTAC24, from STREM CHEMICALS) or are produced by the method

10  
15  
20

described in the above-mentioned reference are used and added  
in a catalytic amount, preferably in an amount of 1 to 10%  
molar equivalents. Further, it is also possible that a  
tertiary amine, such as dimethylaminopyridine or  
5 triethylamine, is added in an amount of from a catalytic  
amount to 1 molar equivalent to accelerate the reaction.

[0041]

The reaction can be carried out in the range of from  
room temperature to reflux temperature and for a period of 1  
10 hour to 1 week. Preferably, the reaction can be carried out  
for 1 to 3 days under reflux conditions, thereby to  
synthesize the compound. Alternatively, the reaction may  
also be carried out using a microwave reactor, for example,  
for a period of from several minutes to several hours under  
15 temperature conditions of 60 to 150°C, thereby to synthesize  
the compound.

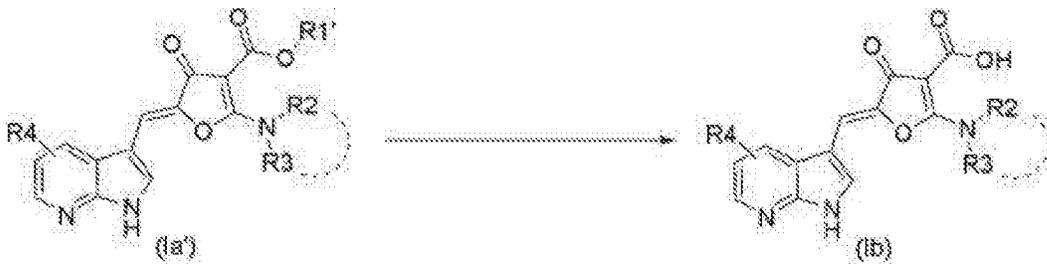
[0042]

This reaction can also be carried out under other  
usual conditions used in the transesterification reaction, as  
20 shown in scheme 5, for example, under acidic or basic  
conditions, or under conditions using a catalyst, such as  
tetravalent titanium.

[Scheme 5]

[0043]

25 [Chemical Formula 8]



wherein R1', R2, R3, and R4 have the same meaning as mentioned above.

[0044]

5           A compound (Ib) of the present invention can be obtained by hydrolysis of a compound (Ia'), which is a lower alkyl ester compound, under reaction conditions used in usual organic synthetic chemistry (using methods described in, for example, T. W. Greene, Protective Groups in Organic Synthesis, 10   3rd Edition, John Wiley & Sons, Inc., 1999, p. 377, or their modified methods). That is, the compound (Ib) can be obtained by reacting the compound (Ia') and a base or acid in an amount of from an equivalent amount to an excess amount in a solvent at a temperature between 0°C and the boiling point 15   of the solvent used.

[0045]

The solvent can be any solvent which is inert in the reaction, and is not limited in particular. For example, 1,4-dioxane, tetrahydrofuran, various alcohols, or the like 20   can be used as the solvent.

As the base or acid, use can be made of, for example,

sodium hydroxide, potassium hydroxide, or hydrochloric acid.

[0046]

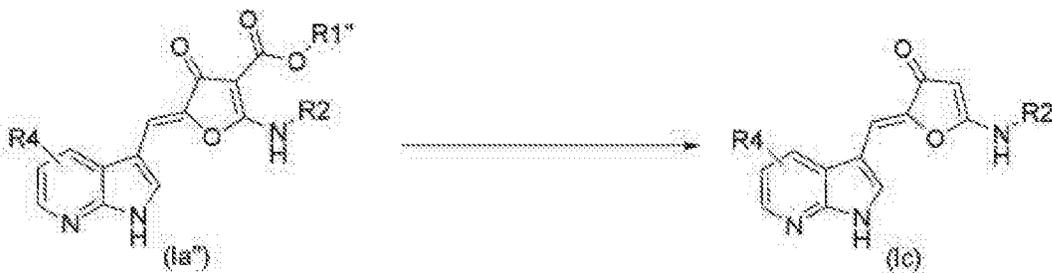
The reaction can be carried out at a temperature between 0°C and the boiling point of the solvent used and for a period of 1 hour to 1 week. Preferably, the reaction can be carried out for 1 hour to 1 day under reflux conditions, thereby to synthesize the compound.

Among the compounds (I) of the present invention, a compound (Ic) wherein A and R3 are hydrogen atoms can be produced, for example, as shown in scheme 6:

[Scheme 6]

[0047]

[Chemical Formula 9]



wherein R2 and R4 have the same meaning as mentioned above, and R1'' represents a hydrogen atom or a substituted or unsubstituted lower alkyl group.

[0048]

A compound (Ic) of the present invention can be synthesized from a compound (Ia''), which is a compound (Ia) wherein R1 is a substituted or unsubstituted lower alkyl

ester group and R3 is hydrogen, using known methods (see, for example, Sheng-Chu Kuo et al., Chem. Pharm. Bull., 38 (2), 340-341 (1990)) or their modified methods.

[0049]

5           The reaction can be carried out by heating a solution or suspension of a compound (Ia'') in N,N-dimethylformamide or N,N-dimethylacetamide at a temperature between 100°C and the boiling point of the solvent used and for a period of 1 to 24 hours. Preferably, the reaction can be carried out for 1 to  
10 12 hours under reflux conditions, thereby to synthesize the compound.

[0050]

          This reaction can also be carried out by heating and stirring in the presence of a base. For example, the  
15 reaction can be carried out by heating to reflux in an alcohol solvent, such as ethanol, in the presence of a highly-concentrated aqueous solution of potassium hydroxide, thereby to synthesize compound.

[0051]

20           Moreover, a compound (I) of the present invention which has a desired functional group at a desired position can be obtained by combining the above-mentioned methods as appropriate and carrying out procedures usually used in organic synthetic chemistry (for example, reactions for  
25 alkylation of amino groups, reactions for oxidation of an

alkylthio group to the corresponding sulfoxide or sulfone group, reactions for converting an alkoxy group to a hydroxy group or vice versa).

[0052]

5           Compounds (I) of the present invention or pharmaceutically acceptable salts thereof can be used as medicines, particularly anti-tumor agents, in the form of conventional pharmaceutical preparations for oral administration or for parenteral administration, such as  
10 instillation.

[0053]

Pharmaceutical preparations for oral administration include solid formulations, such as tablets, granules, powders, and capsules, and liquid formulations, such as  
15 syrups. These formulations can be prepared by conventional methods. Solid formulations can be prepared using conventional pharmaceutical carriers like lactose, starches such as corn starch, crystalline cellulose such as microcrystalline cellulose, hydroxypropylcellulose, calcium  
20 carboxymethylcellulose, talc, magnesium stearate, and others. Capsules can be prepared by encapsulating the granules or powders thus prepared. Syrups can be prepared by dissolving or suspending a compound (I) of the present invention or a pharmaceutically acceptable salt thereof in an aqueous  
25 solution containing sucrose, carboxymethylcellulose, or the

like.

[0054]

Pharmaceutical preparations for parenteral administration include formulations for injection, such as  
5 instillation. Formulations for injection can also be prepared by conventional methods, and may be incorporated in tonicity adjusting agents (for example, mannitol, sodium chloride, glucose, sorbitol, glycerol, xylitol, fructose, maltose, mannose), stabilizing agents (for example, sodium  
10 sulfite, albumin), antiseptics (for example, benzyl alcohol, methyl p-hydroxybenzoate) as appropriate.

[0055]

Compounds (I) of the present invention or pharmaceutically acceptable salts thereof are effective for  
15 medicines, particularly for the treatment of tumors. Tumors include solid tumors, such as breast cancer, colon cancer, and lung cancer, and hematological cancers, such as leukemia, lymphoma, and myeloma.

[0056]

20 The amount of dosage of a compound (I) of the present invention or a pharmaceutically acceptable salt thereof can be varied, according to the severeness of the disease, the age and body weight of the patient, its dosage form, and others, and usually is in the range of 1 mg to 1,000 mg per  
25 day for adult humans, which can be administered once, or

twice or thrice by oral route or by parenteral route.

[Examples]

[0057]

The present invention will be more specifically  
5 described below by way of Examples and Test Examples, which  
are not intended to limit the present invention.

[0058]

The identification of compounds was performed with  
hydrogen nuclear magnetic resonance (<sup>1</sup>H-NMR) spectra and mass  
10 spectra (MS). <sup>1</sup>H-NMR spectra were measured at 400 MHz,  
unless otherwise specified. In the <sup>1</sup>H-NMR spectra,  
exchangeable hydrogens are sometimes not clearly observed,  
depending on the compound being measured and on the  
measurement conditions, and br denotes a broad signal.

15 HPLC preparative chromatography was carried out using a  
commercial available ODS column, and fractions were collected  
using a water/methanol system (containing formic acid) as an  
eluent in a gradient mode, unless otherwise specified.

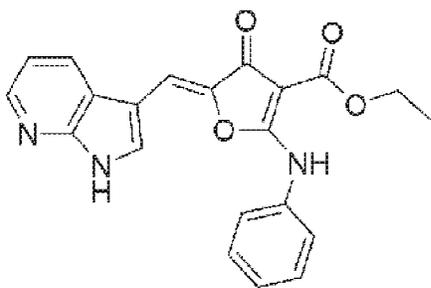
Example 1

20 [0059]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-4-oxo-2-(p  
henylamino)-4,5-dihydrofuran-3-carboxylate

[0060]

[Chemical Formula 10]



[0061]

To a solution of 7-azaindole-3-carboxaldehyde (0.10 g, 0.70 mmol) and ethyl 4-oxo-2-(phenylamino)-4,5-dihydrofuran-3-carboxylate (0.18 g, 0.70 mmol) in ethanol (3.0 mL), piperidine (0.083 mL, 0.84 mmol) was added at ambient temperature. The mixture was refluxed for 12 h. Cooled to ambient temperature, the precipitate was collected by filtration, washed with cold ethanol and isopropyl ether then dried to afford the titled compound (0.13 g, y. 48%).

[0062]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.30 (br. s, 1H), 10.58 (s, 1H), 8.23 (dd, J = 1.25, 4.52 Hz, 1H), 7.98 (d, J = 7.28 Hz, 1H), 7.79 (d, J = 2.76 Hz, 1H), 7.52 - 7.64 (m, 4H), 7.43 - 7.51 (m, 1H), 6.80 - 6.99 (m, 2H), 4.28 (q, J = 7.03 Hz, 2H), 1.30 (t, J = 7.03 Hz, 3H); LCMS (m/z): 376.0 [M+H]<sup>+</sup>.

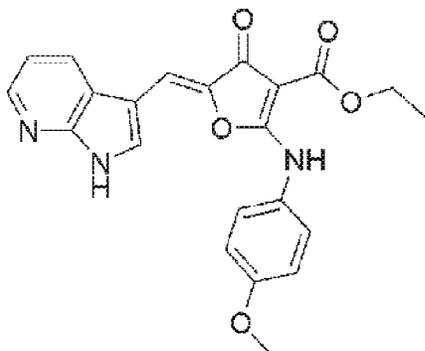
Example 2

[0063]

Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-2-[(4-methoxyphenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[0064]

[Chemical Formula 11]



First Step

5 [0065]

Under a nitrogen atmosphere, to a mixed solution of ethyl 4-chloroacetoacetate (0.82 mL, 6.0 mmol) and 4-methoxyphenyl isocyanate (1.1 g, 7.2 mmol) in diethyl ether/ethyl acetate (10 mL/1.0 mL) that cooled with ice bath, triethylamine (0.96 mL, 6.9 mmol) was added dropwise. The reaction mixture was stirred at ambient temperature for 1.5 h then the precipitate was collected by filtration, washed with diethyl ether, 1M hydrochloric acid solution, water and diethyl ether, and then dried to afford ethyl 2-[(4-methoxyphenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate as solid (1.3 g, y. 78%).

15

[0066]

$^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  (ppm) 10.11 (br. s, 1H), 7.24 - 7.33 (m, 2H), 6.90 - 6.96 (m, 2H), 4.65 (s, 2H), 4.38 (q,  $J = 7.07$  Hz, 2H), 3.83 (s, 3H), 1.40 (t,  $J = 7.20$  Hz, 3H); LCMS ( $m/z$ ): 277.9  $[\text{M}+\text{H}]^+$ .

20

Second Step

[0067]

To a solution of ethyl 2-[(4-methoxyphenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.28 g, 1.0 mmol) and 7-azaindole-3-carboxaldehyde (0.15 g, 1.0 mmol) in ethanol (4.0 mL), piperidine (0.12 mL, 1.2 mmol) was added at ambient temperature. The mixture was refluxed for 12 h. Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol and diisopropyl ether then dried to afford the titled compound (0.092 g, y. 22%).

[0068]

$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.31 (br. s, 1H), 10.47 (s, 1H), 8.24 (dd,  $J = 1.51, 4.52$  Hz, 1H), 7.94 (d,  $J = 7.53$  Hz, 1H), 7.77 (d,  $J = 2.76$  Hz, 1H), 7.50 (d,  $J = 9.03$  Hz, 2H), 7.09 (d,  $J = 8.78$  Hz, 2H), 6.81 - 6.92 (m, 2H), 4.26 (q,  $J = 7.03$  Hz, 2H), 3.87 (s, 3H), 1.29 (t,  $J = 7.03$  Hz, 3H); LCMS (m/z): 406.0 [M+H] $^+$ .

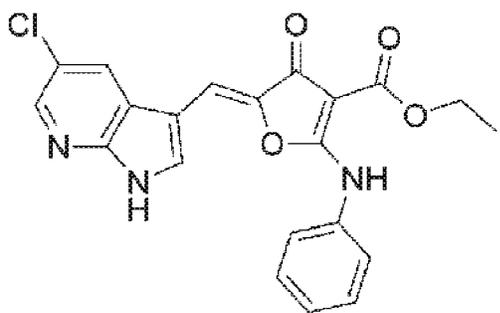
20 Example 3

[0069]

Ethyl 5-[(5-chloro-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-4-oxo-2-(phenylamino)-4,5-dihydrofuran-3-carboxylate

[0070]

25 [Chemical Formula 12]



### First Step

[0071]

To a mixed solution of 2-amino-5-chloropyridine (2.6 g, 0.020  
5 mol) in acetic acid/water (7.8 mL/1.8 mL) that cooled with ice  
bath, conc. sulfuric acid (0.26 mL, 4.9 mmol) was added dropwi  
se, and then periodic acid (0.95 g, 4.2 mmol) and iodine (2.0 g,  
8.0 mmol) were added. The reaction mixture was stirred at 80 °  
C for 6 h. Cooled to ambient temperature, the reaction mixture  
10 was poured into ice water, and neutralized by aqueous 5M sodi  
um hydroxide solution. After removal of the precipitate by fil  
tration, the filtrate was extracted with ethyl acetate. The or  
ganic layer was washed with saturated sodium thiosulfate solut  
ion, aqueous 1M sodium hydroxide solution and brine then dried  
15 over sodium sulfate and concentrated to afford 2-amino-5-chlo  
ro-3-iodopyridine as solid (4.4 g, y. 85%).

[0072]

$^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  (ppm) 7.96 (s, 1H), 7.82 (s, 1H), 4.93 (s, 2  
H); LCMS (m/z) 255.2  $[\text{M}+\text{H}]^+$ .

20

### Second Step

[0073]

Under a nitrogen atmosphere, to a solution of 2-amino-5-chloro-3-iodopyridine (4.2 g, 0.017 mol), copper(I) iodide (0.032 g, 0.17 mmol) and triethylamine (7.0 mL, 0.050 mol) in anhydrous tetrahydrofuran (10 mL), dichlorobis(triphenylphosphine)palladium(II) (0.12 g, 0.17 mmol) and ethynyl trimethylsilane (3.0 mL, 0.021 mol) were added and the mixture was stirred at ambient temperature for 2 h. The reaction mixture was diluted with diethyl ether and removed the precipitate by filtration with Celite. The filtrate was concentrated to afford 2-amino-5-chloro-3-[(trimethylsilyl)ethynyl]pyridine as solid (4.2 g).

[0074]

$^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  (ppm) 7.94 (d, 1H,  $J = 2.28$  Hz), 7.49 (d, 1H,  $J = 2.32$  Hz), 5.02 (s, 2H), 0.18-0.25 (m, 9H); LCMS ( $m/z$ ): 225.5 [M+H] $^+$ .

Third Step

[0075]

Under a nitrogen atmosphere, to a solution of potassium *tert*-butoxide (4.0 g, 0.036 mol) in 1-methyl-2-pyrrolidone (8.0 mL) which stirred with heating at 80 °C, a solution of 2-amino-5-chloro-3-[(trimethylsilyl)ethynyl]pyridine (4.0 g, 0.018 mol) in 1-methyl-2-pyrrolidone (22 mL) was added dropwise and the mixture was stirred for 1 h. Cooled to ambient temperature, the reaction mixture was diluted with brine and stirred, then ext

racted with diethyl ether for 3 times. The organic layer was washed with brine, dried over sodium sulfate and concentrated to afford 5-chloro-7-azaindole as solid (2.3 g, y.85%).

[0076]

5  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  (ppm) 9.46 (s, 1H), 8.26 (s, 1H), 7.91 (d, 1H,  $J = 1.12$  Hz), 7.35 (s, 1H), 6.46 (s, 1H); LCMS (m/z): 153.2 [ $\text{M} + \text{H}$ ] $^+$ .

#### Fourth Step

10 [0077]

To a solution of 5-chloro-7-azaindole (0.50 g, 3.3 mmol) in acetic acid (5.0 mL), hexamethylenetetramine (0.69 g, 4.9 mmol) was added at ambient temperature. The mixture was refluxed for 8 h. Cooled to ambient temperature, the reaction mixture was  
15 diluted with water, extracted with ethyl acetate for 2 times. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated. The residue was purified by chromatography on silica gel (hexane/ethyl acetate) to afford 5-chloro-7-azaindole-3-carboxaldehyde as solid (0.13 g, y.22%).

20 [0078]

$^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  (ppm) 10.01 (s, 1H), 9.77 (br. s, 1H), 8.61 (d, 1H,  $J = 2.04$  Hz), 8.37 (d, 1H,  $J = 2.08$  Hz), 7.99 (d, 1H,  $J = 2.64$  Hz); LCMS (m/z): 181.2 [ $\text{M} + \text{H}$ ] $^+$ .

25 Fifth Step

[0079]

To a solution of 5-chloro-7-azaindole-3-carboxaldehyde (0.019 g, 0.11 mmol) and ethyl 4-oxo-2-(phenylamino)-4,5-dihydrofuran-3-carboxylate (0.025 g, 0.10 mmol) in ethanol (1.0 mL), piperidine (0.012 mL, 0.12 mmol) was added at ambient temperature.

The mixture was refluxed for 2 days. Cooled to ambient temperature, solvents were removed under reduced pressure then the residue was purified by preparative HPLC to afford the titled compound (0.0020 g, y. 4.6%).

[0080]

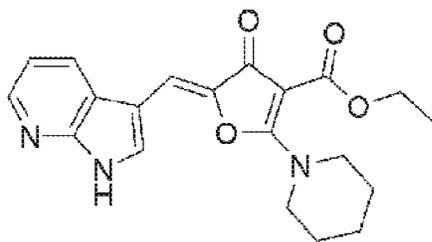
$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.52 (br. s, 1H), 10.58 (s, 1H), 8.42 (d,  $J = 2.26$  Hz, 1H), 8.26 (d,  $J = 2.26$  Hz, 1H), 7.71 (d,  $J = 2.51$  Hz, 1H), 7.55 - 7.63 (m, 2H), 7.51 (t,  $J = 7.78$  Hz, 2H), 7.35 - 7.44 (m, 1H), 7.00 (s, 1H), 4.28 (q,  $J = 7.03$  Hz, 2H), 1.30 (t,  $J = 7.15$  Hz, 3H); LCMS (m/z): 410.0  $[\text{M}+\text{H}]^+$ .

Example 4

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-4-oxo-2-piperidino-4,5-dihydrofuran-3-carboxylate

[0081]

[Chemical Formula 13]



First Step

[0082]

Diethyl malonate (5.0 mL, 0.033 mol) was added dropwise to a solution of sodium hydride (60% w/w in oil, 2.7 g, 0.066 mol) in anhydrous tetrahydrofuran (50 mL) that cooled with ice bath.

The mixture was refluxed for 5 min. The reaction mixture was cooled with ice bath, chloroacetyl chloride (2.8 mL, 0.035 mol)

was added dropwise to the reaction mixture and the mixture was stirred for 1 h then stirred at 45 °C for 1 h. The reaction mixture

was cooled with ice bath again then piperidine (3.9 mL, 0.040 mol) was added dropwise and stirred at ambient temperature for further 12 h. The reaction mixture was diluted with aqueous saturated sodium bicarbonate solution, and extracted with ethyl acetate for 2 times then extracted with chloroform. The

organic layer was washed with brine, dried over sodium sulfate and concentrated. The residue was purified by chromatography on silica gel (chloroform/methanol) to afford ethyl 4-oxo-2-piperidino-4,5-dihydrofuran-3-carboxylate as solid (3.5 g, y. 45%).

[0083]

$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 4.53 (s, 2 H), 4.10 (q,  $J = 7.03$  Hz, 2 H), 3.48 - 3.60 (m, 4 H), 1.56 - 1.67 (m, 6 H), 1.20 (t,  $J = 7.03$  Hz, 16 H); LCMS (m/z): 240.0  $[\text{M}+\text{H}]^+$ .

Second Step

[0083]

$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 4.53 (s, 2 H), 4.10 (q,  $J = 7.03$  Hz, 2 H), 3.48 - 3.60 (m, 4 H), 1.56 - 1.67 (m, 6 H), 1.20 (t,  $J = 7.03$  Hz, 16 H); LCMS (m/z): 240.0  $[\text{M}+\text{H}]^+$ .

Second Step

[0084]

To a solution of ethyl 4-oxo-2-piperidino-4,5-dihydrofuran-3-carboxylate (0.10 g, 0.42 mmol) and 7-azaindole-3-carboxaldehyde (0.061 g, 0.42 mmol) in ethanol (2.0 mL), piperidine (0.041 mL, 0.42 mmol) was added at ambient temperature. The mixture was refluxed for 24 h. Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol and diisopropyl ether then dried to afford the titled compound (0.045 g, y. 29%).

10 [0085]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.29 (br. s, 1H), 8.37 (dd, J = 1.25, 8.03 Hz, 1H), 8.31 (dd, J = 1.51, 4.52 Hz, 1H), 7.96 (d, J = 2.76 Hz, 1H), 7.19 (dd, J = 4.64, 7.91 Hz, 1H), 6.84 (s, 1H), 4.16 (q, J = 7.19 Hz, 2H), 3.70 - 3.80 (m, 4H), 1.65 - 1.78 (m, 6 H), 1.24 (t, J = 7.03 Hz, 3H); LCMS (m/z): 368.0 [M+H]<sup>+</sup>.

15

Example 5

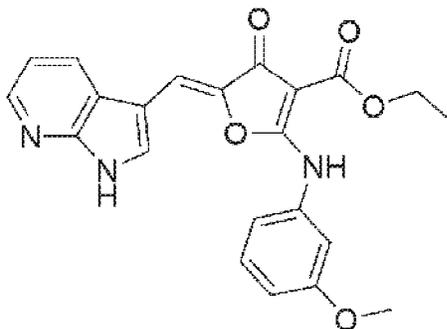
[0086]

Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-2-[(3-methoxyphenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

20

[0087]

[Chemical Formula 14]



[0088]

To a solution of ethyl 2-[(3-methoxyphenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.28 g, 1.0 mmol) which similarly prepared according to the procedure described in the Example 2,

5 First step and 7-azaindole-3-carboxaldehyde (0.15 g, 1.2 mmol) in ethanol (4.0 mL), piperidine (0.12 mL, 1.2 mmol) was added at ambient temperature. The mixture was refluxed for 2 days.

Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol and diisopropyl ether then dried to afford the titled compound (0.17 g, y. 29%).

[0089]

$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.34 (br. s, 1H), 10.52 (s, 1H), 8.25 (dd,  $J = 1.38, 4.64$  Hz, 1H), 8.03 (d,  $J = 7.03$  Hz, 1H), 7.84 (d,  $J = 2.76$  Hz, 1H), 7.45 (t,  $J = 8.03$  Hz, 1H), 7.13 - 7.26 (m, 2H), 7.04 (dd,  $J = 2.01, 8.28$  Hz, 1H), 6.86 - 6.95 (m, 2H), 4.27 (q,  $J = 7.03$  Hz, 2H), 3.77 (s, 3H), 1.30 (t,  $J = 7.15$  Hz, 3H); LCMS (m/z): 406.0  $[\text{M}+\text{H}]^+$ .

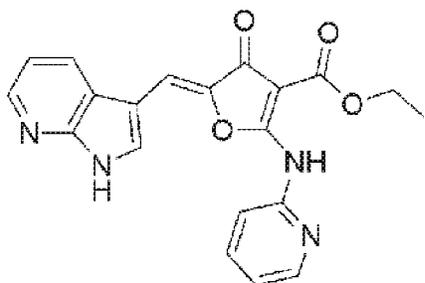
20 Example 6

[0090]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-4-oxo-2-(2-pyridinylamino)-4,5-dihydrofuran-3-carboxylate

[0091]

5 [Chemical Formula 15]



[0092]

To a solution of ethyl 4-oxo-2-(2-pyridinylamino)-4,5-dihydrofuran-3-carboxylate (0.080 g, 0.32 mmol) which similarly prepared according to the procedure described in the Example 4, First step and 7-azaindole-3-carboxaldehyde (0.047 g, 0.32 mmol) in ethanol (2.0 mL), piperidine (0.038 mL, 0.39 mmol) was added at ambient temperature. The mixture was refluxed for 10 h. Cooled to ambient temperature, the precipitate was removed by filtration and the filtrate was purified by preparative HPLC to afford the titled compound as solid (0.0030 g, y. 2.5%).

[0093]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.41 (br. s, 1H), 10.74 (br. s, 1H), 8.60 (d, *J* = 3.26 Hz, 1H), 8.35 (d, *J* = 7.78 Hz, 1H), 8.30 (dd, *J* = 1.38, 4.64 Hz, 1H), 8.24 (br. s, 1H), 7.97 (dt, *J* = 1.88, 7.84 Hz, 1H), 7.61 (d, *J* = 8.03 Hz, 1H), 7.36 - 7.45 (m, 1H), 7.

02 - 7.14 (m, 2H), 4.27 (q, J = 7.03 Hz, 2H), 1.29 (t, J = 7.03 Hz, 3H); LCMS (m/z): 377.0 [M+H]<sup>+</sup>.

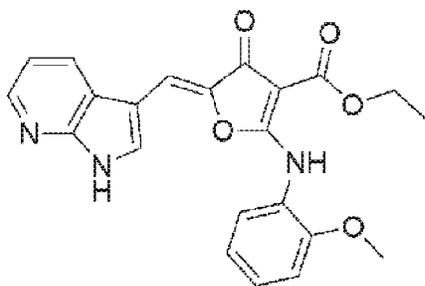
Example 7

5 [0094]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(2-methoxyphenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[0095]

[Chemical Formula 16]



10

[0096]

To a solution of ethyl 2-[(2-methoxyphenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.28 g, 1.0 mmol) which similarly prepared according to the procedure described in the Example 2,

15 First step and 7-azaindole-3-carboxaldehyde (0.15 g, 1.2 mmol) in ethanol (4.0 mL), piperidine (0.12 mL, 1.2 mmol) was added at ambient temperature. The mixture was refluxed for 2 days.

Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol and diisopropyl ether then dried to afford the titled compound (0.30 g, y. 74%).

20

[0097]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.34 (br. s, 1H), 10.35 (s, 1H), 8.25 (dd, J = 1.38, 4.64 Hz, 1H), 8.02 (d, J = 7.03 Hz, 1H), 7.85 (d, J = 2.76 Hz, 1H), 7.66 (dd, J = 1.38, 7.91 Hz, 1H), 7.41 - 7.51 (m, 1H), 7.28 (d, J = 7.53 Hz, 1H), 7.12 (t, J = 7.65 Hz, 1H), 6.88 - 6.99 (m, 2H), 4.28 (q, J = 7.03 Hz, 2H), 3.85 (s, 3 H), 1.30 (t, J = 7.15 Hz, 3H); LCMS (m/z): 406.0 [M+H]<sup>+</sup>.

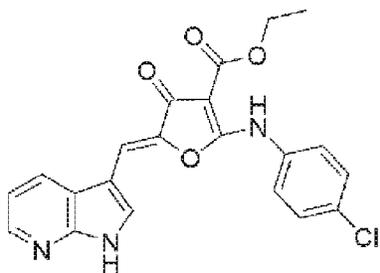
Example 8

[0098]

10 Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(4-chlorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[0099]

[Chemical Formula 17]



15 [0100]

To a solution of ethyl 2-[(4-chlorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.18 g, 0.61 mmol) which similarly prepared according to the procedure described in the Example 2, First step and 7-azaindole-3-carboxaldehyde (0.088 g, 0.61 mmol) in ethanol (10 mL), piperidine (0.0044 mL, 0.044 mmol) was added at ambient temperature. The mixture was refluxed for 6

days. Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol and hexane then dried to afford the titled compound (0.061 g, y. 23%).

[0101]

5  $^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.33 (br. s, 1H), 10.61 (s, 1H), 8.26 (d,  $J = 3.26$  Hz, 1H), 7.96 (d,  $J = 7.53$  Hz, 1H), 7.82 (d,  $J = 2.76$  Hz, 1H), 7.58 - 7.67 (m, 4H), 6.87 - 6.95 (m, 2H), 4.27 (q,  $J = 7.03$  Hz, 2H), 1.29 (t,  $J = 7.03$  Hz, 3H); LCMS (m/z): 409.9 [M+H] $^+$ .

10

Example 9

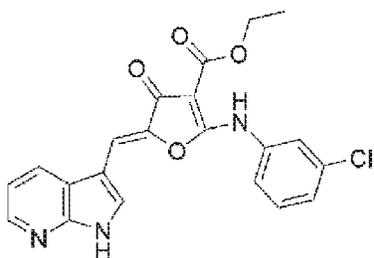
[0102]

Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-2-[(3-chlorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

15

[0103]

[Chemical Formula 18]



[0104]

To a solution of ethyl 2-[(3-chlorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.10 g, 0.36 mmol) which similarly prepared according to the procedure described in the Example 2, First step and 7-azaindole-3-carboxaldehyde (0.051 g, 0.35 mm

20

ol) in ethanol (3.0 mL), piperidine (0.0035 mL, 0.035 mmol) was added at ambient temperature. The mixture was refluxed for 6 days. Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol then dried to afford the titled compound (0.061 g, y. 23%).

[0105]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.36 (br. s, 1H), 10.63 (s, 1H), 8.26 (dd, J = 1.38, 4.64 Hz, 1H), 8.01 (d, J = 7.28 Hz, 1H), 7.82 (d, J = 2.76 Hz, 1H), 7.76 (s, 1H), 7.50 - 7.61 (m, 3H), 6.89 - 6.96 (m, 2H), 4.28 (q, J = 7.03 Hz, 2H), 1.30 (t, J = 7.03 Hz, 3H); LCMS (m/z): 409.9 [M+H]<sup>+</sup>.

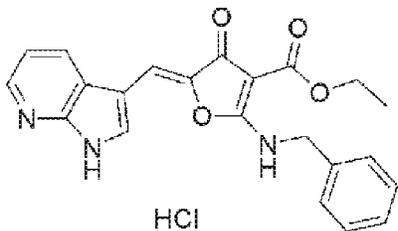
Example 10

[0106]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-(benzylamino)-4-oxo-4,5-dihydrofuran-3-carboxylate hydrochloride

[0107]

[Chemical Formula 19]



[0108]

A solution of ethyl 2-(benzylamino)-4-oxo-4,5-dihydrofuran-3-carboxylate (0.026 g, 0.10 mmol) which similarly prepared acco

rding to the procedure described in the Example 2, First step  
and 7-azaindole-3-carboxaldehyde (0.015 g, 0.10 mmol) in 2M hy  
drochloric acid in ethanol (1.0 mL) was refluxed for 4 h. Cool  
ed to ambient temperature, the precipitate was collected by fi  
5 ltration, washed with ethanol and diisopropyl ether then dried  
to afford the titled compound (0.024 g, y. 56%).

[0109]

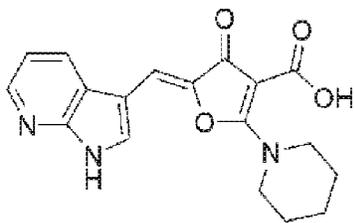
$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.25 - 12.56 (m, 1H), 9.54 (br. s, 1  
H), 8.25 - 8.42 (m, 2H), 7.86 (s, 1H), 7.35 - 7.48 (m, 4H), 7.2  
10 4 - 7.33 (m, 1H), 7.08 - 7.18 (m, 1H), 6.87 (s, 1H), 4.86 (d, J  
= 6.53 Hz, 2H), 4.23 (q, J = 7.19 Hz, 2H), 1.27 (t, J = 7.03 H  
z, 3H); LCMS (m/z): 390.0 [M+H] $^+$ .

Example 11

15 5-[(1H-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-4-oxo-2-piperidi  
no-4,5-dihydrofuran-3-carboxylic acid

[0110]

[Chemical Formula 20]



20 [0111]

To a solution of the compound of Example 4 in dioxane (0.5 mL),  
2M sodium hydroxide solution (0.50 mL, 1.0 mmol) was added at

ambient temperature. The mixture was stirred at 110 °C for 1.5 h. Cooled to ambient temperature, the reaction mixture was neutralized by 2M hydrochloric acid solution then the solvent was removed under reduced pressure. The residue was purified by preparative HPLC to afford the titled compound (0.0044 g, y. 45%).

[0112]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.24 (br. s, 1H), 8.39 (d, J = 8.03 Hz, 1H), 8.30 (dd, J = 1.38, 4.64 Hz, 1H), 7.92 (d, J = 2.26 Hz, 1H), 7.19 (dd, J = 4.77, 8.03 Hz, 1H), 6.73 (s, 1H), 3.35 - 3.62 (m, 4H), 1.45 - 1.69 (m, 6H); LCMS (m/z): 339.9 [M+H]<sup>+</sup>.

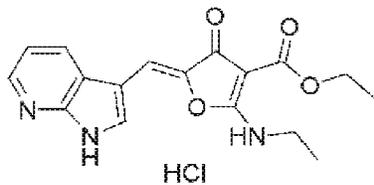
Example 12

[0113]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-(ethylamino)-4-oxo-4,5-dihydrofuran-3-carboxylate hydrochloride

[0114]

[Chemical Formula 21]



[0115]

To a solution of ethyl 2-(ethylamino)-4-oxo-4,5-dihydrofuran-3-carboxylate (0.033 g, 0.17 mmol) which similarly prepared according to the procedure described in the Example 2, First ste

p and 7-azaindole-3-carboxaldehyde (0.024 g, 0.17 mmol) in ethanol (1.5 mL), 2M hydrochloric acid in ethanol (0.17 mL, 0.34 mmol) was added at ambient temperature. The mixture was refluxed for 4 h. Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol and diisopropyl ether then dried to afford the titled compound (0.026 g, y. 42%).

[0116]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.46 (br. s, 1H), 9.03 (t, J = 6.02 Hz, 1H), 8.45 - 8.54 (m, 1H), 8.35 (dd, J = 1.25, 4.77 Hz, 1H), 8.01 (d, J = 1.25 Hz, 1H), 7.25 (dd, J = 4.77, 8.03 Hz, 1H), 6.90 (s, 1H), 4.25 - 4.50 (m, 1H), 4.21 (q, J = 7.19 Hz, 2H), 3.61 - 3.71 (m, 2H), 1.30 (t, J = 7.15 Hz, 3H), 1.26 (t, J = 7.03 Hz, 3H); LCMS (m/z): 328.0 [M+H]<sup>+</sup>.

15

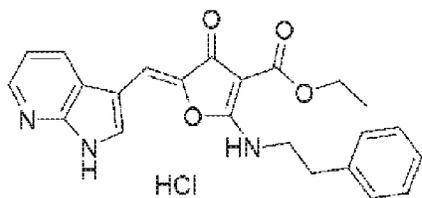
Example 13

[0117]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-4-oxo-2-(phenethylamino)-4,5-dihydrofuran-3-carboxylate hydrochloride

20 [0118]

[Chemical Formula 22]



[0119]

To a solution of ethyl 4-oxo-2-(phenethylamino)-4,5-dihydrofuran-3-carboxylate (0.041 g, 0.15 mmol) which similarly prepared according to the procedure described in the Example 4, First step and 7-azaindole-3-carboxaldehyde (0.022 g, 0.15 mmol) in ethanol (1.0 mL), 2M hydrochloric acid in ethanol (0.16 mL, 0.32 mmol) was added at ambient temperature. The mixture was refluxed for 3 h. Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol and diisopropyl ether then dried to afford the titled compound (0.023 g, y. 32%).

[0120]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.45 (br. s, 1H), 9.02 (t, J = 6.15 Hz, 1H), 8.40 (d, J = 6.78 Hz, 1H), 8.33 (dd, J = 1.38, 4.64 Hz, 1H), 7.94 (d, J = 2.26 Hz, 1H), 7.23 - 7.33 (m, 4H), 7.11 - 7.22 (m, 2H), 6.84 (s, 1H), 4.21 (q, J = 7.19 Hz, 2H), 3.85 (q, J = 6.94 Hz, 2H), 3.00 (t, J = 7.28 Hz, 2H), 1.25 (t, J = 7.03 Hz, 3H); LCMS (m/z): 404.0 [M+H]<sup>+</sup>.

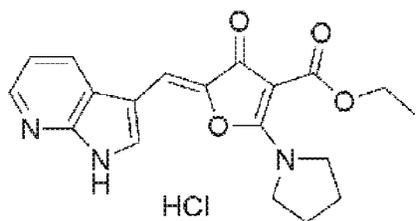
20 Example 14

[0121]

Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-4-oxo-2-pyrrolidinyl-4,5-dihydrofuran-3-carboxylate hydrochloride

[0122]

25 [Chemical Formula 23]



[0123]

To a solution of ethyl 4-oxo-2-pyrrolidinyl-4,5-dihydrofuran-3-carboxylate (0.034 g, 0.15 mmol) which similarly prepared according to the procedure described in the Example 4, First step and 7-azaindole-3-carboxaldehyde (0.022 g, 0.15 mmol) in ethanol (1.0 mL), 2M hydrochloric acid in ethanol (0.16 mL, 0.32 mmol) was added at ambient temperature. The mixture was refluxed for 3 h. Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol and diisopropyl ether then dried to afford the titled compound (0.038 g, y. 61%).

[0124]

$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.38 (br. s, 1H), 8.46 (d,  $J$  = 8.03 Hz, 1H), 8.33 (dd,  $J$  = 1.38, 4.64 Hz, 1H), 7.95 (d,  $J$  = 2.26 Hz, 1H), 7.23 (dd,  $J$  = 4.77, 7.78 Hz, 1H), 6.84 (s, 1H), 4.16 (q,  $J$  = 7.03 Hz, 2H), 3.79 - 3.98 (m, 3H), 3.63 - 3.73 (m, 2H), 1.92 - 2.05 (m, 4H), 1.24 (t,  $J$  = 7.03 Hz, 3H); LCMS ( $m/z$ ): 354.0 [ $M+H$ ] $^+$ .

20

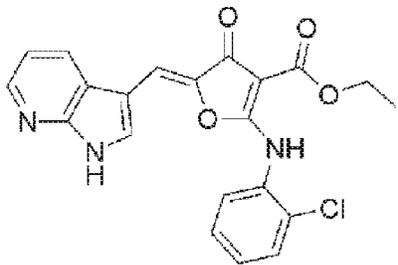
Example 15

[0125]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(2-chlorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[0126]

[Chemical Formula 24]



5

[0127]

To a solution of ethyl 2[(2-chlorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.14 g, 0.50 mmol) which similarly prepared according to the procedure described in the Example 2, First step and 7-azaindole-3-carboxaldehyde (0.073 g, 0.50 mmol) in ethanol (2.0 mL), piperidine (0.054 mL, 0.55 mmol) was added at ambient temperature. The mixture was refluxed for 12 h.

Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol and diisopropyl ether then dried to afford the titled compound (0.099 g, y. 48%).

[0128]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.31 (br. s, 1H), 10.65 (s, 1H), 8.22 (dd, *J* = 1.38, 4.64 Hz, 1H), 7.70 - 7.83 (m, 4H), 7.51 - 7.64 (m, 2H), 6.92 (s, 1H), 6.81 (dd, *J* = 4.64, 7.91 Hz, 1H), 4.29 (q, *J* = 7.11 Hz, 2H), 1.30 (t, *J* = 7.03 Hz, 3H); LCMS (*m/z*): 409.8 [M+H]<sup>+</sup>.

20

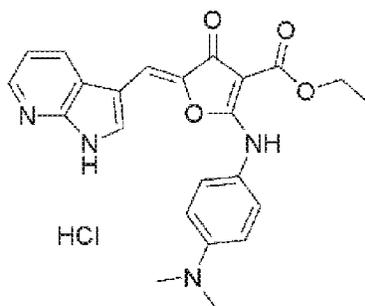
Example 16

[0129]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[[4-(dimethylamino)phenyl]amino]-4-oxo-4,5-dihydrofuran-3-carboxylate hydrochloride

[0130]

[Chemical Formula 25]



10 [0131]

To a solution of ethyl 2-[[4-(dimethylamino)phenyl]amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.073 g, 0.20 mmol) which is similarly prepared according to the procedure described in the Example 2, First step and 7-azaindole-3-carboxaldehyde (0.029 g, 0.20 mmol) in ethanol (1.5 mL), 2M hydrochloric acid in ethanol (0.33 mL, 0.66 mmol) was added at ambient temperature. The mixture was refluxed for 1 h. Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol and diisopropyl ether then dried to afford the titled compound (0.034 g, y. 35%).

[0132]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.51 (br. s, 1H), 10.47 (br. s, 1H), 8.23 - 8.33 (m, 1H), 8.10 (d, J = 7.78 Hz, 1H), 7.81 (s, 1H), 7.50 (d, J = 8.03 Hz, 2H), 7.16 (br. s, 2H), 6.95 (dd, J = 4.77, 7.78 Hz, 1H), 6.90 (s, 1H), 4.40 - 5.20 (m, 1H), 4.27 (q, J = 7.03 Hz, 2H), 3.08 (s, 6H), 1.29 (t, J = 7.15 Hz, 3H); LCMS (m/z): 419.0 [M+H]<sup>+</sup>.

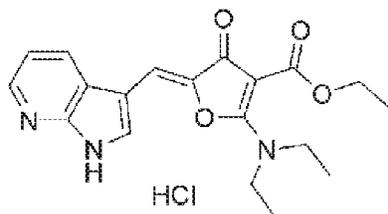
Example 17

[0133]

10 Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-(diethylamino)-4-oxo-4,5-dihydrofuran-3-carboxylate hydrochloride

[0134]

[Chemical Formula 26]



15 [0135]

To a solution of ethyl 2-(diethylamino)-4-oxo-4,5-dihydrofuran-3-carboxylate (0.034 g, 0.15 mmol) which similarly prepared according to the procedure described in the Example 4, First step and 7-azaindole-3-carboxaldehyde (0.022 g, 0.15 mmol) in ethanol (1.0 mL), 2M hydrochloric acid in ethanol (0.16 mL, 0.3  
20 2 mmol) was added at ambient temperature. The mixture was refluxed for 3 h. Cooled to ambient temperature, the precipitate wa

s collected by filtration, washed with ethanol and diisopropyl ether then dried to afford the titled compound (0.023 g, y. 38%).

[0136]

5  $^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.36 (br. s, 1H), 8.41 (d,  $J = 7.78$  Hz, 1H), 8.33 (dd,  $J = 1.25, 4.77$  Hz, 1H), 7.93 (d,  $J = 2.26$  Hz, 1H), 7.22 (dd,  $J = 4.77, 7.78$  Hz, 1H), 6.84 (s, 1H), 4.18 (q,  $J = 7.11$  Hz, 2H), 3.50 - 3.84 (m, 5H), 1.11 - 1.38 (m, 9H); LCMS (m/z): 356.0 [M+H] $^+$ .

10

Example 18

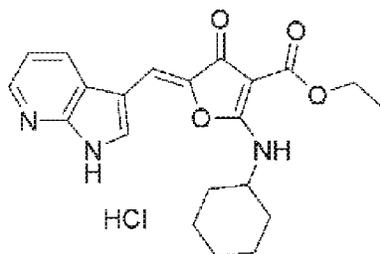
[0137]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-(cyclohexylamino)-4-oxo-4,5-dihydrofuran-3-carboxylate hydrochloride

15

[0138]

[Chemical Formula 27]



[0139]

To a solution of ethyl 2-(cyclohexylamino)-4-oxo-4,5-dihydrofuran-3-carboxylate (0.019 g, 0.075 mmol) which similarly prepared according to the procedure described in the Example 2, First step and 7-azaindole-3-carboxaldehyde (0.011 g, 0.075 mmol)

20

in ethanol (1.0 mL), 2M hydrochloric acid in ethanol (0.079 mL, 0.16 mmol) was added at ambient temperature. The mixture was refluxed for 4 h. Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol and diisopropyl ether then dried to afford the titled compound (0.0070 g, y. 22%).

[0140]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.40 (br. s, 1H), 8.53 (d, J = 8.53 Hz, 1H), 8.46 (d, J = 7.78 Hz, 1H), 8.34 (dd, J = 1.26, 4.52 Hz, 1H), 7.99 (d, J = 2.26 Hz, 1H), 7.22 (dd, J = 4.64, 7.91 Hz, 1H), 6.90 (s, 1H), 4.21 (q, J = 7.03 Hz, 2H), 3.91 - 4.09 (m, 1H), 1.98 (d, J = 9.79 Hz, 2H), 1.79 (d, J = 13.05 Hz, 2H), 1.55 - 1.70 (m, 3H), 1.35 - 1.49 (m, 2H), 1.16 - 1.29 (m, 4H); LCMS (m/z): 382.4 [M+H]<sup>+</sup>.

15

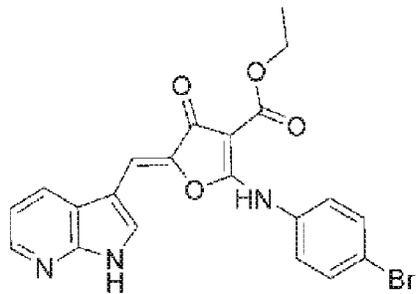
Example 19

[0141]

Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-2-[(4-bromophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

20 [0142]

[Chemical Formula 28]



[0143]

To a solution of ethyl 2-[(4-bromophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.15 g, 0.46 mmol) which similarly prepared according to the procedure described in the Example 4, First step and 7-azaindole-3-carboxaldehyde (0.067 g, 0.46 mmol) in ethanol (5.0 mL), piperidine (0.85 mL, 0.92 mmol) was added at ambient temperature. The mixture was refluxed for 24 h.

Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol then dried to afford the titled compound (0.075 g, y. 36%).

[0144]  $^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.34 (br. s, 1H), 10.61 (br. s, 1H), 8.26 (d,  $J = 3.42$  Hz, 1H), 7.95 (d,  $J = 7.34$  Hz, 1H), 7.84 (br. s, 1H), 7.72 (d,  $J = 8.31$  Hz, 2H), 7.57 (d,  $J = 8.31$  Hz, 2H), 6.77 - 7.05 (m, 2H), 4.07 - 4.42 (m, 2H), 1.29 (t,  $J = 6.85$  Hz, 3H); LCMS (m/z): 382.4  $[\text{M}+\text{H}]^+$ .

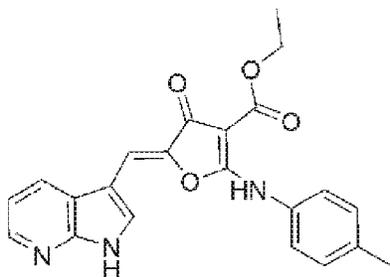
Example 20

[0145]

Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-4-oxo-2-(p-tolylamino)-4,5-dihydrofuran-3-carboxylate

[0146]

[Chemical Formula 29]



The titled compound was similarly prepared according to the procedure described in the Example 19.

[0147]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.30 (br. s, 1H), 10.51 (br. s, 1H), 8.24 (d, J = 3.42 Hz, 1H), 7.97 (d, J = 7.34 Hz, 1H), 7.80 (br. s, 1H), 7.46 (d, J = 7.82 Hz, 2H), 7.34 (d, J = 8.31 Hz, 2H), 6.74 - 7.02 (m, 2H), 4.14 - 4.37 (m, 2H), 2.44 (s, 3H), 1.29 (t, J = 6.85 Hz, 3H); LCMS (m/z): 390.6 [M+H]<sup>+</sup>.

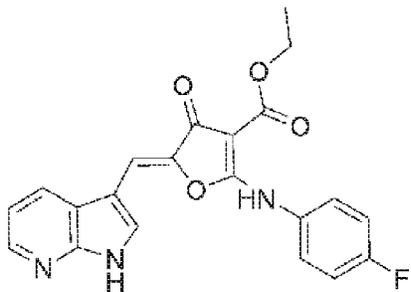
Example 21

[0148]

15 Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-2-[(4-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[0149]

[Chemical Formula 30]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 19.

[0150]

5  $^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.28 (br. s, 1H), 10.57 (br. s, 1H), 8.24 (br. s, 1H), 7.95 (d,  $J = 7.82$  Hz, 1H), 7.75 (br. s, 1H), 7.60 - 7.68 (m, 2H), 7.38 (t,  $J = 8.31$  Hz, 2H), 6.85 - 6.93 (m, 2H), 4.11 - 4.50 (m, 2H), 1.29 (t,  $J = 6.85$  Hz, 3H); LCMS (m/z): 394.2  $[\text{M}+\text{H}]^+$ .

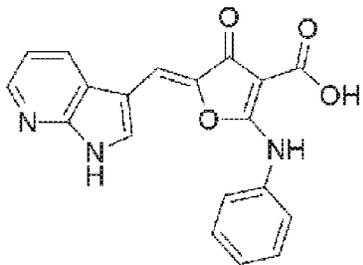
10

Example 22

5-[(1H-Pyrrolo[2,3-b]pyridin-3-yl)methylene]-4-oxo-2-(phenylamino)-4,5-dihydrofuran-3-carboxylic acid

[0151]

15 [Chemical Formula 31]



[0152]

To a solution of the compound (0.050g, 0.13mmol) of Example 1 in ethanol (1.0 mL), 50% potassium hydroxide solution (0.5 mL, 0.13 mmol) was added at ambient temperature. The mixture was refluxed for 1 h. Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol. The crude material was dissolved in water (0.5 mL) and tetrahydrofuran (0.5 mL), then 2M hydrochloric acid (0.023 mL, 0.046 mmol) was added and the mixture was stirred for 30 min. The precipitate was collected by filtration, washed with water and diethyl ether then dried to afford the titled compound (0.012 g, y. 26%).

[0153]

$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.11 (br. s, 2H), 8.21 (dd,  $J = 1.25$ , 4.52 Hz, 1H), 8.06 (d,  $J = 7.78$  Hz, 1H), 7.73 (d,  $J = 2.26$  Hz, 1H), 7.38 - 7.49 (m, 2H), 7.32 (d,  $J = 7.53$  Hz, 2H), 7.19 - 7.27 (m, 1H), 6.91 (dd,  $J = 4.64$ , 7.91 Hz, 1H), 6.66 (s, 1H); LCMS (m/z): 347.9 [M+H] $^+$ .

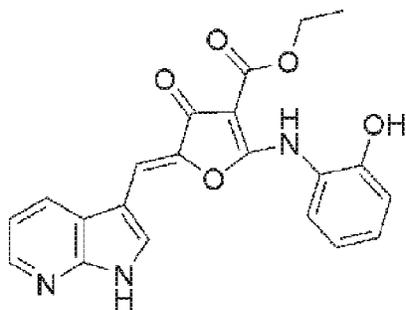
Example 23

[0154]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(2-hydroxyphenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[0155]

[Chemical Formula 32]



[0156]

To a solution of ethyl 2-[(2-hydroxyphenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.050 g, 0.19 mmol) which similarly prepared according to the procedure described in the Example 4 and 7-azaindole-3-carboxaldehyde (0.023 g, 0.16 mmol) in ethanol (1.0 mL), piperidine (0.0010 mL, 0.010 mmol) was added at ambient temperature. The mixture was refluxed for 2 days. The precipitate was collected by filtration, washed with hot ethanol. The solid was washed hexane then dried to afford the titled compound (0.008 g, y. 11%).

[0157]

$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.33 (br. s, 1H), 10.35 (s, 1H), 10.30 (s, 1H), 8.25 (dd,  $J = 1.38, 4.64$  Hz, 1H), 8.06 (d,  $J = 7.03$  Hz, 1H), 7.87 (d,  $J = 2.76$  Hz, 1H), 7.58 (d,  $J = 7.03$  Hz, 1H), 7.24 - 7.33 (m, 1H), 7.07 (dd,  $J = 1.00, 8.28$  Hz, 1H), 6.90 - 7.01 (m, 3H), 4.28 (q,  $J = 7.03$  Hz, 2H), 1.30 (t,  $J = 7.15$  Hz, 3H); LCMS (m/z): 392.0  $[\text{M}+\text{H}]^+$ .

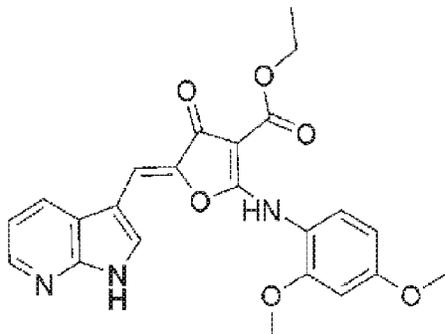
20 Example 24

[0158]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(2,4-dimethoxyphenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[0159]

[Chemical Formula 33]



5

[0160]

To a solution of ethyl 2-[(2,4-dimethoxyphenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.35 g, 1.1 mmol) which similarly prepared according to the procedure described in the Example

10

4, First step and 7-azaindole-3-carboxaldehyde (0.12 g, 1.1 mmol) in ethanol (10 mL), piperidine (0.5 mL, 4.6 mmol) was added at ambient temperature. The mixture was refluxed for 16 h.

Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol then dried to afford the tit

15

led compound (0.13 g, y. 26%).

[0161]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.31 (br. s, 1H), 10.14 (br. s, 1H), 8.24 (br. s, 1H), 7.94 (d, *J* = 7.82 Hz, 1H), 7.80 (br. s, 1H), 7.51 (d, *J* = 8.80 Hz, 1H), 6.78 - 6.93 (m, 3H), 6.68 (d, *J* = 8.

20

31 Hz, 1H), 4.26 (d, *J* = 6.85 Hz, 2H), 3.89 (s, 3H), 3.81 (s, 3

H), 1.29 (t, J = 6.60 Hz, 3H); LCMS (m/z): 436.2 [M+H]<sup>+</sup>.

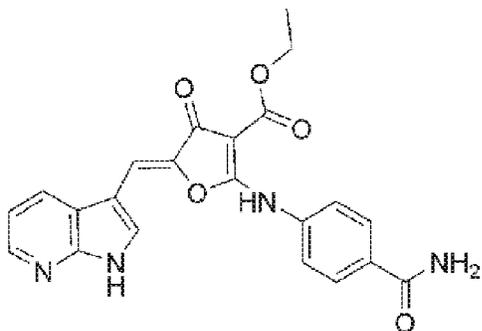
Example 25

[0162]

5 Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-2-[(4-carbamoylphenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[0163]

[Chemical Formula 34]



10 The titled compound(solid) was similarly prepared according to the procedure described in the Example 24.

[0164]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.34 (br. s, 1H), 10.67 (br. s, 1H), 8.24 (br. s, 1H), 7.95 - 8.13 (m, 4H), 7.84 (br. s, 1H), 7.67 (d, J = 7.34 Hz, 2H), 7.49 (br. s, 1H), 6.75 - 7.08 (m, 2H), 4.28 (d, J = 6.85 Hz, 2H), 1.30 (t, J = 6.36 Hz, 3H); LCMS (m/z): 419.0 [M+H]<sup>+</sup>.

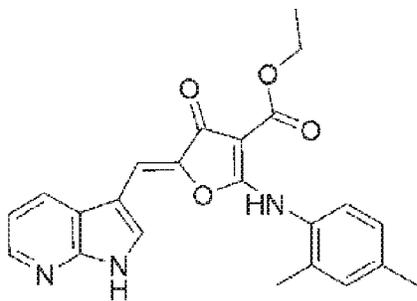
Example 26

20 [0165]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(2,4-di  
methylphenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[0166]

[Chemical Formula 35]



The titled compound(solid) was similarly prepared according to  
the procedure described in the Example 24.

[0167]

10 <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.26 (br. s, 1H), 10.35 (br. s, 1H),  
8.21 (d, *J* = 3.91 Hz, 1H), 7.65 - 7.80 (m, 2H), 7.39 (d, *J* = 8.  
31 Hz, 1H), 7.27 (s, 1H), 7.20 (d, *J* = 7.82 Hz, 1H), 6.84 (s, 1  
H), 6.73 (dd, *J* = 4.40, 7.83 Hz, 1H), 4.27 (q, *J* = 7.01 Hz, 2H),  
2.44 (s, 3H), 2.23 (s, 3H), 1.30 (t, *J* = 6.85 Hz, 3H); LCMS (*m*  
/z): 404.0 [M+H]<sup>+</sup>.

15

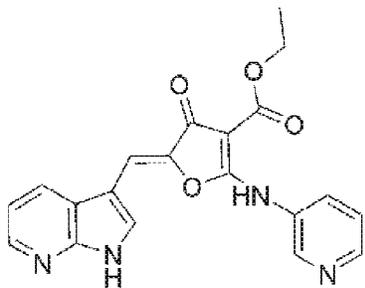
Example 27

[0168]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-4-oxo-2-(3  
-pyridinylamino)-4,5-dihydrofuran-3-carboxylate

20 [0169]

[Chemical Formula 36]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 24.

[0170]

5 <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.33 (br. s, 1H), 10.72 (br. s, 1H), 8.82 (br. s, 1H), 8.65 (br. s., 1H), 8.24 (br. s, 1H), 7.90 - 8.11 (m, 2H), 7.73 (br. s, 1H), 7.54 - 7.62 (m, 1H), 6.87 - 6.97 (m, 2H), 4.28 (d, J = 6.85 Hz, 2H), 1.30 (t, J = 6.36 Hz, 3H); LCMS (m/z): 377.6 [M+H]<sup>+</sup>.

10

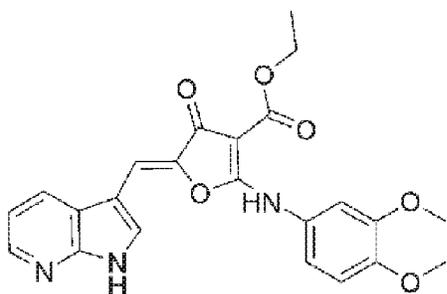
Example 28

[0171]

Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-2-[(3,4-dimethoxyphenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

15 [0172]

[Chemical Formula 37]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 24.

[0173]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.33 (br. s, 1H), 10.44 (s, 1H), 8.24 (d, J = 3.91 Hz, 1H), 7.96 (d, J = 7.82 Hz, 1H), 7.82 (br. s, 1H), 7.24 (s, 1H), 7.06 - 7.14 (m, 2H), 6.78 - 6.94 (m, 2H), 4.27 (q, J = 7.01 Hz, 2H), 3.87 (s, 3H), 3.71 (s, 3H), 1.29 (t, J = 7.09 Hz, 3H); LCMS (m/z): 436.5 [M+H]<sup>+</sup>.

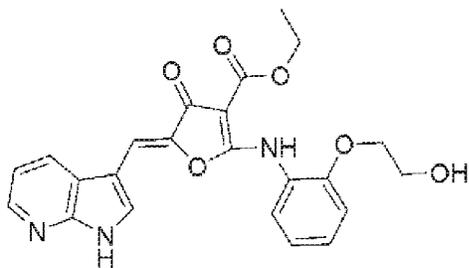
10 Example 29

[0174]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[[2-(2-hydroxyethoxy)phenyl]amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

15 [0175]

[Chemical Formula 38]



First Step

[0176]

20 A solution of ethyl 2-[[2-(2-hydroxyphenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.10 g, 0.38 mmol) which similarly pre

pared according to the procedure described in the Example 4, First step, 2-chloroethanol (0.038 mL, 0.57 mmol) and potassium carbonate (0.11 g, 0.80 mmol) in *N,N*-dimethylformamide (2.0 mL) was stirred at 90 °C for 2 days. Cooled to ambient temperature, ethyl acetate was added to the reaction mixture, the organic layer was washed with aqueous 5% citric acid solution, water and brine, dried over magnesium sulfate and concentrated. To the residue, *tert*-butyl methyl ether was added to precipitate the product. The precipitate was collected by filtration, washed with hexane then dried to afford ethyl 2-([2-(2-hydroxyethoxy)phenyl]amino)-4-oxo-4,5-dihydrofuran-3-carboxylate as solid (0.041 g, y. 35%).

[0177]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 10.40 (s, 1H), 7.66 (d, *J* = 7.53 Hz, 1H), 7.16 - 7.25 (m, 2H), 6.97 - 7.05 (m, 1H), 4.82 (br. s, 1H), 4.75 (s, 2H), 4.24 (q, *J* = 7.03 Hz, 2H), 4.15 (t, *J* = 5.14 Hz, 2H), 3.72 - 3.80 (m, 2H), 1.26 (t, *J* = 7.15 Hz, 3H); LCMS (*m/z*): 308.0 [M+H]<sup>+</sup>.

20 Second Step

[0178]

To a solution of ethyl 2-([2-(2-hydroxyethoxy)phenyl]amino)-4-oxo-4,5-dihydrofuran-3-carboxylate (0.021 g, 0.068 mmol) and 7-azaindole-3-carboxaldehyde (0.0087 g, 0.060 mmol) in ethanol (0.5 mL), 2M hydrochloric acid in ethanol (0.030 mL, 0.059 mm

ol) was added at ambient temperature. The mixture was refluxed for 4 h. Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol and hexane then dried to afford the titled compound as solid (0.021 g, y. 72%).

5 [0179]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.36 (br. s, 1H), 10.33 (s, 1H), 8.24 - 8.29 (m, 1H), 8.07 (d, J = 6.78 Hz, 1H), 7.85 (s, 1H), 7.65 - 7.70 (m, 1H), 7.38 - 7.46 (m, 1H), 7.29 (d, J = 7.78 Hz, 1H), 7.11 (t, J = 7.65 Hz, 1H), 6.92 - 6.99 (m, 2H), 4.41 (br. s, 1H), 4.28 (q, J = 7.20 Hz, 2H), 4.10 (t, J = 5.14 Hz, 2H), 3.65 (t, J = 5.02 Hz, 2H), 1.30 (t, J = 7.03 Hz, 3H); LCMS (m/z): 436 [M+H]<sup>+</sup>.

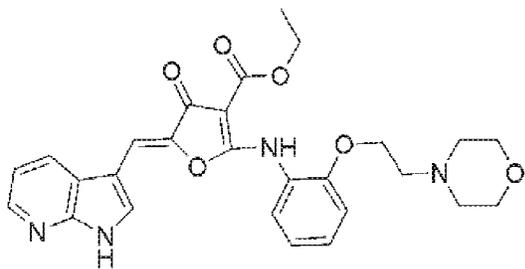
Example 30

15 [0180]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[[2-(2-morpholinoethoxy)phenyl]amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[0181]

20 [Chemical Formula 39]



[0182]

To a solution of ethyl 2-([2-(2-morpholinoethoxy)phenyl]amino)-4-oxo-4,5-dihydrofuran-3-carboxylate (0.021 g, 0.054 mmol) which similarly prepared according to the procedure described in the Example 29, First step and 7-azaindole-3-carboxaldehyde (0.0070 g, 0.048 mmol) in ethanol (0.5 mL), 2M hydrochloric acid in ethanol (0.024 mL, 0.048 mmol) was added at ambient temperature. The mixture was refluxed for 4 h. The reaction mixture was cooled with ice bath. Aqueous 2M sodium hydroxide solution (0.024 mL, 0.048 mmol) was added dropwise to neutralize and the mixture was stirred for 1 h. The precipitate was collected by filtration then purified by preparative HPLC to afford the titled compound as solid (0.0054 g, y. 21%).

[0183]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.31 (br. s, 1H), 10.35 (br. s, 1H), 8.24 (dd, J = 1.25, 4.52 Hz, 1H), 7.94 (d, J = 7.78 Hz, 1H), 7.83 (d, J = 2.01 Hz, 1H), 7.62 (d, J = 7.03 Hz, 1H), 7.42 - 7.50 (m, 1H), 7.28 (d, J = 7.78 Hz, 1H), 7.12 (t, J = 7.28 Hz, 1H), 6.92 (s, 1H), 6.88 (dd, J = 4.64, 7.91 Hz, 1H), 4.27 (q, J = 7.03 Hz, 2H), 4.14 (t, J = 5.14 Hz, 2H), 3.36 - 3.42 (m, 4H), 2.59 (t, J = 5.02 Hz, 2H), 2.25 - 2.35 (m, 4H), 1.30 (t, J = 7.03 Hz, 3H); LCMS (m/z): 505.4 [M+H]<sup>+</sup>.

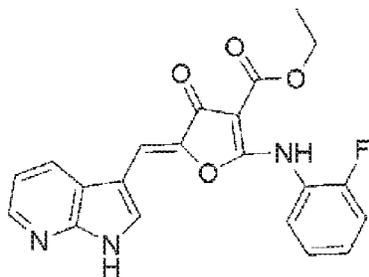
Example 31

[0184]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(2-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[0185]

[Chemical Formula 40]



[0186]

To a solution of ethyl 2-[(2-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.10 g, 0.38 mmol) which similarly prepared according to the procedure described in the Example 4,

10 First step and 7-azaindole-3-carboxaldehyde (0.050 g, 0.34 mmol) in ethanol (2.0 mL), piperidine (0.0034 mL, 0.034 mmol) was added at ambient temperature. The mixture was refluxed for 36 h. The precipitate was collected by filtration, washed with hot ethanol. The solid was washed with hexane then dried to afford the titled compound as solid (0.037 g, y. 27%).

[0187]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.31 (br. s, 1H), 10.55 (s, 1H), 8.22 (dd, *J* = 1.38, 4.64 Hz, 1H), 7.84 (d, *J* = 7.78 Hz, 1H), 7.67 - 7.77 (m, 2H), 7.55 - 7.63 (m, 1H), 7.45 - 7.53 (m, 1H), 7.37 - 7.44 (m, 1H), 6.92 (s, 1H), 6.83 (dd, *J* = 4.64, 7.91 Hz, 1H), 4.28 (q, *J* = 7.03 Hz, 2H), 1.30 (t, *J* = 7.03 Hz, 3H); LCMS (m/

20

z): 393.9 [M+H]<sup>+</sup>.

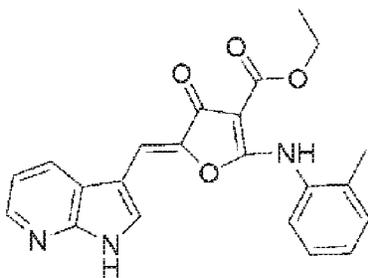
Example 32

[0188]

5 Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-4-oxo-2-(*o*-tolylamino)-4,5-dihydrofuran-3-carboxylate

[0189]

[Chemical Formula 41]



10 [0190]

To a solution of ethyl 4-oxo-2-(*o*-tolylamino)-4,5-dihydrofuran-3-carboxylate (0.098 g, 0.38 mmol) which similarly prepared according to the procedure described in the Example 4, First step and 7-azaindole-3-carboxaldehyde (0.050 g, 0.34 mmol) in ethanol (2.0 mL), piperidine (0.0034 mL, 0.034 mmol) was added at ambient temperature. The mixture was refluxed for 32 h. The precipitate was collected by filtration, washed with hot ethanol. The solid was washed with hexane then dried to afford the titled compound as solid (0.019 g, y. 27%).

20 [0191]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.26 (br. s, 1H), 10.43 (s, 1H), 8.18

- 8.22 (m, 1H), 7.69 - 7.75 (m, 2H), 7.54 (d, J = 7.78 Hz, 1H),  
7.45 - 7.49 (m, 2H), 7.37 - 7.44 (m, 1H), 6.85 (s, 1H), 6.78  
(dd, J = 4.64, 7.91 Hz, 1H), 4.28 (q, J = 7.19 Hz, 2H), 2.28 (s,  
3H), 1.30 (t, J = 7.03 Hz, 3H); LCMS (m/z): 390 [M+H]<sup>+</sup>.

5

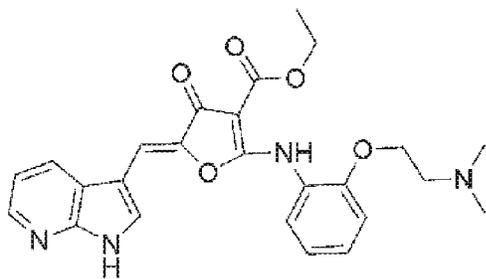
Example 33

[0192]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-({2-[2-  
(dimethylamino)ethoxy]phenyl}amino)-4-oxo-4,5-dihydrofuran-3-  
10 carboxylate

[0193]

[Chemical Formula 42]



[0194]

15 To a solution of ethyl 2-({2-[2-(dimethylamino)ethoxy]phenyl}  
amino)-4-oxo-4,5-dihydrofuran-3-carboxylate (0.010 g, 0.031 m  
mol) which similarly prepared according to the procedure descr  
ibed in the Example 29, First step and 7-azaindole-3-carboxald  
ehyde (0.0042 g, 0.029 mmol) in 2-propanol (0.3 mL), piperidin  
20 e (0.00028 mL, 0.0028 mmol) was added at ambient temperature.  
The mixture was refluxed for 24 h. The precipitate was collect

ed by filtration, washed with hot ethanol. The solid was washed with hexane then dried to afford the titled compound as solid (0.0029 g, y. 22%).

[0195]

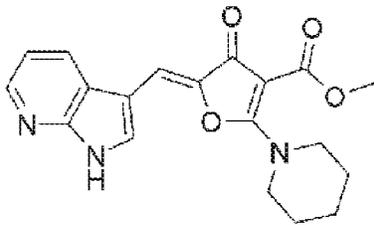
5 <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.24 (br. s, 1H), 8.23 (dd, J = 1.26, 4.52 Hz, 1H), 7.98 (d, J = 7.53 Hz, 1H), 7.79 (s, 1H), 7.58 (d, J = 7.28 Hz, 1H), 7.36 - 7.45 (m, 1H), 7.28 (d, J = 7.53 Hz, 1H), 7.13 (t, J = 7.53 Hz, 1H), 6.89 (dd, J = 4.64, 7.91 Hz, 1H), 6.83 (s, 1H), 4.26 (q, J = 7.19 Hz, 2H), 4.15 (t, J = 5.52 Hz, 2H), 2.55 - 2.65 (m, 2H), 2.19 (s, 6H), 1.29 (t, J = 7.03 Hz, 3H); LCMS (m/z): 463 [M+H]<sup>+</sup>.

Example 34

Methyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-4-oxo-2-piperidino-4,5-dihydrofuran-3-carboxylate

[0196]

[Chemical Formula 43]



[0197]

20 To a solution of methyl 4-oxo-2-(phenylamino)-4,5-dihydrofuran-3-carboxylate (0.047 g, 0.20 mmol) which similarly prepared according to the procedure described in the Example 2, First s

tep using methyl 4-chloroacetoacetate and phenyl isocyanate, and 7-azaindole-3-carboxaldehyde (0.029 g, 0.20 mmol) in methanol (1.0 mL), piperidine (0.022 mL, 0.22 mmol) was added at ambient temperature. The mixture was refluxed for 5 days. Cooled to ambient temperature, the precipitate was collected by filtration, then purified by preparative HPLC, collected former fraction to afford the titled compound as solid (0.0075 g, y. 11%).

[0198]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.30 (br. s, 1H), 8.35 - 8.43 (m, 1H), 8.31 (dd, J = 1.38, 4.64 Hz, 1H), 7.97 (d, J = 2.51 Hz, 1H), 7.19 (dd, J = 4.64, 7.91 Hz, 1H), 6.87 (s, 1H), 3.70 - 3.82 (m, 4H), 3.68 (s, 3H), 1.64 - 1.80 (m, 6H); LCMS (m/z): 354.0 [M+H]<sup>+</sup>

15

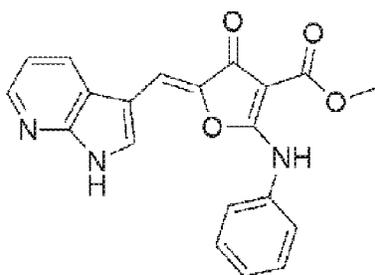
Example 35

[0199]

Methyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-4-oxo-2-(phenylamino)-4,5-dihydrofuran-3-carboxylate

20 [0200]

[Chemical Formula 44]



[0201]

To a solution of methyl 4-oxo-2-(phenylamino)-4,5-dihydrofuran-3-carboxylate (0.047 g, 0.20 mmol) which similarly prepared according to the procedure described in the Example 2, First step using methyl 4-chloroacetoacetate and phenyl isocyanate, and 7-azaindole-3-carboxaldehyde (0.029 g, 0.20 mmol) in 2-propanol (1.0 mL), piperidine (0.022 mL, 0.22 mmol) was added at a ambient temperature. The mixture was refluxed for 5 days. Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol and diisopropyl ether then dried to afford the titled compound as solid (0.031 g, y. 43%).

[0202]

$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.29 (br. s, 1H), 10.59 (s, 1H), 8.23 (dd,  $J = 1.38, 4.64$  Hz, 1H), 7.98 (d,  $J = 7.53$  Hz, 1H), 7.77 (d,  $J = 2.51$  Hz, 1H), 7.52 - 7.64 (m, 4H), 7.44 - 7.51 (m, 1H), 6.93 (s, 1H), 6.89 (dd,  $J = 4.64, 7.91$  Hz, 1H), 3.77 (s, 3H); LCMS (m/z): 361.9 [M+H] $^+$ .

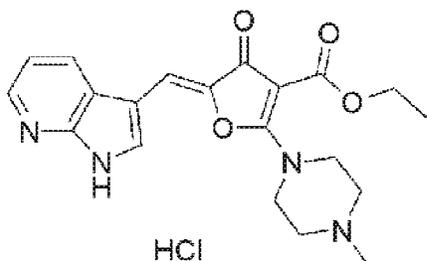
20 Example 36

[0203]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-(4-methylpiperazinyl)-4-oxo-4,5-dihydrofuran-3-carboxylate hydrochloride

[0204]

5 [Chemical Formula 45]



[0205]

To a solution of ethyl 2-(4-methylpiperazinyl)-4-oxo-4,5-dihydrofuran-3-carboxylate (0.038 g, 0.15 mmol) which similarly prepared according to the procedure described in the Example 4,  
10 First step and 7-azaindole-3-carboxaldehyde (0.022 g, 0.15 mmol) in ethanol (1.0 mL), 2M hydrochloric acid in methanol (0.17 mL, 0.34 mmol) was added at ambient temperature. The mixture was refluxed for 40 min. Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol then  
15 dried to afford the titled compound as solid (0.0069 g, yield 9%).

[0206]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.32 - 12.49 (m, 1H), 10.69 (br. s, 1H), 8.39 (d, *J* = 8.03 Hz, 1H), 8.29 - 8.36 (m, 1H), 8.08 (d, *J* = 2.76 Hz, 1H), 7.22 (dd, *J* = 4.64, 7.91 Hz, 1H), 6.95 (s, 1H),

20

4.19 (q,  $J = 7.19$  Hz, 2H), 3.57 - 3.75 (m, 4H), 3.33 - 3.40 (m, 4H), 2.87 (br. s., 3H), 1.16 - 1.34 (m, 3H); LCMS ( $m/z$ ): 383.0 [M+H]<sup>+</sup>.

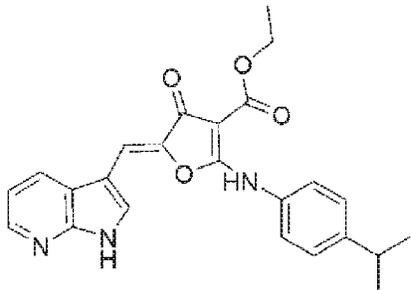
5 Example 37

[0207]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(4-isopropylphenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[0208]

10 [Chemical Formula 46]



[0209]

To a solution of ethyl 2-[(4-isopropylphenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.26 g, 0.90 mmol) which similarly prepared according to the procedure described in the Example 4, First step and 7-azaindole-3-carboxaldehyde (0.13 g, 0.90 mmol) in ethanol (6.0 mL), piperidine (0.045 mL, 0.45 mmol) was added at ambient temperature. The mixture was refluxed for 16 h. Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol then dried to afford the titled compound as solid (0.13 g, y. 35%).

[0210]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.35 (br. s, 1H), 10.50 (br. s, 1H),  
8.24 (d, J = 3.42 Hz, 1H), 8.04 (d, J = 7.82 Hz, 1H), 7.82 (br.  
s, 1H), 7.33 - 7.58 (m, 4H), 6.82 - 6.96 (m, 2H), 4.08 - 4.44  
5 (m, 2H), 2.86 - 3.17 (m, 1H), 1.31 (s, 3H), 1.29 (s, 6H); LCMS  
(m/z): 418.0 [M+H]<sup>+</sup>.

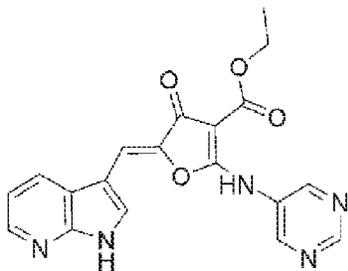
Example 38

[0211]

10 Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-4-oxo-2-(5  
-pyrimidinylamino)-4,5-dihydrofuran-3-carboxylate

[0212]

[Chemical Formula 47]



15 The titled compound(solid) was similarly prepared according to  
the procedure described in the Example 37.

[0213]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.34 (br. s, 1H), 10.80 (br. s, 1H),  
9.19 (s, 1H), 9.02 - 9.12 (m, 2H), 8.25 (d, J = 4.40 Hz, 1H), 8.  
20 03 (d, J = 7.82 Hz, 1H), 7.71 (br. s, 1H), 6.86 - 7.00 (m, 2H),  
4.28 (q, J = 6.85 Hz, 2H), 1.30 (t, J = 6.00 Hz, 3H); LCMS (m/

z): 378.2 [M+H]<sup>+</sup>.

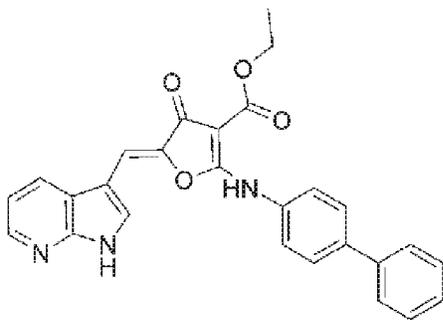
Example 39

[0214]

5 Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(1,1'-biphenyl)-4-ylamino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[0215]

[Chemical Formula 48]



10 The titled compound(solid) was similarly prepared according to the procedure described in the Example 37.

[0216]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.34 (br. s, 1H), 10.63 (br. s, 1H), 8.20 (br. s, 1H), 8.09 (d, *J* = 6.85 Hz, 1H), 7.75 - 7.93 (m, 5 H), 7.62 - 7.74 (m, 2H), 7.50 - 7.58 (m, 2H), 7.39 - 7.48 (m, 1 H), 6.94 (br. s, 1H), 6.83 - 6.91 (m, 1H), 4.29 (d, *J* = 6.36 Hz, 2H), 1.31 (br. s, 3H); LCMS (*m/z*): 452.6 [M+H]<sup>+</sup>.

Example 40

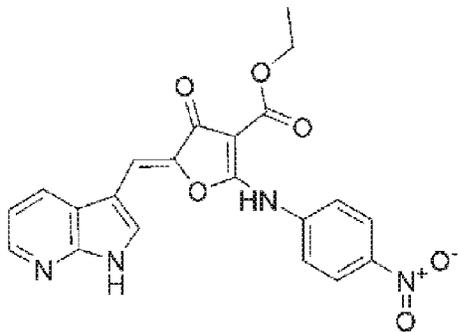
20 [0217]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(4-nitr

ophenyl) amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[0218]

[Chemical Formula 49]



5 The titled compound(solid) was similarly prepared according to the procedure described in the Example 37.

[0219]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.39 (br. s, 1H), 10.89 (br. s, 1H), 8.35 (d, J = 8.80 Hz, 2H), 8.27 (d, J = 3.91 Hz, 1H), 8.17 (d, J = 7.82 Hz, 1H), 7.88 (d, J = 8.80 Hz, 2H), 7.84 (d, J = 2.45 Hz, 1H), 7.03 (s, 1H), 6.98 (dd, J = 4.65, 8.07 Hz, 1H), 4.28 (q, J = 7.17 Hz, 2H), 1.29 (t, J = 7.09 Hz, 3H); LCMS (m/z): 421.4 [M+H]<sup>+</sup>.

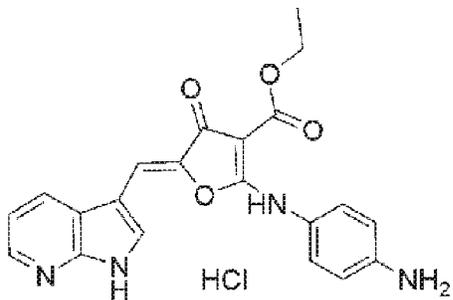
15 Example 41

[0220]

Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-2-[(4-aminophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate hydrochloride

20 [0221]

[Chemical Formula 50]



First Step

[0222]

5 To a solution of ethyl 2-((4-[(*tert*-butoxycarbonyl)amino]phenyl)amino)-4-oxo-4,5-dihydrofuran-3-carboxylate (0.32 g, 0.88 mmol) which similarly prepared according to the procedure described in the Example 4, First step and 7-azaindole-3-carboxaldehyde (0.13 g, 0.88 mmol) in ethanol (5.0 mL), piperidine (0.1  
10 8 mL, 1.8 mmol) was added at ambient temperature. The mixture was refluxed for 16 h. Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol then dried to afford ethyl 5-[(1H-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-((4-[(*tert*-butoxycarbonyl)amino]phenyl)amino)-4-oxo-4,  
15 5-dihydrofuran-3-carboxylate as solid (0.095 g, y. 21%).

[0223]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ 12.30 (br. s, 1H), 10.44 (br. s, 1H), 9.60 (s, 1H), 8.20 (d, *J* = 3.76 Hz, 1H), 7.91 (d, *J* = 7.72 Hz, 1H), 7.82 (s, 1H), 7.60 (d, *J* = 8.40 Hz, 2H), 7.45 (d, *J* = 8.56 Hz, 2H), 6.82 - 6.92 (m, 2H), 4.26 (q, *J* = 6.86 Hz, 2H), 1.53 (s, 9  
20 H), 1.29 (t, *J* = 6.90 Hz, 3H); LCMS (*m/z*): 491.4 [M+H]<sup>+</sup>.

## Second Step

[0224]

A solution of ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-([4-(*tert*-butoxycarbonyl)aminophenyl]amino)-4-oxo-4,5-dihydrofuran-3-carboxylate (0.090 g, 0.18 mmol) in 4M hydrochloric acid in dioxane (3.0 mL) was stirred at ambient temperature for 2 h. The solvent was removed under reduced pressure, and diethyl ether was added to precipitate the product. The precipitate was collected by filtration, washed with diethyl ether then dried to afford the titled compound as solid (0.066 g, y. 92%).

[0225]

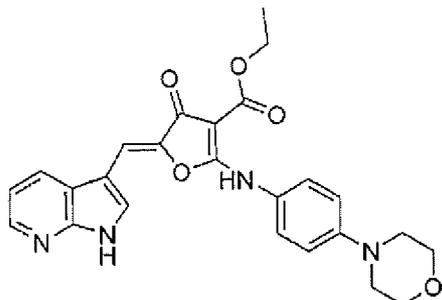
<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.44 (br. s, 1H), 10.61 (br. s, 1H), 8.26 (d, *J* = 3.91 Hz, 1H), 8.02 (d, *J* = 7.82 Hz, 1H), 7.79 (s, 1H), 7.61 (d, *J* = 8.31 Hz, 2H), 7.40 (d, *J* = 7.34 Hz, 2H), 7.01 (dd, *J* = 4.89, 7.83 Hz, 1H), 6.92 (s, 1H), 4.68 (br. s, 3H), 4.27 (q, *J* = 7.01 Hz, 2H), 1.29 (t, *J* = 6.85 Hz, 3H); LCMS (*m/z*): 391.2 [M+H]<sup>+</sup>.

## Example 42

[0226]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-([4-(*morpholinophenyl*)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 51]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 41, First step.

[0227]

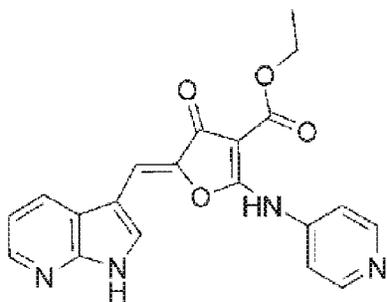
5  $^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.31 (br. s, 1H), 10.39 (br. s, 1H), 8.24 (br. s, 1H), 7.99 (d,  $J = 7.34$  Hz, 1H), 7.79 (br. s, 1H), 7.42 (d,  $J = 8.31$  Hz, 2H), 7.07 (d,  $J = 8.31$  Hz, 2H), 6.81 - 6.96 (m, 2H), 4.26 (d,  $J = 6.85$  Hz, 2H), 3.28 - 3.40 (m, 4H), 3.15 - 3.28 (m, 4H), 1.29 (t,  $J = 6.85$  Hz, 3H); LCMS (m/z): 461.4  
10  $[\text{M}+\text{H}]^+$ .

Example 43

[0228]

Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-4-oxo-2-(4-  
15 -pyridinylamino)-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 52]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 41, First step.

[0229]

5 <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.30 (br. s, 1H), 11.18 (br. s, 1H), 8.59 (d, J = 3.91 Hz, 2H), 8.28 (d, J = 3.91 Hz, 1H), 8.19 (d, J = 7.34 Hz, 1H), 7.88 (br. s, 1H), 7.55 (br. s, 2H), 7.02 (dd, J = 4.40, 7.83 Hz, 1H), 6.93 (br. s, 1H), 4.23 (d, J = 6.85 Hz, 2H), 1.26 (t, J = 6.85 Hz, 3H); LCMS (m/z): 377.6 [M+H]<sup>+</sup>.

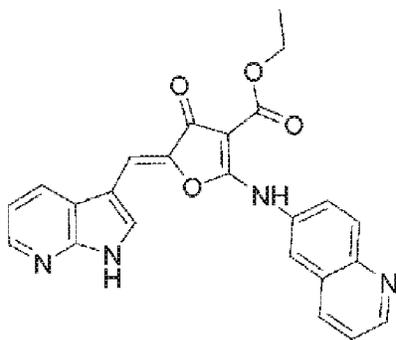
10

Example 44

[0230]

Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-4-oxo-2-(6-quinolinylamino)-4,5-dihydrofuran-3-carboxylate

15 [Chemical Formula 53]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 41, First step.

[0231]

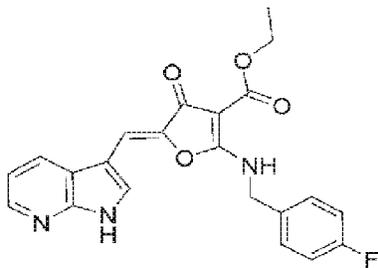
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.29 (br. s, 1H), 10.82 (s, 1H), 9.01  
5 (d, J = 3.42 Hz, 1H), 8.39 (d, J = 8.31 Hz, 1H), 8.23 (br. s, 1H), 8.17 (d, J = 8.80 Hz, 1H), 8.11 (d, J = 3.91 Hz, 1H), 8.00 (d, J = 8.80 Hz, 1H), 7.88 (d, J = 7.34 Hz, 1H), 7.83 (br. s, 1H), 7.62 (dd, J = 4.16, 8.07 Hz, 1H), 6.94 (s, 1H), 6.26 - 6.5  
10 1 (m, 1H), 4.30 (q, J = 6.85 Hz, 2H), 1.32 (t, J = 6.85 Hz, 3 H); LCMS (m/z): 427.4 [M+H]<sup>+</sup>.

Example 45

[0232]

Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-2-[(4-fluorobenzyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 54]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 41, First step.

20 [0233]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.31 (br. s, 1H), 9.51 (br. s, 1H), 8.

22 - 8.37 (m, 2H), 7.86 (br. s, 1H), 7.47 (t, J = 6.30 Hz, 2H),  
7.22 (t, J = 8.31 Hz, 2H), 7.05 - 7.15 (m, 1H), 6.87 (s, 1H),  
4.84 (d, J = 5.87 Hz, 2H), 4.23 (q, J = 6.52 Hz, 2H), 1.27 (t,  
J = 6.85 Hz, 3H); LCMS (m/z): 408.2 [M+H]<sup>+</sup>.

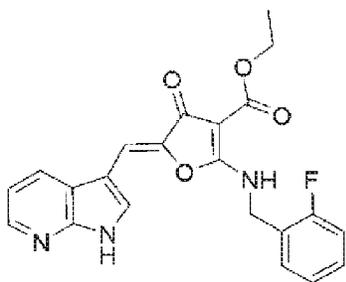
5

Example 46

[0234]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(2-fluoro-*o*-benzyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

10 [Chemical Formula 55]



The titled compound(solid) was similarly prepared according to  
the procedure described in the Example 41, First step.

[0235]

15 <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.35 (br. s, 1H), 9.44 (br. s, 1H), 8.  
15 - 8.42 (m, 2H), 7.86 (s, 1H), 7.45 (t, J = 7.34 Hz, 1H), 7.3  
3 - 7.40 (m, 1H), 7.18 - 7.32 (m, 2H), 7.07 (dd, J = 5.14, 7.58  
Hz, 1H), 6.87 (s, 1H), 4.91 (s, 2H), 4.23 (q, J = 7.17 Hz, 2H),  
1.27 (t, J = 6.85 Hz, 3H); LCMS (m/z): 408.0 [M+H]<sup>+</sup>.

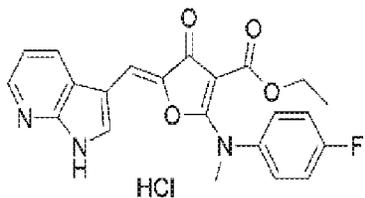
20

Example 47

[0236]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(4-fluorophenyl)-*N*-methylamino]-4-oxo-4,5-dihydrofuran-3-carboxylate hydrochloride

5 [Chemical Formula 56]



First Step

[0237]

A solution of ethyl 2-[(4-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.10 g, 0.38 mmol) which similarly prepared according to the procedure described in the Example 4, First step, potassium carbonate (0.063 g, 0.45 mmol) and methyl iodide (0.026 mL, 0.42 mmol) in anhydrous *N,N*-dimethylformamide (2.0 mL) was stirred at ambient temperature for 12 h. The reaction mixture was diluted with water then extracted with ethyl acetate for 3 times. The organic layer was dried over sodium sulfate and concentrated to afford ethyl 2-[(4-fluorophenyl)-*N*-methylamino]-4-oxo-4,5-dihydrofuran-3-carboxylate as solid (0.13 g).

20 [0238]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 7.38 - 7.47 (m, 2H), 7.21 - 7.32 (m, 2H), 4.65 (s, 2H), 3.60 (q, *J* = 7.03 Hz, 2H), 3.43 (s, 3H), 0.96

(t, J = 7.15 Hz, 3H); LCMS (m/z): 279.9 [M+H]<sup>+</sup>.

## Second Step

[0239]

5 To a solution of ethyl 2-[(4-fluorophenyl)-N-methylamino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.050 g, 0.18 mmol) and 7-azaindole-3-carboxaldehyde (0.026 g, 0.18 mmol) in ethanol (1.0 mL), 2M hydrochloric acid in ethanol (0.19 mL, 0.38 mmol) was added at ambient temperature. The mixture was refluxed for 2 h.  
10 Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol and diisopropyl ether then dried to afford the titled compound as solid (0.011 g, y. 13%).

[0240]

15 <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.38 (br. s, 1H), 8.28 (dd, J = 1.25, 4.77 Hz, 1H), 8.12 (d, J = 7.78 Hz, 1H), 7.81 (d, J = 2.01 Hz, 1H), 7.53 - 7.62 (m, 2H), 7.31 - 7.38 (m, 2H), 7.05 (dd, J = 4.77, 7.78 Hz, 1H), 6.90 (s, 1H), 3.80 (q, J = 7.03 Hz, 2H), 3.63 (s, 3H), 1.01 - 1.10 (m, 3H); LCMS (m/z): 407.9 [M+H]<sup>+</sup>.

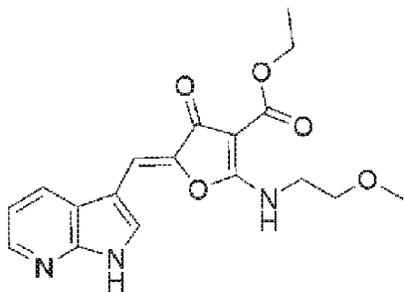
20

## Example 48

[0241]

Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-2-[(2-methoxyethyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

25 [Chemical Formula 57]



[0242]

To a solution of ethyl 2-[(2-methoxyethyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.50 g, 2.2 mmol) which similarly prepared according to the procedure described in the Example 4,  
5 First step and 7-azaindole-3-carboxaldehyde (0.32 g, 2.2 mmol) in ethanol (3.0 mL), piperidine (5 drops) was added at ambient temperature. The mixture was refluxed for 16 h. Cooled to ambient temperature, the precipitate was collected by filtration,  
10 washed with ethanol then dried to afford the titled compound as solid.

[0243]

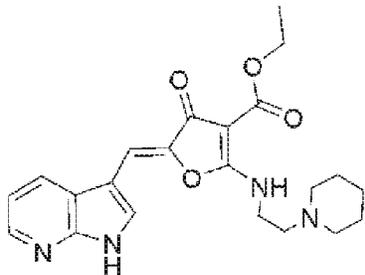
$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.34 (br. s, 1H), 8.89 (br. s, 1H), 8.43 (d,  $J = 7.34$  Hz, 1H), 8.31 (d,  $J = 3.91$  Hz, 1H), 8.03 (s, 1H), 7.19 (dd,  $J = 4.40, 7.83$  Hz, 1H), 6.90 (s, 1H), 4.21 (q,  $J = 7.17$  Hz, 2H), 3.79 (d,  $J = 4.40$  Hz, 2H), 3.62 (t,  $J = 5.14$  Hz, 2H), 3.28 (s, 3H), 1.26 (t,  $J = 7.09$  Hz, 3H); LCMS (m/z): 358.4 [M+H] $^+$ .

20 Example 49

[0244]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-4-oxo-2-  
[(2-piperidinoethyl)amino]-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 58]



5 The titled compound(solid) was similarly prepared according to  
the procedure described in the Example 48.

[0245]

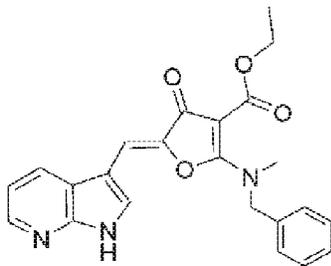
<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.35 (br. s, 1H), 8.83 (br. s, 1H), 8.  
38 - 8.47 (m, 1H), 8.31 (br. s, 1H), 8.02 (br. s, 1H), 7.20 (br.  
10 s, 1H), 6.88 (br. s, 1H), 4.12 - 4.28 (m, 2H), 3.67 - 3.80 (m,  
2H), 2.25 - 2.70 (m, 6H), 1.32 - 1.53 (m, 6H), 1.18 - 1.32 (m,  
3H); LCMS (m/z): 411.5 [M+H]<sup>+</sup>.

Example 50

15 [0246]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-(benzyl-  
N-methylamino)-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 59]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 48.

[0247]

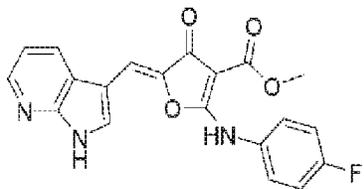
5 <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.28 (br. s, 1H), 8.24 – 8.39 (m, 2H), 7.88 (br. s, 1H), 7.29 – 7.47 (m, 5H), 7.10 (br. s, 1H), 6.87 (s, 1H), 5.01 (s, 2H), 4.14 (d, J = 6.85 Hz, 2H), 3.25 (br. s, 3H), 1.19 (t, J = 6.36 Hz, 3H); LCMS (m/z): 404.6 [M+H]<sup>+</sup>.

10 Example 51

[0248]

Methyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(4-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 60]



15

[0249]

To a solution of methyl 2-[(4-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.25 g, 1.0 mmol) which similarly p

repared according to the procedure described in the Example 2,  
First step using methyl 4-chloroacetoacetate and 4-fluorophenyl isocyanate, and 7-azaindole-3-carboxaldehyde (0.15 g, 1.0 mmol) in 2-propanol (5.0 mL), L-proline (0.023 g, 0.20 mmol) was added at ambient temperature. The mixture was refluxed for 2 days. Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol and diisopropyl ether then dried to afford the titled compound as solid (0.26 g, y. 68%).

10 [0250]

$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.28 (br. s, 1H), 10.58 (s, 1H), 8.25 (dd,  $J = 1.38, 4.64$  Hz, 1H), 7.96 (d,  $J = 8.03$  Hz, 1H), 7.74 (d,  $J = 2.51$  Hz, 1H), 7.59 - 7.69 (m, 2H), 7.36 - 7.43 (m, 2H), 6.92 (s, 1H), 6.89 (dd,  $J = 4.77, 8.03$  Hz, 1H), 3.76 (s, 3H);

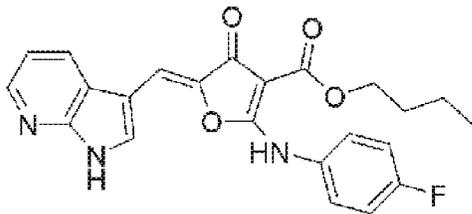
15 LCMS (m/z): 379.8  $[\text{M}+\text{H}]^+$ .

Example 52

[0251]

20 *n*-Butyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(4-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 61]



First Step

[0252]

Under a nitrogen atmosphere, a solution of methyl 2-[(4-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.13 g, 0.50 mmol) which similarly prepared according to the procedure described in the Example 2, First step using methyl 4-chloroacetate and 4-fluorophenyl isocyanate, and zinc cluster catalyst ( $Zn_4(OCOCF_3)_6O$ ) (0.0062 g, 0.0065 mmol) in 1-butanol (2.0 mL) was stirred at 80 °C for 3 days then stirred at ambient temperature for further 3 days. The precipitate was collected by filtration, washed with 2-propanol and diisopropyl ether then dried to afford *n*-butyl 2-[(4-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate as solid (0.078 g, y. 53%).

[0253]

$^1H$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 10.25 (s, 1H), 7.45 - 7.55 (m, 2H), 7.21 - 7.31 (m, 2H), 4.65 (s, 2H), 4.17 (t,  $J = 6.53$  Hz, 2H), 1.57 - 1.67 (m, 2H), 1.33 - 1.45 (m, 2H), 0.92 (t,  $J = 7.40$  Hz, 3H); LCMS (m/z): 293.8 [M+H] $^+$ .

Second Step

[0254]

To a solution of *n*-butyl 2-[(4-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.035 g, 0.12 mmol) and 7-azaindole-3-carboxaldehyde (0.018 g, 0.12 mmol) in 2-propanol (1.0 mL), L-proline (0.0028 g, 0.024 mmol) was added at ambient tempera

ture. The mixture was refluxed for 2 days. Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol and diisopropyl ether then dried to afford the titled compound as solid (0.019 g, y. 36%).

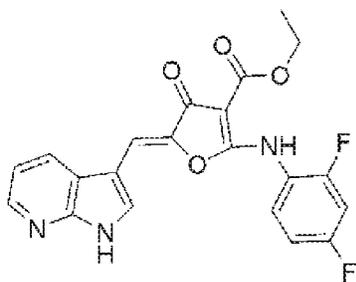
5 [0255]

$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.28 (br. s, 1H), 10.56 (s, 1H), 8.25 (dd,  $J = 1.38, 4.64$  Hz, 1H), 7.95 (d,  $J = 7.78$  Hz, 1H), 7.75 (d,  $J = 2.76$  Hz, 1H), 7.60 - 7.68 (m, 2H), 7.35 - 7.42 (m, 2H), 6.85 - 6.95 (m, 2H), 4.22 (t,  $J = 6.65$  Hz, 2H), 1.60 - 1.72 (m, 2H), 1.37 - 1.49 (m, 2H), 0.94 (t,  $J = 7.40$  Hz, 3H); LCMS (m/z): 421.9  $[\text{M}+\text{H}]^+$ .

Example 53

[0256]

15 Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(2,4-difluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate  
[Chemical Formula 62]



[0257]

20 To a solution of ethyl 2-[(2,4-difluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.15 g, 0.54 mmol) which similar

ly prepared according to the procedure described in the Example 2, First step and 7-azaindole-3-carboxaldehyde (0.074 g, 0.50 mmol) in 2-propanol (2.5 mL), 2M hydrochloric acid in ethanol (0.25 mL, 0.50 mmol) was added at ambient temperature then refluxed for 24 h. Cooled with ice bath, aqueous 2M sodium hydroxide solution (0.024 mL, 0.048 mmol) was added dropwise to neutralize and the mixture was refluxed for 1 h. The precipitate was collected by filtration, washed with ethanol and hexane then dried to afford the titled compound as solid (0.14 g, y. 69%).

[0258]

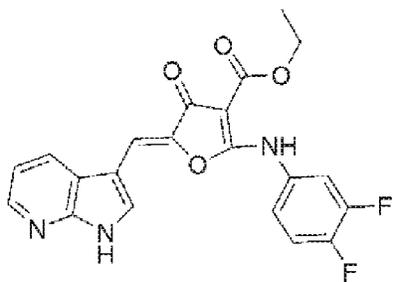
$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.27 (br. s, 1H), 10.51 (s, 1H), 8.24 (dd,  $J = 1.38, 4.64$  Hz, 1H), 7.84 (d,  $J = 7.78$  Hz, 1H), 7.66 - 7.77 (m, 2H), 7.50 - 7.59 (m, 1H), 7.29 (t,  $J = 7.78$  Hz, 1H), 6.80 - 6.89 (m, 2H), 4.26 (q,  $J = 7.03$  Hz, 2H), 1.29 (t,  $J = 7.03$  Hz, 3H); LCMS (m/z): 411.8 [M+H] $^+$ .

Example 54

[0259]

Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-2-[(3,4-difluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 63]



[0260]

To a solution of ethyl 2-[(3,4-difluorophenyl)amino]-4-oxo-4,  
5-dihydrofuran-3-carboxylate (0.084 g, 0.30 mmol) which simila  
5 rly prepared according to the procedure described in the Examp  
le 4, First step and 7-azaindole-3-carboxaldehyde (0.041 g, 0.  
28 mmol) in 2-propanol (2.0 mL), 2M hydrochloric acid in ethan  
ol (0.14 mL, 0.28 mmol) was added at ambient temperature. The  
mixture was refluxed for 18 h. Cooled with ice bath, aqueous 2  
10 M sodium hydroxide solution (0.13 mL, 0.26 mmol) was added dro  
pwise to neutralize, ethanol (5.0 mL) was added and the mixtur  
e was refluxed for 1.5 h. The precipitate was collected by fil  
tration, washed with hot ethanol. The solid was washed with he  
xane then dried to afford the titled compound as solid (0.051  
15 g, y. 44%).

[0261]

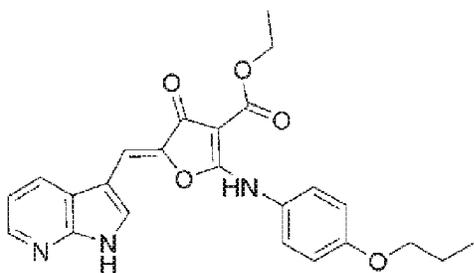
$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.07 (br. s, 1H), 10.63 (br. s, 1H),  
8.22 (dd,  $J = 1.38, 4.64$  Hz, 1H), 8.00 (d,  $J = 7.78$  Hz, 1H), 7.  
65 (s, 1H), 7.33 - 7.51 (m, 2H), 7.13 (br. s, 1H), 6.88 (dd,  $J$   
20 = 4.64, 7.91 Hz, 1H), 6.56 (br. s, 1H), 4.16 (q,  $J = 6.86$  Hz, 2  
H), 1.24 (t,  $J = 7.15$  Hz, 3H); LCMS (m/z): 411.8 [M+H] $^+$ .

Example 55

[0262]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-4-oxo-2-  
5 { [4-(1-propoxy)phenyl]amino}-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 64]



[0263]

To a solution of ethyl 4-oxo-2-[[4-(1-propoxy)phenyl]amino]-4,  
10 5-dihydrofuran-3-carboxylate (0.15 g, 0.50 mmol) which similar  
ly prepared according to the procedure described in the Examp  
le 4, First step and 7-azaindole-3-carboxaldehyde (0.072 g, 0.5  
0 mmol) in ethanol (6.0 mL), L-proline (0.0060 g, 0.05 mmol) w  
as added at ambient temperature. The mixture was refluxed for  
15 16 h. Cooled to ambient temperature, the precipitate was colle  
cted by filtration, washed with ethanol then dried to afford t  
he titled compound as solid (0.060 g, y. 28%).

[0264]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.30 (br. s, 1H), 10.44 (br. s, 1H),  
20 8.22 (br. s, 1H), 7.85 - 7.99 (m, 1H), 7.79 (br. s, 1H), 7.48  
(d, J = 6.85 Hz, 2H), 7.07 (d, J = 7.34 Hz, 2H), 6.86 (br. s, 2

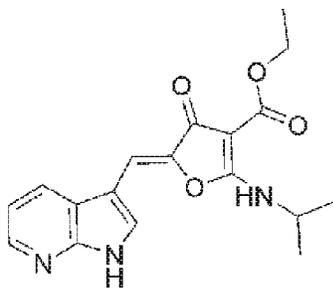
H), 4.18 - 4.37 (m, 2H), 3.93 - 4.11 (m, 2H), 1.70 - 1.90 (m, 2H), 1.22 - 1.38 (m, 3H), 0.98 - 1.12 (m, 3H); LCMS (m/z): 433.9 [M+H]<sup>+</sup>.

5 Example 56

[0265]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-(isopropylamino)-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 65]



[0266]

To a solution of ethyl 2-(isopropylamino)-4-oxo-4,5-dihydrofuran-3-carboxylate (0.50 g, 2.3 mmol) which similarly prepared according to the procedure described in the Example 4, First step and 7-azaindole-3-carboxaldehyde (0.34 g, 2.3 mmol) in ethanol (15 mL), L-proline (0.027 g, 0.23 mmol) was added at ambient temperature. The mixture was refluxed for 16 h. Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol then dried to afford the titled compound as solid (0.45 g, y. 56%).

15

20

[0267]

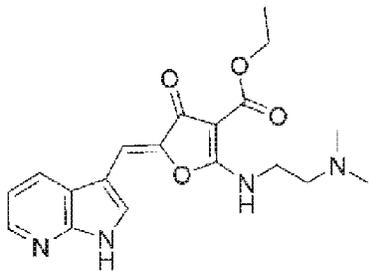
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.32 (br. s, 1H), 8.56 (br. s, 1H), 8.41 (d, J = 7.82 Hz, 1H), 8.32 (d, J = 3.91 Hz, 1H), 7.99 (s, 1H), 7.20 (dd, J = 4.40, 7.83 Hz, 1H), 6.90 (s, 1H), 4.39 (br. s, 1H), 4.21 (q, J = 7.01 Hz, 2H), 1.38 (d, J = 6.36 Hz, 6H), 1.26 (t, J = 6.85 Hz, 3H); LCMS (m/z): 342.3 [M+H]<sup>+</sup>.

Example 57

[0268]

Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-2-[[2-(dimethylamino)ethyl]amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 66]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 56.

15 [0269]

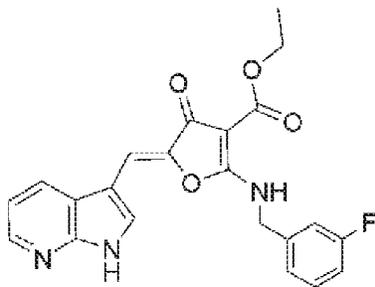
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.37 (br. s, 1H), 8.82 (br. s, 1H), 8.42 (d, J = 7.82 Hz, 1H), 8.31 (d, J = 3.91 Hz, 1H), 8.03 (s, 1H), 7.20 (dd, J = 4.89, 7.83 Hz, 1H), 6.90 (s, 1H), 4.20 (q, J = 7.34 Hz, 2H), 3.68 - 3.80 (m, 2H), 2.38 - 2.65 (m, 2H), 2.23 (s, 6H), 1.26 (t, J = 7.09 Hz, 3H); LCMS (m/z): 371.2 [M+H]<sup>+</sup>.

Example 58

[0270]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(3-fluorobenzyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

5 [Chemical Formula 67]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 56.

[0271]

10 <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.33 (br. s, 1H), 9.54 (br. s, 1H), 8.28 (d, *J* = 5.87 Hz, 2H), 7.88 (s, 1H), 7.44 (q, *J* = 7.34 Hz, 1H), 7.20 - 7.33 (m, 2H), 7.03 - 7.18 (m, 2H), 6.87 (s, 1H), 4.87 (br. s, 2H), 4.23 (q, *J* = 6.85 Hz, 2H), 1.27 (t, *J* = 6.85 Hz, 3H); LCMS (*m/z*): 408.0 [M+H]<sup>+</sup>.

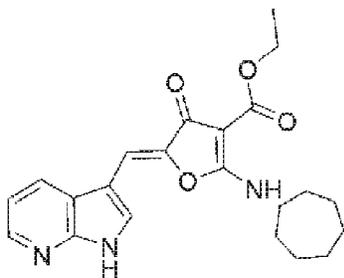
15

Example 59

[0272]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-(cycloheptylamino)-4-oxo-4,5-dihydrofuran-3-carboxylate

20 [Chemical Formula 68]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 56.

[0273]

5 <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.37 (br. s, 1H), 8.56 (d, J = 8.16 Hz, 1H), 8.42 (d, J = 7.82 Hz, 1H), 8.32 (d, J = 3.91 Hz, 1H), 7.99 (s, 1H), 7.19 (dd, J = 4.89, 7.82 Hz, 1H), 6.90 (s, 1H), 4.21 (q, J = 6.85 Hz, 2H), 3.39 – 3.50 (m, 1H), 1.94 – 2.08 (m, 2H), 1.77 – 1.91 (m, 2H), 1.48 – 1.76 (m, 8H), 1.26 (t, J = 7.09 Hz, 3H); LCMS (m/z): 396.0 [M+H]<sup>+</sup>.

10

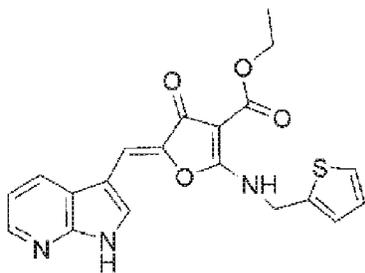
Example 60

[0274]

Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-4-oxo-2-[(2-thienylmethyl)amino]-4,5-dihydrofuran-3-carboxylate

15

[Chemical Formula 69]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 56.

[0275]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.36 (br. s, 1H), 9.55 (br. s, 1H), 8.37 (d, J = 7.82 Hz, 1H), 8.30 (d, J = 3.91 Hz, 1H), 8.03 (s, 1H), 7.45 (d, J = 4.89 Hz, 1H), 7.09 - 7.22 (m, 2H), 7.00 (t, J = 3.96 Hz, 1H), 6.91 (s, 1H), 5.01 (br. s, 2H), 4.22 (q, J = 7.01 Hz, 2H), 1.26 (t, J = 6.85 Hz, 3H); LCMS (m/z): 395.8 [M+H]<sup>+</sup>.

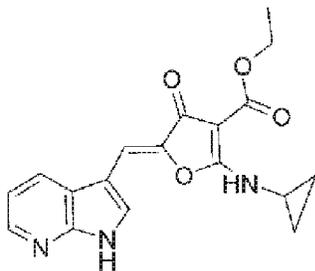
10

Example 61

[0276]

Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-2-(cyclopropylamino)-4-oxo-4,5-dihydrofuran-3-carboxylate

15 [Chemical Formula 70]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 56.

[0277]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.33 (br. s, 1H), 8.86 (br. s, 1H), 8.57 (d, J = 7.82 Hz, 1H), 8.31 (d, J = 3.91 Hz, 1H), 8.06 (s, 1

20

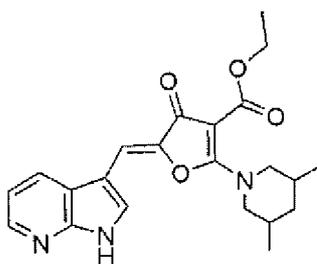
H), 7.21 (dd,  $J = 4.89, 7.82$  Hz, 1H), 6.92 (s, 1H), 4.19 (q,  $J = 7.01$  Hz, 2H), 3.08 - 3.20 (m, 1H), 1.24 (t,  $J = 6.85$  Hz, 3H), 0.84 - 1.01 (m, 4H); LCMS ( $m/z$ ): 340.0  $[M+H]^+$ .

5 Example 62

[0278]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-(3,5-dimethylpiperidino)-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 71]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 56.

[0279]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>)  $\delta$  (ppm) 12.32 (br. s, 1H), 8.38 (d,  $J = 7.82$  Hz, 1H), 8.31 (d,  $J = 3.91$  Hz, 1H), 7.96 (s, 1H), 7.11 - 7.26 (m, 1H), 6.84 (s, 1H), 4.00 - 4.25 (m, 4H), 2.81 (t,  $J = 11.98$  Hz, 2H), 1.74 - 1.93 (m, 3H), 1.24 (t,  $J = 6.85$  Hz, 3H), 0.82 - 1.02 (m, 7H); LCMS ( $m/z$ ): 396.0  $[M+H]^+$ .

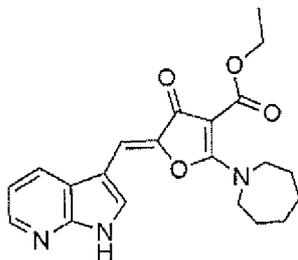
15

20 Example 63

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-azepinyl

-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 72]



The titled compound(solid) was similarly prepared according to  
 5 the procedure described in the Example 56.

[0280]

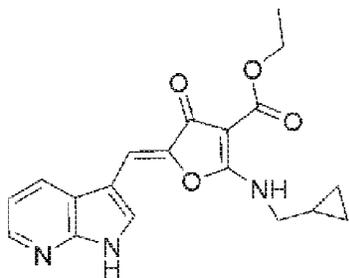
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.29 (br. s, 1H), 8.38 (d, J = 7.78 Hz,  
 1H), 8.31 (dd, J = 1.51, 4.77 Hz, 1H), 7.93 (d, J = 2.26 Hz, 1  
 H), 7.19 (dd, J = 4.64, 7.91 Hz, 1H), 6.84 (s, 1H), 4.17 (q, J  
 10 = 7.19 Hz, 2H), 3.73 - 3.84 (m, 4H), 1.75 - 1.93 (m, 4H), 1.51  
 - 1.64 (m, 4H), 1.24 (t, J = 7.03 Hz, 3H); LCMS (m/z): 382.0 [M  
 +H]<sup>+</sup>.

Example 64

15 [0281]

Ethyl 5-((1H-pyrrolo[2,3-b]pyridin-3-yl)methylene)-2-((cyclopropylmethyl)amino)-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 73]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 56.

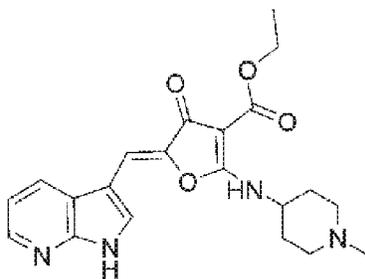
[0282]

5 <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.33 (br. s, 1H), 9.06 (br. s, 1H), 8.41 (d, J = 7.82 Hz, 1H), 8.31 (d, J = 3.91 Hz, 1H), 8.00 (br. s, 1H), 7.19 (dd, J = 4.65, 7.58 Hz, 1H), 6.89 (s, 1H), 4.22 (q, J = 7.01 Hz, 2H), 3.52 (t, J = 6.36 Hz, 2H), 1.15 - 1.35 (m, 4 H), 0.52 (d, J = 6.85 Hz, 2H), 0.36 (d, J = 4.40 Hz, 2H); LCMS  
10 (m/z): 354.2 [M+H]<sup>+</sup>.

Example 65

[0283]

Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-2-[(1-methyl-4-piperidinyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate  
15 [Chemical Formula 74]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 56.

[0284]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.36 (br. s, 1H), 8.58 (br. s, 1H), 8.42 (d, J = 7.83 Hz, 1H), 8.33 (d, J = 3.42 Hz, 1H), 7.98 (s, 1H), 7.19 (dd, J = 4.65, 7.58 Hz, 1H), 6.90 (s, 1H), 4.21 (q, J = 6.85 Hz, 2H), 3.90 - 4.07 (m, 1H), 2.79 (d, J = 10.27 Hz, 2H), 2.21 (s, 3H), 2.08 (t, J = 10.27 Hz, 2H), 1.80 - 1.99 (m, 4H), 1.26 (t, J = 6.85 Hz, 3H); LCMS (m/z): 397.2 [M+H]<sup>+</sup>.

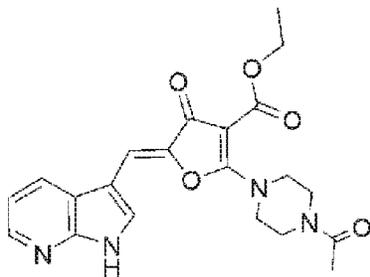
10

Example 66

[0285]

Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-2-(4-acetyl piperazinyl)-4-oxo-4,5-dihydrofuran-3-carboxylate

15 [Chemical Formula 75]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 56.

[0286]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.37 (br. s, 1H), 8.38 (d, J = 7.34 Hz, 1H), 8.32 (d, J = 3.42 Hz, 1H), 8.01 (s, 1H), 7.21 (dd, J = 4.

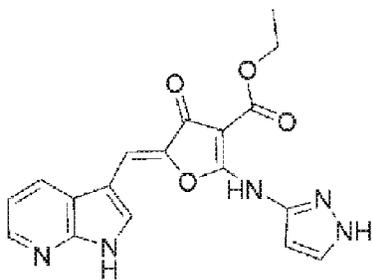
89, 7.82 Hz, 1H), 6.89 (s, 1H), 4.18 (q, J = 7.34 Hz, 2H), 3.77 - 3.95 (m, 4H), 3.62 - 3.77 (m, 4H), 2.07 (s, 3H), 1.25 (t, J = 6.85 Hz, 3H); LCMS (m/z): 411.4 [M+H]<sup>+</sup>.

5 Example 67

[0287]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(3-pyrazolyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 76]



[0288]

To a solution of ethyl 2-[(3-pyrazolyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.30 g, 1.3 mmol) which similarly prepared according to the procedure described in the Example 4, First step, and 7-azaindole-3-carboxaldehyde (0.19 g, 1.3 mmol) in ethanol (6.0 mL), L-proline (0.015 g, 0.13 mmol) was added at ambient temperature. The mixture was refluxed for 16 h. Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol then dried to afford the titled compound as solid (0.20 g, y. 35%).

15

20

[0289]

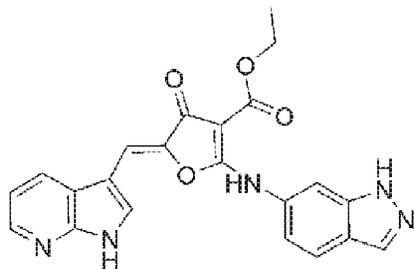
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 13.07 (br. s, 1H), 12.34 (br. s, 1H),  
10.46 (br. s, 1H), 8.27 (d, J = 3.91 Hz, 1H), 8.14 (d, J = 7.82  
Hz, 1H), 7.91 - 8.20 (m, 2H), 7.08 (dd, J = 4.65, 7.58 Hz, 1H),  
6.94 (s, 1H), 6.47 (br. s, 1H), 4.26 (q, J = 6.85 Hz, 2H), 1.2  
5 9 (t, J = 7.09 Hz, 3H); LCMS (m/z): 366.0 [M+H]<sup>+</sup>.

Example 68

[0290]

Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-2-[(6-inda  
10 zolyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 77]



The titled compound(solid) was similarly prepared according to  
the procedure described in the Example 67.

15 [0291]

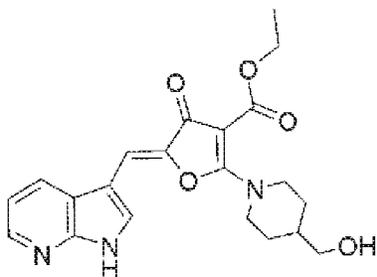
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 13.22 (br. s, 1H), 12.24 (br. s, 1H),  
10.66 (br. s, 1H), 8.22 (br. s, 1H), 8.12 (br. s, 1H), 7.91 (d,  
J = 8.31 Hz, 1H), 7.71 - 7.86 (m, 3H), 7.33 (d, J = 7.83 Hz, 1  
H), 6.89 (s, 1H), 6.33 (br. s, 1H), 4.29 (d, J = 6.85 Hz, 2H),  
20 1.31 (t, J = 6.60 Hz, 3H); LCMS (m/z): 416.4 [M+H]<sup>+</sup>.

Example 69

[0292]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[4-(hydroxymethyl)piperidino]-4-oxo-4,5-dihydrofuran-3-carboxylate

5 [Chemical Formula 78]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 67.

[0293]

10 <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.30 (br. s, 1H), 8.37 (d, *J* = 7.82 Hz, 1H), 8.31 (d, *J* = 3.91 Hz, 1H), 7.97 (br. s, 1H), 7.19 (dd, *J* = 4.40, 7.82 Hz, 1H), 6.84 (s, 1H), 4.57 (t, *J* = 4.89 Hz, 1H), 4.08 - 4.32 (m, 4H), 3.22 - 3.40 (m, 4H), 1.70 - 1.95 (m, 3H), 1.37 (q, *J* = 11.09 Hz, 2H), 1.24 (t, *J* = 6.85 Hz, 3H); LCMS (*m/z*): 398.0 [M+H]<sup>+</sup>.

15

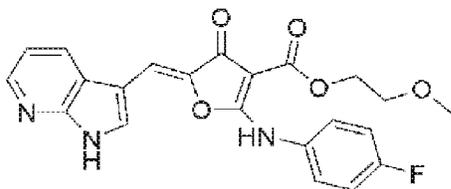
Example 70

[0294]

2-Methoxyethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(4-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

20

[Chemical Formula 79]



First Step

[0295]

5 A solution of methyl 2-[(4-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.063 g, 0.25 mmol) which similarly prepared according to the procedure described in the Example 2, First step using methyl 4-chloroacetoacetate and 4-fluorophenyl isocyanate, 2-methoxyethanol (0.2 mL, 2.5 mmol) and zinc cluster catalyst ( $Zn_4(OCOCF_3)_6O$ ) (0.0048 g, 0.0050 mmol) in anhydrous dioxane (1.0 mL) was stirred with the microwave synthesizer (Biotage Initiator™) at 120 °C for 1 h. Cooled to ambient temperature, the reaction mixture was concentrated under reduced pressure. The residue was purified by chromatography on silica gel (chloroform/ethyl acetate) to afford 2-methoxyethyl 2-[(4-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate as solid (0.024 g, y. 33%).

15  $^1H$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 10.22 (s, 1H), 7.43 - 7.56 (m, 2H), 7.27 (t, J = 8.78 Hz, 2H), 4.66 (s, 2H), 4.22 - 4.37 (m, 2H), 3.52 - 3.66 (m, 2H), 3.30 (s, 3H); LCMS (m/z): 295.8 [M+H]<sup>+</sup>

20

Second Step

[0296]

To a solution of 2-methoxyethyl 2-[(4-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.023 g, 0.078 mmol) and 7-azaindole-3-carboxaldehyde (0.011 g, 0.078 mmol) in 2-propanol (1.0 mL), L-proline (0.0018 g, 0.016 mmol) was added at ambient temperature. The mixture was refluxed for 2 days. Cooled to ambient temperature, the precipitate was collected by filtration. The solid was purified by preparative HPLC to afford the titled compound as solid (0.046 g, y. 14%).

[0297]

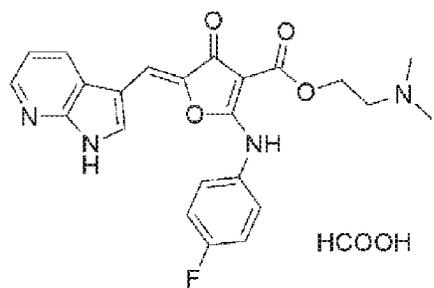
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.22 (br. s, 1H), 10.65 (br. s, 1H), 8.24 (dd, J = 1.25, 4.52 Hz, 1H), 7.96 (d, J = 7.53 Hz, 1H), 7.72 (d, J = 2.26 Hz, 1H), 7.52 - 7.63 (m, 2H), 7.35 (t, J = 8.78 Hz, 2H), 6.89 (dd, J = 4.77, 8.03 Hz, 1H), 6.82 (br. s, 1H), 4.32 (t, J = 4.77 Hz, 2H), 3.54 - 3.72 (m, 2H), 3.33 (s, 3H); LCM S (m/z): 423.8 [M+H]<sup>+</sup>.

Example 71

[0298]

2-(Dimethylamino)ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-2-[(4-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate formate

[Chemical Formula 80]



[0299]

Under a nitrogen atmosphere, a solution of methyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(4-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.038 g, 0.10 mmol) which  
 5 afforded in the Example 51, 2-(dimethylamino)ethanol (0.10 mL, 1.0 mmol) and zinc cluster catalyst ( $Zn_4(OCOCF_3)_6O$ ) (0.0019 g, 0.0020 mmol) in *N,N*-dimethylacetamide (0.9 mL) was stirred with the microwave synthesizer (Biotage Initiator<sup>TM</sup>) at 130 °C for  
 10 r 1 h. Cooled to ambient temperature, the reaction mixture was purified by preparative HPLC to afford the titled compound as solid (0.016 g, y. 36%).

[0300]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.15 (br. s, 1H), 8.23 (dd, *J* = 1.38, 4.64 Hz, 1H), 8.14 (s, 1H), 7.97 (d, *J* = 7.53 Hz, 1H), 7.68 (d, *J* = 2.01 Hz, 1H), 7.45 (dd, *J* = 5.14, 8.41 Hz, 2H), 7.27 - 7.36 (m, 2H), 6.89 (dd, *J* = 4.64, 7.91 Hz, 1H), 6.72 (s, 1H), 4.30 (t, *J* = 5.77 Hz, 2H), 2.80 (t, *J* = 5.77 Hz, 2H), 2.41 (s, 6H);  
 LCMS (*m/z*): 436.9 [M+H]<sup>+</sup>.

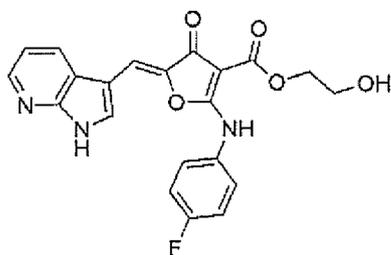
20

Example 72

[0301]

2-Hydroxyethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-  
-[(4-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

5 [Chemical Formula 81]



[0302]

Under a nitrogen atmosphere, a solution of the compound (0.038  
g, 0.10mmol) of Example 51, ethylene glycol (0.50 mL, 9.0 mmol)  
10 and zinc cluster catalyst ( $Zn_4(OCOCF_3)_6O$ ) (0.0019 g, 0.0020  
mmol) in *N,N*-dimethylacetamide (0.5 mL) was stirred with the microwave synthesizer (Biotage Initiator™) at 150 °C for 1 h. Cooled to ambient temperature, the precipitate was removed by filtration. The filtrate was purified by preparative HPLC to afford the titled compound as solid (0.0040 g, y. 10%).

[0303]

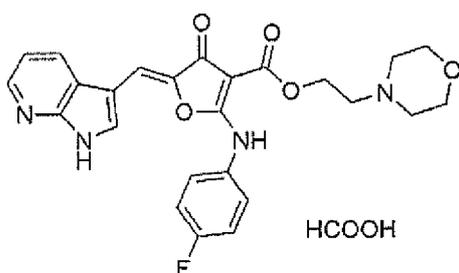
$^1H$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.24 (br. s, 1H), 10.52 (br. s, 1H),  
8.21 - 8.28 (m, 1H), 7.96 (d,  $J = 7.78$  Hz, 1H), 7.74 (d,  $J = 2.40$  Hz, 1H), 7.58 (br. s, 2H), 7.36 (t,  $J = 8.66$  Hz, 2H), 6.80 -  
20 6.94 (m, 2H), 4.90 (br. s, 1H), 4.22 (t,  $J = 5.27$  Hz, 2H), 3.67 (t,  $J = 5.27$  Hz, 2H); LCMS ( $m/z$ ): 409.8  $[M+H]^+$ .

Example 73

[0304]

2-Morpholinoethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]  
 5 e]-2-[(4-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxy-  
 late formate

[Chemical Formula 82]



[0305]

10 Under a nitrogen atmosphere, a solution of the compound (0.038  
 g, 0.10mmol) of Example 51, *N*-(2-hydroxyethyl)morpholine (0.2  
 0 mL, 1.6 mmol) and zinc cluster catalyst ( $Zn_4(OCOCF_3)_6O$ ) (0.00  
 19 g, 0.0020 mmol) in *N,N*-dimethylacetamide (0.8 mL) was stirr  
 ed with the microwave synthesizer (Biotage Initiator<sup>TM</sup>) at 150  
 15 °C for 40 min. Cooled to ambient temperature, the precipitate w  
 as removed by filtration. The filtrate was purified by prepara  
 tive HPLC to afford the titled compound as solid (0.0075 g, y.  
 15%).

[0306]

20 <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.25 (br. s, 1H), 8.24 (d, *J* = 4.02 Hz,  
 1H), 8.15 (s, 1H), 7.95 (d, *J* = 7.78 Hz, 1H), 7.72 (s, 1H), 7.6

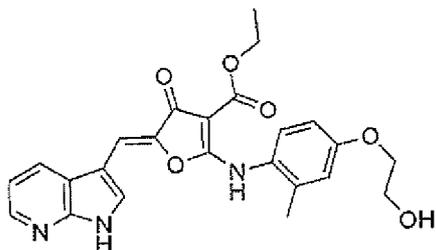
0 (br. s, 2H), 7.33 - 7.43 (m, 2H), 6.84 - 6.93 (m, 2H), 4.31  
 (t, J = 5.77 Hz, 2H), 3.47 - 3.58 (m, 4H), 2.78 (s, 2H), 2.62 -  
 2.70 (m, 2H), 2.35 - 2.42 (m, 2H); LCMS (m/z): 478.9 [M+H]<sup>+</sup>.

5 Example 74

[0307]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-([4-(2-h  
 ydroxyethoxy)-2-methylphenyl]amino)-4-oxo-4,5-dihydrofuran-3-  
 carboxylate

10 [Chemical Formula 83]



First Step

[0308]

A solution of 4-nitro-*m*-cresol (1.4 g, 9.4 mmol), 2-bromoethan  
 15 ol (1.0 mL, 0.014 mol) and potassium carbonate (3.3g, 0.024 mo  
 l) in *N,N*-dimethylformamide (10 mL) was stirred with heating a  
 t 70 °C for 12 h. Cooled to ambient temperature, the reaction m  
 ixture was poured into ice water and extracted with ethyl acet  
 ate. The organic layer was washed with water and brine, dried  
 20 over sodium sulfate, filtered and concentrated. The residue wa  
 s purified by chromatography on silica gel( hexane/ethyl aceta

te) to afford 2-(3-methyl-4-nitrophenoxy)ethanol as solid (1.3 g, y. 70%).

[0309]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 8.04 (d, J = 9.08 Hz, 1H), 7.03 (br. s, 1H), 6.98 (dd, J = 2.44, 9.04 Hz, 1H), 4.92 (t, J = 5.42 Hz, 1H), 4.11 (t, J = 4.80 Hz, 2H), 3.73 (q, J = 4.99 Hz, 2H), 2.55 (s, 3H); LCMS (m/z): 198.3 [M+H]<sup>+</sup>.

Second Step

[0310]

Under a nitrogen atmosphere, 2-(3-methyl-4-nitrophenoxy)ethanol (1.0 g, 5.3 mmol) was dissolved in methanol/tetrahydrofuran (30 mL/30 mL) and 10% palladium on carbon (0.37 g) was added at ambient temperature. The reaction mixture was agitated under a hydrogen atmosphere for 4 h. Palladium on carbon was removed by filtration with Celite and the solvent was removed under reduced pressure to afford 4-(2-hydroxyethoxy)-2-methylaniline as solid (0.80 g, y. 90%).

[0311]

<sup>1</sup>H NMR DMSO-d<sub>6</sub>) δ (ppm) 6.57 (br. s, 1H), 6.52 (br. s, 2H), 4.74 (t, J = 5.56 Hz, 1H), 4.34 (br. s, 2H), 3.82 (t, J = 5.16 Hz, 2H), 3.63 (q, J = 5.30 Hz, 2H), 2.02 (s, 3H); LCMS (m/z): 168.0 [M+H]<sup>+</sup>.

Third Step

[0312]

Diethyl malonate (8.0 mL, 0.052 mol) was added dropwise to a solution of sodium hydride (60% w/w in oil, 4.2 g, 0.11 mol) in anhydrous tetrahydrofuran (130 mL) that cooled with ice bath. The mixture was refluxed for 7 min. The reaction mixture was cooled with ice bath, chloroacetyl chloride (4.2 mL, 0.052 mol) was added dropwise to the reaction mixture and stirred for 1 h then stirred at 45 °C for 1 h. Cooled to ambient temperature, the reaction mixture was diluted with water, and extracted with chloroform for 4 times. The organic layer was dried over magnesium sulfate and concentrated. The residue was purified by chromatography on silica gel (chloroform/methanol) to afford ethyl 2-ethoxy-4-oxo-4,5-dihydrofuran-3-carboxylate as solid (5.0 g, y. 48%).

[0313]

$^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  (ppm) 4.58 - 4.70 (m, 4H), 4.30 (q,  $J = 7.03$  Hz, 2H), 1.53 (t,  $J = 7.03$  Hz, 3H), 1.33 (t,  $J = 7.15$  Hz, 3H)

Fourth Step

[0314]

A solution of 4-(2-hydroxyethoxy)-2-methylaniline (0.69 g, 4.1 mmol) and ethyl 2-ethoxy-4-oxo-4,5-dihydrofuran-3-carboxylate (0.83 g, 4.2 mmol) in ethanol (8.3 mL) was stirred at ambient temperature for 16 h. The solvent was removed under reduced pressure, and ethanol was added to precipitate the product. The

precipitate was collected by filtration then dried to afford ethyl 2-([4-(2-hydroxyethoxy)-2-methylphenyl]amino)-4-oxo-4,5-dihydrofuran-3-carboxylate as solid (0.55 g, y. 42%).

[0315]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 9.99 (br. s, 1H), 7.24 (d, J = 7.84 Hz, 1H), 6.89 (br. s, 1H), 6.80 (d, J = 8.40 Hz, 1H), 4.83 - 4.91 (m, 1H), 4.56 (br. s, 2H), 4.20 (q, J = 6.95 Hz, 2H), 3.97 (t, J = 4.88 Hz, 2H), 3.65 - 3.74 (m, 2H), 2.20 (s, 3H), 1.24 (t, J = 7.04 Hz, 3H); LCMS (m/z): 322.2 [M+H]<sup>+</sup>.

10

Fifth Step

[0316]

To a solution of 7-azaindole-3-carboxaldehyde (0.16 g, 1.1 mmol) and ethyl 2-([4-(2-hydroxyethoxy)-2-methylphenyl]amino)-4-oxo-4,5-dihydrofuran-3-carboxylate (0.36 g, 1.1 mmol) in ethanol (11 mL), L-proline (0.022 g, 0.19 mmol) was added at ambient temperature. The mixture was refluxed for 2 days. Cooled to ambient temperature, the precipitate was collected by filtration, washed with diethyl ether then dried to afford the titled compound as solid (0.24 g, y. 48%).

20

[0317]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.27 (br. s, 1H), 10.29 (br. s, 1H), 8.19 (d, J = 3.91 Hz, 1H), 7.75 (br. s, 1H), 7.68 (d, J = 7.83 Hz, 1H), 7.41 (d, J = 8.31 Hz, 1H), 7.03 (br. s, 1H), 6.94 (d, J = 8.31 Hz, 1H), 6.72 - 6.86 (m, 2H), 4.97 (t, J = 5.38 Hz, 1

25

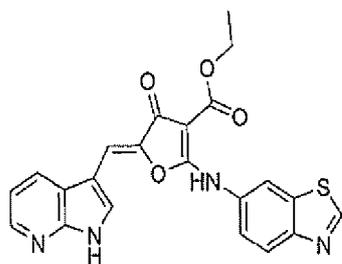
H), 4.26 (q, J = 6.85 Hz, 2H), 4.09 (t, J = 4.65 Hz, 2H), 3.80 (dd, J = 5.14, 9.98 Hz, 2H), 2.23 (s, 3H), 1.29 (t, J = 7.09 Hz, 3H); LCMS (m/z): 450.2 [M+H]<sup>+</sup>.

5 Example 75

[0318]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-(benzo[d]thiazol-6-ylamino)-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 84]



[0319]

To a solution of ethyl 2-(benzo[d]thiazol-6-ylamino)-4-oxo-4,5-dihydrofuran-3-carboxylate (0.070 g, 0.23 mmol) which similarly prepared according to the procedure described in the Example 4, First step and 7-azaindole-3-carboxaldehyde (0.034 g, 0.23 mmol) in ethanol (6.0 mL), L-proline (0.0030 g, 0.023 mmol) was added at ambient temperature. The mixture was refluxed for 16 h. Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol then dried to afford the titled compound as solid (0.045 g, y. 45%).

15

20

[0320]

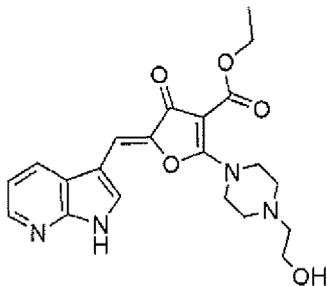
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.25 (br. s, 1H), 10.77 (br. s, 1H), 9.52 (s, 1H), 8.40 (s, 1H), 8.23 (d, J = 8.80 Hz, 1H), 8.12 (d, J = 3.42 Hz, 1H), 7.69 - 7.85 (m, 3H), 6.89 (s, 1H), 6.36 (t, J = 5.94 Hz, 1H), 4.16 - 4.47 (m, 2H), 1.31 (t, J = 6.85 Hz, 3 H); LCMS (m/z): 433.2 [M+H]<sup>+</sup>.

Example 76

[0321]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[4-(2-hydroxyethyl)piperazinyl]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 85]



[0322]

To a solution of ethyl 2-[4-(2-hydroxyethyl)piperazinyl]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.35 g, 1.2 mmol) which similarly prepared according to the procedure described in the Example 74, Fourth step and 7-azaindole-3-carboxaldehyde (0.18 g, 1.2 mmol) in ethanol (6.0 mL), piperidine (0.12 mL, 1.4 mmol) was added at ambient temperature. The mixture was refluxed for 16 h. Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol then dried to afford

the titled compound as solid (0.050 g, y. 10%).

[0323]

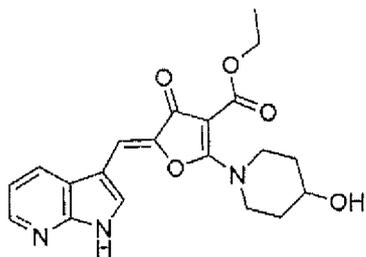
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.34 (br. s, 1H), 8.37 (d, J = 7.82 Hz, 1H), 8.31 (d, J = 3.91 Hz, 1H), 7.99 (s, 1H), 7.20 (dd, J = 4.89, 7.82 Hz, 1H), 6.87 (s, 1H), 4.50 (br. s, 1H), 4.16 (q, J = 7.34 Hz, 2H), 3.71 - 3.88 (m, 4H), 3.55 (t, J = 5.87 Hz, 2H), 2.57 - 2.72 (m, 4H), 2.40 - 2.58 (m, 2H), 1.24 (t, J = 7.09 Hz, 3 H); LCMS (m/z): 413.2 [M+H]<sup>+</sup>.

10 Example 77

[0324]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-(4-hydroxypiperidino)-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 86]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 76.

[0325]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.30 (br. s, 1H), 8.37 (d, J = 7.82 Hz, 1H), 8.31 (d, J = 3.42 Hz, 1H), 7.98 (s, 1H), 7.19 (dd, J = 4.40, 7.83 Hz, 1H), 6.85 (s, 1H), 4.92 (d, J = 3.91 Hz, 1H), 4.17

20

(q,  $J = 6.85$  Hz, 2H), 3.92 - 4.02 (m, 2H), 3.80 - 3.90 (m, 1H),  
 3.58 (t,  $J = 9.29$  Hz, 2H), 1.94 (d,  $J = 3.42$  Hz, 2H), 1.52 - 1.  
 69 (m, 2H), 1.24 (t,  $J = 6.85$  Hz, 3H); LCMS ( $m/z$ ): 384.2  $[M+H]^+$ .

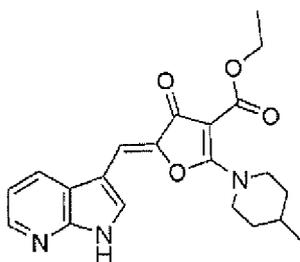
5

Example 78

[0326]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-(4-methy  
 lpiperidino)-4-oxo-4,5-dihydrofuran-3-carboxylate

10 [Chemical Formula 87]



The titled compound(solid) was similarly prepared according to  
 the procedure described in the Example 76.

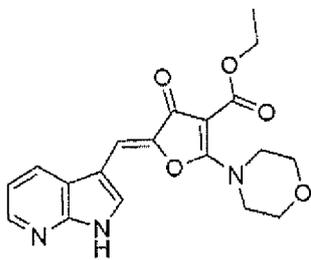
[0327]

15  $^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.30 (br. s, 1H), 8.37 (d,  $J = 7.34$  Hz,  
 1H), 8.31 (d,  $J = 3.91$  Hz, 1H), 7.97 (s, 1H), 7.19 (dd,  $J = 4.$   
 40, 7.82 Hz, 1H), 6.84 (s, 1H), 4.08 - 4.29 (m, 4H), 3.22 - 3.4  
 0 (m, 2H), 1.68 - 1.92 (m, 3H), 1.28 - 1.42 (m, 2H), 1.24 (t,  $J$   
 = 6.85 Hz, 3H), 0.96 (d,  $J = 5.87$  Hz, 3H); LCMS ( $m/z$ ): 382.2  
 20  $[M+H]^+$ .

Example 79

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-morpholino-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 88]



5

The titled compound(solid) was similarly prepared according to the procedure described in the Example 76.

[0328]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.34 (br. s, 1H), 8.37 (d, *J* = 7.82 Hz, 1H), 8.31 (d, *J* = 3.42 Hz, 1H), 8.00 (s, 1H), 7.20 (dd, *J* = 4.40, 7.82 Hz, 1H), 6.89 (s, 1H), 4.16 (q, *J* = 7.17 Hz, 2H), 3.73 - 3.89 (m, 8H), 1.24 (t, *J* = 7.09 Hz, 3H); LCMS (*m/z*): 370.4 [M+H]<sup>+</sup>.

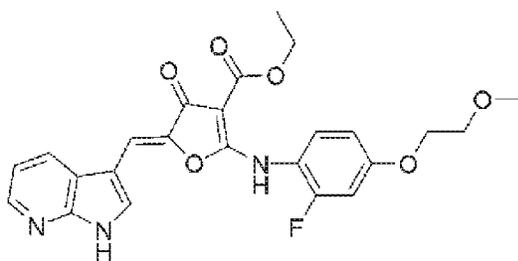
10

15 Example 80

[0329]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(2-fluoro-4-(2-methoxyethoxy)phenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

20 [Chemical Formula 89]



[0330]

To a solution of ethyl 2-([2-fluoro-4-(2-methoxyethoxy)phenyl  
 1]amino)-4-oxo-4,5-dihydrofuran-3-carboxylate (0.011 g, 0.032  
 5 mmol) which similarly prepared according to the procedure des-  
 cribed in the Example 29, First step and 7-azaindole-3-carboxa-  
 ldehyde (0.0045 g, 0.031 mmol) in ethanol (0.2 mL), 2M hydroch-  
 loric acid in ethanol (0.016 mL, 0.032 mmol) was added at ambi-  
 ent temperature. The mixture was refluxed for 4 h. Cooled with  
 10 ice bath, 2M sodium hydroxide solution (0.015 mL, 0.029 mmol)  
 was added dropwise to neutralize, and ethanol (1.5 mL) was ad-  
 ded. The mixture was refluxed for further 30 min. The precipit-  
 ate was collected by filtration, washed with hot ethanol. The  
 solid was washed with hexane then dried to afford the titled c-  
 15 ompound as solid (0.0051 g, y. 32%).

[0331]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.34 (br. s, 1H), 10.38 (s, 1H), 8.21  
 (dd, J = 1.38, 4.64 Hz, 1H), 7.81 (d, J = 7.53 Hz, 1H), 7.75  
 (d, J = 2.51 Hz, 1H), 7.58 (t, J = 9.03 Hz, 1H), 7.13 (dd, J =  
 20 2.51, 12.05 Hz, 1H), 6.98 (dd, J = 2.26, 8.78 Hz, 1H), 6.89 (s,  
 1H), 6.82 (dd, J = 4.64, 7.91 Hz, 1H), 4.20 - 4.31 (m, 4H), 3.  
 71 - 3.77 (m, 2H), 3.37 (br. s, 3H), 1.29 (t, J = 7.03 Hz, 3H);

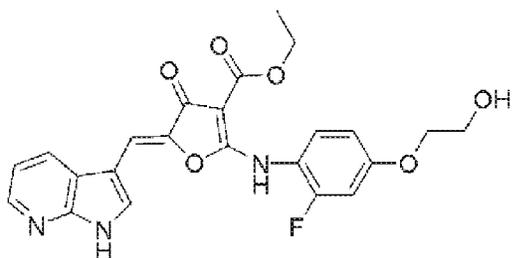
LCMS (m/z): 467.9 [M+H]<sup>+</sup>.

Example 81

[0332]

5 Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[[2-fluoro-4-(2-hydroxyethoxy)phenyl]amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 90]



10 [0333]

To a solution of ethyl 2-[[2-fluoro-4-(2-hydroxyethoxy)phenyl]amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.017 g, 0.052 mmol) which similarly prepared according to the procedure described in the Example 29, First step and 7-azaindole-3-carboxaldehyde (0.0075 g, 0.051 mmol) in ethanol (0.2 mL), 2M hydrochloric acid in ethanol (0.052 mL, 0.10 mmol) was added at ambient temperature. The mixture was refluxed for 8.5 h. Cooled with ice bath, 2M sodium hydroxide solution (0.047 mL, 0.094 mmol) was added dropwise to neutralize, and ethanol (0.5 mL) was added and refluxed for further 16 min. The precipitate was collected by filtration, washed with hot ethanol. The solid was washed with hexane then dried to afford the titled compound as

20

solid (0.014 g, y. 59%).

[0334]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.14 (br. s, 1H), 10.38 (s, 1H), 8.21  
(dd, J = 1.20, 4.80 Hz, 1H), 7.87 (d, J = 7.20 Hz, 1H), 7.65  
5 (br. s, 1H), 7.38 (br. s, 1H), 6.95 - 7.07 (m, 1H), 6.85 - 6.95  
(m, 1H), 6.83 (dd, J = 4.80, 8.00 Hz, 1H), 6.64 (br. s, 1H), 4.  
96 (t, J = 5.40 Hz, 1H), 4.15 - 4.25 (m, 2H), 4.09 (t, J = 4.80  
Hz, 2H), 3.78 (q, J = 5.07 Hz, 2H), 1.26 (t, J = 7.00 Hz, 3H);  
LCMS (m/z): 453.8 [M+H]<sup>+</sup>.

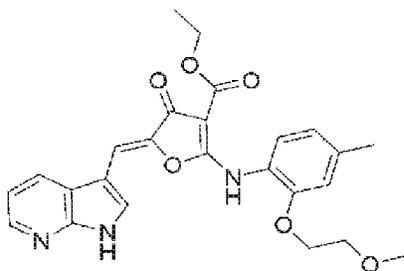
10

Example 82

[0335]

Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-2-[[2-(2-m  
ethoxyethoxy)-4-methylphenyl]amino]-4-oxo-4,5-dihydrofuran-3-  
15 carboxylate

[Chemical Formula 91]



[0336]

To a solution of ethyl 2-[[2-(2-methoxyethoxy)-4-methylpheny  
20 l]amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.015 g, 0.045  
mmol) which similarly prepared according to the procedure des

cribed in the Example 29, First step and 7-azaindole-3-carboxaldehyde (0.0067 g, 0.046 mmol) in ethanol (0.2 mL), 2M hydrochloric acid in ethanol (0.023 mL, 0.045 mmol) was added at ambient temperature. The mixture was refluxed for 4 h. Cooled to ambient temperature, the solvent was removed under reduced pressure. The residue was purified by preparative HPLC to afford the titled compound as solid (0.0090g, y. 43%).

[0337]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.29 (br. s, 1H), 10.30 (br. s, 1H), 8.25 (dd, J = 1.38, 4.64 Hz, 1H), 8.00 (d, J = 7.03 Hz, 1H), 7.83 (s, 1H), 7.49 (d, J = 7.78 Hz, 1H), 7.10 (s, 1H), 6.84 - 6.95 (m, 3H), 4.26 (q, J = 7.03 Hz, 2H), 4.09 - 4.17 (m, 2H), 3.53 - 3.60 (m, 2H), 3.17 (s, 3H), 2.43 (s, 3H), 1.29 (t, J = 7.03 Hz, 3H); LCMS (m/z): 463.9 [M+H]<sup>+</sup>.

15

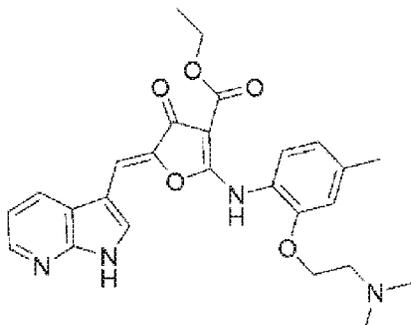
Example 83

[0338]

Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-2-({2-[2-(dimethylamino)ethoxy]-4-methylphenyl}amino)-4-oxo-4,5-dihydrofuran-3-carboxylate

20

[Chemical Formula 92]



[0339]

To a stirred solution of ethyl 2-((2-[2-(dimethylamino)ethoxy]-4-methylphenyl)amino)-4-oxo-4,5-dihydrofuran-3-carboxylate (0.011 g, 0.030 mmol) which similarly prepared according to the procedure described in the Example 29, First step and 7-azaindole-3-carboxaldehyde (0.0044 g, 0.030 mmol) in ethanol (0.2 mL), 2M hydrochloric acid in ethanol (0.045 mL, 0.091 mmol) was added at ambient temperature. The mixture was refluxed for 9 h. Cooled with ice bath, 2M sodium hydroxide solution (0.041 mL, 0.082 mmol) was added dropwise to neutralize, and ethanol (0.5 mL) was added. The mixture was refluxed for further 16 min. The precipitate was collected by filtration, washed with hot ethanol. The solid was washed with hexane then dried to afford the titled compound as solid (0.00079 g, y. 5%).

[0340]

$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.27 (br. s, 1H), 8.24 (d,  $J$  = 4.52 Hz, 1H), 8.16 (s, 1H), 7.96 (d,  $J$  = 8.03 Hz, 1H), 7.79 - 7.82 (m, 1H), 7.46 (d,  $J$  = 7.53 Hz, 1H), 7.09 - 7.12 (m, 1H), 6.93 (d,  $J$  = 7.53 Hz, 1H), 6.81 - 6.89 (m, 2H), 4.25 (q,  $J$  = 6.94 Hz, 2H),

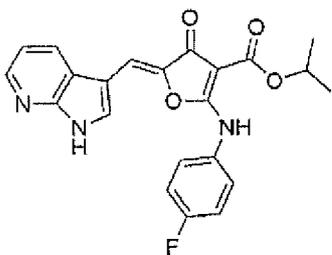
4.10 (t, J = 4.64 Hz, 2H), 2.52 - 2.58 (m, 2H), 2.43 (s, 3H),  
2.13 (s, 6H), 1.29 (t, J = 7.03 Hz, 3H); LCMS (m/z): 477.0 [M+  
H]<sup>+</sup>.

5 Example 84

[0341]

Isopropyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(4-  
fluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 93]



10

[0342]

Under a nitrogen atmosphere, a solution of the compound (0.039  
g, 0.10mmol) of Example 21, 4-dimethylaniline (0.0024 g, 0.02  
0 mmol) and zinc cluster catalyst ( $Zn_4(OCO_2CF_3)_6O$ ) (0.0012 g, 0.  
15 0013 mmol) in 2-propanol (1.0 mL) and *N,N*-dimethylacetamide (1.  
0 mL) was stirred with the microwave synthesizer (Biotage Init  
iator<sup>TM</sup>) at 150 °C for 1.5 h. Cooled to ambient temperature, th  
e precipitate was removed by filtration. The filtrate was puri  
fied by preparative HPLC to afford the titled compound as soli  
20 d (0.011 g, y. 27%).

[0343]

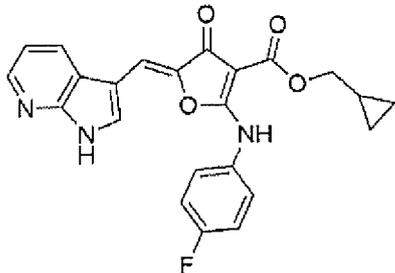
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.29 (br. s, 1H), 10.54 (s, 1H), 8.25 (dd, J = 1.51, 4.77 Hz, 1H), 7.94 (d, J = 7.03 Hz, 1H), 7.76 (d, J = 2.76 Hz, 1H), 7.56 - 7.70 (m, 2H), 7.28 - 7.44 (m, 2H), 6.80 - 6.98 (m, 2H), 5.08 - 5.17 (m, 1H), , 1.31 (d, J = 6.27 Hz, 6H); LCMS (m/z): 408.0 [M+H]<sup>+</sup>.

Example 85

[0344]

Cyclopropylmethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(4-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 94]



[0345]

Under a nitrogen atmosphere, a solution of the compound (0.038 g, 0.10mmol) of Example 51, cyclopropyl carbinol (0.10 mL, 1.3 mmol) and zinc cluster catalyst (Zn<sub>4</sub>(OCOCF<sub>3</sub>)<sub>6</sub>O) (0.0019 g, 0.0020 mmol) in *N,N*-dimethylacetamide (0.9mL) was stirred with the microwave synthesizer (Biotage Initiator<sup>TM</sup>) at 150 °C for 30 min. Cooled to ambient temperature, the precipitate was removed by filtration. The filtrate was purified by preparative HPL

C to afford the titled compound as solid (0.0080 g, y. 19%).

[0346]

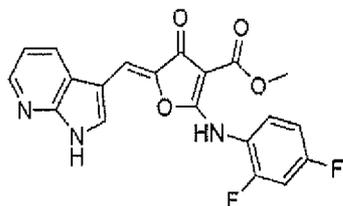
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.29 (br. s, 1H), 10.57 (s, 1H), 8.25 (d, J = 3.51 Hz, 1H), 7.95 (d, J = 7.78 Hz, 1H), 7.75 (d, J = 2.51 Hz, 1H), 7.60 - 7.69 (m, 2H), 7.34 - 7.43 (m, 2H), 6.85 - 6.95 (m, 2H), 4.08 (d, J = 7.03 Hz, 2H), 1.16 - 1.31 (m, 1H), 0.55 (dd, J = 1.51, 8.03 Hz, 2H), 0.36 (d, J = 5.02 Hz, 2H); LCMS (m/z): 419.8 [M+H]<sup>+</sup>.

10 Example 86

[0347]

Methyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(2,4-difluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 95]



15

[0348]

To a solution of methyl 2-[(2,4-difluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.27 g, 1.0 mmol) which similarly prepared according to the procedure described in the Example 2, First step using methyl 4-chloroacetoacetate and 2,4-difluorophenyl isocyanate, and 7-azaindole-3-carboxaldehyde (0.15 g, 1.0 mmol) in 2-propanol (5.0 mL), L-proline (0.023 g, 0.20

20

mmol) was added at ambient temperature. The mixture was refluxed for 12 h. Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol and diisopropyl ether then dried to afford the titled compound as solid (0.30 g, y. 75%).

[0349]

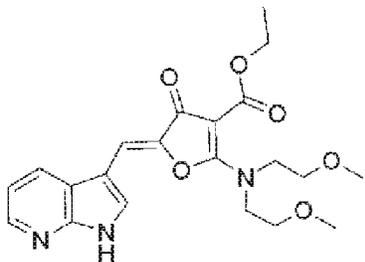
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.32 (br. s, 1H), 10.53 (s, 1H), 8.24 (dd, J = 1.38, 4.64 Hz, 1H), 7.74 - 7.87 (m, 2H), 7.70 (d, J = 2.51 Hz, 1H), 7.54 - 7.63 (m, 1H), 7.27 - 7.37 (m, 1H), 6.94 (s, 1H), 6.84 (dd, J = 4.77, 8.03 Hz, 1H), 3.77 (s, 3H); LCMS (m/z): 397.9 [M+H]<sup>+</sup>.

Example 87

[0350]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[bis(2-methoxyethyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 96]



[0351]

To a solution of ethyl 2-[bis(2-methoxyethyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.30 g, 1.0 mmol) which similarly

prepared according to the procedure described in the Example 4, First step and 7-azaindole-3-carboxaldehyde (0.15 g, 1.0 mmol) in ethanol (5.0 mL), L-proline (0.023 g, 0.20 mmol) was added at ambient temperature. The mixture was refluxed for 2 days. Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol then dried to afford the titled compound as solid (0.048 g, y. 11%).

[0352]

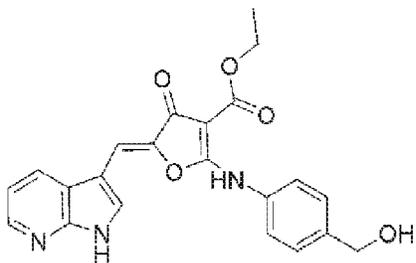
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.36 (br. s, 1H), 8.38 (d, J = 7.82 Hz, 1H), 8.31 (d, J = 4.89 Hz, 1H), 7.98 (s, 1H), 7.19 (dd, J = 4.65, 8.07 Hz, 1H), 6.85 (s, 1H), 4.16 (q, J = 6.85 Hz, 2H), 3.97 (t, J = 5.14 Hz, 4H), 3.57 - 3.67 (m, 4H), 3.25 (s, 6H), 1.24 (t, J = 7.09 Hz, 3H); LCMS (m/z): 416.2 [M+H]<sup>+</sup>.

15 Example 88

[0353]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[[4-(hydroxymethyl)phenyl]amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

20 [Chemical Formula 97]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 87.

[0354]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.27 (br. s, 1H), 10.66 (br. s, 1H),  
5 8.22 (d, J = 3.42 Hz, 1H), 7.97 (d, J = 7.34 Hz, 1H), 7.79 (br.  
s, 1H), 7.42 - 7.55 (m, 4H), 6.86 - 6.94 (m, 1H), 6.84 (br. s,  
1H), 5.34 (br. s, 1H), 4.62 (d, J = 4.40 Hz, 2H), 4.26 (d, J =  
6.85 Hz, 2H), 1.29 (t, J = 6.85 Hz, 3H); LCMS (m/z): 406.4 [M+  
H]<sup>+</sup>.

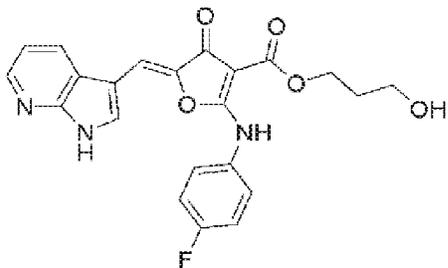
10

Example 89

[0355]

3-Hydroxypropyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-  
2-[(4-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylat  
15 e

[Chemical Formula 98]



[0356]

A solution of the compound of Example 51 and zinc cluster catalyst (Zn<sub>4</sub>(OCOCF<sub>3</sub>)<sub>6</sub>O) (0.0019 g, 0.0020 mmol) in 1,3-propanediol  
20 (0.5 mL) and *N,N*-dimethylacetamide (0.5 mL) was stirred at 12

0 °C for 2 h then at 100 °C for 12 h. Cooled to ambient temperature, the reaction mixture was diluted with water, and the precipitate was collected by filtration. Ethyl acetate was added to the filtrate, and the precipitate was collected by filtration. Those precipitates were combined then purified by preparative HPLC to afford the titled compound as solid (0.0067 g, y. 16%).

[0357]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.22 (br. s, 1H), 10.72 (br. s, 1H), 8.24 (dd, J = 1.38, 4.64 Hz, 1H), 7.97 (d, J = 7.03 Hz, 1H), 7.72 (d, J = 2.51 Hz, 1H), 7.50 - 7.60 (m, 2H), 7.35 (t, J = 8.78 Hz, 2H), 6.89 (dd, J = 4.52, 8.03 Hz, 1H), 6.81 (br. s, 1H), 4.77 (br. s, 1H), 4.25 (t, J = 6.27 Hz, 2H), 3.59 (t, J = 5.77 Hz, 2H), 1.79 - 1.87 (m, 2H); LCMS (m/z): 423.8 [M+H]<sup>+</sup>.

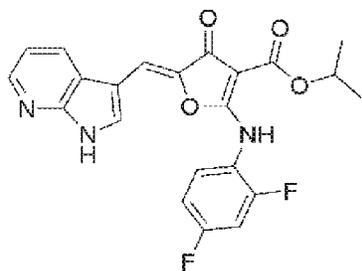
15

Example 90

[0358]

Isopropyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(2,4-difluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

20 [Chemical Formula 99]



[0359]

A solution of the compound (0.040g, 0.10mmol) of Example 86 and zinc cluster catalyst ( $Zn_4(OCOCF_3)_6O$ ) (0.0012 g, 0.0013 mmol) in 2-propanol (0.5 mL) was stirred at 95 °C for 4 days. Cooled to ambient temperature, the reaction mixture was purified by preparative HPLC to afford the titled compound as solid (0.0061 g, y. 13%).

[0360]

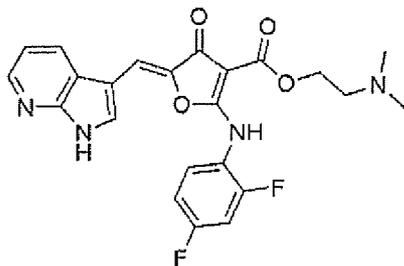
$^1H$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.32 (br. s, 1H), 10.47 (s, 1H), 8.24 (dd,  $J = 1.51, 4.52$  Hz, 1H), 7.67 - 7.88 (m, 3H), 7.54 - 7.63 (m, 1H), 7.26 - 7.38 (m, 1H), 6.88 (s, 1H), 6.83 (dd,  $J = 4.64, 7.91$  Hz, 1H), 5.10 - 5.18 (m, 1H), 1.31 (d,  $J = 6.27$  Hz, 6H); LCMS (m/z): 426.2 [M+H] $^+$ .

Example 91

[0361]

2-(Dimethylamino)ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(2,4-difluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 100]



[0362]

A solution of the compound (0.040g, 0.10mmol) of Example 86, 2-dimethylaminoethanol (0.10 mL, 1.0 mmol) and zinc cluster catalyst ( $Zn_4(OCOCF_3)_6O$ ) (0.0019 g, 0.0020 mmol) in *N,N*-dimethylacetamide (0.9 mL) was stirred at 100 °C for 24 h. Cooled to ambient temperature, the precipitate was removed by filtration. The filtrate was purified by preparative HPLC to afford the titled compound as solid (0.010 g, y. 22%).

[0363]

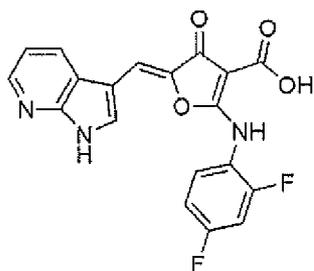
<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 11.97 (br. s, 1H), 8.19 (dd, *J* = 1.51, 4.52 Hz, 1H), 8.14 (s, 1H), 7.93 (d, *J* = 7.78 Hz, 1H), 7.52 (br. s, 1H), 7.16 - 7.36 (m, 2H), 7.03 - 7.13 (m, 1H), 6.83 (dd, *J* = 4.89, 7.91 Hz, 1H), 6.42 (s, 1H), 4.35 (t, *J* = 5.27 Hz, 2H), 3.22 (t, *J* = 5.27 Hz, 2H), 2.67 - 2.87 (m, 6H); LCMS (*m/z*): 455.2 [M+H]<sup>+</sup>.

Example 92

[0364]

5-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(2,4-difluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylic acid

[Chemical Formula 101]



[0365]

To a solution of the compound (0.20g, 0.45mmol) of Example 53 in ethanol (2.0 mL), aqueous 50% w/v potassium hydroxide solution (0.5 mL) was added at ambient temperature. The mixture was stirred at 95 °C for 3 h. Cooled to ambient temperature, diluted with water and conc. hydrochloric acid was added dropwise to neutralize. The precipitate was collected by filtration, washed with ethanol and diisopropyl ether then dried to afford the titled compound as solid (0.19 g, y. 98%).

[0366]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.36 (br. s, 1H), 8.25 (dd, J = 1.51, 4.52 Hz, 1H), 7.86 (d, J = 7.03 Hz, 1H), 7.69 - 7.82 (m, 2H), 7.57 (ddd, J = 2.76, 8.97, 10.35 Hz, 1H), 7.25 - 7.37 (m, 1H), 7.01 (s, 1H), 6.85 (dd, J = 4.77, 8.03 Hz, 1H); LCMS (m/z): 381.9 [M-H]<sup>-</sup>

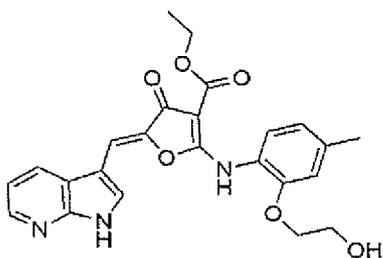
Example 93

[0367]

Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-2-[[2-(2-hydroxyethoxy)-4-methylphenyl]amino]-4-oxo-4,5-dihydrofuran-3-

carboxylate

[Chemical Formula 102]



[0368]

5 To a solution of ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-2-[(2,4-difluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.017 g, 0.052 mmol) which similarly prepared according to the procedure described in the Example 29, First step and 7-azaindole-3-carboxaldehyde (0.0075 g, 0.051 mmol) in  
 10 ethanol (0.2 mL), 2M hydrochloric acid in ethanol (0.052 mL, 0.10 mmol) was added at ambient temperature. The mixture was refluxed for 8.5 h. Cooled with ice bath, 2M sodium hydroxide solution (0.047 mL, 0.094 mmol) was added dropwise to neutralize then the solvent was removed under reduced pressure. The residue  
 15 was purified by preparative HPLC to afford the titled compound as solid (0.0066 g, y. 28%).

[0369]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.30 (br. s, 1H), 10.22 (br. s, 1H), 8.25 (d, J = 3.51 Hz, 1H), 8.03 (d, J = 7.78 Hz, 1H), 7.83 (br. s, 1H), 7.43 - 7.56 (m, 1H), 7.10 (s, 1H), 6.85 - 6.95 (m, 3H),  
 20 4.79 (br. s, 1H), 4.26 (q, J = 7.19 Hz, 2H), 4.06 (t, J = 5.14

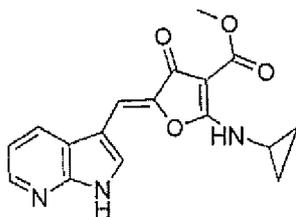
Hz, 2H), 3.62 (t,  $J = 5.20$  Hz, 2H), 2.42 (s, 3H), 1.29 (t,  $J = 7.15$  Hz, 3H); LCMS ( $m/z$ ): 449.5  $[M+H]^+$ .

Example 94

[0370]

Methyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-(cyclopropylamino)-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 103]



[0371]

To a solution of methyl 2-(cyclopropylamino)-4-oxo-4,5-dihydrofuran-3-carboxylate (0.50 g, 2.5 mmol) which similarly prepared according to the procedure described in the Example 4, First step using dimethyl malonate, chloroacetyl chloride and cyclopropylamine, and 7-azaindole-3-carboxaldehyde (0.37 g, 2.5 mmol) in ethanol (6.0 mL), L-proline (0.029 g, 0.25 mmol) was added at ambient temperature. The mixture was refluxed for 16 h.

Cooled to ambient temperature, the precipitate was collected by filtration, washed with methanol then dried to afford the titled compound as solid (0.012 g, y. 30%).

[0372]

$^1\text{H}$  NMR ( $\text{DMSO-}d_6$ )  $\delta$  (ppm) 12.33 (br. s, 1H), 8.88 (br. s, 1H), 8.

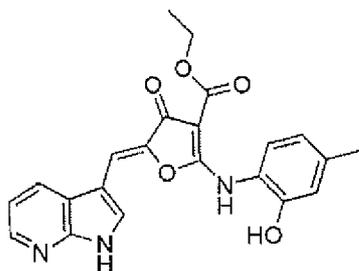
57 (d,  $J = 7.82$  Hz, 1H), 8.31 (d,  $J = 3.91$  Hz, 1H), 8.06 (s, 1H), 7.20 (dd,  $J = 4.89, 7.82$  Hz, 1H), 6.94 (s, 1H), 3.69 (s, 3H), 3.08 - 3.20 (m, 1H), 0.84 - 1.00 (m, 4H); LCMS ( $m/z$ ): 326.0 [M+H]<sup>+</sup>.

Example 95

[0373]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(2-hydroxy-4-methylphenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 104]



[0374]

To a solution of ethyl 2-[(2-hydroxy-4-methylphenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.10 g, 0.36 mmol) which is similarly prepared according to the procedure described in the Example 74, Fourth step and 7-azaindole-3-carboxaldehyde (0.061 g, 0.42 mmol) in ethanol (2.5 mL), 2M hydrochloric acid in ethanol (0.56 mL, 1.1 mmol) was added at ambient temperature. The mixture was refluxed for 19 h. Cooled with ice bath, 2M sodium hydroxide solution (0.49 mL, 0.97 mmol) was added dropwise to

o neutralize, and ethanol (8.0 mL) was added and the mixture was refluxed for 30 min. The precipitate was collected by filtration, washed with hot ethanol. The solid was washed with hexane then dried to afford the titled compound as solid (0.027 g, 18%).

[0375]

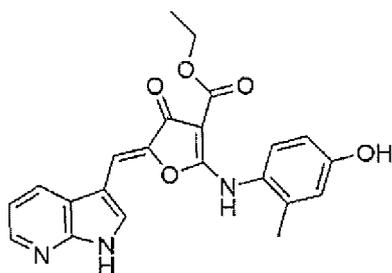
$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.32 (br. s, 1H), 10.21 (s, 1H), 10.19 (s, 1H), 8.22 - 8.30 (m, 1H), 8.04 (d,  $J = 7.53$  Hz, 1H), 7.87 (d,  $J = 2.26$  Hz, 1H), 7.44 (d,  $J = 8.03$  Hz, 1H), 6.84 - 6.94 (m, 3H), 6.77 (d,  $J = 8.03$  Hz, 1H), 4.27 (q,  $J = 7.03$  Hz, 2H), 2.35 (s, 3H), 1.30 (t,  $J = 7.03$  Hz, 3H); LCMS (m/z): 405.9 [ $\text{M} + \text{H}$ ] $^+$ .

Example 96

[0376]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(4-hydroxy-2-methylphenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 105]



[0377]

To a solution of ethyl 2-[(4-hydroxy-2-methylphenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.10 g, 0.37 mmol) which is similarly prepared according to the procedure described in the Example 74, Fourth step and 7-azaindole-3-carboxaldehyde (0.063 g, 0.43 mmol) in ethanol (2.5 mL), 2M hydrochloric acid in ethanol (0.46 mL, 0.92 mmol) was added at ambient temperature. The mixture was refluxed for 2.5 days. Cooled with ice bath, 2M sodium hydroxide solution (0.46 mL, 0.92 mmol) was added dropwise to neutralize, and ethanol (11 mL) was added and the mixture was refluxed for further 40 min. The precipitate was collected by filtration, washed with hot ethanol. The solid was washed with hexane then dried to afford the titled compound as solid (0.10 g, y. 70%).

[0378]

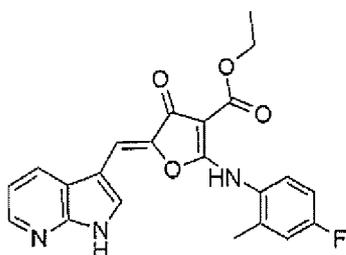
$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.27 (br. s, 1H), 10.20 (s, 1H), 9.76 (s, 1H), 8.20 (dd,  $J = 1.25, 4.52$  Hz, 1H), 7.81 (d,  $J = 2.51$  Hz, 1H), 7.64 (d,  $J = 7.53$  Hz, 1H), 7.28 (d,  $J = 8.28$  Hz, 1H), 6.72 - 6.87 (m, 4H), 4.26 (q,  $J = 7.03$  Hz, 2H), 2.16 (s, 3H), 1.29 (t,  $J = 7.03$  Hz, 3H); LCMS (m/z): 405.8 [M+H] $^+$ .

Example 97

[0379]

Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-2-[(4-fluoro-2-methylphenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 106]



[0380]

To a solution of ethyl 2-[(4-fluoro-2-methylphenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.30 g, 1.1 mmol) which similarly prepared according to the procedure described in the Example 4, First step and 7-azaindole-3-carboxaldehyde (0.16 g, 1.1 mmol) in ethanol (7.0 mL), L-proline (0.013 g, 0.10 mmol) was added at ambient temperature. The mixture was refluxed for 3 days. Cooled to ambient temperature, the precipitate was collected by filtration, washed with methanol then dried to afford the titled compound as solid (0.25 g, y. 58%).

[0381]

$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.28 (br. s, 1H), 10.40 (s, 1H), 8.22 (d,  $J = 3.91$  Hz, 1H), 7.66 - 7.76 (m, 2H), 7.59 (dd,  $J = 5.62, 8.56$  Hz, 1H), 7.36 (dd,  $J = 2.45, 9.78$  Hz, 1H), 7.18 - 7.28 (m, 1H), 6.85 (s, 1H), 6.78 (dd,  $J = 4.89, 7.83$  Hz, 1H), 4.27 (q,  $J = 7.01$  Hz, 2H), 2.27 (s, 3H), 1.30 (t,  $J = 7.09$  Hz, 3H); LCMS (m/z): 408.4 [M+H] $^+$ .

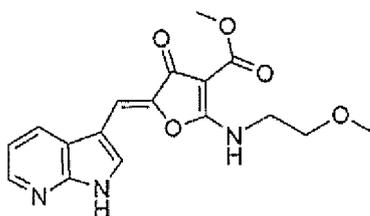
20

Example 98

[0382]

Methyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(2-methoxyethyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 107]



5

The titled compound(solid) was similarly prepared according to the procedure described in the Example 97.

[0383]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.36 (br. s, 1H), 8.94 (br. s, 1H), 8.44 (d, *J* = 7.83 Hz, 1H), 8.31 (d, *J* = 4.40 Hz, 1H), 8.03 (s, 1H), 7.19 (dd, *J* = 4.40, 7.82 Hz, 1H), 6.92 (s, 1H), 3.76 - 3.84 (m, 2H), 3.71 (s, 3H), 3.62 (t, *J* = 5.14 Hz, 2H), 3.31 (br. s, 3H); LCMS (*m/z*): 344.2 [M+H]<sup>+</sup>.

10

15 Example 99

[0384]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[[4-(2-methoxyethoxy)-2-methylphenyl]amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

20

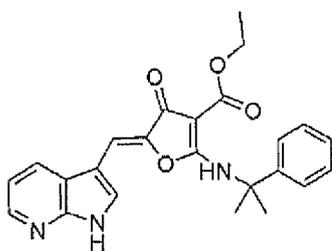
[Chemical Formula 108]

Example 112

[0420]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-4-oxo-2-  
[(2-phenyl-2-propynyl)amino]-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 121]



[0421]

To a solution of ethyl 4-oxo-2-[(2-phenyl-2-propynyl)amino]-4,  
5-dihydrofuran-3-carboxylate (0.40 g, 1.4 mmol) which similarl  
y prepared according to the procedure described in the Example  
4, First step and 7-azaindole-3-carboxaldehyde (0.20 g, 1.4 m  
mol) in ethanol (10 mL), L-proline (0.016 g, 0.14 mmol) was ad  
ded at ambient temperature. The mixture was refluxed for 3 day  
s. Cooled to ambient temperature, the precipitate was collecte  
d by filtration, washed with methanol then dried to afford the  
titled compound as solid (0.15 g, y. 26%).

[0422]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.22 (br. s, 1H), 8.92 (br. s, 1H), 8.  
25 (d, *J* = 3.42 Hz, 1H), 8.10 (d, *J* = 7.82 Hz, 1H), 7.58 (d, *J*  
= 7.34 Hz, 2H), 7.44 - 7.53 (m, 2H), 7.23 - 7.33 (m, 1H), 7.06  
(dd, *J* = 4.65, 7.09 Hz, 1H), 6.90 (br. s, 1H), 6.78 (br. s, 1H),

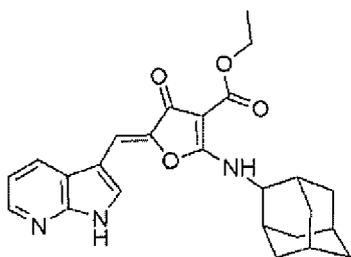
4.27 (q,  $J = 6.52$  Hz, 2H), 1.85 (br. s, 6H), 1.29 (t,  $J = 6.85$  Hz, 3H); LCMS ( $m/z$ ): 418.0  $[M+H]^+$ .

Example 113

[0423]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-(2-adamantylamino)-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 122]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 112.

[0424]

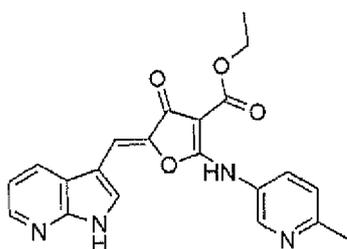
$^1\text{H}$  NMR ( $\text{DMSO-}d_6$ )  $\delta$  (ppm) 12.37 (br. s, 1H), 8.71 (d,  $J = 6.85$  Hz, 1H), 8.42 (d,  $J = 7.82$  Hz, 1H), 8.32 (d,  $J = 3.91$  Hz, 1H), 7.99 (s, 1H), 7.20 (dd,  $J = 4.89, 7.83$  Hz, 1H), 6.92 (s, 1H), 4.30 - 4.40 (m, 1H), 4.24 (q,  $J = 7.01$  Hz, 2H), 2.10 - 2.19 (m, 2H), 1.81 - 1.99 (m, 8H), 1.67 - 1.80 (m, 4H), 1.27 (t,  $J = 7.09$  Hz, 3H); LCMS ( $m/z$ ): 433.8  $[M+H]^+$ .

Example 114

[0425]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[3-(6-methylpyridinyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 123]



5

The titled compound(solid) was similarly prepared according to the procedure described in the Example 112.

[0426]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.23 (br. s, 1H), 8.41 - 8.61 (m, 2H), 8.25 (d, *J* = 4.40 Hz, 1H), 8.02 (br. s, 1H), 7.79 (d, *J* = 1.96 Hz, 1H), 7.50 (br. s, 1H), 6.89 - 7.00 (m, 1H), 6.78 - 6.89 (m, 1H), 4.08 - 4.28 (m, 2H), 2.27 (s, 3H), 1.18 - 1.30 (m, 3H); L CMS (m/z): 391.4 [M+H]<sup>+</sup>.

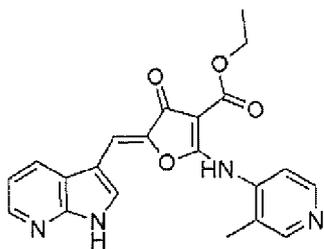
10

15 Example 115

[0427]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[4-(3-methylpyridinyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 124]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 112.

[0428]

5 <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.23 (br. s, 1H), 8.41 - 8.61 (m, 2H), 8.25 (d, J = 4.40 Hz, 1H), 8.02 (br. s, 1H), 7.79 (d, J = 1.96 Hz, 1H), 7.50 (br. s, 1H), 6.89 - 7.00 (m, 1H), 6.83 (br. s, 1H), 4.19 (br. s, 2H), 2.27 (s, 3H), 1.24 (br. s, 3H); LCMS (m/z): 391.4 [M+H]<sup>+</sup>.

10

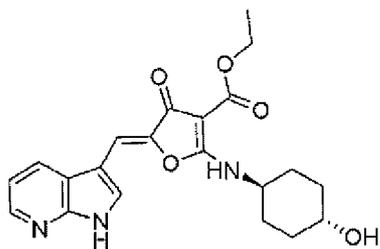
Example 116

[0429]

Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-2-[(trans-4-hydroxycyclohexyl) amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

15

[Chemical Formula 125]



[0430]

To a solution of ethyl 2-[(*trans*-4-hydroxycyclohexyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.30 g, 1.1 mmol) which is similarly prepared according to the procedure described in the Example 4, First step and 7-azaindole-3-carboxaldehyde (0.16 g, 1.1 mmol) in ethanol (20 mL), L-proline (0.013 g, 0.11 mmol) was added at ambient temperature. The mixture was refluxed for 2 days. Cooled to ambient temperature, the precipitate was collected by filtration, washed with methanol then dried to afford the titled compound as solid (0.14 g, y. 40%).

[0431]

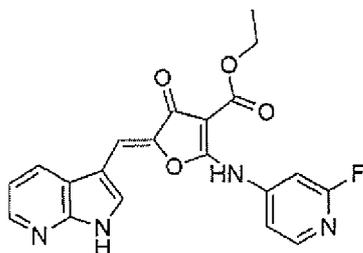
<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.36 (br. s, 1H), 8.39 - 8.54 (m, 2H), 8.33 (d, *J* = 4.40 Hz, 1H), 7.99 (s, 1H), 7.20 (dd, *J* = 4.89, 7.83 Hz, 1H), 6.89 (s, 1H), 4.69 (d, *J* = 3.91 Hz, 1H), 4.20 (q, *J* = 7.34 Hz, 2H), 3.97 (br. s, 1H), 3.41 - 3.53 (m, 1H), 1.86 - 2.03 (m, 4H), 1.61 - 1.76 (m, 2H), 1.29 - 1.42 (m, 2H), 1.25 (t, *J* = 7.09 Hz, 3H); LCMS (*m/z*): 398.1 [M+H]<sup>+</sup>.

Example 117

[0432]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[4-(2-fluoropyridinyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 126]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 116.

[0433]

- 5  $^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.44 (br. s, 1H), 10.86 (br. s, 1H), 8.30 (d,  $J = 5.38$  Hz, 2H), 8.21 (d,  $J = 7.82$  Hz, 1H), 7.94 (d,  $J = 1.96$  Hz, 1H), 7.63 (d,  $J = 5.38$  Hz, 1H), 7.44 (s, 1H), 7.00 - 7.09 (m, 2H), 4.29 (q,  $J = 7.01$  Hz, 2H), 1.30 (t,  $J = 7.09$  Hz, 3H); LCMS (m/z): 395.0  $[\text{M}+\text{H}]^+$ .

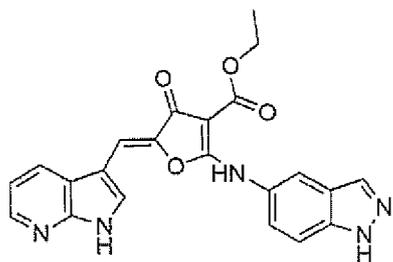
10

Example 118

[0434]

Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-2-[(5-indazolyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

15 [Chemical Formula 127]



The titled compound(solid) was similarly prepared according to

the procedure described in the Example 116.

[0435]

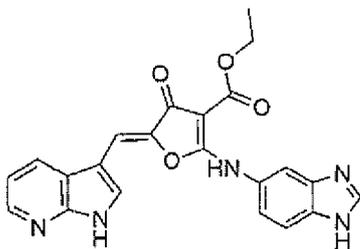
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 13.36 (s, 1H), 12.25 (br. s, 1H), 10.6  
2 (br. s, 1H), 8.17 (s, 1H), 8.09 (d, J = 3.91 Hz, 1H), 7.99 (s,  
5 1H), 7.78 (d, J = 1.96 Hz, 1H), 7.63 - 7.72 (m, 2H), 7.52 (d,  
J = 7.82 Hz, 1H), 6.85 (s, 1H), 6.12 - 6.27 (m, 1H), 4.28 (q, J  
= 7.01 Hz, 2H), 1.30 (t, J = 6.85 Hz, 3H); LCMS (m/z): 416.2  
[M+H]<sup>+</sup>.

10 Example 119

[0436]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(5-benz  
imidazolyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 128]



[0437]

To a solution of ethyl 2-[(5-benzimidazolyl)amino]-4-oxo-4,5-  
dihydrofuran-3-carboxylate (0.30 g, 1.0 mmol) which similarly  
prepared according to the procedure described in the Example 7  
20 4, Fourth step and 7-azaindole-3-carboxaldehyde (0.15 g, 1.0  
mol) in ethanol (5.0 mL), piperidine (0.20 mL, 3.1 mmol) was a

added at ambient temperature. The mixture was refluxed for 24 h.  
Cooled to ambient temperature, the precipitate was collected  
by filtration, washed with methanol then dried to afford the t  
itled compound as solid (0.015 g, y. 4%).

5 [0438]

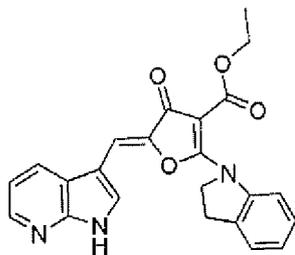
$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.28 (br. s, 1H), 10.82 (s, 1H), 9.55  
(s, 1H), 8.16 (d,  $J = 3.91$  Hz, 1H), 8.08 (s, 1H), 7.98 (d,  $J =$   
8.80 Hz, 1H), 7.87 (d,  $J = 7.34$  Hz, 1H), 7.59 - 7.89 (m, 1H),  
7.74 (s, 1H), 6.93 (s, 1H), 6.53 (dd,  $J = 4.89, 7.34$  Hz, 1H), 4.  
10 30 (q,  $J = 7.34$  Hz, 2H), 1.31 (t,  $J = 7.09$  Hz, 3H); LCMS (m/z):  
416.2 [M+H] $^+$ .

Example 120

[0439]

15 Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-indoliny  
1-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 129]



First Step

20 [0440]

To a solution of potassium tert-butoxide (0.56 g, 5.0 mmol) in

tetrahydrofuran (5.0 mL) that cooled with ice bath, a solution of indoline (0.36 g, 3.0 mmol) in tetrahydrofuran (5.0 mL) was added dropwise. The mixture was stirred at ambient temperature for 30 min. Then the reaction mixture was cooled with ice bath, a solution of ethyl 2-ethoxy-4-oxo-4,5-dihydrofuran-3-carboxylate (0.50 g, 2.5 mmol) which afforded in the Example 74, Third step dissolved in tetrahydrofuran (5.0 mL) was added dropwise. The mixture was stirred at ambient temperature for further 16 h. The reaction mixture was poured into ice water, extracted with ethyl acetate for 3 times. The combined organic layer was dried over sodium sulfate and concentrated. The residue was purified by chromatography on silica gel. Eluted with hexane/ethyl acetate to afford 2-indolinyl-4-oxo-4,5-dihydrofuran-3-carboxylate as solid (0.095 g, y. 8%).

[0441]

$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 7.49 (d,  $J$  = 8.00 Hz, 1H), 7.35 (d,  $J$  = 7.60 Hz, 1H), 7.24 (t,  $J$  = 7.46 Hz, 1H), 7.13 (t,  $J$  = 7.46 Hz, 1H), 4.73 (s, 2H), 4.05 - 4.20 (m, 4H), 3.20 (t,  $J$  = 8.12 Hz, 2H), 1.21 (t,  $J$  = 7.08 Hz, 3H); LCMS (m/z): 274.0 [M+H] $^+$ .

Second Step

[0442]

To a solution of 2-indolinyl-4-oxo-4,5-dihydrofuran-3-carboxylate (0.090 g, 0.32 mmol) and 7-azaindole-3-carboxaldehyde (0.048 g, 0.32 mmol) in ethanol (5.0 mL), L-proline (0.0040 g, 0.

030 mmol) was added at ambient temperature. The mixture was re-  
fluxed for 2 days. Cooled to ambient temperature, the precipit-  
ate was collected by filtration, washed with ethanol then drie-  
d to afford the titled compound as solid (0.076 g, y. 58%).

5 [0443]

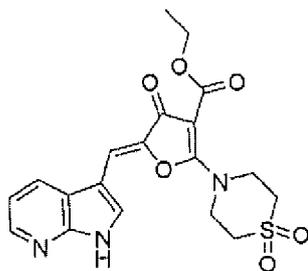
$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.40 (br. s, 1H), 8.36 (d,  $J$  = 6.85 Hz,  
1H), 8.31 (d,  $J$  = 3.91 Hz, 1H), 8.01 (s, 1H), 7.56 - 7.63 (m,  
1H), 7.44 (d,  $J$  = 7.34 Hz, 1H), 7.33 (t,  $J$  = 7.58 Hz, 1H), 7.21  
- 7.27 (m, 1H), 7.12 (dd,  $J$  = 4.89, 7.83 Hz, 1H), 7.00 (s, 1H),  
10 4.26 (t,  $J$  = 7.82 Hz, 2H), 4.19 (q,  $J$  = 7.17 Hz, 2H), 3.24 - 3.  
28 (m, 2H), 1.22 (t,  $J$  = 7.09 Hz, 3H); LCMS (m/z): 402.0 [M+H] $^+$ .

Example 121

15 [0444]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-(1,1-dio-  
xidothiomorpholino)-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 130]



20 [0445]

To a solution of ethyl 2-(1,1-dioxidothiomorpholino)-4-oxo-4,

5-dihydrofuran-3-carboxylate (0.027 g, 0.092 mmol) which similarly prepared according to the procedure described in the Example 74, Fourth step and 7-azaindole-3-carboxaldehyde (0.014 g, 0.092 mmol) in ethanol (0.5 mL), piperidine (0.00092 mL, 0.0093 mmol) was added at ambient temperature. The mixture was refluxed for 2 days. The precipitate was collected by filtration, washed with hot ethanol. The solid was washed with hexane then dried to afford the titled compound as solid (0.037 g, y. 47%).

10 [0446]

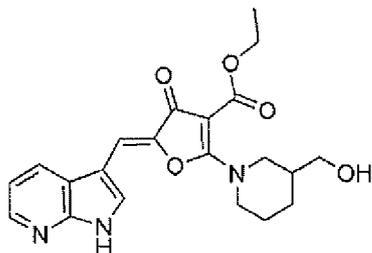
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.40 (br. s, 1H), 8.38 (d, J = 8.03 Hz, 1H), 8.32 (dd, J = 1.51, 4.77 Hz, 1H), 8.03 (d, J = 2.51 Hz, 1H), 7.22 (dd, J = 4.64, 7.91 Hz, 1H), 6.94 (s, 1H), 4.12 - 4.25 (m, 6H), 3.47 - 3.55 (m, 4H), 1.25 (t, J = 7.03 Hz, 3H); LCMS (m/z): 418.0 [M+H]<sup>+</sup>.

15

Example 122

[0447]

Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-2-[3-(hydroxymethyl)piperidino]-4-oxo-4,5-dihydrofuran-3-carboxylate  
20 [Chemical Formula 131]



[0448]

To a solution of ethyl 2-[(3-hydroxymethyl)piperidino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.30 g, 1.0 mmol) which similarly prepared according to the procedure described in the Example 74, Fourth step and 7-azaindole-3-carboxaldehyde (0.16 g, 1.0 mmol) in ethanol (5.0 mL), L-proline (0.0040 g, 0.030 mmol) was added at ambient temperature. The mixture was refluxed for 2 days. Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol then dried to afford the titled compound as solid (0.045 g, y. 10%).

[0449]

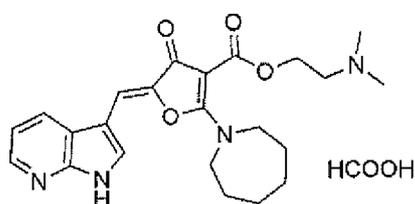
$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.33 (br. s, 1H), 8.38 (d,  $J = 7.82$  Hz, 1H), 8.31 (d,  $J = 4.40$  Hz, 1H), 7.98 (s, 1H), 7.19 (dd,  $J = 4.89, 7.82$  Hz, 1H), 6.84 (s, 1H), 4.72 (br. s, 1H), 4.12 - 4.24 (m, 2H), 3.24 - 3.50 (m, 4H), 3.17 (t,  $J = 11.74$  Hz, 2H), 1.74 - 1.91 (m, 2H), 1.60 - 1.72 (m, 2H), 1.29 - 1.41 (m, 1H), 1.24 (t,  $J = 6.85$  Hz, 3H); LCMS (m/z): 398.2 [M+H] $^+$ .

20 Example 123

[0450]

2-(Dimethylamino)ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-azepinyl-4-oxo-4,5-dihydrofuran-3-carboxylate formate

[Chemical Formula 132]



5

[0451]

A solution of the compound (0.052g, 0.14mmol) of Example 63, 2-dimethylaminoethanol (0.14 mL, 1.4 mmol), zinc cluster catalyst ( $Zn_4(OCO_2CF_3)_6O$ ) (0.0019 g, 0.0020 mmol) and 4-dimethylaminopyridine (0.0049 g, 0.040 mmol) in *N,N*-dimethylacetamide (1.0 mL) was stirred with the microwave synthesizer (Biotage Initiator™) at 150 °C for 1 h. The reaction mixture was purified by preparative HPLC to afford the titled compound as solid (0.018 g, y. 24%).

15 [0452]

$^1H$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.31 (br. s, 1H), 8.39 (dd,  $J = 1.25, 7.78$  Hz, 1H), 8.31 (dd,  $J = 1.38, 4.64$  Hz, 1H), 8.16 (s, 1H), 7.94 (d,  $J = 1.76$  Hz, 1H), 7.20 (dd,  $J = 4.77, 7.78$  Hz, 1H), 6.86 (s, 1H), 4.22 (t,  $J = 5.77$  Hz, 2H), 3.72 - 3.92 (m, 4H), 2.54 - 2.60 (m, 2H), 2.24 (s, 6H), 1.78 - 1.90 (m, 4H), 1.52 - 1.63 (m, 4H); LCMS ( $m/z$ ): 425.1 [ $M+H$ ] $^+$ .

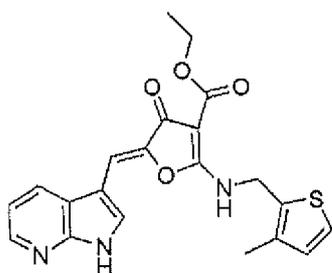
20

Example 124

[0453]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[[2-(3-methylthienyl)methyl]amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 133]



[0454]

To a solution of ethyl 2-[[2-(3-methylthienyl)methyl]amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.38 g, 1.4 mmol) which is similarly prepared according to the procedure described in the Example 74, Fourth step and 7-azaindole-3-carboxaldehyde (0.20 g, 1.4 mmol) in ethanol (4.0 mL), piperidine (0.014 mL, 0.14 mmol) was added at ambient temperature. The mixture was refluxed for 5 days. The precipitate was collected by filtration, washed with hot ethanol. The solid was washed with hexane then dried to afford the titled compound as solid (0.12 g, y. 21%).

[0455]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.38 (br. s, 1H), 9.47 (t, *J* = 6.27 Hz, 1H), 8.35 (d, *J* = 8.03 Hz, 1H), 8.30 (dd, *J* = 1.38, 4.64 Hz, 1H), 7.97 (d, *J* = 2.26 Hz, 1H), 7.32 (d, *J* = 5.02 Hz, 1H), 7.15

(dd,  $J = 4.64, 7.91$  Hz, 1H), 6.92 (s, 1H), 6.88 (d,  $J = 5.02$  Hz, 1H), 4.95 (d,  $J = 6.27$  Hz, 2H), 4.22 (q,  $J = 7.03$  Hz, 2H), 2.28 (s, 3H), 1.26 (t,  $J = 7.03$  Hz, 3H); LCMS ( $m/z$ ): 410.0 [M+H]<sup>+</sup>.

5

Example 125

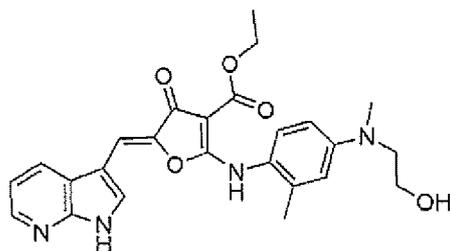
[0456]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-({4-[(2-hydroxyethyl)-*N*-methylamino]-2-methylphenyl}amino)-4-oxo-4,5-

10

dihydrofuran-3-carboxylate

[Chemical Formula 134]



First Step

[0457]

15

A solution of 5-fluoro-2-nitrotoluene (1.5 g, 9.6 mmol), *N*-methyl ethanolamine (0.90 mL, 0.012 mol) and triethylamine (1.6 mL, 0.012 mol) in *N*-methyl-2-pyrrolidone (15 mL) was stirred at 60 °C for 12 h. Cooled to ambient temperature, the reaction mixture was poured into ice water, extracted with ethyl acetate.

20

The organic layer was washed with water and brine, dried over sodium sulfate and concentrated to afford 2-[(3-methyl-4-nitro

phenyl)-*N*-methylamino]ethanol as solid (2.0 g, y. 98%).

[0458]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 7.99 (d, *J* = 9.32 Hz, 1H), 6.58 - 6.71 (m, 2H), 4.78 (t, *J* = 5.22 Hz, 1H), 3.46 - 3.63 (m, 4H), 3.06 (s, 3H), 2.56 (s, 3H); LCMS (m/z): 211.2 [M+H]<sup>+</sup>.

Second Step

[0459]

2-[(3-Methyl-4-nitrophenyl)-*N*-methylamino]ethanol (0.70 g, 3.3 mmol) was dissolved in ethanol (10 mL) and 10% palladium on carbon (0.050 g) was added at ambient temperature. The reaction mixture was agitated under a hydrogen atmosphere at ambient temperature for 4 h. Palladium on carbon was removed by filtration with Celite and the solvent was removed under reduced pressure to afford 2-[(4-amino-3-methylphenyl)-*N*-methylamino]ethanol as solid (0.58 g, y. 97%).

[0460]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 6.49 (d, *J* = 8.44 Hz, 1H), 6.43 (d, *J* = 2.60 Hz, 1H), 6.38 (q, *J* = 6.13 Hz, 1H), 4.50 (t, *J* = 5.38 Hz, 1H), 4.12 (br. s, 2H), 3.48 (dd, *J* = 6.38, 12.00 Hz, 2H), 3.16 (t, *J* = 6.58 Hz, 2H), 2.73 (s, 3H), 2.02 (s, 3H); LCMS (m/z): 181.1 [M+H]<sup>+</sup>.

Third Step

[0461]

A solution of ethyl 2-ethoxy-4-oxo-4,5-dihydrofuran-3-carboxylate (0.70 g, 3.5 mmol) which afforded in the Example 74, Third step and 2-[(4-amino-3-methylphenyl)-*N*-methylamino]ethanol (0.60 g, 3.5 mmol) in ethanol (8.3 mL) was stirred at ambient temperature for 16 h. The solvent was removed under reduced pressure, and ethanol was added to precipitate the product. The precipitate was collected by filtration, washed with ethanol then dried to afford 2-[(4-[(2-hydroxyethyl)-*N*-methylamino]-2-methylphenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate as solid (0.60 g, y. 60%).

[0462]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 9.86 (br. s, 1H), 7.12 (d, *J* = 8.76 Hz, 1H), 6.60 (d, *J* = 2.60 Hz, 1H), 5.54 (dd, *J* = 2.74, 8.80 Hz, 1H), 4.65 (br. s, 1H), 4.57 (s, 2H), 4.20 (q, *J* = 7.06 Hz, 2H), 3.53 (t, *J* = 6.14 Hz, 2H), 3.38 (t, *J* = 6.22 Hz, 2H), 2.92 (s, 3H), 2.17 (s, 3H); LCMS (*m/z*): 335.0 [M+H]<sup>+</sup>.

#### Fourth Step

[0463]

To a solution of 2-[(4-[(2-hydroxyethyl)-*N*-methylamino]-2-methylphenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.20 g, 0.60 mmol) and 7-azaindole-3-carboxaldehyde (0.097 g, 0.60 mmol) in ethanol (11 mL), piperidine (0.10 mL, 1.0 mmol) was added at ambient temperature. The mixture was refluxed for 2 days. Cooled to ambient temperature, the precipitate was collected

by filtration, washed with diethyl ether then dried to afford the titled compound as solid (0.055 g, y. 19%).

[0464]

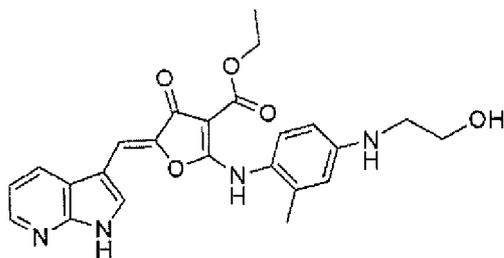
<sup>1</sup>H NMR DMSO-d<sub>6</sub> δ (ppm) 12.22 (br. s, 1H), 10.12 (br. s, 1H), 8.15 (d, J = 4.40 Hz, 1H), 7.77 (br. s, 1H), 7.68 (d, J = 7.82 Hz, 1H), 7.22 (d, J = 8.80 Hz, 1H), 6.77 (s, 1H), 6.67 - 6.73 (m, 2H), 6.63 (d, J = 8.31 Hz, 1H), 4.69 (t, J = 5.14 Hz, 1H), 4.23 (q, J = 6.85 Hz, 2H), 3.55 - 3.63 (m, 2H), 3.43 - 3.50 (m, 2H), 3.01 (s, 3H), 2.15 (s, 3H), 1.26 (t, J = 6.85 Hz, 3H); LCMS (m/z): 463.2 [M+H]<sup>+</sup>.

Example 126

[0465]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-({4-[(2-hydroxyethyl)amino]-2-methylphenyl}amino)-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 135]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 125.

[0466]

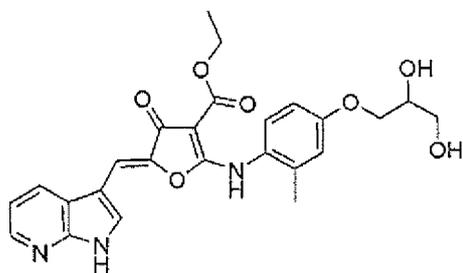
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.25 (br. s, 1H), 10.11 (s 1H), 8.18 (d, J = 4.40 Hz, 1H), 7.81 - 7.87 (m, 1H), 7.70 (d, J = 7.83 Hz, 1H), 7.16 (d, J = 8.31 Hz, 1H), 6.75 - 6.87 (m, 2H), 6.53 - 6.67 (m, 2H), 5.85 (t, J = 5.38 Hz, 1H), 4.75 (t, J = 5.38 Hz, 1H), 4.26 (q, J = 6.85 Hz, 2H), 3.63 (q, J = 5.87 Hz, 2H), 3.20 (q, J = 5.71 Hz, 2H), 2.13 (s, 3H), 1.29 (t, J = 7.09 Hz, 3H); LCMS (m/z): 449.2 [M+H]<sup>+</sup>.

Example 127

10 [0467]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[[4-(2,3-dihydroxypropoxy)-2-methylphenyl]amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 136]



15

[0468]

To a stirred solution of ethyl 2-[[4-(2,3-dihydroxypropoxy)-2-methylphenyl]amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.17 g, 0.50 mmol) which similarly prepared according to the procedure described in the Example 74, First step to Fourth step and 7-azaindole-3-carboxaldehyde (0.070 g, 0.50 mmol) in ethan

20

ol (5.0 mL), piperidine (0.10 mL, 1.0 mmol) was added at ambient temperature. The mixture was refluxed for 2 days. Cooled to ambient temperature, the precipitate was collected by filtration, washed with diethyl ether then dried to afford the titled compound as solid (0.054 g, y. 23%).

[0469]

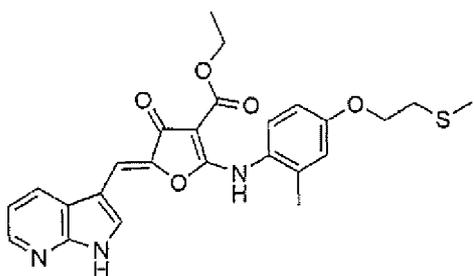
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.28 (br. s, 1H), 10.30 (br. s, 1H), 8.18 (d, J = 2.93 Hz, 1H), 7.78 (br. s, 1H), 7.64 (d, J = 7.34 Hz, 1H), 7.41 (d, J = 8.31 Hz, 1H), 7.03 (br. s, 1H), 6.94 (d, J = 7.34 Hz, 1H), 6.82 (s, 1H), 6.70 - 6.79 (m, 1H), 5.06 (d, J = 4.40 Hz, 1H), 4.76 (t, J = 5.04 Hz, 1H), 4.20 - 4.32 (m, 2H), 4.05 - 4.15 (m, 1H), 3.93 - 4.02 (m, 1H), 3.83 - 3.92 (m, 1H), 3.47 - 3.57 (m, 2H), 2.22 (br. s, 3H), 1.29 (t, J = 6.60 Hz, 3H); LCMS (m/z): 480.2 [M+H]<sup>+</sup>.

Example 128

[0470]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(2-methyl-4-[2-(methylthio)ethoxy]phenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 137]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 127.

[0471]

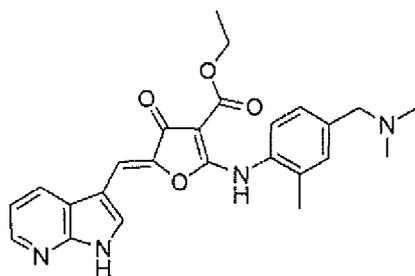
5 <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.28 (br. s, 1H), 10.30 (br. s, 1H),  
 8.19 (d, J = 4.40 Hz, 1H), 7.77 (s, 1H), 7.65 (d, J = 7.82 Hz,  
 1H), 7.42 (d, J = 8.80 Hz, 1H), 7.05 (br. s, 1H), 6.95 (dd, J =  
 2.69, 8.56 Hz, 1H), 6.82 (br. s, 1H), 6.76 (dd, J = 4.40, 7.83  
 Hz, 1H), 4.21 - 4.32 (m, 4H), 2.94 (t, J = 6.36 Hz, 2H), 2.23  
 10 (s, 3H), 2.22 (s, 3H), 1.29 (t, J = 7.09 Hz, 3H); LCMS (m/z): 4  
 80.2 [M+H]<sup>+</sup>.

Example 129

[0472]

15 Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-2-((4-[(di  
 methylamino)methyl]-2-methylphenyl)amino)-4-oxo-4,5-dihydrofu  
 ran-3-carboxylate

[Chemical Formula 138]



### First Step

[0473]

A solution of 3-methyl-4-nitrobenzyl bromide (1.0 g, 4.3 mmol),  
 5 anhydrous dimethylamine (0.34 mL, 5.1 mmol) and potassium car-  
 bonate (1.5 g, 0.011 mol) in *N,N*-dimethylformamide (4.5 mL) wa-  
 s stirred at 70 °C for 12 h. Cooled to ambient temperature, the  
 reaction mixture was poured into ice water, extracted with et-  
 hyl acetate. The organic layer was washed with water and brine,  
 10 dried over sodium sulfate and concentrated to afford *N,N*-dime-  
 thyl-1-(3-methyl-4-nitrophenyl)methanamine as oil (0.80 g, y.  
 95%).

[0474]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 7.65 (d, *J* = 8.32 Hz, 1H), 7.41 (s, 1H),  
 15 7.36 (d, *J* = 8.36 Hz, 1H), 3.44 (s, 2H), 2.52 (s, 3H), 2.15 (s,  
 6H); LCMS (*m/z*): 195.4 [M+H]<sup>+</sup>.

### Second Step

[0475]

20 *N,N*-Dimethyl-1-(3-methyl-4-nitrophenyl)methanamine (0.80 g, 4.  
 1 mmol) was dissolved in ethanol (5.0 mL) and 10% palladium on

carbon (0.18 g) was added at ambient temperature. The reaction mixture was agitated under a hydrogen atmosphere at ambient temperature for 4 h. Palladium on carbon was removed by filtration with Celite and the solvent was removed under reduced pressure to afford 4-[(dimethylamino)methyl]-2-methylaniline (0.65 g, y. 96%).

[0476]

$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 6.81 (s, 1H), 6.77 (d,  $J = 7.92$  Hz, 1H), 6.52 (d,  $J = 7.96$  Hz, 1H), 4.68 (s, 2H), 3.16 (s, 2H), 2.07 (s, 6H), 2.02 (s, 3H).

Third Step

[0477]

A solution of ethyl 2-ethoxy-4-oxo-4,5-dihydrofuran-3-carboxylate (0.47 g, 2.3 mmol) which afforded in the Example 74, Third step and 4-[(dimethylamino)methyl]-2-methylaniline (0.35 g, 2.1 mmol) in ethanol (10 mL) was stirred at ambient temperature for 16 h. The solvent was removed under reduced pressure, and ethanol was added to precipitate the product. The precipitate was collected by filtration to afford ethyl 2-((4-[(dimethylamino)methyl]-2-methylphenyl)amino)-4-oxo-4,5-dihydrofuran-3-carboxylate (0.26 g, crude material) as solid.

[0478]

$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 10.18 (br. s, 1H), 7.48 (d,  $J = 6.96$  Hz, 1H), 7.25 - 7.40 (m, 2H), 4.65 (s, 2H), 4.23 (q,  $J = 7.04$  Hz,

2H), 2.40 - 2.60 (m, 9H), 1.26 (t, J = 7.04 Hz, 3H); LCMS (m/z): 319.2 [M+H]<sup>+</sup>.

#### Fourth Step

5 [0479]

To a solution of ethyl 2-((4-[(dimethylamino)methyl]-2-methylphenyl)amino)-4-oxo-4,5-dihydrofuran-3-carboxylate (0.26 g, 0.82 mmol) and 7-azaindole-3-carboxaldehyde (0.12 g, 0.82 mmol) in ethanol (5.0 mL), piperidine (0.16 mL, 1.6 mmol) was added at ambient temperature. The mixture was refluxed for 2 days. Cooled to ambient temperature, the precipitate was collected by filtration, washed with diethyl ether then dried to afford the titled compound as solid (0.015 g, y. 4%).

[0480]

15 <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.26 (br. s, 1H), 8.20 (d, J = 3.91 Hz, 1H), 8.15 (s, 1H), 7.82 (d, J = 7.34 Hz, 1H), 7.72 (s, 1H), 7.47 (d, J = 7.83 Hz, 1H), 7.37 (s, 1H), 7.30 (d, J = 8.31 Hz, 1H), 6.83 (s, 1H), 6.79 (dd, J = 4.89, 7.82 Hz, 1H), 4.26 (q, J = 7.17 Hz, 2H), 3.54 (s, 2H), 2.22 - 2.29 (m, 9H), 1.29 (t, J = 6.85 Hz, 3H); LCMS (m/z): 447.4 [M+H]<sup>+</sup>

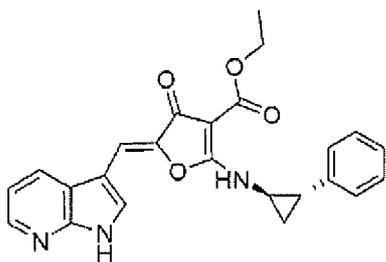
#### Example 130

[0481]

25 Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-4-oxo-2-[[*(1R,2S)*-2-phenylcyclopropyl]amino)-4,5-dihydrofuran-3-carbo

xylate

[Chemical Formula 139]



[0482]

5 To a solution of ethyl 4-oxo-2-((1*R*,2*S*)-2-phenylcyclopropyl)amino)-4,5-dihydrofuran-3-carboxylate (0.090 g, 0.31 mmol) which similarly prepared according to the procedure described in the Example 74, Fourth step and 7-azaindole-3-carboxaldehyde (0.045 g, 0.30 mmol) in ethanol (5.0 mL), L-proline (0.0035 g, 0.031 mmol) was added at ambient temperature. The mixture was  
10 refluxed for 2 days. Cooled to ambient temperature, the solvent was removed under reduced pressure then the residue was purified by preparative HPLC to afford the titled compound as solid (0.018 g, y. 14%).

15 [0483]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.11 (br. s, 1H), 9.10 (br. s, 1H), 8.41 (d, *J* = 7.34 Hz, 1H), 8.26 (d, *J* = 3.91 Hz, 1H), 7.81 (s, 1H), 7.28 - 7.36 (m, 2H), 7.19 - 7.27 (m, 3H), 7.03 (dd, *J* = 4.40, 7.82 Hz, 1H), 6.88 (s, 1H), 4.21 (q, *J* = 6.85 Hz, 2H), 3.40  
20 - 3.48 (m, 1H), 2.88 - 3.10 (m, 1H), 1.63 - 1.72 (m, 1H), 1.35 - 1.43 (m, 1H), 1.26 (t, *J* = 7.08 Hz, 3H); LCMS (*m/z*): 415.8 [M

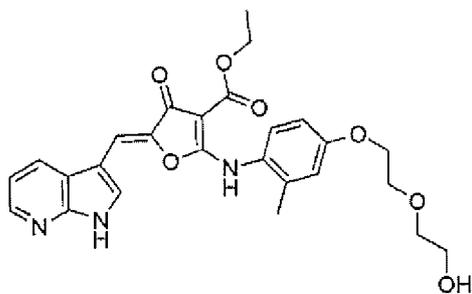
+H]<sup>+</sup>.

Example 131

[0484]

5 Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-((4-[2-(2-hydroxyethoxy)ethoxy]-2-methylphenyl)amino)-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 140]



10 [0485]

To a solution of ethyl 2-((4-[2-(2-hydroxyethoxy)ethoxy]-2-methylphenyl)amino)-4-oxo-4,5-dihydrofuran-3-carboxylate (0.15 g, 0.50 mmol) which similarly prepared according to the procedure described in the Example 74, First step to Fourth step and

15 7-azaindole-3-carboxaldehyde (0.070 g, 0.50 mmol) in ethanol (10 mL), L-proline (0.010 g, 0.087 mmol) was added at ambient temperature. The mixture was refluxed for 2 days. Cooled to ambient temperature, the precipitate was collected by filtration, washed with diethyl ether then dried to afford the titled compound

20 (0.031 g, y. 15%) as solid.

[0486]

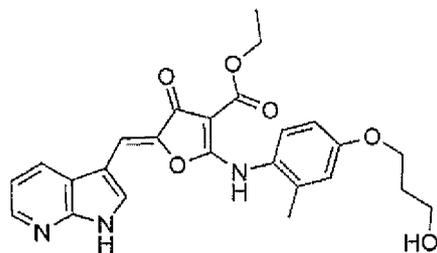
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.28 (br. s, 1H), 10.29 (br. s, 1H), 8.20 (d, J = 3.91 Hz, 1H), 7.75 (br. s, 1H), 7.68 (d, J = 7.82 Hz, 1H), 7.42 (d, J = 8.80 Hz, 1H), 7.05 (br. s, 1H), 6.95 (dd, J = 2.40, 8.60 Hz, 1H), 6.83 (s, 1H), 6.77 (dd, J = 4.40, 7.83 Hz, 1H), 4.64 - 4.70 (m, 1H), 4.26 (q, J = 6.85 Hz, 2H), 4.17 - 4.23 (m, 2H), 3.79 - 3.87 (m, 2H), 3.52 - 3.62 (m, 4H), 2.23 (s, 3H), 1.29 (t, J = 6.85 Hz, 3H); LCMS (m/z): 494.0 [M+H]<sup>+</sup>.

Example 132

[0487]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[[4-(3-hydroxypropoxy)-2-methylphenyl]amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 141]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 131.

[0488]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.25 (br. s, 1H), 8.19 (d, J = 4.40 Hz, 1H), 7.74 (s, 1H), 7.67 (d, J = 7.82 Hz, 1H), 7.36 (d, J = 8.80 Hz, 1H), 7.00 (d, J = 2.4 Hz, 1H), 6.91 (d, J = 8.31 Hz, 1H),

6.71 - 6.79 (m, 2H), 4.59 - 4.65 (m, 1H), 4.25 (q, J = 6.85 Hz, 2H), 4.14 (t, J = 6.11 Hz, 2H), 3.60 - 3.67 (m, J = 5.38 Hz, 2H), 2.21 (s, 3H), 1.94 (t, J = 6.11 Hz, 2H), 1.28 (t, J = 7.06 Hz, 3H); LCMS (m/z): 464.2 [M+H]<sup>+</sup>.

5

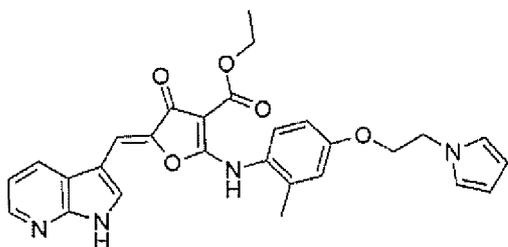
Example 133

[0489]

Ethyl 2-({4-[2-(1H-pyrrol-1-yl)ethoxy]-2-methylphenyl}amino)-5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-4-oxo-4,5-dihydrofuran-3-carboxylate

10

[Chemical Formula 142]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 131.

15

[0490]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.04 (br. s, 1H), 8.08 (d, J = 3.91 Hz, 1H), 7.60 - 7.76 (m, 2H), 7.16 (br. s, 1H), 6.88 - 6.94 (m, 3H), 6.84 (d, J = 7.82 Hz, 1H), 6.60 - 6.68 (m, 1H), 6.48 - 6.57 (m, 1H), 6.02 - 6.07 (m, 2H), 4.22 - 4.37 (m, 4H), 4.13 - 4.22 (m, 2H), 2.14 (s, 3H), 1.25 (t, J = 6.85 Hz, 3H); LCMS (m/z): 499.2 [M+H]<sup>+</sup>.

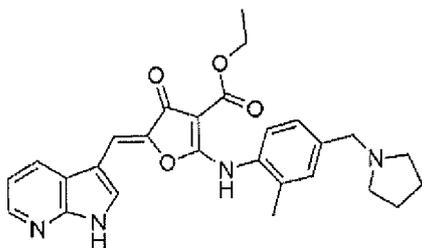
20

Example 134

[0491]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[[2-methyl-4-(1-pyrrolidinylmethyl)phenyl]amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 143]



[0492]

To a solution of 2-[[2-methyl-4-(1-pyrrolidinylmethyl)phenyl]amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.25 g, 0.70 mmol) which similarly prepared according to the procedure described in the Example 129, First step to Third step and 7-azaindole-3-carboxaldehyde (0.10 g, 0.70 mmol) in ethanol (10 mL), piperidine (0.014 mL, 0.14 mmol) was added at ambient temperature.

The mixture was refluxed for 2 days. Cooled to ambient temperature then the reaction mixture was purified by preparative HPLC to afford the titled compound as solid (0.035 g, y. 10%).

[0493]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.27 (br. s, 1H), 8.20 (d, *J* = 3.91 Hz, 1H), 8.14 (s, 1H), 7.72 - 7.82 (m, 2H), 7.48 (d, *J* = 7.83 Hz,

1H), 7.41 (s, 1H), 7.34 (d,  $J = 7.34$  Hz, 1H), 6.76 - 6.86 (m, 2 H), 4.26 (q,  $J = 6.85$  Hz, 2H), 3.81 (br. s, 2H), 2.57 - 2.69 (m, 4H), 2.27 (s, 3H), 1.70 - 1.85 (m, 4H), 1.29 (t,  $J = 6.85$  Hz, 3H); LCMS (m/z): 473.2 [M+H]<sup>+</sup>.

5

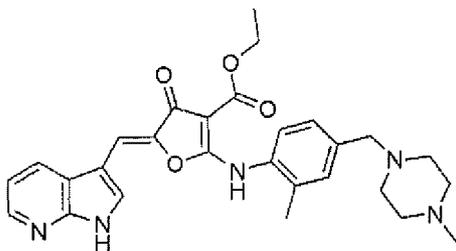
Example 135

[0494]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-({2-methyl-4-[(4-methylpiperazinyl)methyl]phenyl}amino)-4-oxo-4,5-dihydrofuran-3-carboxylate

10

[Chemical Formula 144]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 134.

15

[0495]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>)  $\delta$  (ppm) 12.43 (br. s, 1H), 8.18 (br. s, 1H), 8.01 (br. s, 1H), 7.41 (br. s, 1H), 6.99 - 7.17 (m, 3H), 6.87 (br. s, 2H), 6.40 (d,  $J = 12.72$  Hz, 1H), 4.26 (br. s, 2H), 3.57 (br. s, 2H), 2.42 (br. s, 8H), 2.28 (br. s, 3H), 2.08 (br. s, 3H), 1.12 - 1.39 (m, 3H); LCMS (m/z): 502.4 [M+H]<sup>+</sup>.

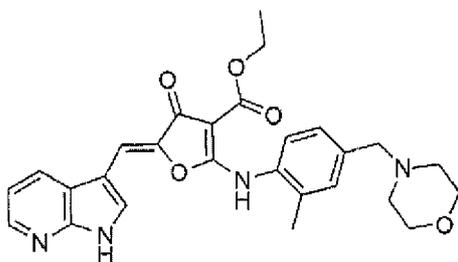
20

Example 136

[0496]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-([2-methyl-4-(morpholinomethyl)phenyl]amino)-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 145]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 134.

10 [0497]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.29 (br. s, 1H), 10.38 (br. s, 1H), 8.21 (d, *J* = 4.40 Hz, 1H), 7.72 - 7.83 (m, 2H), 7.46 - 7.54 (m, 1H), 7.28 - 7.44 (m, 2H), 6.86 (s, 1H), 6.75 - 6.81 (m, 1H), 4.27 (q, *J* = 7.17 Hz, 2H), 3.51 - 3.74 (m, 6H), 2.35 - 2.59 (m, 4H), 2.27 (s, 3H), 1.30 (t, *J* = 7.09 Hz, 3H); LCMS (*m/z*): 489.2 [M+H]<sup>+</sup>.

15

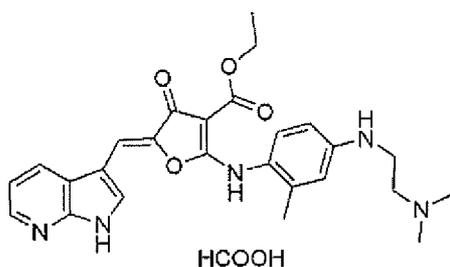
Example 137

[0498]

20 Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(4-([2-(dimethylamino)ethyl]amino)-2-methylphenyl)amino]-4-oxo-4,5-d

ihydrofuran-3-carboxylate formate

[Chemical Formula 146]



[0499]

5 To a solution of ethyl 2-[(4-[[2-(dimethylamino)ethyl]amino]-  
2-methylphenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.  
27 g, 0.70 mmol) which similarly prepared according to the pro-  
cedure described in the Example 125, First step to Third step  
and 7-azaindole-3-carboxaldehyde (0.11 g, 0.70 mmol) in ethano-  
10 l (5.0 mL), piperidine (0.10 mL, 1.0 mmol) was added at ambien-  
t temperature. The mixture was refluxed for 16 h. Cooled to am-  
bient temperature, the solvent was removed under reduced press-  
ure then the residue was purified by preparative HPLC to affor-  
d the titled compound as solid (0.015 g, y. 8%).

15 [0500]

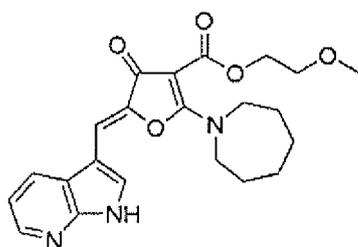
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.29 (br. s, 1H), 10.12 (br. s, 1H),  
8.11 - 8.23 (m, 2H), 7.86 (s, 1H), 7.67 (d, J = 7.82 Hz, 1H), 7.  
17 (d, J = 8.31 Hz, 1H), 6.75 - 6.83 (m, 2H), 6.51 - 6.69 (m, 2  
H), 5.79 (br. s, 1H), 4.25 (q, J = 6.85 Hz, 2H), 3.16 - 3.28 (m,  
20 2H), 2.58 (t, J = 6.11 Hz, 2H), 2.29 (s, 6H), 2.13 (s, 3H), 1.  
29 (t, J = 6.85 Hz, 3H); LCMS (m/z): 476.0 [M+H]<sup>+</sup>.

Example 138

[0501]

2-Methoxyethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-azepinyl-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 147]



First Step

[0502]

10 A solution of ethyl malonyl chloride (0.10 mL, 0.78 mmol) and 2-methoxyethanol (0.061 mL, 0.78 mmol) in dichloromethane (1.5 mL) was cooled with ice bath. To this solution, triethylamine (0.13 mL, 0.94 mmol) was added and stirred at ambient temperature for 1.5 h. The reaction mixture was diluted with water, e  
15 xtracted with dichloromethane. The organic layer was washed with brine, dried over magnesium sulfate and concentrated. The residue was purified by chromatography on silica gel (hexane/ethyl acetate) to afford ethyl 2-methoxyethyl malonate (0.10 g, y.  
69%) as oil.

20 [0503]

$^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  (ppm) 4.28 - 4.34 (m, 2H), 4.21 (q,  $J = 7.11$  Hz,

2H), 3.59 - 3.64 (m, 2H), 3.42 (s, 2H), 3.39 (s, 3H), 1.29 (t, J = 7.15 Hz, 3H)

Second Step

5 [0504]

A solution of ethyl 2-methoxyethyl malonate (0.10 g, 0.53 mmol) in anhydrous tetrahydrofuran (1.5 mL) was added dropwise to a solution of sodium hydride (60% w/w in oil, 0.043 g, 1.1 mmol) in anhydrous tetrahydrofuran (2.0 mL) that cooled with ice bath. The mixture was refluxed for 5 min. The reaction mixture was cooled with ice bath, chloroacetyl chloride (0.042 mL, 0.53 mmol) was added dropwise to the reaction mixture and the mixture was stirred for 1 h then stirred with heating at 45 °C for 1 h. The reaction mixture was cooled to ambient temperature then hexamethyleneimine (0.071 mL, 0.63 mmol) was added dropwise and the mixture was stirred at ambient temperature for further 1 h. The reaction mixture was diluted with water, and extracted with chloroform. The organic layer was dried over magnesium sulfate and concentrated. The residue was purified by chromatography on silica gel, eluted with chloroform/methanol to afford 2-methoxyethyl 2-azepinyl-4-oxo-4,5-dihydrofuran-3-carboxylate as oil (0.065 g, y. 43%).

[0505]

<sup>1</sup>H NMR (CDCl<sub>3</sub>) δ (ppm) 4.51 (s, 2H), 4.35 - 4.39 (m, 2H), 3.56 - 3.75 (m, 6H), 3.40 (s, 3H), 1.80 (br. s, 4H), 1.61 (br. s, 4

H); LCMS (m/z): 284.1 [M+H]<sup>+</sup>.

### Third Step

[0506]

5 To a solution of 2-methoxyethyl 2-azepinyl-4-oxo-4,5-dihydrofuran-3-carboxylate (0.065 g, 0.23 mmol) and 7-azaindole-3-carboxaldehyde (0.033 g, 0.23 mmol) in ethanol (0.5 mL), hexamethylenimine (0.026 mL, 0.023 mmol) was added at ambient temperature. The mixture was refluxed for 3 days. Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol and hexane then dried to afford the titled compound as solid (0.019 g, y. 20%).

[0507]

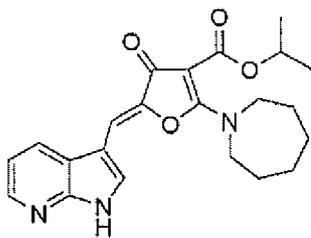
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.31 (br. s, 1H), 8.39 (dd, J = 1.38, 7.91 Hz, 1H), 8.31 (dd, J = 1.38, 4.64 Hz, 1H), 7.94 (s, 1H), 7.20 (dd, J = 4.64, 7.91 Hz, 1H), 6.85 (s, 1H), 4.21 - 4.28 (m, 2H), 3.70 - 3.90 (m, 4H), 3.54 - 3.62 (m, 2H), 3.29 (s, 3H), 1.78 - 1.91 (m, 4H), 1.51 - 1.63 (m, 4H); LCMS (m/z): 412.1 [M+H]<sup>+</sup>.

### 20 Example 139

[0508]

Isopropyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-azepinyl-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 148]



[0509]

To a stirred solution of isopropyl 2-azepinyl-4-oxo-4,5-dihydrofuran-3-carboxylate (0.033 g, 0.12 mmol) which similarly prepared according to the procedure described in the Example 4, First step and 7-azaindole-3-carboxaldehyde (0.019 g, 0.13 mmol) in 2-propanol (1.0 mL), hexamethyleneimine (0.0014 mL, 0.012 mmol) was added at ambient temperature. The mixture was refluxed for 12 days. Cooled to ambient temperature, the reaction mixture was purified by preparative HPLC to afford the titled compound as solid (0.024 g, y. 49%).

[0510]

$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.30 (br. s, 1H), 8.37 (dd,  $J = 1.38$ , 7.91 Hz, 1H), 8.31 (dd,  $J = 1.38$ , 4.64 Hz, 1H), 7.93 (s, 1H), 7.20 (dd,  $J = 4.77$ , 7.78 Hz, 1H), 6.81 (s, 1H), 4.94 - 5.05 (m, 1H), 3.70 - 3.90 (m, 4H), 1.75 - 1.91 (m, 4H), 1.52 - 1.62 (m, 4H), 1.25 (d,  $J = 6.27$  Hz, 6H); LCMS (m/z): 396.1 [M+H] $^+$ .

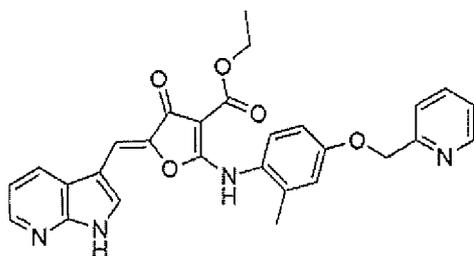
Example 140

[0511]

Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-2-[[2-methyl-4-(2-pyridinylmethoxy)phenyl]amino]-4-oxo-4,5-dihydrofuran

-3-carboxylate

[Chemical Formula 149]



[0512]

5 The titled compound was similarly prepared as solid according to the procedure described in the Example 1, using ethyl 2-([2-methyl-4-(2-pyridinylmethoxy)phenyl]amino)-4-oxo-4,5-dihydrofuran-3-carboxylate which similarly prepared according to the procedure described in the Example 74, First step to Fourth step and 7-azaindole-3-carboxaldehyde as starting materials.

[0513]

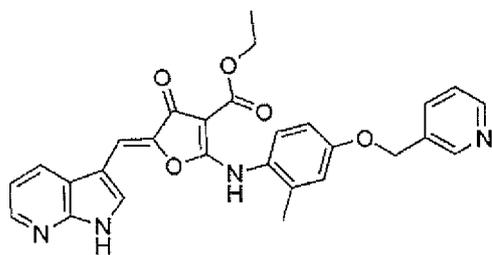
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.29 (br. s, 1H), 10.30 (br. s, 1H), 8.63 (d, J = 3.91 Hz, 1H), 8.17 (d, J = 3.91 Hz, 1H), 7.89 (t, J = 7.09 Hz, 1H), 7.67 - 7.79 (m, 2H), 7.62 (d, J = 7.34 Hz, 1H), 7.34 - 7.49 (m, 2H), 7.16 (br. s, 1H), 7.04 (d, J = 8.31 Hz, 1H), 6.83 (s, 1H), 6.70 - 6.77 (m, 1H), 5.29 (s, 2H), 4.26 (q, J = 6.85 Hz, 2H), 2.23 (s, 3H), 1.29 (t, J = 7.09 Hz, 3H); LCM S (m/z): 497.0 [M+H]<sup>+</sup>.

20 Example 141

[0514]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[[2-methyl-4-(3-pyridinylmethoxy)phenyl]amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 150]



5

[0515]

To a solution of ethyl 2-[[2-methyl-4-(3-pyridinylmethoxy)phenyl]amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.080 g, 0.20 mmol) which similarly prepared according to the procedure described in the Example 74, First step to Fourth step and 7-aza indole-3-carboxaldehyde (0.032 g, 0.20 mmol) in ethanol (5.0 mL), L-proline (0.0050 g, 0.043 mmol) was added at ambient temperature. The mixture was refluxed for 2 days. Cooled to ambient temperature, the reaction mixture was purified by preparative HPLC to afford the titled compound as solid (0.010 g, y. 9%).

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[0516]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.25 (br. s, 1H), 10.25 (br. s, 1H), 8.76 (s, 1H), 8.59 (d, *J* = 3.42 Hz, 1H), 8.18 (d, *J* = 4.40 Hz, 1H), 7.96 (d, *J* = 7.83 Hz, 1H), 7.69 - 7.79 (m, 2H), 7.45 - 7.53 (m, 1H), 7.41 (d, *J* = 8.80 Hz, 1H), 7.14 (br. s, 1H), 7.04 (d,

20

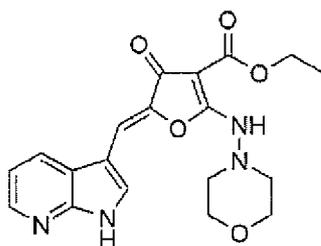
$J = 8.31$  Hz, 1H), 6.79 (br. s, 1H), 6.68 - 6.76 (m, 1H), 5.27 (s, 2H), 4.20 - 4.30 (m, 2H), 2.23 (s, 3H), 1.29 (t,  $J = 7.09$  Hz, 3H); LCMS (m/z): 497.4 [M+H]<sup>+</sup>.

5 Example 142

[0517]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-(morpholino)-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 151]



[0518]

A solution of ethyl 2-ethoxy-4-oxo-4,5-dihydrofuran-3-carboxylate (0.10 g, 0.50 mmol) which afforded in the Example 74, Third step and 4-aminomorpholine (0.046 mL, 0.48 mmol) in ethanol (2.0 mL) was stirred at ambient temperature for 15 h. To this reaction mixture, 7-azaindole-3-carboxaldehyde (0.061 g, 0.42 mmol) and piperidine (0.0048 mL, 0.048 mmol) were added. The mixture was refluxed for 3 days. The precipitate was collected by filtration, washed with hot ethanol. The solid was washed with hexane then dried to afford the titled compound (0.045 g, y. 24%) as solid.

15

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[0519]

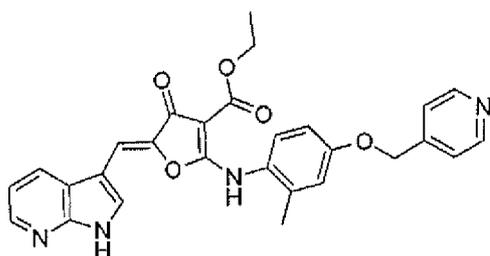
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.34 (br. s, 1H), 10.07 (s, 1H), 8.93 (d, J = 7.78 Hz, 1H), 8.33 (d, J = 3.51 Hz, 1H), 8.12 (br. s, 1H), 7.20 - 7.26 (m, 1H), 6.88 (s, 1H), 4.21 (q, J = 6.78 Hz, 2 H), 3.74 - 3.88 (m, 4H), 3.02 - 3.14 (br. s, 4H), 1.26 (t, J = 6.90 Hz, 3H); LCMS (m/z): 385.1 [M+H]<sup>+</sup>.

Example 143

[0520]

10 Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(2-methyl-4-(4-pyridinylmethoxy)phenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 152]



15 The titled compound(solid) was similarly prepared according to the procedure described in the Example 141.

[0521]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.28 (br. s, 1H), 10.30 (br. s, 1H), 8.62 (d, J = 4.40 Hz, 2H), 8.17 (d, J = 4.40 Hz, 1H), 7.67 - 7.79 (m, 2H), 7.52 (d, J = 4.89 Hz, 2H), 7.45 (d, J = 8.31 Hz, 1 H), 7.15 (br. s, 1H), 7.03 (d, J = 8.31 Hz, 1H), 6.83 (s, 1H),

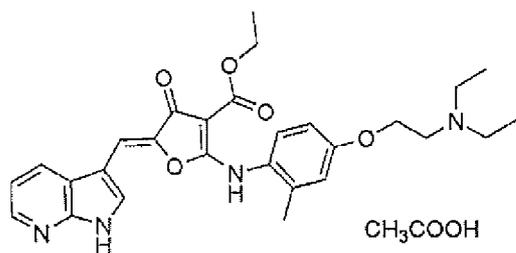
6.68 - 6.75 (m, 1H), 5.31 (s, 2H), 4.26 (q, J = 7.17 Hz, 2H), 2.23 (s, 3H), 1.29 (t, J = 6.85 Hz, 3H); LCMS (m/z): 496.8 [M+H]<sup>+</sup>.

5 Example 144

[0522]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(4-[2-(diethylamino)ethoxy]-2-methylphenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate acetate

10 [Chemical Formula 153]



[0523]

The crude material, which similarly prepared according to the procedure described in the Example 141, was purified by preparative HPLC (aqueous ammonium acetate/acetonitrile) to afford the titled compound(solid).

[0524]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.17 (br. s, 1H), 8.16 (d, J = 3.91 Hz, 1H), 7.75 (s, 1H), 7.68 (d, J = 7.34 Hz, 1H), 7.34 (d, J = 8.31 Hz, 1H), 7.00 (br. s, 1H), 6.91 (d, J = 8.80 Hz, 1H), 6.70 - 6.79 (m, 2H), 4.19 - 4.30 (m, 2H), 4.10 (t, J = 5.87 Hz, 2H), 2.

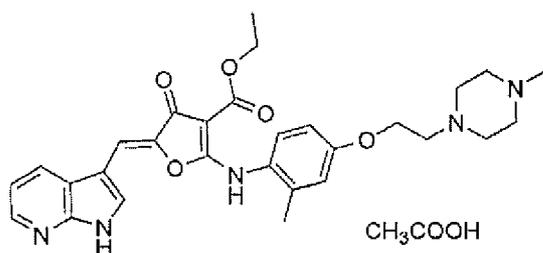
86 (t,  $J = 5.87$  Hz, 2H), 2.61 (q,  $J = 6.85$  Hz, 4H), 2.20 (s, 3H), 1.90 (s, 3H), 1.28 (t,  $J = 6.85$  Hz, 3H), 1.02 (t,  $J = 7.09$  Hz, 6H); LCMS ( $m/z$ ): 505.6  $[M+H]^+$ .

5 Example 145

[0525]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-({2-methyl-4-[2-(4-methylpiperazinyl)ethoxy]phenyl}amino)-4-oxo-4,5-dihydrofuran-3-carboxylate acetate

10 [Chemical Formula 154]



First Step

[0526]

A solution of 4-nitro-*m*-cresol (2.0 g, 0.013 mol), 1-bromo-2-chloroethane (1.7 mL, 0.020 mol) and potassium carbonate (4.7 g, 0.034 mol) in *N,N*-dimethylformamide (21 mL) was stirred at 70 °C for 18 h. Cooled to ambient temperature, the reaction mixture was poured into ice water, extracted with ethyl acetate. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated. The residue was purified by chromatography on silica gel (hexane/ethyl acetate) to afford 4-(2

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-chloroethoxy)-2-methyl-1-nitrobenzene as solid (2.1 g, y. 73%).

[0527]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 8.05 (d, J = 9.12 Hz, 1H), 7.08 (d, J = 2.48 Hz, 1H), 7.01 (dd, J = 2.72, 9.08 Hz, 1H), 4.38 (t, J = 5.04 Hz, 2H), 3.98 (t, J = 5.08 Hz, 2H), 2.55 (s, 3H); LCMS (m/z): 216.2[M+H]<sup>+</sup>.

Second Step

[0528]

A solution of 4-(2-chloroethoxy)-2-methyl-1-nitrobenzene (2.1 g, 9.7 mmol), *N*-methylpiperazine (1.5 g, 15 mmol) and potassium carbonate (3.4 g, 0.025 mol) in *N,N*-dimethylformamide (15 mL) was stirred with heating at 70 °C for 18 h. Cooled to ambient temperature, the reaction mixture was poured into ice water, extracted with ethyl acetate. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated. The residue was purified by chromatography on silica gel (dichloromethane/methanol) to afford 1-methyl-4-[2-(3-methyl-4-nitrophenoxy)ethyl]piperazine as solid (1.8 g, y. 64%).

[0529]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 8.03 (d, J = 9.12 Hz, 1H), 7.05 (d, J = 2.68 Hz, 1H), 6.98 (dd, J = 2.76, 9.08 Hz, 1H), 4.18 (t, J = 5.78 Hz, 2H), 2.69 (t, J = 5.74 Hz, 2H), 2.54 (s, 3H), 2.39 - 2.52 (m, 4H), 2.22 - 2.37 (m, 4H), 2.14 (s, 3H); LCMS (m/z): 280.2

[M+H]<sup>+</sup>.

Third Step

[0530]

5 1-Methyl-4-[2-(3-methyl-4-nitrophenoxy)ethyl]piperazine (0.69 g, 2.5 mmol) was dissolved in ethanol (10 mL) and 10%wt palladium on carbon (0.055 g) was added at ambient temperature. The reaction mixture was agitated under a hydrogen atmosphere at a  
10 mbient temperature for 4 h. Palladium on carbon was removed by filtration with Celite and the solvent was removed under reduced pressure to afford 2-methyl-4-[2-(4-methylpiperazinyl)ethoxy]aniline as oil (0.60 g, y. 97%).

[0531]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 6.57 (br. s, 1H), 6.51 (br. s, 2H), 4.35 (br. s, 2H), 3.90 (t, J = 5.90 Hz, 2H), 3.17 (br. s, 3H), 2.60 (t, J = 5.88 Hz, 2H), 2.38 - 2.54 (m, 4H), 2.30 (br. s, 4H), 2.14 (s, 3H); LCMS (m/z): 250.4 [M+H]<sup>+</sup>.

Fourth Step

20 [0532]

A solution of ethyl 2-ethoxy-4-oxo-4,5-dihydrofuran-3-carboxylate (0.32 g, 1.6 mmol) which afforded in the Example 74, Third step and 2-methyl-4-[2-(4-methylpiperazinyl)ethoxy]aniline (0.40 g, 1.6 mmol) in ethanol (5.0 mL) was stirred at 60 °C for  
25 30 min. The solvent was removed under reduced pressure, then

the residue was purified by chromatography on silica gel (dichloromethane/methanol) to afford 2-((2-methyl-4-[2-(4-methylpiperazinyl)ethoxy]phenyl)amino)-4-oxo-4,5-dihydrofuran-3-carboxylate as solid (0.30 g, y. 46%).

5 [0533]

$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 9.99 (br. s, 1H), 7.26 (d,  $J$  = 8.56 Hz, 1H), 6.91 (d,  $J$  = 2.28 Hz, 1H), 6.78 - 6.86 (m, 1H), 4.58 (s, 2H), 4.21 (q,  $J$  = 7.04 Hz, 2H), 4.03 - 4.12 (m, 2H), 3.31 (s, 3H), 2.27 - 2.80 (m, 10H), 2.20 (s, 3H), 1.25 (t,  $J$  = 7.04 Hz, 3H); LCMS (m/z): 404.2 [M+H] $^+$ .

#### Fifth Step

[0534]

To a solution of 2-((2-methyl-4-[2-(4-methylpiperazinyl)ethoxy]phenyl)amino)-4-oxo-4,5-dihydrofuran-3-carboxylate (0.22 g, 0.55 mmol) and 7-azaindole-3-carboxaldehyde (0.080 g, 0.55 mmol) in ethanol (14 mL), L-proline (0.014 g, 0.12 mmol) was added at ambient temperature. The mixture was refluxed for 2 days.

The solvent was removed under reduced pressure, and then the residue was purified by preparative HPLC (aqueous ammonium acetate/acetonitrile) to afford the titled compound as solid. (0.032 g, y. 11%).

[0535]

$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.16 (br. s, 1H), 8.17 (d,  $J$  = 4.40 Hz, 1H), 7.64 - 7.79 (m, 2H), 7.31 (d,  $J$  = 8.31 Hz, 1H), 7.00 (br.

s, 1H), 6.90 (d, J = 8.31 Hz, 1H), 6.65 - 6.80 (m, 2H), 4.10 - 4.30 (m, 4H), 2.76 (t, J = 5.62 Hz, 2H), 2.25 - 2.65 (m, 9H), 2.19 - 2.21 (m, 5H), 1.86 (s, 3H), 1.28 (t, J = 6.85 Hz, 3H); LCMS (m/z): 532.3 [M+H]<sup>+</sup>.

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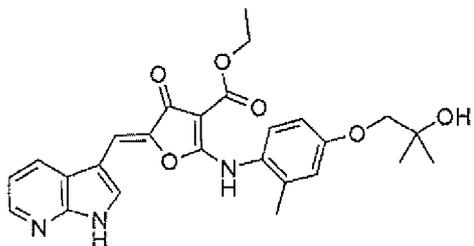
Example 146

[0536]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[[4-(2-hydroxy-2-methylpropoxy)-2-methylphenyl]amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

10

[Chemical Formula 155]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 141.

15

[0537]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.28 (br. s, 1H), 10.30 (br. s, 1H), 8.16 (d, J = 3.91 Hz, 1H), 7.80 (s, 1H), 7.60 (d, J = 7.82 Hz, 1H), 7.40 (d, J = 8.31 Hz, 1H), 7.03 (br. s, 1H), 6.94 (d, J = 8.31 Hz, 1H), 6.81 (s, 1H), 6.73 (dd, J = 4.40, 7.82 Hz, 1H), 4.72 (s, 1H), 4.27 (q, J = 7.17 Hz, 2H), 3.81 (s, 2H), 2.22 (s, 3H), 1.25 - 1.33 (m, 9H); LCMS (m/z): 478.2 [M+H]<sup>+</sup>.

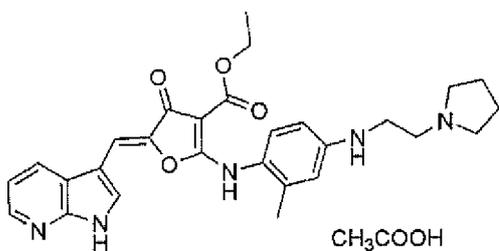
20

Example 147

[0538]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(2-methyl-4-([2-(pyrrolidino)ethyl]amino)phenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate acetate

[Chemical Formula 156]



[0539]

10 To a solution of 2-[(2-methyl-4-([2-(pyrrolidino)ethyl]amino)phenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.32 g, 0.85 mmol) which similarly prepared according to the procedure described in the Example 125, First step to Third step and 7-azaindole-3-carboxaldehyde (0.13 g, 0.85 mmol) in ethanol (5.0 m

15 L), piperidine (0.10 mL, 1.0 mmol) was added at ambient temperature. The mixture was refluxed for 24 h. Cooled to ambient temperature, the reaction mixture was purified by preparative HPLC (aqueous ammonium acetate/acetonitrile) to afford the title d compound as solid (0.010 g, y. 3%).

20 [0540]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.05 (br. s, 1H), 8.11 - 8.20 (m, 1H),

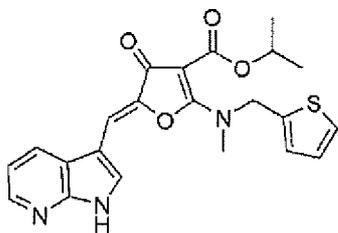
7.71 - 7.84 (m, 2H), 7.01 - 7.10 (m, 1H), 6.77 - 6.85 (m, 1H),  
 6.49 - 6.68 (m, 3H), 5.57 (br. s, 1H), 4.15 - 4.25 (m, 2H), 3.  
 21 (br. s, 2H), 2.63 - 2.73 (m, 2H), 2.52 - 2.61 (m, 4H), 2.10  
 (s, 3H), 1.85 (s, 3H), 1.65 - 1.78 (m, 4H), 1.27 (t,  $J = 6.85$  H  
 5 z, 3H); LCMS (m/z): 502.4 [M+H]<sup>+</sup>.

Example 148

[0541]

10 Isopropyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[*N*-methyl-*N*-(2-thienylmethyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 157]



[0542]

15 A solution of isopropyl 2-isopropoxy-4-oxo-4,5-dihydrofuran-3-carboxylate (0.10 g, 0.44 mmol) which similarly prepared according to the procedure described in the Example 74, Third step using diisopropyl malonate and chloroacetyl chloride, *N*-methyl-*N*-(2-thienylmethyl)amine (0.061 mg, 0.048 mmol) and triethyl  
 20 amine (0.18 mL, 1.3 mmol) in 2-propanol (2.0 mL) was stirred for 7 days then refluxed for further 24 h. To this reaction mixture, 7-azaindole-3-carboxaldehyde (0.065 g, 0.44 mmol) was add

ed then the mixture was refluxed for 24 h. Cooled to ambient temperature, the reaction mixture was purified by preparative HPLC to afford the titled compound as solid (0.0038 g, y. 2%).

[0543]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.33 (br. s, 1H), 8.35 (d, J = 8.03 Hz, 1H), 8.28 - 8.32 (m, 1H), 8.02 (s, 1H), 7.53 (dd, J = 1.13, 5.14 Hz, 1H), 7.14 - 7.22 (m, 2H), 7.04 (dd, J = 3.51, 5.02 Hz, 1H), 6.88 (s, 1H), 5.19 (s, 2H), 4.97 - 5.05 (m, 1H), 3.26 (s, 3H), 1.24 (d, J = 6.27 Hz, 6H); LCMS (m/z): 424.1 [M+H]<sup>+</sup>.

10

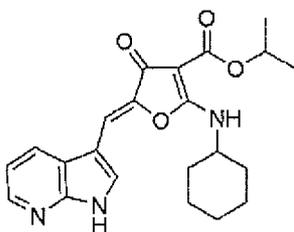
Example 149

[0544]

Isopropyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-(cyclohexylamino)-4-oxo-4,5-dihydrofuran-3-carboxylate

15

[Chemical Formula 158]



[0545]

A solution of isopropyl 2-isopropoxy-4-oxo-4,5-dihydrofuran-3-carboxylate (0.10 g, 0.44 mmol) which similarly prepared according to the procedure described in the Example 74, Third step using diisopropyl malonate and chloroacetyl chloride, and cyclohexylamine (0.055 mL, 0.48 mmol) in 2-propanol (2.0 mL) was

20

stirred at ambient temperature for 14 h. To this reaction mixture, 7-azaindole-3-carboxaldehyde (0.065 g, 0.44 mmol) and piperidine (0.0044 mL, 0.044 mmol) were added then the mixture was refluxed for further 8 days. Cooled to ambient temperature, the reaction mixture was purified by preparative HPLC to afford the titled compound as solid (0.0079 g, y. 4%).

[0546]

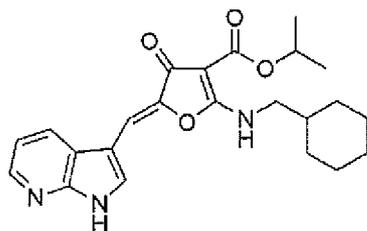
$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.35 (br. s, 1H), 8.51 (d,  $J = 8.28$  Hz, 1H), 8.41 (d,  $J = 7.78$  Hz, 1H), 8.32 (dd,  $J = 1.38, 4.64$  Hz, 1H), 7.99 (d,  $J = 2.51$  Hz, 1H), 7.20 (dd,  $J = 4.64, 7.91$  Hz, 1H), 6.86 (s, 1H), 5.00 - 5.12 (m, 1H), 3.96 - 4.05 (m, 1H), 1.93 - 2.04 (m, 2H), 1.72 - 1.84 (m, 2H), 1.54 - 1.69 (m, 3H), 1.35 - 1.49 (m, 2H), 1.18 - 1.31 (m, 7H); LCMS (m/z): 396.2  $[\text{M}+\text{H}]^+$ .

15 Example 150

[0547]

Isopropyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(cyclohexylmethyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 159]



20

[0548]

A solution of isopropyl 2-isopropoxy-4-oxo-4,5-dihydrofuran-3-

-carboxylate (0.10 g, 0.44 mmol) which similarly prepared according to the procedure described in the Example 74, Third step using diisopropyl malonate and chloroacetyl chloride, and aminomethylcyclohexane (0.063 mL, 0.48 mmol) in 2-propanol (2.0 mL) was stirred at ambient temperature for 14 h. To this reaction mixture, 7-azaindole-3-carboxaldehyde (0.065 g, 0.44 mmol) and piperidine (0.0044 mL, 0.044 mmol) were added then the mixture was refluxed for further 8 days. Cooled to ambient temperature, the reaction mixture was purified by preparative HPLC to afford the titled compound as solid (0.036 g, y. 19%).

[0549]

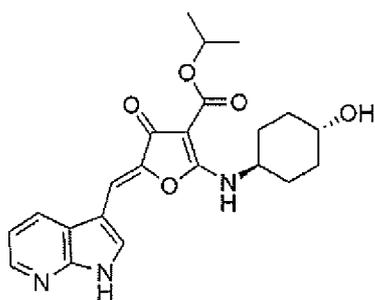
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.35 (br. s, 1H), 8.90 - 8.98 (m, 1H), 8.41 (d, J = 6.78 Hz, 1H), 8.32 (dd, J = 1.38, 4.64 Hz, 1H), 7.99 (s, 1H), 7.19 (dd, J = 4.77, 8.03 Hz, 1H), 6.84 (s, 1H), 5.00 - 5.13 (m, 1H), 3.45 - 3.53 (m, 2H), 1.56 - 1.81 (m, 5H), 1.27 (d, J = 6.27 Hz, 6H), 1.08 - 1.24 (m, 4H), 0.94 - 1.07 (m, 2H); LCMS (m/z): 410.2 [M+H]<sup>+</sup>.

Example 151

[0550]

Isopropyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(*trans*-4-hydroxycyclohexyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 160]



[0551]

A solution of isopropyl 2-[(*trans*-4-hydroxycyclohexyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.10 g, 0.44 mmol) which similarly prepared according to the procedure described in the Example 74, Third step using diisopropyl malonate and chloroacetyl chloride, and *trans*-4-aminomethylcyclohexanol (0.056 mg, 0.49 mmol) in 2-propanol (1.0 mL) was stirred at ambient temperature for 20 h. To this reaction mixture, 7-azaindole-3-carboxaldehyde (0.065 g, 0.44 mmol) and L-proline (0.0050 g, 0.044 mmol) were added then the mixture was refluxed for further 1.5 days. The precipitate was collected by filtration, washed with hot ethanol. The solid was washed with hexane then dried to afford isopropyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(*trans*-4-hydroxycyclohexyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate as solid (0.0076 g, y. 4%).

[0552]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.36 (br. s, 1H), 8.46 (d, *J* = 8.28 Hz, 1H), 8.42 (d, *J* = 7.53 Hz, 1H), 8.33 (dd, *J* = 1.38, 4.64 Hz, 1H), 7.99 (d, *J* = 2.51 Hz, 1H), 7.20 (dd, *J* = 4.64, 7.91 Hz, 1H), 6.85 (s, 1H), 5.01 - 5.09 (m, 1H), 4.69 (d, *J* = 4.27 Hz, 1H),

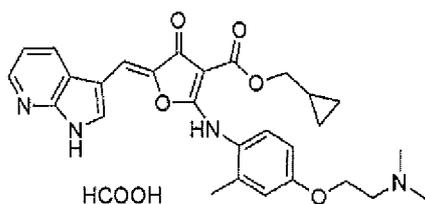
3.93 - 3.99 (m, 1H), 3.43 - 3.51 (m, 1H), 1.86 - 2.03 (m, 4H),  
 1.60 - 1.73 (m, 2H), 1.29 - 1.42 (m, 2H), 1.26 (d,  $J = 6.27$  Hz,  
 6H); LCMS ( $m/z$ ): 412.1  $[M+H]^+$ .

5 Example 152

[0553]

Cyclopropylmethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-((4-[2-(dimethylamino)ethoxy]-2-methylphenyl)amino)-4-oxo-4,5-dihydrofuran-3-carboxylate formate

10 [Chemical Formula 161]



[0554]

A solution of ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-((4-[2-(dimethylamino)ethoxy]-2-methylphenyl)amino)-4-oxo-4,5-dihydrofuran-3-carboxylate (0.033 g, 0.070 mmol) which  
 15 similarly prepared according to the procedure described in the  
 Example 111, cyclopropyl carbinol (0.10 mL, 1.3 mmol) and zinc cluster catalyst ( $Zn_4(OCOCH_3)_6O$ ) (0.0033 g, 0.0035 mmol) in *N,N*-dimethylacetamide (0.9 mL) was stirred with the microwave synthesis  
 20 nthesizer (Biotage Initiator™) at 150 °C for 30 min. Cooled to ambient temperature, the precipitate was removed by filtration. The filtrate was purified by preparative HPLC to afford the

titled compound as solid (0.0029 g, y. 8%).

[0555]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.25 (br. s, 1H), 8.04 - 8.29 (m, 2H),  
 7.75 (s, 1H), 7.68 (d, J = 7.78 Hz, 1H), 7.38 (d, J = 8.28 Hz,  
 1H), 7.03 (d, J = 2.51 Hz, 1H), 6.93 (d, J = 8.78 Hz, 1H), 6.7  
 0 - 6.83 (m, 2H), 6.55 (br. s, 1H), 4.15 (t, J = 5.65 Hz, 2H),  
 4.06 (d, J = 6.78 Hz, 2H), 2.70 (t, J = 5.80 Hz, 2H), 2.28 (s,  
 6H), 2.22 (s, 3H), 1.15 - 1.32 (m, 1H), 0.49 - 0.62 (m, 2H), 0.  
 32 - 0.39 (m, 2H); LCMS (m/z): 503.2 [M+H]<sup>+</sup>.

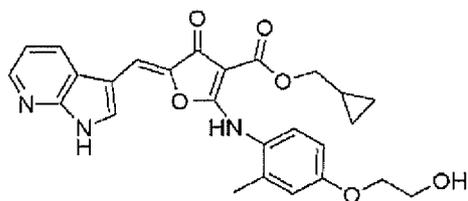
10

Example 153

[0556]

Cyclopropylmethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylen  
 e]-2-([4-(2-hydroxyethoxy)-2-methylphenyl]amino)-4-oxo-4,5-di  
 15 hydrofuran-3-carboxylate

[Chemical Formula 162]



[0557]

A solution of the compound (0.032g, 0.070mmol) of Example 74,  
 20 cyclopropyl carbinol (0.10 mL, 1.3 mmol) and zinc cluster cata  
 lyst (Zn<sub>4</sub>(OCOCF<sub>3</sub>)<sub>6</sub>O) (0.0033 g, 0.0035 mmol) in *N,N*-dimethylace  
 tamide (0.9 mL) was stirred with the microwave synthesizer (Bi

otage Initiator™) at 150 °C for 30 min. Cooled to ambient temperature, the precipitate was removed by filtration. The filtrate was purified by preparative HPLC to afford the titled compound as solid (0.0040 g, y. 11%).

5 [0558]

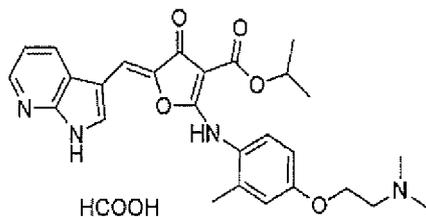
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.23 (br. s, 1H), 10.36 (br. s, 1H), 8.19 (d, J = 3.51 Hz, 1H), 7.65 - 7.80 (m, 2H), 7.38 (d, J = 8.53 Hz, 1H), 7.01 (d, J = 2.26 Hz, 1H), 6.92 (dd, J = 2.51, 8.53 Hz, 1H), 6.72 - 6.84 (m, 2H), 4.95 (t, J = 5.40 Hz, 1H), 4.01 - 4.12 (m, 4H), 3.79 (q, J = 5.02 Hz, 2H), 2.22 (s, 3H), 1.14 - 1.26 (m, 1H), 0.51 - 0.58 (m, 2H), 0.31 - 0.39 (m, 2H); LCMS (m/z): 476.1 [M+H]<sup>+</sup>.

Example 154

15 [0559]

Isopropyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-({4-[2-(dimethylamino)ethoxy]-2-methylphenyl}amino)-4-oxo-4,5-dihydrofuran-3-carboxylate formate

[Chemical Formula 163]



20 [0560]

A solution of ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methyle

ne]-2-((4-[2-(dimethylamino)ethoxy]-2-methylphenyl)amino)-4-oxo-4,5-dihydrofuran-3-carboxylate (0.033 g, 0.070 mmol) which similarly prepared according to the procedure described in the Example 111, and zinc cluster catalyst ( $Zn_4(OCOCF_3)_6O$ ) (0.0033 g, 0.0035 mmol) in 2-propanol (0.5 mL) and *N,N*-dimethylacetamide (0.5 mL) was stirred with the microwave synthesizer (Biota ge Initiator™) at 150 °C for 30 min. Cooled to ambient temperature, the precipitate was removed by filtration. The filtrate was purified by preparative HPLC to afford the titled compound as solid (0.0046 g, y. 11%).

[0561]

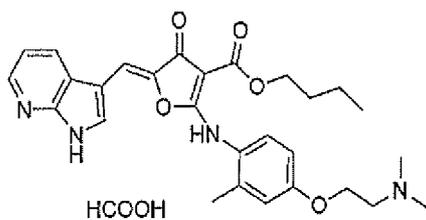
$^1H$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.28 (br. s, 1H), 10.20 (br. s, 1H), 8.18 (dd,  $J = 1.60, 4.40$  Hz, 1H), 8.14 (s, 1H), 7.78 (s, 1H), 7.67 (d,  $J = 8.03$  Hz, 1H), 7.42 (d,  $J = 8.53$  Hz, 1H), 7.04 (d,  $J = 2.51$  Hz, 1H), 6.94 (dd,  $J = 2.76, 8.78$  Hz, 1H), 6.72 - 6.81 (m, 2H), 5.10 - 5.17 (m, 1H), 4.16 (t,  $J = 5.65$  Hz, 2H), 2.75 (t,  $J = 5.52$  Hz, 2H), 2.31 (s, 6H), 2.23 (s, 3H), 1.31 (d,  $J = 6.27$  Hz, 6H); LCMS (m/z): 491.2 [M+H] $^+$ .

20 Example 155

[0562]

*n*-Butyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-((4-[2-(dimethylamino)ethoxy]-2-methylphenyl)amino)-4-oxo-4,5-dihydrofuran-3-carboxylate formate

25 [Chemical Formula 164]



[0563]

A solution of ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-((4-[2-(dimethylamino)ethoxy]-2-methylphenyl)amino)-4-oxo-4,5-dihydrofuran-3-carboxylate (0.033 g, 0.070 mmol) which similarly prepared according to the procedure described in the Example 111, and zinc cluster catalyst ( $Zn_4(OCOCF_3)_6O$ ) (0.0033 g, 0.0035 mmol) in *n*-butanol (0.5 mL) and *N,N*-dimethylacetamide (0.5 mL) was stirred with the microwave synthesizer (Biotage Initiator™) at 150 °C for 30 min. Cooled to ambient temperature, the precipitate was removed by filtration. The filtrate was purified by preparative HPLC to afford the titled compound as solid (0.011 g, y. 31%).

[0564]

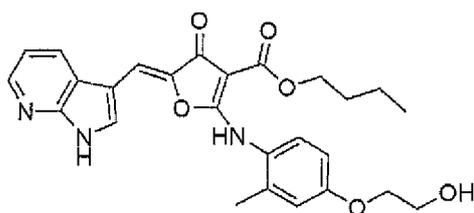
$^1H$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.28 (br. s, 1H), 10.32 (br. s, 1H), 8.18 (dd,  $J = 1.38, 4.64$  Hz, 1H), 8.15 (s, 1H), 7.76 (s, 1H), 7.67 (d,  $J = 7.78$  Hz, 1H), 7.41 (d,  $J = 8.78$  Hz, 1H), 7.04 (d,  $J = 2.51$  Hz, 1H), 6.94 (dd,  $J = 2.76, 8.78$  Hz, 1H), 6.81 (s, 1H), 6.75 (dd,  $J = 4.77, 8.03$  Hz, 1H), 4.22 (t,  $J = 6.78$  Hz, 2H), 4.16 (t,  $J = 5.65$  Hz, 2H), 2.74 (t,  $J = 5.65$  Hz, 2H), 2.30 (s, 6H), 2.22 (s, 3H), 1.60 - 1.72 (m, 2H), 1.34 - 1.51 (m, 2H), 0.94 (t,  $J = 7.40$  Hz, 3H); LCMS ( $m/z$ ): 505.2  $[M+H]^+$ .

Example 156

[0565]

*n*-Butyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[[4-(2-hydroxyethoxy)-2-methylphenyl]amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 165]



[0566]

10 A solution of the compound (0.032g, 0.070mmol) of Example 74, and zinc cluster catalyst ( $Zn_4(OCOCF_3)_6O$ ) (0.0033 g, 0.0035 mmol) in *n*-butanol (0.5 mL) and *N,N*-dimethylacetamide (0.5 mL) was stirred with the microwave synthesizer (Biotage Initiator™) at 150 °C for 30 min. Cooled to ambient temperature, the precipitate was removed by filtration. The filtrate was purified by preparative HPLC to afford the titled compound as solid (0.015 g, y. 44%).

[0567]

20  $^1H$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.27 (br. s, 1H), 10.27 (s, 1H), 8.19 (dd,  $J = 1.13, 4.64$  Hz, 1H), 7.74 (d,  $J = 2.26$  Hz, 1H), 7.69 (d,  $J = 7.78$  Hz, 1H), 7.42 (d,  $J = 8.78$  Hz, 1H), 7.03 (d,  $J = 2.76$  Hz, 1H), 6.94 (dd,  $J = 2.64, 8.66$  Hz, 1H), 6.74 - 6.85 (m, 2

H), 4.88 - 5.05 (m, 1H), 4.22 (t,  $J = 6.65$  Hz, 2H), 4.09 (t,  $J = 4.89$  Hz, 2H), 3.75 - 3.85 (m, 2H), 2.23 (s, 3H), 1.59 - 1.73 (m, 2H), 1.36 - 1.49 (m, 2H), 0.94 (t,  $J = 7.40$  Hz, 3H); LCMS ( $m/z$ ): 478.2  $[M+H]^+$ .

5

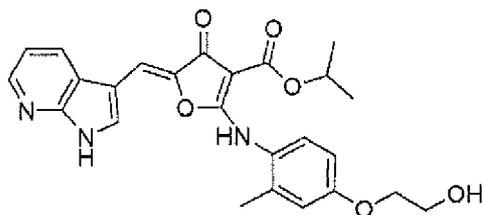
Example 157

[0568]

Isopropyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-([4-(2-hydroxyethoxy)-2-methylphenyl]amino)-4-oxo-4,5-dihydrofuran-3-carboxylate

10

[Chemical Formula 166]



[0569]

A solution of the compound (0.032g, 0.070mmol) of Example 74, and zinc cluster catalyst ( $Zn_4(OCOCF_3)_6O$ ) (0.0033 g, 0.0035 mmol) in 2-propanol (0.5 mL) and *N,N*-dimethylacetamide (0.5 mL) was stirred with the microwave synthesizer (Biotage Initiator<sup>TM</sup>) at 150 °C for 30 min. Cooled to ambient temperature, the precipitate was removed by filtration. The filtrate was purified by preparative HPLC to afford the titled compound as solid (0.010 g, y. 28%).

20

[0570]

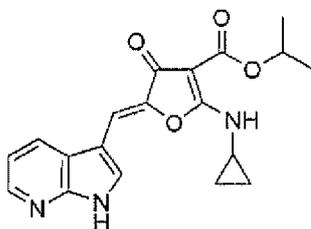
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.27 (br. s, 1H), 10.22 (s, 1H), 8.19 (dd, J = 1.26, 4.77 Hz, 1H), 7.76 (d, J = 2.51 Hz, 1H), 7.69 (d, J = 7.78 Hz, 1H), 7.42 (d, J = 8.53 Hz, 1H), 7.03 (d, J = 2.51 Hz, 1H), 6.94 (dd, J = 2.76, 8.78 Hz, 1H), 6.73 - 6.84 (m, 2 H), 5.08 - 5.18 (m, 1H), 4.95 (t, J = 5.40 Hz, 1H), 4.09 (t, J = 4.89 Hz, 2H), 3.80 (q, J = 5.27 Hz, 2H), 2.23 (s, 3H), 1.31 (d, J = 6.27 Hz, 6H); LCMS (m/z): 464.1 [M+H]<sup>+</sup>.

Example 158

10 [0571]

Isopropyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-(cyclopropylamino)-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 167]



15 [0572]

A solution of isopropyl 2-isopropoxy-4-oxo-4,5-dihydrofuran-3-carboxylate (0.10 g, 0.44 mmol) which similarly prepared according to the procedure described in the Example 74, Third step using diisopropyl malonate and chloroacetyl chloride, and cyclopropylamine (0.034 mL, 0.48 mmol) in 2-propanol (2.0 mL) was stirred at ambient temperature for 14 h. To this reaction mixture, 7-azaindole-3-carboxaldehyde (0.065 g, 0.44 mmol) and pi

peridine (0.0044 mL, 0.044 mmol) were added then the mixture was refluxed for further 12 days. Cooled to ambient temperature, the reaction mixture was purified by preparative HPLC to afford the titled compound as solid (0.0020 g, y. 1%).

5 [0573]

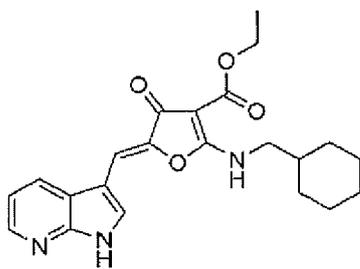
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.33 (br. s, 1H), 8.81 (br. s, 1H), 8.56 (d, J = 7.28 Hz, 1H), 8.31 (d, J = 3.51 Hz, 1H), 8.06 (d, J = 2.26 Hz, 1H), 7.21 (dd, J = 4.64, 7.91 Hz, 1H), 6.88 (s, 1H), 4.99 - 5.10 (m, 1H), 3.09 - 3.18 (m, 1H), 1.26 (d, J = 6.27 Hz, 6H), 0.89 - 0.97 (m, 4H); LCMS (m/z): 354.1 [M+H]<sup>+</sup>.

Example 159

[0574]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(cyclohexylmethyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 168]



[0575]

A solution of ethyl 2-ethoxy-4-oxo-4,5-dihydrofuran-3-carboxylate (0.10 g, 0.51 mmol) which afforded in the Example 74, Third step and aminomethylcyclohexane (0.072 mL, 0.55 mmol) in et

hanol (2.0 mL) was stirred at ambient temperature for 1.5 h. To this reaction mixture, 7-azaindole-3-carboxaldehyde (0.073 g, 0.50 mmol) and L-proline (0.012 mg, 0.10 mmol) were added then the mixture was refluxed for further 5 days. The precipitate was collected by filtration, washed with hot ethanol. The solid was washed with hexane then dried to afford the titled compound as solid (0.024 g, y. 12%).

[0576]

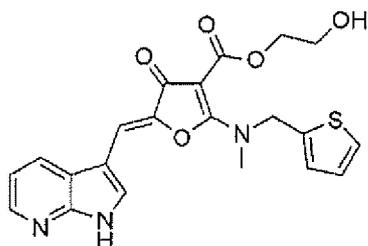
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.35 (br. s, 1H), 8.98 (t, J = 6.27 Hz, 1H), 8.42 (d, J = 7.78 Hz, 1H), 8.32 (dd, J = 1.38, 4.64 Hz, 1H), 7.99 (d, J = 2.51 Hz, 1H), 7.19 (dd, J = 4.64, 7.91 Hz, 1H), 6.88 (s, 1H), 4.21 (q, J = 7.03 Hz, 2H), 3.48 (t, J = 6.40 Hz, 2H), 1.65 - 1.81 (m, 5H), 1.62 (d, J = 9.29 Hz, 1H), 1.09 - 1.30 (m, 6H), 0.95 - 1.06 (m, 2H); LCMS (m/z): 396.2 [M+H]<sup>+</sup>.

Example 160

[0577]

2-Hydroxyethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[*N*-methyl-*N*-(2-thienylmethyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 169]



[0578]

A solution of the compound (0.050g, 0.12mmol) of Example 108, ethylene glycol (0.20 mL, 3.6 mmol), 4-dimethylaminopyridine (0.0030 g, 0.024 mmol) and zinc cluster catalyst ( $Zn_4(OCOCF_3)_6$ ) (0.0058 g, 0.0061 mmol) in *N,N*-dimethylacetamide (0.5 mL) was stirred with the microwave synthesizer (Biotage Initiator<sup>™</sup>) at 150 °C for 30 min. Cooled to ambient temperature, the precipitate was removed by filtration. The filtrate was purified by preparative HPLC to afford the titled compound as solid (0.0061 g, y. 10%).

[0579]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.34 (br. s, 1H), 11.7 (br. s, 1H), 8.35 - 8.44 (m, 1H), 8.30 (dd, *J* = 1.38, 4.64 Hz, 1H), 8.04 (s, 1H), 7.53 (dd, *J* = 1.13, 5.14 Hz, 1H), 7.21 (d, *J* = 3.01 Hz, 1H), 7.17 (dd, *J* = 4.64, 7.91 Hz, 1H), 7.04 (dd, *J* = 3.51, 5.02 Hz, 1H), 6.94 (s, 1H), 5.20 (s, 2H), 4.17 (t, *J* = 5.14 Hz, 2H), 3.62 (q, *J* = 5.52 Hz, 2H), 3.23 - 3.37 (m, 3H); LCMS (*m/z*): 426.1 [M+H]<sup>+</sup>.

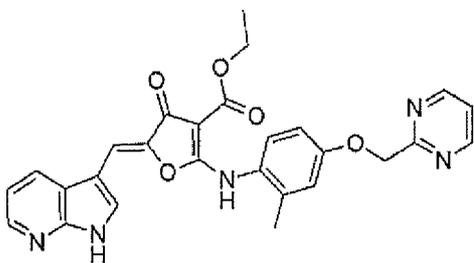
20

Example 161

[0580]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(2-methyl-4-(2-pyrimidinylmethoxy)phenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

5 [Chemical Formula 170]



First Step

[0581]

A solution of 4-nitro-*m*-cresol (0.25 g, 1.6 mmol), 2-(chloromethyl)pyrimidine hydrochloride (0.40 g, 2.4 mmol) and potassium carbonate (0.50 g, 4.0 mmol) in *N,N*-dimethylformamide (6.0 mL) was stirred at 70 °C for 18 h. Cooled to ambient temperature, the reaction mixture was poured into ice water, extracted with ethyl acetate. The organic layer was washed with water and brine, dried over sodium sulfate, filtered and concentrated to afford 2-[(3-methyl-4-nitrophenoxy)methyl]pyrimidine as crude material (0.32 g, y. 81%) as solid.

[0582]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 8.84 (d, *J* = 4.92 Hz, 2H), 8.03 (d, *J* = 9.08 Hz, 1H), 7.48 (t, *J* = 4.90 Hz, 1H), 7.10 (d, *J* = 2.68 Hz, 1H), 7.00 (dd, *J* = 2.80, 9.12 Hz, 1H), 5.43 (s, 2H), 2.53 (s,

3H); LCMS (m/z): 246.4 [M+H]<sup>+</sup>.

#### Second Step

[0583]

5 To a solution of 2-[(3-methyl-4-nitrophenoxy)methyl]pyrimidin  
e (0.18 g, 0.7 mmol) in ethanol (4.0 mL) and water (1.0 mL), ir  
on (0.40 g, 7.2 mmol) and ammonium chloride (0.020 g, 0.37 mmo  
l) were added. The mixture was refluxed for 1.5 h. Cooled to am  
bient temperature, the reaction mixture was filtered over Celi  
10 te to remove unneeded materials and the filtrate was concentra  
ted to afford 2-methyl-4-(2-pyrimidinylmethoxy)aniline (0.15  
g, crude material) as solid.

[0584]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 8.82 (d, J = 4.88 Hz, 2H), 7.45 (t, J =  
15 4.90 Hz, 1H), 6.62 (d, J = 2.64 Hz, 1H), 6.55 (dd, J = 2.74, 8.  
60 Hz, 1H), 6.50 (d, J = 8.52 Hz, 1H), 5.08 (s, 2H), 4.40 (br.  
s, 2H), 2.01 (s, 3H); LCMS (m/z): 216.0 [M+H]<sup>+</sup>.

#### Third Step

20 [0585]

A solution of ethyl 2-ethoxy-4-oxo-4,5-dihydrofuran-3-carboxy  
late (0.14 g, 0.60 mmol) which afforded in the Example 74, Thi  
rd step and 2-methyl-4-(2-pyrimidinylmethoxy)aniline (0.13 g,  
0.6 mmol) in ethanol (5.0 mL) was stirred at 60 °C for 30 h. Th  
25 e solvent was removed under reduced pressure, then the residue

was purified by chromatography on silica gel (hexane/ethyl acetate) to afford ethyl 2-([2-methyl-4-(2-pyrimidinylmethoxy)phenyl]amino)-4-oxo-4,5-dihydrofuran-3-carboxylate as solid (0.035 g, y. 15%).

5 [0586]

$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 9.98 (br. s, 1H), 8.84 (d,  $J$  = 4.88 Hz, 2H), 7.47 (t,  $J$  = 4.90 Hz, 1H), 7.25 (d,  $J$  = 8.76 Hz, 1H), 6.96 (d,  $J$  = 2.72 Hz, 1H), 6.84 (dd,  $J$  = 2.82, 8.70 Hz, 1H), 5.28 (s, 2H), 4.57 (s, 2H), 4.21 (q,  $J$  = 7.07 Hz, 2H), 2.19 (s, 3H),  
10 1.24 (t,  $J$  = 7.04 Hz, 3H); LCMS (m/z): 370.0 [M+H] $^+$ .

Fourth Step

[0587]

To a solution of ethyl 2-([2-methyl-4-(2-pyrimidinylmethoxy)phenyl]amino)-4-oxo-4,5-dihydrofuran-3-carboxylate (0.035 g, 0.10 mmol) and 7-azaindole-3-carboxaldehyde (0.014 g, 0.10 mmol) in ethanol (5.0 mL), piperidine (0.050 mL, 0.50 mmol) was added at ambient temperature then the mixture was refluxed for 3 days. Cooled to ambient temperature, the solvent was removed under reduced pressure. The residue was suspended in ethanol, then the precipitate was collected by filtration, washed with ethanol then dried to afford the titled compound as solid (9.0 mg, y. 19%).

[0588]

25  $^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.28 (br. s, 1H), 10.27 (br. s, 1H),

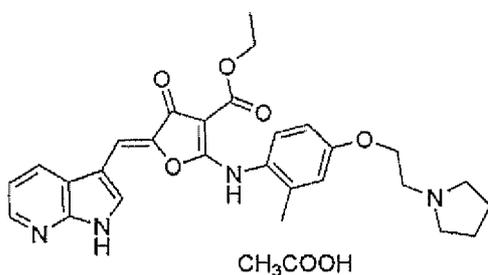
8.88 (d,  $J = 4.40$  Hz, 2H), 8.19 (d,  $J = 3.42$  Hz, 1H), 7.77 (br. s, 1H), 7.68 (d,  $J = 7.34$  Hz, 1H), 7.50 (t,  $J = 4.60$  Hz, 1H), 7.42 (d,  $J = 8.80$  Hz, 1H), 7.10 (br. s, 1H), 6.98 (d,  $J = 8.31$  Hz, 1H), 6.74 - 6.86 (m, 2H), 5.39 (s, 2H), 4.19 - 4.32 (m,  $J = 6.80$  Hz, 2H), 2.22 (br. s, 3H), 1.18 - 1.47 (m, 3H); LCMS ( $m/z$ ): 498.4  $[M+H]^+$ .

Example 162

[0589]

10 Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-((2-methyl-4-[2-(1-pyrrolidinyl)ethoxy]phenyl)amino)-4-oxo-4,5-dihydrofuran-3-carboxylate acetate

[Chemical Formula 171]



15 [0590]

The mixture, which similarly prepared according to the procedure described in the Example 161, was purified by preparative HPLC (aqueous ammonium acetate/acetonitrile were used as eluents) to afford the titled compound(solid).

20 [0591]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>)  $\delta$  (ppm) 12.25 (br. s, 1H), 8.16 (d,  $J = 3.91$  Hz,

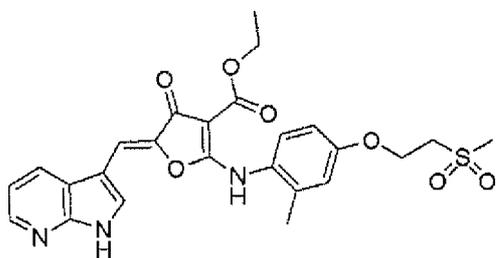
1H), 7.74 (s, 1H), 7.68 (d,  $J = 7.82$  Hz, 1H), 7.35 (d,  $J = 7.8$   
 2 Hz, 1H), 7.02 (br. s, 1H), 6.86 - 6.96 (m, 2H), 6.70 - 6.80  
 (m, 1H), 4.20 - 4.35 (m, 2H), 4.16 (t,  $J = 5.62$  Hz, 2H), 2.87  
 (t,  $J = 5.62$  Hz, 2H), 2.50 - 2.72 (m, 4H), 2.21 (s, 3H), 1.90  
 5 (s, 3H), 1.68 - 1.78 (m, 4H), 1.28 (t,  $J = 7.09$  Hz, 3H); LCMS  
 (m/z): 503.2 [M+H]<sup>+</sup>.

Example 163

[0592]

10 Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-({2-meth  
 yl-4-[2-(methylsulfonyl)ethoxy]phenyl)amino)-4-oxo-4,5-dihydr  
 ofuran-3-carboxylate

[Chemical Formula 172]



15 [0593]

To a mixed solution of the compound (0.070g, 0.14mmol) of Exam  
 ple 128 and saturated sodium bicarbonate solution (0.80 mL) in  
 methanol (0.4 mL) and dichloromethane (1.6 mL) that cooled wi  
 th ice bath, 3-chloroperoxybenzoic acid (0.050 g, 0.28 mmol) w  
 20 as added at 0 °C. The mixture was stirred for 1 h. The reaction  
 mixture was extracted with dichloromethane, and the organic 1

ayer was washed with saturated sodium bicarbonate solution, dried over sodium sulfate and concentrated. The residue was purified by preparative HPLC to afford the titled compound as solid (0.010 g, y. 13%).

[0594]

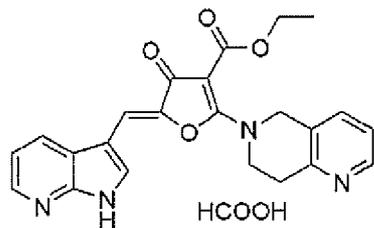
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.18 (br. s, 1H), 10.4 (br. s, 1H), 8.19 (d, J = 4.40 Hz, 1H), 7.74 (br. s, 1H), 7.64 (d, J = 7.34 Hz, 1H), 7.36 (d, J = 8.31 Hz, 1H), 7.06 (br. s, 1H), 6.97 (d, J = 8.31 Hz, 1H), 6.66 - 6.80 (m, 2H), 4.44 (t, J = 5.38 Hz, 2H), 4.18 - 4.30 (m, J = 6.80 Hz, 2H), 3.66 - 3.76 (m, 2H), 3.15 (s, 3H), 2.21 (s, 3H), 1.28 (t, J = 7.09 Hz, 3H); LCMS (m/z): 512.2 [M+H]<sup>+</sup>.

Example 164

[0595]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-(7,8-dihydro-1,6-naphthyridin-6(5*H*)-yl)-4-oxo-4,5-dihydrofuran-3-carboxylate formate

[Chemical Formula 173]



[0596]

To a solution of 5,6,7,8-tetrahydro-1,6-naphthyridine dihydro

chloride (0.049 g, 0.24 mmol) in ethanol (1.0 mL), 4M sodium hydroxide solution (0.13 mL, 0.52 mmol) was added at ambient temperature and the mixture was stirred for 5 min. To this reaction mixture, ethyl 2-ethoxy-4-oxo-4,5-dihydrofuran-3-carboxylate (0.049 g, 0.24 mmol), which afforded in the Example 74, Third step was added and stirred for 1 h. The solvent was removed under reduced pressure, then chloroform and water were added to the residue and two phases were separated. The organic layer was washed with brine, dried over magnesium sulfate and concentrated. To this residue, 7-azaindole-3-carboxaldehyde (0.027 g, 0.18 mmol), 5,6,7,8-tetrahydro-1,6-naphthyridine (0.0063 g, 0.047 mmol) and ethanol (1.0 mL) were added and the mixture was refluxed for further 14 days. The reaction mixture was filtered and washed with hot ethanol. The solid was purified by preparative HPLC to afford the titled compound as solid (0.0058 g, y. 5%).

[0597]

$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.38 (br. s, 1H), 8.46 (d,  $J = 3.51$  Hz, 1H), 8.42 (d,  $J = 7.78$  Hz, 1H), 8.33 (dd,  $J = 1.13, 4.64$  Hz, 1H), 8.10 (s, 1H), 7.71 (d,  $J = 7.78$  Hz, 1H), 7.31 (dd,  $J = 4.77, 7.78$  Hz, 1H), 7.22 (dd,  $J = 4.64, 7.91$  Hz, 1H), 6.91 (s, 1H), 5.01 - 5.07 (m, 2H), 4.22 (q,  $J = 7.03$  Hz, 2H), 4.07 - 4.13 (m, 2H), 3.19 (t,  $J = 5.90$  Hz, 2H), 1.27 (t,  $J = 7.03$  Hz, 3H); LCM S (m/z): 417.1 [M+H] $^+$ .

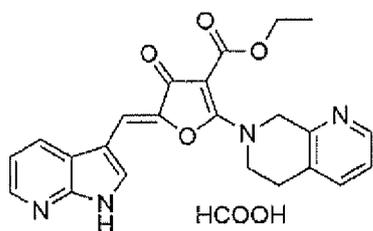
25

Example 165

[0598]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-(5,6-dihydro-1,7-naphthyridin-7(8*H*)-yl)-4-oxo-4,5-dihydrofuran-3-carboxylate formate

[Chemical Formula 174]



[0599]

To a solution of 5,6,7,8-tetrahydro-1,7-naphthyridine dihydrochloride (0.050 g, 0.24 mmol) in ethanol (1.3 mL), 4M sodium hydroxide solution (0.13 mL, 0.52 mmol) was added at ambient temperature and the mixture was stirred for 5 min. To this reaction mixture, ethyl 2-ethoxy-4-oxo-4,5-dihydrofuran-3-carboxylate (0.049 g, 0.24 mmol), which afforded in the Example 74, Third step was added and stirred for 1 h. The solvent was removed under reduced pressure, then chloroform and water were added to the residue and two phases were separated. The organic layer was washed with brine, dried over magnesium sulfate and concentrated. To this residue, 7-azaindole-3-carboxaldehyde (0.023 g, 0.15 mmol), 5,6,7,8-tetrahydro-1,7-naphthyridine dihydrochloride (0.0056 g, 0.042 mmol) and ethanol (1.0 mL) were added and refluxed for further 14 days. Cooled to ambient temperature

ure, the reaction mixture was purified by preparative HPLC to afford the titled compound as solid (0.0033 g, y. 3%).

[0600]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.39 (br. s, 1H), 8.39 - 8.49 (m, 2H),  
 5 8.33 (d, J = 4.52 Hz, 1H), 8.05 (d, J = 2.26 Hz, 1H), 7.70 (d,  
 J = 7.03 Hz, 1H), 7.31 (dd, J = 4.77, 7.78 Hz, 1H), 7.21 (dd,  
 J = 4.77, 7.78 Hz, 1H), 6.92 (s, 1H), 5.00 (br. s, 2H), 4.22 (q,  
 J = 7.03 Hz, 2H), 4.02 - 4.10 (m, 2H), 3.12 (t, J = 5.52 Hz, 2  
 H), 1.27 (t, J = 7.03 Hz, 3H); LCMS (m/z): 417.1 [M+H]<sup>+</sup>.

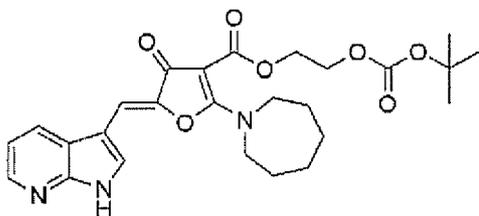
10

Example 166

[0601]

2-[(*tert*-Butoxycarbonyl)oxy]ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridi  
 n-3-yl)methylene]-2-azepinyl-4-oxo-4,5-dihydrofuran-3-carboxy  
 15 late

[Chemical Formula 175]



First Step

[0602]

20 To a solution of triethylamine (0.65 mL, 4.7 mmol) in ethylene  
 glycol (1.8 mL, 0.031 mol) that cooled with ice bath, ethyl ma  
 lonyl chloride (0.40 mL, 3.1 mmol) was added dropwise and the

mixture was stirred for 2.5 h. The reaction was terminated by addition of aqueous 10% citric acid solution, the reaction mixture was extracted with chloroform. The organic layer was dried over magnesium sulfate, filtered and concentrated. The residue was purified by chromatography on silica gel (chloroform/methanol) to afford ethyl (2-hydroxyethyl) malonate as oil (0.37 g, y. 66%).

[0603]

$^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  (ppm) 4.28 - 4.35 (m, 2H), 4.22 (q,  $J = 7.19$  Hz, 2H), 3.80 - 3.88 (m, 2H), 3.43 (s, 2H), 2.18 (br. s, 1H), 1.29 (t,  $J = 7.15$  Hz, 3H)

Second Step

[0604]

To a solution of ethyl 2-hydroxyethyl malonate (0.36 mg, 2.1 mmol) and di-*tert*-butyl dicarbonate (0.57 mL, 2.5 mmol) in tetrahydrofuran (2.0 mL) that cooled with ice bath, triethylamine (0.43 mL, 3.1 mmol) was added dropwise and 4-dimethylaminopyridine (0.019 mg, 0.16 mmol) was added then the mixture was stirred at ambient temperature for 2 weeks. The reaction mixture was diluted with water, and extracted with ethyl acetate. The organic layer was washed with brine, dried over magnesium sulfate and concentrated. The residue was purified by chromatography on silica gel (hexane/ethyl acetate) to afford 2-[(*tert*-butoxycarbonyl)oxy]ethyl ethyl malonate as oil (0.37 g, y. 43%).

[0605]

<sup>1</sup>H NMR (CDCl<sub>3</sub>) δ (ppm) 4.33 - 4.39 (m, 2H), 4.26 - 4.31 (m, 2H),  
4.21 (q, J = 7.03 Hz, 2H), 3.41 (s, 2H), 1.49 (s, 9H), 1.28 (t,  
J = 7.15 Hz, 3H)

5

Third Step

[0606]

A solution of 2-[(*tert*-butoxycarbonyl)oxy]ethyl ethyl malonate (0.36 g, 1.3 mmol) in anhydrous tetrahydrofuran (1.0 mL) was  
10 added dropwise to a solution of sodium hydride (60% w/w in oil, 0.10 g, 2.6 mmol) in anhydrous tetrahydrofuran (4.0 mL) that cooled with ice bath. The mixture was refluxed for 14 min. The reaction mixture was cooled with ice bath, chloroacetyl chloride (0.11 mL, 1.3 mmol) was added dropwise to the reaction mixture and the mixture was stirred for 1 h then stirred at 45 °C for further 1 h. The reaction mixture was diluted with water, extracted with chloroform for 2 times. The organic layer was dried over magnesium sulfate and concentrated. The residue was purified by chromatography on silica gel (ethyl acetate/methanol) then concentrated. To this residue (ca. 0.11 g) in ethanol (3.0 mL), hexamethylenimine (0.046 mL, 0.41 mmol) was added dropwise and the mixture was stirred at ambient temperature for 30 min. Then to the reaction mixture, 7-azaindole-3-carboxaldehyde (0.043 g, 0.30 mmol) was added at ambient temperature then the mixture was refluxed for further 4 days. Cooled to ambi  
15  
20  
25

ent temperature, the reaction mixture was purified by preparative HPLC to afford the titled compound as solid (0.020 g, y. 3%).

[0607]

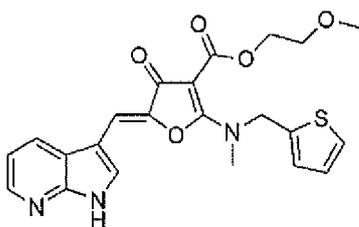
5 <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.31 (br. s, 1H), 8.39 (d, J = 8.03 Hz, 1H), 8.31 (dd, J = 1.38, 4.64 Hz, 1H), 7.95 (d, J = 2.51 Hz, 1H), 7.20 (dd, J = 4.64, 7.91 Hz, 1H), 6.85 (s, 1H), 4.30 - 4.36 (m, 2H), 4.21 - 4.27 (m, 2H), 3.70 - 3.90 (m, 4H), 1.80 - 1.90 (m, 4H), 1.53 - 1.62 (m, 4H), 1.42 (s, 9H); LCMS (m/z): 498.2  
10 [M+H]<sup>+</sup>.

Example 167

[0608]

2-Methoxyethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[*N*-methyl-*N*-(2-thienylmethyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 176]



[0609]

20 A solution of the compound (0.050g, 0.12mmol) of Example 108, 2-methoxyethanol (0.20 mL, 2.6 mmol), 4-dimethylaminopyridine (0.0030 g, 0.024 mmol) and zinc cluster catalyst (Zn<sub>4</sub>(OCOCF<sub>3</sub>)<sub>6</sub>)

0) (0.0058 g, 0.0061 mmol) in *N,N*-dimethylacetamide (0.5 mL) was stirred with the microwave synthesizer (Biotage Initiator<sup>T</sup> M) at 150 °C for 3.5 h. Cooled to ambient temperature, the reaction mixture was purified by preparative HPLC to afford the titled compound as solid (0.0029 g, y. 5%).

[0610]

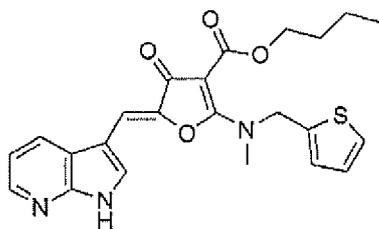
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.34 (br. s, 1H), 8.38 (d, *J* = 8.03 Hz, 1H), 8.30 (dd, *J* = 1.38, 4.64 Hz, 1H), 8.03 (d, *J* = 2.26 Hz, 1H), 7.53 (dd, *J* = 1.00, 5.02 Hz, 1H), 7.13 - 7.22 (m, 2H), 7.04 (dd, *J* = 3.51, 5.02 Hz, 1H), 6.93 (s, 1H), 5.20 (s, 2H), 4.23 - 4.28 (m, 2H), 3.55 - 3.60 (m, 2H), 3.22 - 3.32 (m, 6H); LCMS (*m/z*): 440.1 [M+H]<sup>+</sup>.

Example 168

[0611]

*n*-Butyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[*N*-methyl-*N*-(2-thienylmethyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 177]



[0612]

A solution of the compound (0.050g, 0.12mmol) of Example 108,

1-butanol (0.50 mL, 5.5 mmol), 4-dimethylaminopyridine (0.0030 g, 0.024 mmol) and zinc cluster catalyst ( $Zn_4(OCOCF_3)_6O$ ) (0.0058 g, 0.0061 mmol) in *N,N*-dimethylacetamide (0.5 mL) was stirred with the microwave synthesizer (Biotage Initiator™) at 150 °C for 1.5 h. Cooled to ambient temperature, the reaction mixture was purified by preparative HPLC to afford the titled compound as solid (0.0044 g, y. 6%).

[0613]

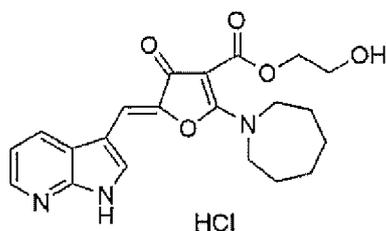
$^1H$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.33 (br. s, 1H), 8.37 (d,  $J = 7.78$  Hz, 1H), 8.30 (dd,  $J = 1.25, 4.52$  Hz, 1H), 8.01 - 8.04 (m, 1H), 7.53 (dd,  $J = 1.25, 5.02$  Hz, 1H), 7.14 - 7.22 (m, 2H), 7.04 (dd,  $J = 3.51, 5.02$  Hz, 1H), 6.91 (s, 1H), 5.21 (s, 2H), 4.13 (t,  $J = 6.53$  Hz, 2H), 3.24 - 3.31 (m, 3H), 1.55 - 1.65 (m, 2H), 1.36 - 1.47 (m, 2H), 0.90 (t,  $J = 7.40$  Hz, 3H); LCMS ( $m/z$ ): 438.1 [M+H] $^+$ .

Example 169

[0614]

2-Hydroxyethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-azepinyl-4-oxo-4,5-dihydrofuran-3-carboxylate hydrochloride

[Chemical Formula 178]



[0615]

To a mixed solution of the compound (0.018g, 0.037mmol) of Example 166 in dioxane (0.2 mL) and chloroform (1.0 mL) that cooled with ice bath, 4M hydrochloric acid in dioxane (0.25 mL, 1.0 mmol) was added dropwise. The mixture was stirred at ambient temperature for 24 h. The precipitate was collected by filtration, washed with chloroform and hexane then dried to afford the titled compound as solid (6.3 mg, y. 37%).

[0616]

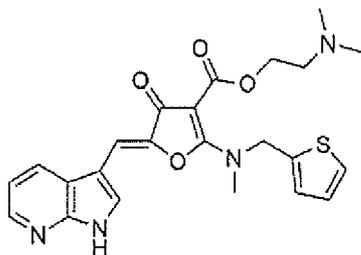
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.39 (br. s, 1H), 8.44 (d, J = 7.78 Hz, 1H), 8.33 (dd, J = 1.38, 4.64 Hz, 1H), 7.96 (s, 1H), 7.23 (dd, J = 4.77, 8.03 Hz, 1H), 6.89 (s, 1H), 4.16 (t, J = 5.27 Hz, 2H), 3.67 - 3.95 (m, 6H), 3.62 (t, J = 5.14 Hz, 2H), 1.75 - 1.93 (m, 4H), 1.50 - 1.65 (m, 4H); LCMS (m/z): 398.1 [M+H]<sup>+</sup>.

Example 170

[0617]

2-(Dimethylamino)ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[*N*-methyl-*N*-(2-thienylmethyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 179]



[0618]

A solution of the compound (0.10g, 0.25mmol) of Example 108, 2-(dimethylamino)ethanol (0.40 mL, 4.0 mmol), 4-dimethylaminopyridine (0.0060 g, 0.049 mmol) and zinc cluster catalyst ( $Zn_4(OCOCF_3)_6O$ ) (0.012 g, 0.012 mmol) in *N,N*-dimethylacetamide (0.5 mL) was stirred with the microwave synthesizer (Biotage Initiator™) at 150 °C for 30 min. Cooled to ambient temperature, the reaction mixture was purified by preparative HPLC to afford the titled compound as solid (0.0023 g, y. 2%).

[0619]

$^1H$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.33 (br. s, 1H), 8.38 (d,  $J = 8.03$  Hz, 1H), 8.28 - 8.32 (m, 1H), 8.03 (s, 1H), 7.53 (dd,  $J = 1.00, 5.02$  Hz, 1H), 7.14 - 7.22 (m, 2H), 7.04 (dd,  $J = 3.51, 5.02$  Hz, 1H), 6.92 (s, 1H), 5.20 (s, 2H), 4.21 (t,  $J = 5.90$  Hz, 2H), 3.51 (s, 3H), 3.25 - 3.29 (m, 2H), 2.18 (s, 6H); LCMS (m/z): 453.1 [M+H] $^+$ .

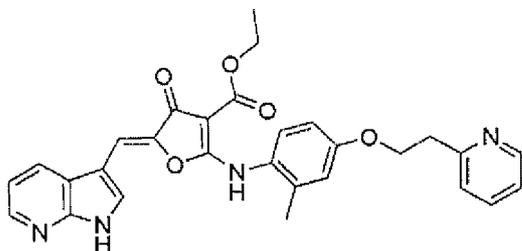
Example 171

[0620]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-((2-meth

yl-4-[2-(2-pyridinyl)ethoxy]phenyl)amino)-4-oxo-4,5-dihydrofu  
ran-3-carboxylate

[Chemical Formula 180]



5 First Step

[0621]

To a solution of 4-nitro-*m*-cresol (3.0 g, 0.020 mmol) and trip  
henylphosphine (7.7 g, 0.029 mmol) in tetrahydrofuran (50 mL)  
cooled with ice bath, diisopropyl azodicarboxylate (5.8 mL, 0.  
10 030 mmol) was added dropwise. The mixture was stirred at ambie  
nt temperature for 30 min. The reaction mixture was cooled wit  
h ice bath, and a solution of 2-pyridineethanol (2.6 mL, 0.024  
mmol) in tetrahydrofuran (5.0 mL) was added dropwise to the r  
eaction mixture then the mixture was stirred at ambient temper  
15 ature for further 16 h. The solvent was removed under reduced  
pressure, then the residue was purified by chromatography on s  
ilica gel (hexane/ethyl acetate) to afford 2-methyl-4-[2-(2-py  
ridinyl)ethoxy]-1-nitrobenzene as solid (2.0 g, y. 40%).

[0622]

20 <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 8.43 - 8.59 (m, 1H), 8.03 (d, *J* = 9.08  
Hz, 1H), 7.73 (t, *J* = 7.62 Hz, 1H), 7.37 (d, *J* = 7.80 Hz, 1H),

7.25 (t, J = 6.12 Hz, 1H), 7.03 (s, 1H), 6.98 (d, J = 9.20 Hz, 1H), 4.49 (t, J = 6.46 Hz, 2H), 3.22 (t, J = 6.54 Hz, 2H), 2.53 (s, 3H); LCMS (m/z): 259.0 [M+H]<sup>+</sup>.

5 Second Step

[0623]

Under a nitrogen atmosphere, 2-methyl-4-[2-(2-pyridinyl)ethoxy]-1-nitrobenzene (2.0 g, 7.7 mmol) was dissolved in tetrahydrofuran (40 mL) and 10% palladium on carbon (0.20 g) was added at ambient temperature. The reaction mixture was agitated under a hydrogen atmosphere at ambient temperature for 4 h. Palladium on carbon was removed by filtration with Celite and the solvent was removed under reduced pressure to afford 2-methyl-4-[2-(2-pyridinyl)ethoxy]aniline as solid (1.4 g, y. 80%).

15 [0624]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 8.49 (d, J = 4.36 Hz, 1H), 7.71 (t, J = 7.64 Hz, 1H), 7.33 (d, J = 7.76 Hz, 1H), 7.22 (t, J = 6.10 Hz, 1H), 6.45 - 6.58 (m, 3H), 4.35 (br. s, 2H), 4.18 (t, J = 6.66 Hz, 2H), 3.10 (t, J = 6.62 Hz, 2H), 2.00 (s, 3H); LCMS (m/z): 20 29.4 [M+H]<sup>+</sup>.

Third Step

[0625]

A solution of ethyl 2-ethoxy-4-oxo-4,5-dihydrofuran-3-carboxylate (0.35 g, 1.8 mmol) which afforded in the Example 74, Thir

d step and 2-methyl-4-[2-(2-pyridinyl)ethoxy]aniline (0.40 g, 1.8 mmol) in ethanol (5.0 mL) was stirred at ambient temperature for 1.5 days. The solvent was removed under reduced pressure, then the residue was purified by preparative HPLC to afford ethyl 2-((2-methyl-4-[2-(2-pyridinyl)ethoxy]phenyl)amino)-4-oxo-4,5-dihydrofuran-3-carboxylate as solid (0.15 g, y. 22%).

[0626]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 9.98 (br. s, 1H), 8.51 (d, J = 4.52 Hz, 1H), 7.70 - 7.78 (m, 1H), 7.37 (d, J = 7.92 Hz, 1H), 7.22 - 7.28 (m, 2H), 6.87 - 6.92 (m, 1H), 6.77 - 6.84 (m, 1H), 4.57 (s, 2H), 4.36 (t, J = 6.62 Hz, 2H), 4.21 (q, J = 7.06 Hz, 2H), 3.13 - 3.25 (m, 2H), 2.19 (s, 3H), 1.21 (s, 3H); LCMS (m/z): 383.2 [M+H]<sup>+</sup>.

15 Fourth Step

[0627]

To a stirred solution of ethyl 2-((2-methyl-4-[2-(2-pyridinyl)ethoxy]phenyl)amino)-4-oxo-4,5-dihydrofuran-3-carboxylate (0.15 g, 0.39 mmol) and 7-azaindole-3-carboxaldehyde (0.057 g, 0.39 mmol) in ethanol (5.0 mL), L-proline (5.0 mg, 0.043 mmol) was added at ambient temperature. The mixture was refluxed for 3 days. The solvent was removed under reduced pressure and the residue was purified by preparative HPLC to afford the titled compound as solid (0.015 g, y. 8%).

25 [0628]

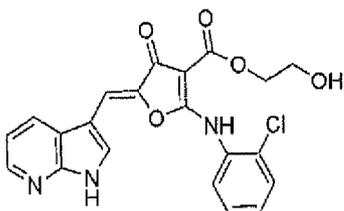
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 8.57 (d, J = 3.91 Hz, 1H), 8.11 (d, J = 3.91 Hz, 1H), 7.78 (t, J = 7.58 Hz, 1H), 7.65 - 7.73 (m, 2H), 7.44 (d, J = 7.82 Hz, 1H), 7.24 - 7.33 (m, 2H), 6.97 (br. s, 1H), 6.88 (d, J = 8.31 Hz, 1H), 6.63 - 6.72 (m, 2H), 4.45 (t, J = 6.36 Hz, 2H), 4.21 (d, J = 6.85 Hz, 2H), 3.23 - 3.27 (m, 2H), 2.17 (s, 3H), 1.27 (t, J = 6.85 Hz, 3H); LCMS (m/z): 511.2 [M+H]<sup>+</sup>.

Example 172

[0629]

2-Hydroxyethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(2-chlorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 181]



[0630]

A solution of the compound (0.10g, 0.24mmol) of Example 15, ethylene glycol (0.14 mL, 2.5 mmol) and zinc cluster catalyst (Zn<sub>4</sub>(OCOCF<sub>3</sub>)<sub>6</sub>O) (0.012 g, 0.012 mmol) in *N,N*-dimethylacetamide (2.0 mL) was stirred with the microwave synthesizer (Biotage Initiator™) at 130 °C for 1 h. Cooled to ambient temperature, the reaction mixture was purified by preparative HPLC to afford the

titled compound as solid (0.030 g, y. 29%).

[0631]

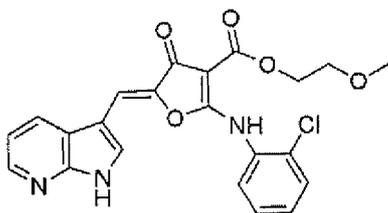
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.11 (br. s, 1H), 8.18 (d, J = 4.24 Hz, 1H), 7.82 (d, J = 7.34 Hz, 1H), 7.59 - 7.66 (m, 2H), 7.29 - 7.55 (m, 3H), 6.79 (dd, J = 4.65, 7.58 Hz, 1H), 6.62 (br. s, 1H), 4.12 - 4.22 (m, 2H), 3.65 (t, J = 4.89 Hz, 2H); LCMS (m/z): 426 [M+H]<sup>+</sup>.

Example 173

[0632]

2-Methoxyethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(2-chlorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 182]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 172.

[0633]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.12 (br. s, 1H), 8.18 (d, J = 4.04 Hz, 1H), 7.82 (d, J = 7.34 Hz, 1H), 7.58 - 7.67 (m, 2H), 7.32 - 7.54 (m, 3H), 6.79 (dd, J = 4.65, 7.58 Hz, 1H), 6.63 (br. s, 1H), 4.22 - 4.32 (m, 2H), 3.56 - 3.66 (m, 2H), 3.30 (s, 3H); LCMS

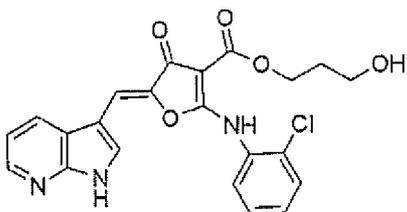
(m/z): 440.2 [M+H]<sup>+</sup>.

Example 174

[0634]

5 3-Hydroxypropyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-  
2-[(2-chlorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylat  
e

[Chemical Formula 183]



10 The titled compound(solid) was similarly prepared according to  
the procedure described in the Example 172.

[0635]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.23 (br. s, 1H), 10.70 (br. s, 1H),  
8.20 (d, *J* = 3.42 Hz, 1H), 7.62 - 7.85 (m, 4H), 7.43 - 7.58 (m,  
15 2H), 6.73 - 6.83 (m, 2H), 4.72 (br. s, 1H), 4.20 - 4.30 (m, 2  
H), 3.58 (t, *J* = 5.38 Hz, 2H), 1.75 - 1.89 (m, 2H); LCMS (m/z):  
440.2 [M+H]<sup>+</sup>.

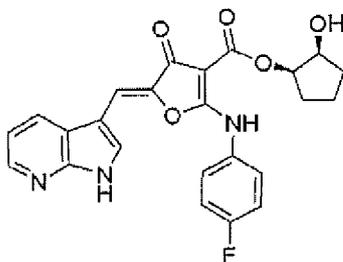
Example 175

20 [0636]

(1*R*,2*S*)-2-Hydroxycyclopentyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-*y*  
l)methylene]-2-[(4-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran

-3-carboxylate

[Chemical Formula 184]



[0637]

5 A solution of the compound (0.10g, 0.25mmol) of Example 21, (1  
*R*,2*S*)-1,2-cyclopentanediol (0.26 g, 2.5 mmol) and zinc cluster  
 catalyst ( $Zn_4(OCOCF_3)_6O$ ) (0.012 g, 0.012 mmol) in *N,N*-dimethyl  
 acetamide (1.5 mL) was stirred with the microwave synthesizer  
 (Biotage Initiator™) at 130 °C for 2 h. Cooled to ambient temp  
 10 erature, the precipitate was removed by filtration. The filtra  
 te was purified by preparative HPLC to afford the titled compo  
 und as solid (0.025 g, y. 20%).

[0638]

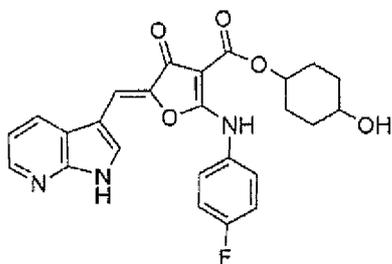
<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.26 (br. s, 1H), 10.60 (br. s, 1H),  
 15 8.26 (d, *J* = 4.40 Hz, 1H), 8.05 (d, *J* = 7.82 Hz, 1H), 7.77 (br.  
 s, 1H), 7.52 - 7.61 (m, 2H), 7.36 (t, *J* = 8.31 Hz, 2H), 6.94  
 (dd, *J* = 4.65, 7.58 Hz, 1H), 6.87 (br. s, 1H), 5.37 (br. s, 1H),  
 4.88 - 4.98 (m, 1H), 4.09 - 4.18 (m, 1H), 1.94 - 2.06 (m, 1H),  
 1.70 - 1.90 (m, 3H), 1.43 - 1.69 (m, 2H); LCMS (*m/z*): 450.2 [*M*  
 20 +H]<sup>+</sup>.

## Example 176

[0639]

4-Hydroxycyclohexyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(4-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 185]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 175.

10 [0640]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.26 (br. s, 1H), 10.65 (br. s, 1H), 8.25 (d, *J* = 2.93 Hz, 1H), 7.95 (d, *J* = 7.34 Hz, 1H), 7.75 (br. s, 1H), 7.55 - 7.65 (br. s, 2H), 7.36 (t, *J* = 8.07 Hz, 2H), 6.87 - 6.94 (m, 1H), 6.82 (br. s, 1H), 4.94 (br. s, 1H), 4.53 (br. s, 1H), 3.56 - 3.68 (m, 1H), 1.79 - 1.95 (m, 2H), 1.46 - 1.77 (m, 6H); LCMS (*m/z*): 463.8 [M+H]<sup>+</sup>.

15

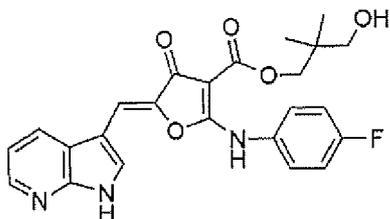
## Example 177

[0641]

20 3-Hydroxy-2,2-dimethylpropyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(4-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran

-3-carboxylate

[Chemical Formula 186]



[0642]

5 A solution of the compound (0.10g, 0.25mmol) of Example 21, 2,  
2-dimethyl-1,3-propanediol (0.40 g, 3.8 mmol) and zinc cluster  
catalyst ( $Zn_4(OCOCF_3)_6O$ ) (0.018 g, 0.019 mmol) in *N,N*-dimethyl  
acetamide (1.5 mL) was stirred with the microwave synthesizer  
(Biotage Initiator™) at 130 °C for 24 h. Cooled to ambient tem  
10 perature, the precipitate was removed by filtration. The filtrate  
was purified by preparative HPLC to afford the titled compound  
as solid (0.020 g, y. 17%).

[0643]

$^1H$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.27 (br. s, 1H), 10.68 (br. s, 1H),  
15 8.25 (d,  $J = 3.91$  Hz, 1H), 7.97 (d,  $J = 7.82$  Hz, 1H), 7.74 (br.  
s, 1H), 7.57 - 7.65 (m, 2H), 7.37 (t,  $J = 8.31$  Hz, 2H), 6.83 -  
6.97 (m, 2H), 4.88 (br. s, 1H), 3.93 - 4.02 (m, 2H), 3.26 - 3.  
36 (m, 2H), 0.93 (s, 6H); LCMS (m/z): 452.4  $[M+H]^+$ .

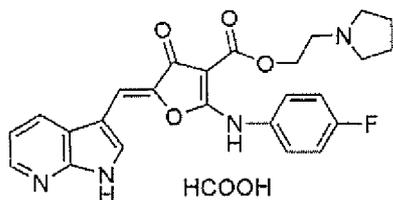
20 Example 178

[0644]

2-(1-Pyrrolidinyl)ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)met

ethylene]-2-[(4-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate formate

[Chemical Formula 187]



- 5 The titled compound(solid) was similarly prepared according to the procedure described in the Example 177.

[0645]

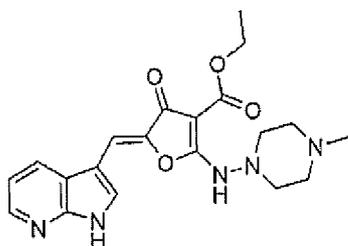
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.11 (br. s, 1H), 8.21 (d, J = 4.12 Hz, 1H), 8.17 (s, 1H), 7.96 (d, J = 7.83 Hz, 1H), 7.65 (s, 1H), 7.34 - 7.43 (m, 2H), 7.24 - 7.33 (m, 2H), 6.87 (dd, J = 4.89, 7.34 Hz, 1H), 6.65 (s, 1H), 4.25 - 4.38 (m, 2H), 3.03 - 3.12 (m, 2H), 2.87 - 3.00 (m, 4H), 1.65 - 1.80 (m, 4H); LCMS (m/z): 463.2 [M+H]<sup>+</sup>.

- 15 Example 179

[0646]

Ethyl 5-[(1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-2-[(4-methyl-1-piperazinyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 188]



[0647]

To a solution of ethyl 2-[(4-methyl-1-piperazinyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.080 g, 0.30 mmol) which si  
 5 milarly prepared according to the procedure described in the E  
 xample 74, Fourth step and 7-azaindole-3-carboxaldehyde (0.040  
 g, 0.30 mmol) in ethanol (2.0 mL), L-proline (0.020 g, 0.17 mm  
 ol) was added at ambient temperature. The mixture was refluxed  
 for 1.5 days. Cooled to ambient temperature, the precipitate  
 10 was collected by filtration, washed with ethanol and hexane th  
 en dried to afford the titled compound as solid (0.017 g, y. 1  
 4%).

[0648]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.36 (br. s, 1H), 9.95 (br. s, 1H), 8.  
 15 96 (d, J = 7.34 Hz, 1H), 8.35 (d, J = 3.42 Hz, 1H), 8.11 (br. s,  
 1H), 7.23 (dd, J = 4.65, 7.58 Hz, 1H), 6.85 (br. s, 1H), 4.21  
 (q, J = 7.30 Hz, 2H), 3.06 (br. s, 3H), 2.43 - 2.70 (m, 6H), 2.  
 24 - 2.35 (m, 2H), 1.26 (t, J = 6.85 Hz, 3H); LCMS (m/z): 398.2  
 [M+H]<sup>+</sup>.

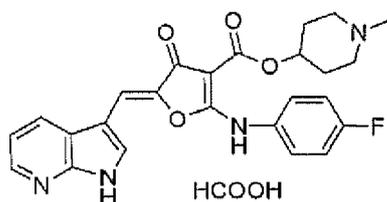
20

Example 180

[0649]

1-Methyl-4-piperidinyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(4-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate formate

5 [Chemical Formula 189]



[0650]

A solution of the compound (0.10g, 0.25mmol) of Example 21, 4-hydroxy-1-methylpiperidine (0.44 g, 3.8 mmol) and zinc cluster catalyst ( $Zn_4(OCOCH_3)_6O$ ) (0.018 g, 0.019 mmol) in *N,N*-dimethyl acetamide (1.0 mL) was stirred at 180 °C for 16 h then at 130 °C for further 16 h. Cooled to ambient temperature, the precipitate was removed by filtration. The filtrate was purified by preparative HPLC to afford the titled compound as solid (0.016 g, 15 y. 13%).

[0651]

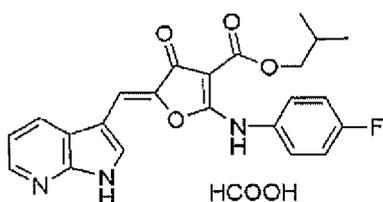
$^1H$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.15 (br. s, 1H), 8.23 (d,  $J = 3.91$  Hz, 1H), 8.18 (s, 1H), 7.96 (d,  $J = 7.82$  Hz, 1H), 7.69 (s, 1H), 7.42 - 7.49 (m, 2H), 7.25 - 7.36 (m, 2H), 6.89 (dd,  $J = 4.89, 7.8$  20 3 Hz, 1H), 6.68 (s, 1H), 4.83 - 4.93 (m, 1H), 2.77 - 2.87 (m, 2H), 2.35 - 2.45 (m, 2H), 2.30 (s, 3H), 1.85 - 1.95 (m, 2H), 1.68 - 1.80 (m, 2H); LCMS (m/z): 463.2 [M+H] $^+$ .

Example 181

[0652]

Isobutyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(4-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate formate

[Chemical Formula 190]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 180.

[0653]

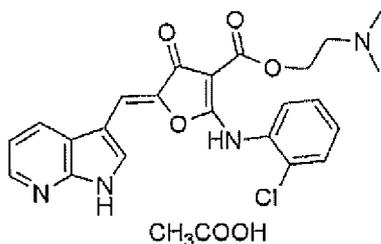
<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.17 (br. s, 1H), 8.23 (d, *J* = 3.91 Hz, 1H), 8.19 (s, 1H), 7.96 (d, *J* = 7.82 Hz, 1H), 7.70 (s, 1H), 7.43 - 7.54 (m, 2H), 7.31 (t, *J* = 8.07 Hz, 2H), 6.84 - 6.96 (m, 1H), 6.72 (br. s, 1H), 3.96 (d, *J* = 5.87 Hz, 2H), 1.90 - 2.05 (m, 1H), 0.97 (d, *J* = 6.36 Hz, 6H); LCMS (*m/z*): 422.2 [M+H]<sup>+</sup>.

Example 182

[0654]

2-(Dimethylamino)ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(2-chlorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate acetate

[Chemical Formula 191]



[0655]

A solution of the compound (0.10g, 0.24mmol) of Example 15, 2-(dimethylamino)ethanol (0.40 mL, 4.0 mmol), 4-dimethylaminopyridine (0.010 g, 0.082 mmol) and zinc cluster catalyst (Zn<sub>4</sub>(OCOCF<sub>3</sub>)<sub>6</sub>O) (0.018 g, 0.019 mmol) in *N,N*-dimethylacetamide (2.0 mL) was stirred at 130 °C for 24 h. Cooled to ambient temperature, the precipitate was removed by filtration. The filtrate was purified by preparative HPLC (aqueous ammonium acetate/acetonitrile as eluents) to afford the titled compound as solid (0.012 g, y. 11%).

[0656]

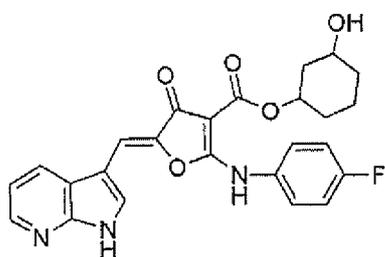
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 11.92 (br. s, 1H), 8.15 (d, J = 3.91 Hz, 1H), 7.86 (d, J = 7.82 Hz, 1H), 7.48 - 7.55 (m, 2H), 7.30 - 7.37 (m, 1H), 7.15 - 7.23 (m, 2H), 6.73 - 6.79 (m, 1H), 6.39 (s, 1H), 4.30 - 4.39 (m, 2H), 3.12 - 3.22 (m, 2H), 2.73 (br. s, 6H), 1.91 (s, 3H); LCMS (m/z): 453.0 [M+H]<sup>+</sup>.

20 Example 183

[0657]

3-Hydroxycyclohexyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(4-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 192]



5

[0658]

A solution of the compound (0.10g, 0.25mmol) of Example 21, 1, 3-cyclohexanediol (0.44 g, 3.8 mmol) and zinc cluster catalyst ( $Zn_4(OCOCF_3)_6O$ ) (0.018 g, 0.019 mmol) in *N,N*-dimethylacetamide (1.0 mL) was stirred at 130 °C for 1.5 days. Cooled to ambient temperature, the precipitate was removed by filtration. The filtrate was purified by preparative HPLC to afford the titled compound as solid (0.010 g, y. 13%).

10

[0659]

$^1H$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.25 (br. s, 1H), 8.24 (d,  $J = 3.91$  Hz, 1H), 7.92 - 8.00 (m, 1H), 7.74 (br. s, 1H), 7.55 - 7.65 (m, 2 H), 7.31 - 7.42 (m, 2H), 6.90 (dd,  $J = 4.89, 7.82$  Hz, 1H), 6.78 - 6.86 (m, 1H), 5.19 - 5.28 (m, 1H), 4.92 - 5.02 (m, 1H), 4.55 (d,  $J = 3.42$  Hz, 1H), 1.15 - 2.08 (m, 8H); LCMS ( $m/z$ ): 463.8

15

20

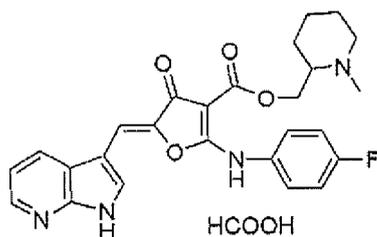
[ $M+H$ ] $^+$ .

## Example 184

[0660]

(1-Methyl-2-piperidinyl)methyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(4-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate formate

[Chemical Formula 193]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 183.

10 [0661]

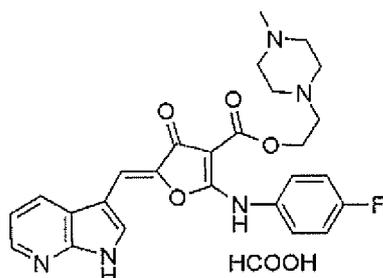
<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.11 (br. s, 1H), 8.22 (d, *J* = 4.40 Hz, 1H), 8.16 (s, 1H), 7.98 (d, *J* = 7.82 Hz, 1H), 7.66 (s, 1H), 7.34 - 7.42 (m, 2H), 7.25 - 7.33 (m, 2H), 6.88 (dd, *J* = 4.65, 7.58 Hz, 1H), 6.65 (s, 1H), 4.23 - 4.35 (m, 2H), 2.90 - 3.00 (m, 1H), 2.62 - 2.72 (m, 1H), 2.46 - 2.56 (m, 4H), 1.18 - 1.83 (m, 6H); LCMS (*m/z*): 477.4 [M+H]<sup>+</sup>.

## Example 185

[0662]

20 2-(4-Methyl-1-piperazinyl)ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(4-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate formate

[Chemical Formula 194]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 183.

5 [0663]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.14 (br. s, 1H), 8.16 - 8.25 (m, 2H), 7.95 (d, J = 6.85 Hz, 1H), 7.67 (br. s, 1H), 7.38 - 7.48 (m, 2H), 7.25 - 7.36 (m, 2H), 6.84 - 6.91 (m, 1H), 6.68 (br. s, 1H), 4.20 - 4.34 (m, 2H), 2.22 - 2.71 (m, 10H), 2.13 (br. s, 3H); L

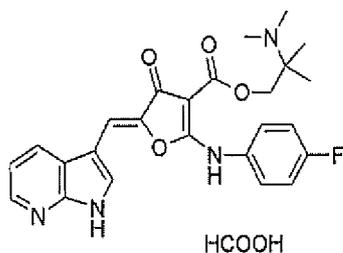
10 CMS (m/z): 492.4 [M+H]<sup>+</sup>.

Example 186

[0664]

2-(*N,N*-Dimethylamino)-2-methylpropyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(4-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate formate

[Chemical Formula 195]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 183.

[0665]

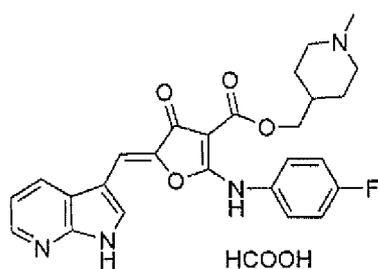
5  $^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.01 (br. s, 1H), 8.15 - 8.29 (m, 2H), 7.98 (d,  $J = 7.34$  Hz, 1H), 7.60 (br. s, 1H), 7.05 - 7.33 (m, 4H), 6.83 - 6.93 (m, 1H), 6.47 (s, 1H), 4.20 (br. s, 2H), 2.55 (br. s, 6H), 1.22 (br. s, 6H); LCMS (m/z): 465.0 [M+H] $^+$ .

10 Example 187

[0666]

(1-Methyl-4-piperidinyl)methyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(4-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate formate

15 [Chemical Formula 196]



The titled compound(solid) was similarly prepared according to

the procedure described in the Example 183.

[0667]

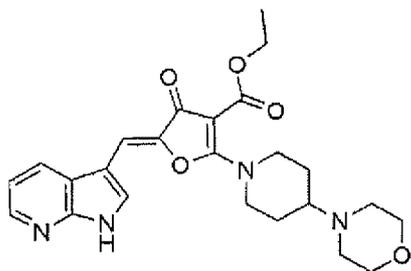
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.09 (br. s, 1H), 8.18 - 8.24 (m, 2H),  
7.96 (d, J = 7.82 Hz, 1H), 7.66 (s, 1H), 7.33 - 7.43 (m, 2H),  
7.22 - 7.32 (m, 2H), 6.89 (dd, J = 4.89, 7.83 Hz, 2H), 6.59 (s,  
1H), 4.01 (d, J = 6.36 Hz, 2H), 2.88 - 2.96 (m, 2H), 2.29 (s,  
3H), 2.03 - 2.15 (m, 2H), 1.62 - 1.82 (m, 3H), 1.26 - 1.41 (m,  
2H); LCMS (m/z): 477.3 [M+H]<sup>+</sup>.

10 Example 188

[0668]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-(4-morpholinopiperidin-1-yl)-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 197]



15

[0669]

To a stirred solution of ethyl 2-(4-morpholinopiperidin-1-yl)-  
4-oxo-4,5-dihydrofuran-3-carboxylate (0.10 g, 0.31 mmol) which  
was similarly prepared according to the procedure described in the  
Example 74, Fourth step and 7-azaindole-3-carboxaldehyde (0.  
045 g, 0.31 mmol) in ethanol (10 mL), piperidine (0.020 mL, 0.

20

20 mmol) was added at ambient temperature. The mixture was refluxed for 16 h. Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol and hexane then dried to afford the titled compound (0.018 g, y. 13%) as solid.

[0670]

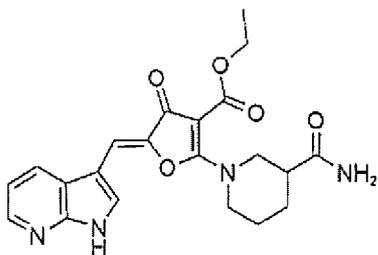
$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.31 (br. s, 1H), 8.37 (d,  $J = 7.34$  Hz, 1H), 8.31 (d,  $J = 3.42$  Hz, 1H), 7.97 (br. s, 1H), 7.16 - 7.23 (m, 1H), 6.85 (s, 1H), 4.11 - 4.30 (m, 4H), 3.52 - 3.64 (m, 4H), 3.23 - 3.43 (m, 7H), 1.90 - 2.02 (m, 2H), 1.54 - 1.76 (m, 2H), 1.24 (t,  $J = 6.60$  Hz, 3H); LCMS ( $m/z$ ): 453.2  $[\text{M}+\text{H}]^+$ .

Example 189

[0671]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-(3-carbamoylpiperidino)-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 198]



[0672]

To a solution of ethyl 2-(3-carbamoylpiperidino)-4-oxo-4,5-dihydrofuran-3-carboxylate (0.15 g, 0.53 mmol) which similarly p

repared according to the procedure described in the Example 74,  
Fourth step and 7-azaindole-3-carboxaldehyde (0.078 g, 0.53 mmol) in ethanol (10 mL), piperidine (0.020 mL, 0.20 mmol) was added at ambient temperature. The mixture was refluxed for 16 h. Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol and hexane then dried to afford the titled compound as solid (0.018 g, y. 9%).

[0673]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.34 (br. s, 1H), 8.38 (d, J = 7.52 Hz, 1H), 8.31 (d, J = 3.72 Hz, 1H), 7.97 (br. s, 1H), 7.44 (br. s, 1H), 7.13 - 7.23 (m, 1H), 6.99 (br. s, 1H), 6.85 (s, 1H), 4.10 - 4.22 (m, 4H), 3.25 - 3.46 (m, 2H), 2.54 - 2.64 (m, 1H), 1.96 - 2.06 (m, 1H), 1.82 - 1.92 (m, 1H), 1.60 - 1.74 (m, 2H), 1.24 (t, J = 6.85 Hz, 3H); LCMS (m/z): 411.4 [M+H]<sup>+</sup>.

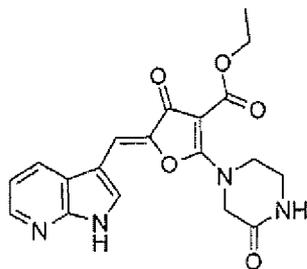
15

Example 190

[0674]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-4-oxo-2-(3-oxopiperazino)-4,5-dihydrofuran-3-carboxylate

20 [Chemical Formula 199]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 189.

[0675]

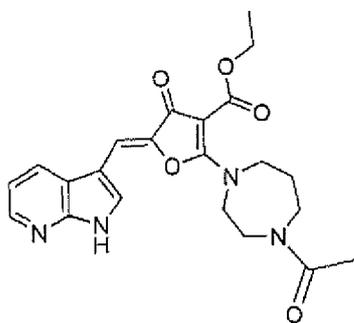
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.38 (br. s, 1H), 8.29 - 8.44 (m, 2H),  
5 8.01 (br. s, 1H), 7.15 - 7.25 (m, 1H), 6.92 (br. s, 1H), 4.30  
- 4.40 (m, 2H), 4.11 - 4.23 (m, 2H), 3.92 - 4.04 (m, 2H), 3.41  
- 3.49 (m, 2H), 1.18 - 1.31 (m, 3H); LCMS (m/z): 383.0 [M+H]<sup>+</sup>.

Example 191

10 [0676]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-(4-acety  
1-1,4-diazepanyl)-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 200]



15 The titled compound (solid) was similarly prepared according to the procedure described in the Example 189.

[0677]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.36 (br. s, 1H), 8.41 (d, J = 7.68 Hz,  
1H), 8.35 (d, J = 4.36 Hz, 1H), 7.99 (br. s, 1H), 7.17 - 7.29  
20 (m, 1H), 6.89 (d, J = 3.91 Hz, 1H), 4.15 - 4.27 (m, 2H), 3.92 -

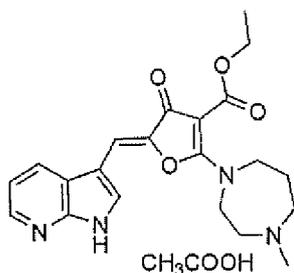
4.10 (m, 3H), 3.73 - 3.90 (m, 3H), 3.51 - 3.64 (m, 2H), 1.83 - 2.08 (m, 5H), 1.28 (t,  $J = 6.60$  Hz, 3H); LCMS ( $m/z$ ): 425.3 [ $M+H$ ]<sup>+</sup>.

5 Example 192

[0678]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-(4-methyl-1,4-diazepanyl)-4-oxo-4,5-dihydrofuran-3-carboxylate acetate

10 [Chemical Formula 201]



[0679]

The titled compound(solid) was similarly prepared according to the procedure described in the Example 189. Further, preparative HPLC (aqueous ammonium acetate/acetonitrile) was used as purification procedure.

[0680]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>)  $\delta$  (ppm) 12.48 (br. s, 1H), 8.36 (d,  $J = 7.82$  Hz, 1H), 8.30 (d,  $J = 4.40$  Hz, 1H), 7.96 (s, 1H), 7.18 (dd,  $J = 4.89, 7.82$  Hz, 1H), 6.85 (s, 1H), 4.16 (q,  $J = 7.34$  Hz, 2H), 3.70 - 3.92 (m, 4H), 2.72 - 2.82 (m, 2H), 2.53 - 2.63 (m, 2H), 2.28

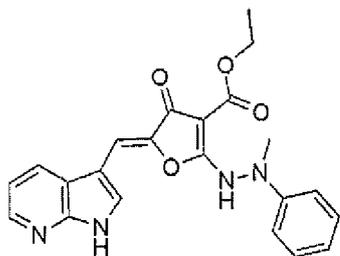
(s, 3H), 1.92 -2.02 (m, 2H), 1.62 (s, 3H), 1.24 (t, J = 7.09 Hz, 3H); LCMS (m/z): 397.2 [M+H]<sup>+</sup>.

Example 193

[0681]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-(2-methyl-1-2-phenylhydrazinyl)-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 202]



[0682]

To a solution of ethyl 2-(2-methyl-2-phenylhydrazinyl)-4-oxo-4,5-dihydrofuran-3-carboxylate (0.10 g, 0.36 mmol) which similarly prepared according to the procedure described in the Example 74, Fourth step and 7-azaindole-3-carboxaldehyde (0.053 g, 0.36 mmol) in ethanol (10 mL), L-proline (0.020 g, 0.17 mmol) was added at ambient temperature. The mixture was refluxed for 2 days. Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol and hexane then dried to afford the titled compound as solid (0.015 g, y. 10%).

[0683]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.28 (br. s, 1H), 10.79 (s, 1H), 8.48

(d,  $J = 8.31$  Hz, 1H), 8.22 (d,  $J = 3.91$  Hz, 1H), 7.90 (br. s, 1H), 7.32 (t,  $J = 7.82$  Hz, 2H), 6.83 - 7.05 (m, 5H), 4.25 (q,  $J = 6.85$  Hz, 2H), 3.34 (s, 3H), 1.29 (t,  $J = 6.85$  Hz, 3H); LCMS (m/z): 405.2 [M+H]<sup>+</sup>.

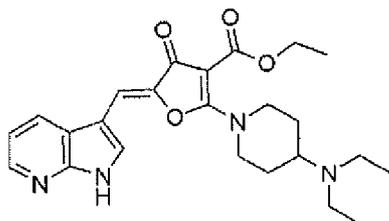
5

Example 194

[0684]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[4-(diethylamino)piperidino]-4-oxo-4,5-dihydrofuran-3-carboxylate

10 {Chemical Formula 203}



First Step

[0685]

Under a nitrogen atmosphere, to a solution of *tert*-butyl 4-oxopiperidine-1-carboxylate (5.0 g, 0.025 mol) and diethylamine (9.1 mL, 0.090 mol) in methanol (40 mL), 10% palladium on carbon (0.50 g) was added at ambient temperature. The reaction mixture was agitated under a hydrogen atmosphere at ambient temperature for 16 h. Palladium on carbon was removed by filtration with Celite and the solvent was removed under reduced pressure, then the residue was purified by chromatography on silica gel (dichloromethane/methanol) to afford *tert*-butyl 4-(diethyla

15  
20

mino)piperidine-1-carboxylate as solid (6.1 g, y. 95%).

[0686]

$^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  (ppm) 4.12 (br. s, 2H), 3.76 - 3.89 (m, 1H), 2.45 - 2.72 (m, 6H), 1.30 - 1.53 (m, 13H), 0.90 - 1.10 (m, 6H)

5

Second Step

[0687]

Cooled with ice bath, 4M hydrochloric acid in dioxane (25 mL) was added to *tert*-butyl 4-(*N,N*-diethylamino)piperidine-1-carboxylate (6.1 g, 0.024 mol) and the mixture was stirred at ambient temperature for 2 h. The solvent was removed under reduced pressure, and the residue was suspended in diethyl ether, then the precipitate was collected by filtration, washed with diethyl ether and then dried to afford 4-(diethylamino)piperidine dihydrochloride as solid (3.9 g, y. 99%).

10  
15

Third Step

[0688]

To a solution of 4-(diethylamino)piperidine dihydrochloride (3.0 g, 0.019 mmol) in water (20 mL), 2M sodium hydroxide solution (5.0 mL) was added at ambient temperature. The mixture was stirred for 30 min. The solvent was removed under reduced pressure, and methanol (10 mL) was added to the crude material, then the residue was removed by filtration. The filtrate was concentrated and dried to afford 4-(diethylamino)piperidine (1.7 g,

20  
25

y. 77%) as solid.

[0689]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 3.20 - 3.29 (m, 2H), 3.09 - 3.14 (m, 1  
H), 2.77 - 2.93 (m, 3H), 2.52 - 2.62 (m, 4H), 1.64 - 1.90 (m, 4  
5 H), 1.00 (t, J = 7.04 Hz, 6H)

#### Fourth Step

[0690]

A solution of 4-(diethylamino)piperidine (0.50 g, 3.2 mmol), e  
10 thyl 2-ethoxy-4-oxo-4,5-dihydrofuran-3-carboxylate (0.76 g, 3.  
8 mmol) which afforded in the Example 74, Third step and triet  
hylamine (0.60 mL, 4.3 mmol) in tetrahydrofuran (10 mL) was st  
irred at ambient temperature for 24 h. The solvent was removed  
under reduced pressure, then the crude material was purified  
15 by chromatography on silica gel (dichloromethane/methanol) to a  
fford ethyl 2-[4-(diethylamino)piperidino]-4-oxo-4,5-dihydrof  
uran-3-carboxylate as oil (0.29 g, y. 30%).

[0691]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 4.53 (s, 2H), 4.03 - 4.15 (m, 4H), 3.0  
20 5 - 3.19 (m, 2H), 2.82 (br. s, 1H), 2.42 - 2.58 (m, 4H), 1.73 -  
1.86 (m, 2H), 1.40 - 1.59 (m, 2H), 1.20 (t, J = 7.08 Hz, 3H),  
0.91 - 1.02 (m, 6H); LCMS (m/z): 311.0 [M+H]<sup>+</sup>

#### Fifth Step

25 [0692]

To a solution of ethyl 2-[4-(diethylamino)piperidino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.10 g, 0.30 mmol) and 7-azaindole-3-carboxaldehyde (0.047 g, 0.30 mmol) in ethanol (5.0 mL), L-proline (0.0040 mg, 0.035 mmol) was added at ambient temperature. The mixture was refluxed for 16 h. Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol and hexane then dried to afford the titled compound as solid (0.035 g, y. 25%).

[0693]

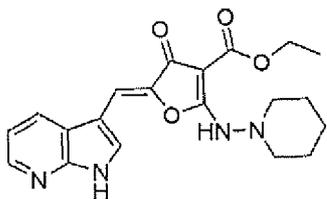
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.30 (br. s, 1H), 8.37 (d, J = 7.82 Hz, 1H), 8.31 (d, J = 3.91 Hz, 1H), 7.97 (s, 1H), 7.19 (dd, J = 4.89, 7.82 Hz, 1H), 6.84 (s, 1H), 4.11 - 4.33 (m, 4H), 3.27 - 3.37 (m, 2H), 2.82 - 2.92 (m, 1H), 2.41 - 2.60 (m, 4H), 1.82 - 1.92 (m, 2H), 1.56 - 1.71 (m, 2H), 1.24 (t, J = 6.85 Hz, 3H), 0.98 (t, J = 7.09 Hz, 6H); LCMS (m/z): 439.4 [M+H]<sup>+</sup>.

Example 195

[0694]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-4-oxo-2-(*N*-piperidinoamino)-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 204]



[0695]

To a solution of ethyl 4-oxo-2-(*N*-piperidinoamino)-4,5-dihydrofuran-3-carboxylate (0.25 g, 0.98 mmol) which similarly prepared according to the procedure described in the Example 74, Forth step and 7-azaindole-3-carboxaldehyde (0.14 g, 0.98 mmol) in ethanol (10 mL), L-proline (0.011 mg, 0.096 mmol) was added at ambient temperature. The mixture was refluxed for 2 days. Cooled to ambient temperature, the precipitate was collected by filtration, washed with ethanol and diethyl ether then dried to afford the titled compound as solid (0.015 g, y. 4%).

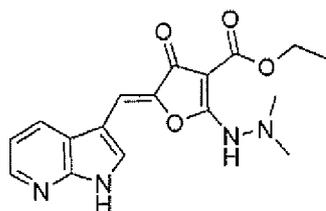
[0696]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.34 (br. s, 1H), 9.86 (br. s, 1H), 9.00 (d, *J* = 7.82 Hz, 1H), 8.33 (d, *J* = 3.91 Hz, 1H), 8.10 (d, *J* = 2.45 Hz, 1H), 7.18 (dd, *J* = 4.65, 8.07 Hz, 1H), 6.85 (s, 1H), 4.20 (q, *J* = 6.85 Hz, 2H), 2.95 - 3.05 (m, 4H), 1.69 - 1.79 (m, 4H), 1.42 - 1.53 (m, 2H), 1.26 (t, *J* = 6.85 Hz, 3H); LCMS (*m/z*): 383.2 [M+H]<sup>+</sup>.

Example 196

[0697]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-(2,2-dimethylhydrazinyl)-4-oxo-4,5-dihydrofuran-3-carboxylate  
[Chemical Formula 205]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 195.

[0698]

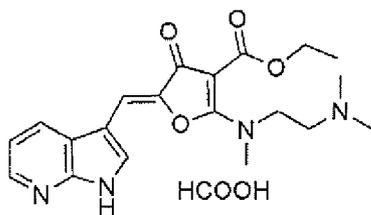
- 5  $^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 11.85 (br. s, 1H), 8.52 (d,  $J = 7.82$  Hz, 1H), 8.23 (d,  $J = 3.91$  Hz, 1H), 7.83 (s, 1H), 7.10 (dd,  $J = 4.89$ , 7.82 Hz, 1H), 6.14 (s, 1H), 4.02 (q,  $J = 6.85$  Hz, 2H), 1.70 (s, 6H), 1.18 (t,  $J = 7.09$  Hz, 3H); LCMS (m/z): 342.8 [M+H] $^+$ .

10 Example 197

[0699]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[[2-(dimethylamino)ethyl]-*N*-methylamino]-4-oxo-4,5-dihydrofuran-3-carboxylate formate

15 [Chemical Formula 206]



[0700]

To a solution of ethyl 2-[[2-(dimethylamino)ethyl]-*N*-methylamino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.20 g, 0.78 mmol)

which similarly prepared according to the procedure described in the Example 74, Fourth step and 7-azaindole-3-carboxaldehyde (0.11 g, 0.78 mmol) in ethanol (6.0 mL), L-proline (0.0093 mg, 0.078 mmol) was added at ambient temperature. The mixture was refluxed for 20 h. Cooled to ambient temperature, the reaction mixture was purified by preparative HPLC to afford the titled compound as solid (0.035 g, y. 12%).

[0701]

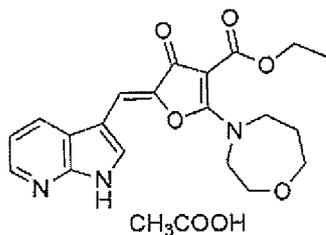
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.35 (br. s, 1H), 8.38 (d, J = 7.83 Hz, 1H), 8.27 - 8.34 (m, 1H), 8.18 (s, 1H), 7.98 (s, 1H), 7.16 - 7.22 (m, 1H), 6.85 (s, 1H), 4.17 (q, J = 6.85 Hz, 2H), 3.83 (t, J = 6.60 Hz, 2H), 3.29 (br. s, 3H), 2.54 - 2.61 (m, 2H), 2.19 (s, 6H), 1.21 - 1.28 (m, 3H); LCMS (m/z): 385.0 [M+H]<sup>+</sup>.

15 Example 198

[0702]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-(1,4-oxazepan-4-yl)-4-oxo-4,5-dihydrofuran-3-carboxylate acetate

[Chemical Formula 207]



[0703]

The titled compound (solid) was similarly prepared according t

o the procedure described in the Example 197. Further, preparative HPLC (aqueous ammonium acetate/acetonitrile) was used as purification procedure.

[0704]

5  $^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 8.35 (d,  $J = 7.82$  Hz, 1H), 8.30 (d,  $J = 4.40$  Hz, 1H), 7.97 (s, 1H), 7.18 (dd,  $J = 4.89, 7.82$  Hz, 1H), 6.87 (s, 1H), 4.17 (q,  $J = 7.17$  Hz, 2H), 3.80 - 4.01 (m, 6H), 3.74 (t,  $J = 5.14$  Hz, 2H), 1.95 - 2.07 (m, 2H), 1.63 (s, 3H), 1.24 (t,  $J = 7.09$  Hz, 3H); LCMS ( $m/z$ ): 383.8  $[\text{M}+\text{H}]^+$ .

10

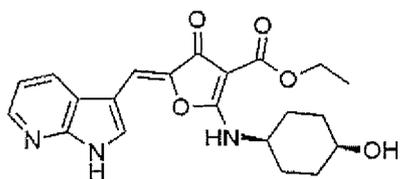
Example 199

[0705]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(*cis*-4-hydroxycyclohexyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

15

[Chemical Formula 208]



First Step

[0706]

20 Cooled with ice bath, to a mixed solution of cyclohexanone oxime (4.0 g, 0.035 mol) in dichloromethane (40 mL) and ethanol (5.0 mL), *tert*-butyl hypochlorite (4.7 mL, 0.038 mol) was added dropwise and the reaction mixture was cooled to  $-20$  °C then s

tirred for 30 min. To this reaction mixture, 1,3-cyclohexadiene (5.0 mL, 0.052 mol) was added dropwise and the reaction mixture was allowed to warm to 0 °C then stirred for 4 days. The reaction mixture was concentrated under reduced pressure to half the solvents, and then diethyl ether (80 mL) was added at ambient temperature then the mixture was stirred for further 1 day. To this reaction mixture, ethanol (10 mL) was added and the mixture was stirred for further 4 h, then the precipitate was collected by filtration. The solid was washed with mixed solution of diethyl ether/ethanol (10/1), diethyl ether and hexane then dried to afford 2-oxa-3-azabicyclo[2.2.2]-5-octene hydrochloride as solid (4.2 g, y. 82%).

[0707]

<sup>1</sup>H NMR (CDCl<sub>3</sub>) δ (ppm) 12.43 (br. s, 1H), 11.29 (br. s, 1H), 6.81 - 6.88 (m, 1H), 6.64 - 6.71 (m, 1H), 4.87 - 4.93 (m, 1H), 4.58 - 4.65 (m, 1H), 2.54 - 2.66 (m, 1H), 2.31 - 2.47 (m, 1H), 1.45 - 1.59 (m, 2H)

Second Step

[0708]

Under a nitrogen atmosphere, to a mixed solution of 2-oxa-3-azabicyclo[2.2.2]-5-octene hydrochloride (0.20 g, 1.4 mol) in ethanol (2.0 mL) and methanol (1.0 mL), platinum oxide (0.12 g, 0.53 mmol) was added at ambient temperature. The reaction mixture was agitated under a hydrogen atmosphere at ambient temperature

rature for 6.5 h. Platinum oxide was removed by filtration with Celite, cooled this filtrate with ice bath, and 2M hydrochloric acid in ethanol (1.6 mL, 3.2 mmol) was added then the mixture was stirred for 10 min. The solvent was removed under reduced pressure, then 2-propanol (2.0 mL) and ethanol (0.20 mL) were added to the residue then the mixture was refluxed for 40 min and filtered. The filtrate was refluxed for further 10 min, stirred at ambient temperature for 14 h, then cooled with ice bath and stirred for further 30 min. The precipitate was collected by filtration, washed with ice-cold 2-propylalcohol and hexane then dried to afford *cis*-4-aminocyclohexanol hydrochloride as solid (0.056 g, y. 27%).

[0709]

$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 7.92 (br. s, 3H), 4.47 (br. s, 1H), 3.70 - 3.82 (m, 1H), 2.89 - 3.04 (m, 1H), 1.57 - 1.76 (m, 6H), 1.37 - 1.51 (m, 2H)

Third Step

[0710]

To a solution of *cis*-4-aminocyclohexanol hydrochloride (0.051 g, 0.34 mmol) and ethyl 2-ethoxy-4-oxo-4,5-dihydrofuran-3-carboxylate (0.073 g, 0.37 mmol) which afforded in the Example 74, Third step in ethanol (0.8 mL), triethylamine (0.052 mL, 0.37 mmol) was added. The mixture was stirred at ambient temperature for 1 h. To this reaction mixture, 7-azaindole-3-carboxaldehyde

hyde (0.044 g, 0.30 mmol) and piperidine (0.0067 mL, 0.067 mmol) was added at ambient temperature then the mixture was refluxed for 4 days. Ethanol (2.0 mL) was added then the mixture was refluxed for further 1 h, the precipitate was collected by filtration, washed with hot ethanol. The solid was washed with hexane then dried to afford the titled compound as solid (0.013 g, y. 11%).

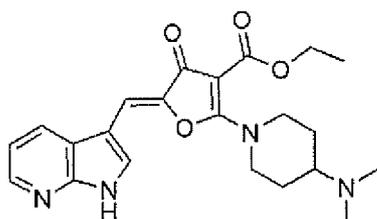
[0711]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.33 (br. s, 1H), 8.50 (d, J = 8.03 Hz, 1H), 8.42 (d, J = 7.78 Hz, 1H), 8.32 (dd, J = 1.38, 4.64 Hz, 1H), 8.02 (d, J = 2.51 Hz, 1H), 7.20 (dd, J = 4.64, 7.91 Hz, 1H), 6.90 (s, 1H), 4.55 (d, J = 3.26 Hz, 1H), 4.22 (q, J = 7.03 Hz, 2H), 4.03 - 4.14 (m, 1H), 3.74 - 3.82 (m, 1H), 1.90 - 2.02 (m, 2H), 1.72 - 1.81 (m, 2H), 1.61 - 1.69 (m, 4H), 1.26 (t, J = 7.15 Hz, 3H); LCMS (m/z): 396.1 [M+H]<sup>+</sup>.

Example 200

[0712]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[4-(dimethylamino)piperidino]-4-oxo-4,5-dihydrofuran-3-carboxylate  
[Chemical Formula 209]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 194.

[0713]

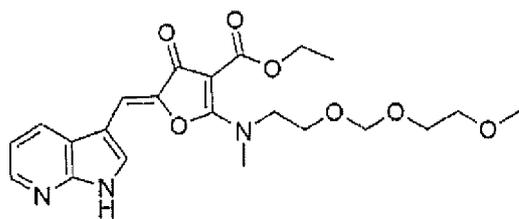
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.37 (br. s, 1H), 8.39 (d, J = 7.00 Hz, 1H), 8.33 (d, J = 5.16 Hz, 1H), 8.01 (s, 1H), 7.21 (dd, J = 5.12, 7.72 Hz, 1H), 6.89 (s, 1H), 4.35 - 4.45 (m, 2H), 4.13 - 4.23 (m, 2H), 3.88 - 3.98 (m, 1H), 3.61 - 3.71 (m, 1H), 3.51 - 3.61 (m, 1H), 2.50 (s, 6H), 2.18 - 2.28 (m, 1H), 1.95 - 2.05 (m, 1H), 1.80 - 1.95 (m, 1H), 1.25 (t, J = 6.96 Hz, 3H); LCMS (m/z): 411.2 [M+H]<sup>+</sup>.

Example 201

[0714]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(2-methoxyethoxy)methoxy]ethyl)-*N*-methylamino)-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 210]



First Step

[0715]

To a solution of ethyl 2-[(2-hydroxyethyl)-*N*-methylamino]-4-oxo-4,5-dihydrofuran-3-carboxylate (0.5 g, 2.18 mmol) which sim

ilarly prepared according to the procedure described in the Example 74, Fourth step in dichloromethane (6.0 mL) that cooled with ice bath, diisopropylethylamine (0.75 mL, 4.36 mmol) then 2-methoxyethoxymethyl chloride (0.5 mL, 4.36 mmol) were added.

5 The reaction mixture was allowed to warm to ambient temperature and stirred for 16 h. The reaction mixture was diluted with water, extracted with ethyl acetate for 3 times. The organic layer was dried over sodium sulfate and concentrated. The residue was purified by chromatography on silica gel (hexane/ethyl acetate) to afford ethyl 2-((2-((2-methoxyethoxy)methoxy)ethyl)-N-methylamino)-4-oxo-4,5-dihydrofuran-3-carboxylate as oil (0.31 g, y. 46%).

[0716]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 4.62 (s, 2H), 4.54 (s, 2H), 4.10 (q, J = 7.04 Hz, 2H), 3.63 - 3.80 (m, 4H), 3.52 - 3.62 (m, 2H), 3.38 - 3.48 (m, 2H), 3.24 (s, 3H), 3.12 (s, 3H), 1.20 (t, J = 7.04 Hz, 3H); LCMS (m/z): 230.0 [M+H]<sup>+</sup>

Second Step

20 [0717]

To a solution of ethyl 2-((2-((2-methoxyethoxy)methoxy)ethyl)-N-methylamino)-4-oxo-4,5-dihydrofuran-3-carboxylate (0.146 g, 0.46 mmol) and 7-azaindole-3-carboxaldehyde (0.067 g, 0.46 mmol) in ethanol (6.0 mL), L-proline (0.005 g, 0.046 mmol) was added at ambient temperature. The mixture was refluxed for 16 h.

Cooled to ambient temperature, the reaction mixture was purified by chromatography on silica gel (hexane/ethyl acetate) to afford the titled compound as solid (0.035 g, y. 17%).

[0718]

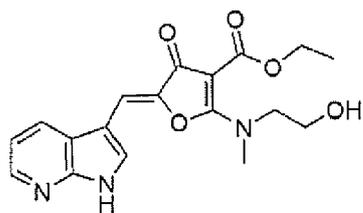
5 <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.33 (br. s, 1H), 8.39 (d, J = 7.34 Hz, 1H), 8.31 (d, J = 4.40 Hz, 1H), 7.98 (s, 1H), 7.19 (dd, J = 4.65, 7.58 Hz, 1H), 6.85 (s, 1H), 4.64 (s, 2H), 4.16 (q, J = 7.17 Hz, 2H), 3.93 - 4.00 (m, 2H), 3.75 - 3.83 (m, 2H), 3.51 - 3.59 (m, 2H), 3.36 - 3.42 (m, 2H), 3.25 - 3.37 (m, 3H), 3.17 (s, 3  
10 H), 1.24 (t, J = 7.09 Hz, 3H); LCMS (m/z): 446.2 [M+H]<sup>+</sup>

Example 202

[0719]

15 Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(2-hydroxyethyl)-*N*-methylamino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 211]



[0720]

20 Cooled with ice bath, 4M hydrochloric acid in dioxane (4.0 mL) was added to ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-[(2-[(2-methoxyethoxy)methoxy]ethyl)-*N*-methylamino]-4-oxo-

oxo-4,5-dihydrofuran-3-carboxylate (0.020 mg, 0.046 mmol) which afforded in the Example 201. The mixture was stirred at ambient temperature for 3 h. The solvent was removed under reduced pressure, and the precipitate was suspended in diethyl ether, then collected by filtration. The solid was washed with diethyl ether then dried to afford the titled compound as solid (0.012 g, y. 75%).

[0721]

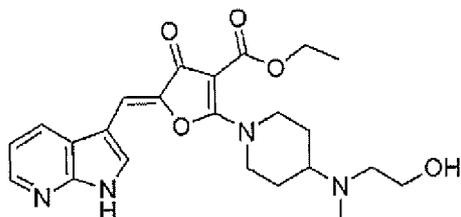
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.35 (br. s, 1H), 8.42 (d, J = 7.82 Hz, 1H), 8.32 (d, J = 3.91 Hz, 1H), 7.99 (s, 1H), 7.21 (dd, J = 4.89, 7.82 Hz, 1H), 6.84 (s, 1H), 4.16 (q, J = 6.85 Hz, 2H), 3.80 - 3.86 (m, 2H), 3.65 - 3.78 (m, 2H), 3.31 (br. s., 3H), 1.24 (t, J = 7.09 Hz, 4H); LCMS (m/z): 358.2 [M+H]<sup>+</sup>

15 Example 203

[0722]

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-(4-[(2-hydroxyethyl)-*N*-methylamino]piperidino)-4-oxo-4,5-dihydrofuran-3-carboxylate

20 [Chemical Formula 212]



The titled compound(solid) was similarly prepared according to

the procedure described in the Example 194.

[0723]

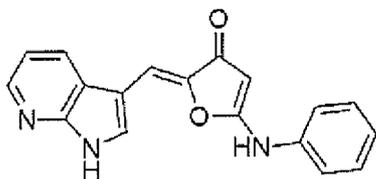
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.30 (br. s, 1H), 8.37 (d, J = 7.82 Hz, 1H), 8.31 (d, J = 4.40 Hz, 1H), 7.97 (s, 1H), 7.20 (dd, J = 4.65, 7.58 Hz, 1H), 6.85 (s, 1H), 4.22 - 4.38 (m, 4H), 4.17 (q, J = 6.85 Hz, 2H), 3.45 (q, J = 5.87 Hz, 2H), 3.25 - 3.40 (m, 2H), 2.69 - 2.81 (m, 1H), 2.23 (s, 3H), 1.85 - 1.95 (m, 2H), 1.58 - 1.72 (m, 2H), 1.25 (t, J = 6.85 Hz, 3H); LCMS (m/z): 441.2 [M+H]<sup>+</sup>.

10

Example 204

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-(phenylamino) furan-3(2*H*)-one

[Chemical Formula 213]



15

[0724]

A solution of the compound (0.050g, 0.13mmol) of Example 1 in *N,N*-dimethylformamide (1.0 mL) was refluxed for 6 h. Cooled to ambient temperature, the reaction mixture was purified by preparative HPLC to afford the titled compound as solid (0.010 g, y. 25%).

20

[0725]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.36 (br. s, 1H), 10.74 (s, 1H), 8.42

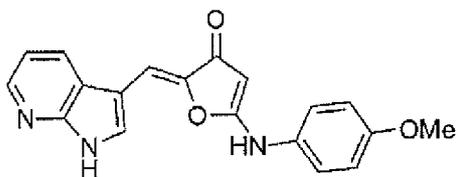
(d,  $J = 7.53$  Hz, 1H), 8.31 (dd,  $J = 1.25, 4.52$  Hz, 1H), 8.10 (d,  $J = 2.26$  Hz, 1H), 7.41 - 7.49 (m, 2H), 7.34 (d,  $J = 7.53$  Hz, 2H), 7.13 - 7.25 (m, 2H), 6.81 (s, 1H), 5.25 (s, 1H); LCMS (m/z): 304.0  $[M+H]^+$ .

5

Example 205

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-[(4-methoxyphenyl)amino]furan-3(2*H*)-one

[Chemical Formula 214]



10

[0726]

To a solution of the compound (0.31g, 0.76mmol) of Example 2 in ethanol (6.0 mL), 18M potassium hydroxide solution (0.41 mL, 7.4 mmol) was added at ambient temperature. The mixture was refluxed for 24 h. Cooled to ambient temperature, the precipitate was removed by filtration. The filtrate was purified by preparative HPLC to afford the titled compound as solid (0.031 g, y. 12%).

15

[0727]

$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.31 (br. s, 1H), 10.56 (s, 1H), 8.39 (d,  $J = 7.53$  Hz, 1H), 8.30 (dd,  $J = 1.51, 4.52$  Hz, 1H), 8.05 (s, 1H), 7.25 - 7.32 (m, 2H), 7.14 (dd,  $J = 4.64, 7.91$  Hz, 1H), 6.99 - 7.04 (m, 2H), 6.76 (s, 1H), 5.05 (s, 1H), 3.79 (s, 3H);

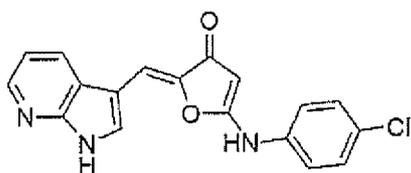
20

LCMS (m/z): 334.0 [M+H]<sup>+</sup>.

Example 206

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-[(4-chlorophenyl)amino]furan-3(2*H*)-one

[Chemical Formula 215]



[0728]

A solution of the compound (0.050g, 0.12mmol) of Example 8 in *N,N*-dimethylformamide (1.0 mL) was refluxed for 6 h. Cooled to ambient temperature, the reaction mixture was purified by preparative HPLC to afford the titled compound as solid (0.0072 g, y. 17%).

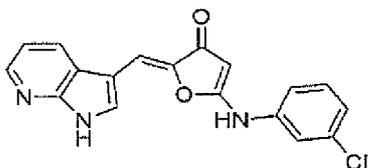
[0729]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.36 (br. s, 1H), 10.87 (br. s, 1H), 8.41 (d, *J* = 7.28 Hz, 1H), 8.31 (dd, *J* = 1.38, 4.64 Hz, 1H), 8.08 (d, *J* = 2.26 Hz, 1H), 7.48 (d, *J* = 8.78 Hz, 2H), 7.36 (d, *J* = 8.78 Hz, 2H), 7.17 (dd, *J* = 4.64, 7.91 Hz, 1H), 6.82 (s, 1H), 5.27 (s, 1H); LCMS (m/z): 337.9 [M+H]<sup>+</sup>.

Example 207

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-[(3-chlorophenyl)amino]furan-3(2*H*)-one

[Chemical Formula 216]



[0730]

A solution of the compound (0.040g, 0.098mmol) of Example 9 in  
 5 *N,N*-dimethylformamide (1.0 mL) was refluxed for 6 h. Cooled to  
 ambient temperature, the reaction mixture was purified by pre-  
 parative HPLC to afford the titled compound as solid (0.0075  
 g, y. 23%).

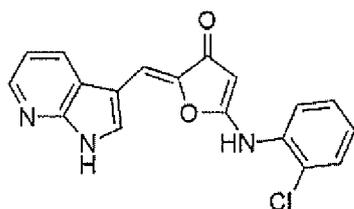
[0731]

10 <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.40 (br. s, 1H), 10.85 (s, 1H), 8.41  
 (d, *J* = 7.28 Hz, 1H), 8.32 (dd, *J* = 1.38, 4.64 Hz, 1H), 8.09  
 (d, *J* = 2.76 Hz, 1H), 7.42 - 7.51 (m, 1H), 7.36 - 7.41 (m, 1H),  
 7.32 (d, *J* = 8.03 Hz, 1H), 7.26 (dd, *J* = 1.00, 8.03 Hz, 1H), 7.  
 17 (dd, *J* = 4.64, 7.91 Hz, 1H), 6.85 (s, 1H), 5.31 (s, 1H); LCM  
 15 S (m/z): 337.9 [M+H]<sup>+</sup>.

Example 208

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-[(2-chlorophen-  
 yl)amino]furan-3(2*H*)-one

20 [Chemical Formula 217]



[0732]

A solution of the compound (0.050g, 0.12mmol) of Example 15 in *N,N*-dimethylformamide (1.0 mL) was stirred at 150 °C for 6 h.

5 Cooled to ambient temperature, the reaction mixture was purified by preparative HPLC to afford the titled compound as solid (0.0050 g, y. 11%).

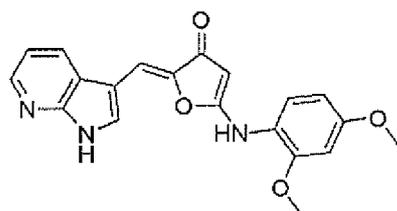
[0733]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.29 (br. s, 1H), 10.63 (br. s, 1H),  
 10 8.21 - 8.32 (m, 2H), 8.01 (br. s, 1H), 7.63 (d, *J* = 8.03 Hz, 1H), 7.57 (d, *J* = 7.28 Hz, 1H), 7.45 (t, *J* = 7.40 Hz, 1H), 7.32 - 7.39 (m, 1H), 7.06 (dd, *J* = 4.77, 7.53 Hz, 1H), 6.75 (s, 1H), 4.89 (br. s, 1H); LCMS (*m/z*): 337.9 [M+H]<sup>+</sup>.

15 Example 209

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-[(2,4-dimethoxyphenyl)amino]furan-3(2*H*)-one

[Chemical Formula 218]



[0734]

A solution of the compound (0.10g, 0.23mmol) of Example 24 in *N,N*-dimethylformamide (3.0 mL) was refluxed for 7 h. Cooled to ambient temperature, the reaction mixture was purified by preparative HPLC to afford the titled compound as solid (0.015 g, y. 18%).

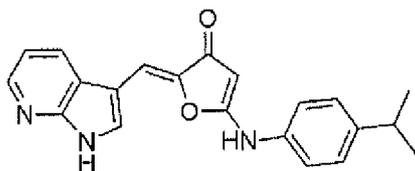
[0735]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.27 (br. s, 1H), 10.11 (br. s, 1H), 8.25 - 8.36 (br. s, 2H), 8.03 (br. s, 1H), 7.30 (d, *J* = 8.31 Hz, 1H), 7.08 (br. s, 1H), 6.72 (d, *J* = 17.12 Hz, 2H), 6.60 (d, *J* = 8.31 Hz, 1H), 4.74 (br. s, 1H), 3.75 - 3.92 (m, 6H); LCMS (*m/z*): 364.2 [M+H]<sup>+</sup>.

Example 210

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-[(4-isopropylphenyl)amino]furan-3(2*H*)-one

[Chemical Formula 219]



[0736]

A solution of the compound (0.12g, 0.29mmol) of Example 37 in *N,N*-dimethylformamide (3.0 mL) was refluxed for 6 h. Cooled to ambient temperature, the reaction mixture was purified by preparative HPLC to afford 2-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)met

hylene]-5-[(4-isopropylphenyl)amino]furan-3(2H)-one as solid  
(0.0050 g, y. 5%).

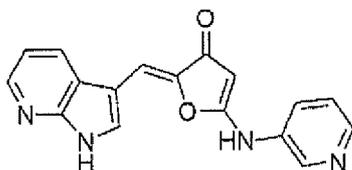
[0737]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.34 (br. s, 1H), 10.68 (br. s, 1H),  
5 8.41 (d, J = 7.82 Hz, 1H), 8.30 (d, J = 3.91 Hz, 1H), 8.09 (br.  
s, 1H), 7.21 - 7.37 (m, 4H), 7.15 (d, J = 4.40 Hz, 1H), 6.77  
(s, 1H), 5.18 (br. s, 1H), 2.84 - 3.00 (m, 1H), 1.22 (d, J = 6.  
85 Hz, 6H); LCMS (m/z): 346.2 [M+H]<sup>+</sup>.

10 Example 211

2-[(1H-Pyrrolo[2,3-b]pyridin-3-yl)methylene]-5-(3-pyridinylamino)furan-3(2H)-one

[Chemical Formula 220]



15 The titled compound(solid) was similarly prepared according to  
the procedure described in the Example 210, using the compound  
of Example 27.

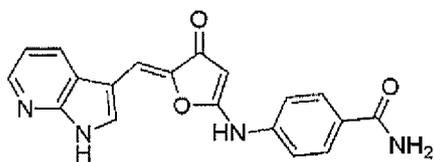
[0738]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.35 (br. s, 1H), 10.95 (br. s, 1H),  
20 8.58 (br. s, 1H), 8.35 - 8.43 (m, 2H), 8.27 - 8.33 (m, 1H), 8.0  
6 (br. s, 1H), 7.76 (d, J = 6.85 Hz, 1H), 7.38 - 7.53 (m, 1H),  
7.09 - 7.24 (m, 1H), 6.81 (br. s, 1H), 5.27 (br. s, 1H); LCMS  
(m/z): 305.2 [M+H]<sup>+</sup>.

## Example 212

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-[(4-carbamoylp  
henyl)amino]furan-3(2*H*)-one

5 [Chemical Formula 221]



The titled compound (solid) was similarly prepared according to  
the procedure described in the Example 210, using the compou  
nd of Example 25.

10 [0739]

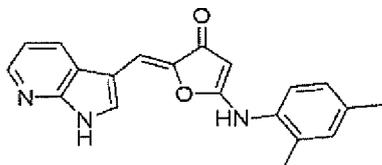
<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.37 (br. s, 1H), 8.42 (d, *J* = 7.34 Hz,  
1H), 8.32 (br. s, 1H), 8.12 (br. s, 1H), 7.85 - 8.04 (m, 4H),  
7.28 - 7.44 (m, 3H), 7.14 - 7.21 (m, 1H), 6.83 (br. s, 1H), 5.3  
8 (br. s, 1H); LCMS (*m/z*): 347.2 [M+H]<sup>+</sup>.

15

## Example 213

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-[(2,4-dimethyl  
phenyl)amino]furan-3(2*H*)-one

[Chemical Formula 222]



20

The titled compound(solid) was similarly prepared according to

the procedure described in the Example 210, using the compound of Example 26.

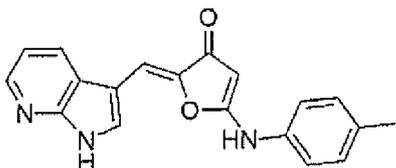
[0740]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.22 (br. s, 1H), 10.21 (br. s, 1H), 8.11 - 8.34 (m, 2H), 7.94 (br. s, 1H), 7.25 (d, J = 7.92 Hz, 1H), 7.17 (br. s, 1H), 6.99 - 7.14 (m, 2H), 6.74 (s, 1H), 4.78 (br. s, 1H), 2.31 (s, 3H), 2.22 (s, 3H); LCMS (m/z): 332.2 [M+H]<sup>+</sup>.

10 Example 214

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-(*p*-tolylamino) furan-3(2*H*)-one

[Chemical Formula 223]



15 The titled compound(solid) was similarly prepared according to the procedure described in the Example 210, using the compound of Example 20.

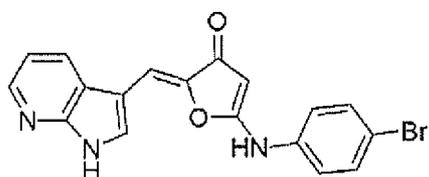
[0741]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.32 (br. s, 1H), 8.40 (d, J = 7.34 Hz, 1H), 8.30 (br. s, 1H), 8.06 (br. s, 1H), 7.10 - 7.36 (m, 5H), 6.74 (br. s, 1H), 5.12 (br. s, 1H), 2.32 (s, 3H); LCMS (m/z): 318.4 [M+H]<sup>+</sup>.

## Example 215

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-[(4-bromophenyl)amino]furan-3(2*H*)-one

[Chemical Formula 224]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 210, using the compound of Example 19.

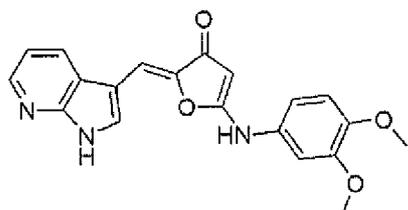
[0742]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.31 (br. s, 1H), 8.39 (d, *J* = 7.76 Hz, 1H), 8.23 - 8.35 (m, 1H), 8.05 (s, 1H), 7.58 (d, *J* = 8.31 Hz, 2H), 7.27 (d, *J* = 8.31 Hz, 2H), 7.18 (dd, *J* = 4.65, 7.58 Hz, 1H), 6.80 (s, 1H), 5.20 (br. s, 1H); LCMS (*m/z*): 382.5 [M+H]<sup>+</sup>.

## Example 216

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-[(3,4-dimethoxyphenyl)amino]furan-3(2*H*)-one

[Chemical Formula 225]



[0743]

A solution of the compound (0.043g, 0.099mmol) of Example 28 in *N,N*-dimethylformamide (1.2 mL) was refluxed for 6 h. Cooled to ambient temperature, the reaction mixture was purified by preparative HPLC to afford the titled compound (0.0050 g, y. 12%).

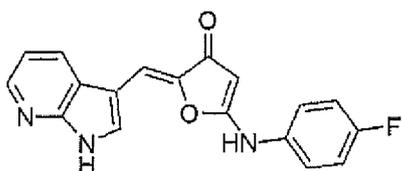
[0744]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.35 (br. s, 1H), 10.56 (br. s, 1H), 8.40 (d, *J* = 7.34 Hz, 1H), 8.30 (d, *J* = 3.91 Hz, 1H), 8.06 (br. s, 1H), 7.08 - 7.22 (m, 1H), 7.01 (d, *J* = 8.31 Hz, 1H), 6.92 (br. s, 1H), 6.87 (d, *J* = 8.31 Hz, 1H), 6.77 (s, 1H), 5.12 (s, 1H), 3.78 (s, 6H); LCMS (*m/z*): 364.0 [M+H]<sup>+</sup>.

#### Example 217

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-[(4-fluorophenyl)amino]furan-3(2*H*)-one

[Chemical Formula 226]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 216, using the compound of Example 21.

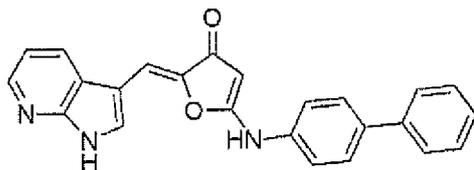
[0745]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.34 (br. s, 1H), 10.72 (br. s, 1H), 8.40 (d, *J* = 7.34 Hz, 1H), 8.31 (d, *J* = 3.91 Hz, 1H), 8.06 (br.

s, 1H), 7.33 - 7.46 (m, 2H), 7.22 - 7.33 (m, 2H), 7.16 (dd, J = 4.65, 7.58 Hz, 1H), 6.80 (s, 1H), 5.18 (s, 1H); LCMS (m/z): 322.0 [M+H]<sup>+</sup>.

5 Example 218

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-[(1,1'-biphenyl)-4-ylamino]furan-3(2*H*)-one  
[Chemical Formula 227]



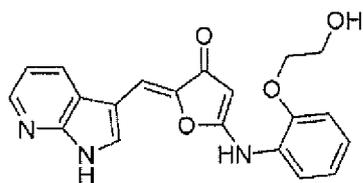
10 The titled compound(solid) was similarly prepared according to the procedure described in the Example 216, using the compound of Example 39.

[0746]

15 <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.29 (br. s, 1H), 8.24 - 8.49 (m, 3H), 8.07 (br. s, 1H), 7.70 (br. s, 3H), 7.48 (br. s, 2H), 7.38 (br. s, 3H), 7.15 (br. s, 1H), 6.72 (br. s, 1H), 5.19 (br. s, 1H); LCMS (m/z): 380.2 [M+H]<sup>+</sup>.

Example 219

20 2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-([2-(2-hydroxyethoxy)phenyl]amino)furan-3(2*H*)-one  
[Chemical Formula 228]



[0747]

A solution of the compound (0.015g, 0.034mmol) of Example 29 in *N,N*-dimethylformamide (0.50 mL) was refluxed for 4 h. Cooled to ambient temperature, the reaction mixture was purified by preparative HPLC to afford the titled compound as solid (0.0013 g, y. 11%).

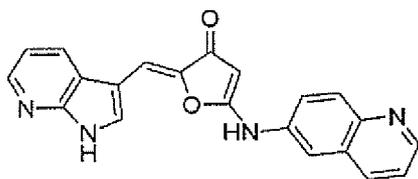
[0748]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.24 (br. s, 1H), 8.44 (br. s, 1H), 8.24 - 8.35 (m, 2H), 8.03 (br. s, 1H), 7.32 - 7.41 (m, 1H), 6.96 - 7.25 (m, 4H), 6.67 (br. s, 1H), 4.90 (br. s, 1H), 4.01 - 4.12 (m, 2H), 3.67 - 3.80 (m, 2H); LCMS (m/z): 363.9 [M+H]<sup>+</sup>.

Example 220

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-(6-quinolinylamino) furan-3(2*H*)-one

[Chemical Formula 229]



[0749]

A solution of the compound (0.075g, 0.18mmol) of Example 44 in *N,N*-dimethylformamide (4.0 mL) was refluxed for 6 h. Cooled t

o ambient temperature, the reaction mixture was purified by preparative HPLC to afford the titled compound as solid (0.0080 g, y. 13%).

[0750]

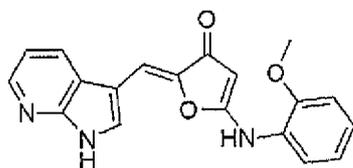
5  $^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.41 (br. s, 1H), 11.07 (br. s, 1H), 8.81 - 8.87 (m, 1H), 8.42 (t,  $J = 8.56$  Hz, 2H), 8.31 (d,  $J = 3.91$  Hz, 1H), 8.15 (br. s, 1H), 8.07 (d,  $J = 8.80$  Hz, 1H), 7.88 (br. s, 1H), 7.73 (d,  $J = 8.80$  Hz, 1H), 7.55 (dd,  $J = 3.91, 7.82$  Hz, 1H), 7.15 (d,  $J = 4.40$  Hz, 1H), 6.85 (br. s, 1H), 5.56 (br. s, 1H); LCMS (m/z): 355.2  $[\text{M}+\text{H}]^+$ .

10

Example 221

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-[(2-methoxyphenyl)amino]furan-3(2*H*)-one

15 [Chemical Formula 230]



[0751]

A solution of the compound (0.099g, 0.24mmol) of Example 7 in *N,N*-dimethylformamide (2.0 mL) was refluxed for 9 h. Cooled to ambient temperature, the reaction mixture was diluted with 2-butanol and washed with 4M sodium hydroxide solution. The organic layer was concentrated then purified by chromatography on silica gel (chloroform/methanol) to afford the titled compound

20

as solid (0.0097 g, y. 12%).

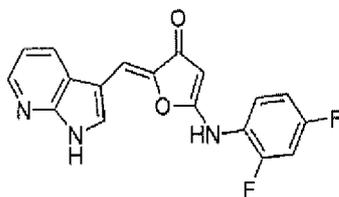
[0752]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.31 (br. s, 1H), 10.29 (s, 1H), 8.33 (d, J = 7.78 Hz, 1H), 8.27 - 8.30 (m, 1H), 8.12 (s, 1H), 7.42 (d, J = 7.78 Hz, 1H), 7.26 - 7.33 (m, 1H), 7.18 (d, J = 7.28 Hz, 1H), 7.10 (dd, J = 4.77, 8.03 Hz, 1H), 7.04 (t, J = 7.65 Hz, 1H), 6.75 (s, 1H), 4.90 - 4.94 (m, 1H), 3.88 (s, 3H); LCMS (m/z): 333.9 [M+H]<sup>+</sup>.

10 Example 222

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-[(2,4-difluorophenyl)amino]furan-3(2*H*)-one

[Chemical Formula 231]



15 [0753]

A solution of the compound (0.099g, 0.24mmol) of Example 53 in *N,N*-dimethylformamide (1.0 mL) was refluxed for 4 h. Cooled to ambient temperature, the reaction mixture was purified by preparative HPLC to afford the titled compound as solid (0.0030 g, y. 4%).

[0754]

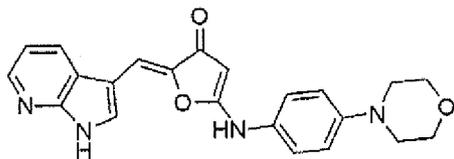
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.31 (br. s, 1H), 10.60 (br. s, 1H),

8.26 - 8.36 (m, 2H), 8.01 (br. s, 1H), 7.55 - 7.65 (m, 1H), 7.44 - 7.54 (m, 1H), 7.16 - 7.25 (m, 1H), 7.06 - 7.14 (m, 1H), 6.79 (br. s, 1H), 4.95 (br. s, 1H); LCMS (m/z): 339.8 [M+H]<sup>+</sup>.

5 Example 223

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-[(4-morpholino phenyl) amino]furan-3(2*H*)-one

[Chemical Formula 232]



10 [0755]

A solution of the compound (0.080g, 0.17mmol) of Example 42 in *N,N*-dimethylacetamide (3.0 mL) was stirred at 160 °C for 4 h. Cooled to ambient temperature, the reaction mixture was diluted with water and the precipitate was collected by filtration.

15 The solid was washed with water, tetrahydrofuran and diethyl ether then dried to afford the titled compound as solid (0.015 g, y. 22%).

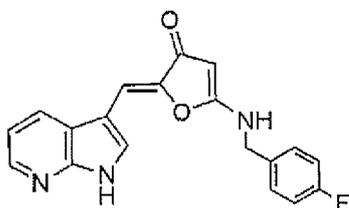
[0756]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.32 (br. s, 1H), 10.53 (br. s, 1H),  
20 8.41 (d, *J* = 8.12 Hz, 1H), 8.31 (d, *J* = 4.28 Hz, 1H), 8.05 (br. s, 1H), 7.23 (d, *J* = 8.31 Hz, 2H), 7.12 - 7.18 (m, 1H), 7.02 (d, *J* = 8.31 Hz, 2H), 6.75 (s, 1H), 5.05 (s, 1H), 3.70 - 3.83 (m, 4H), 3.05 - 3.18 (m, 4H); LCMS (m/z): 389.4 [M+H]<sup>+</sup>.

## Example 224

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-[(4-fluorobenzyl)amino]furan-3(2*H*)-one

5 [Chemical Formula 233]



[0757]

A solution of the compound (0.10g, 0.31mmol) of Example 45 in *N,N*-dimethylacetamide (3.0 mL) was refluxed for 7 h. Cooled to ambient temperature, the reaction mixture was diluted with water and the precipitate was collected by filtration. The solid was washed with water and diethyl ether then dried to afford the titled compound as solid (0.0070 g, y. 9%).

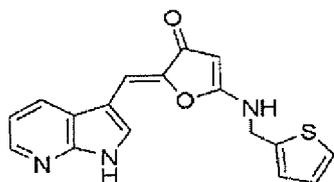
[0758]

15 <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.23 (br. s, 1H), 9.08 (s, 1H), 8.40 (br. s, 1H), 8.21 - 8.32 (m, 2H), 7.96 (br. s, 1H), 7.34 - 7.50 (m, 1H), 7.05 - 7.32 (m, 3H), 6.67 (s, 1H), 4.91 (s, 1H), 4.35 - 4.60 (m, 2H); LCMS (m/z): 336.0 [M+H]<sup>+</sup>.

## 20 Example 225

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-[(2-thienylmethyl)amino]furan-3(2*H*)-one

[Chemical Formula 234]



[0759]

A solution of the compound (0.10g, 0.26mmol) of Example 60 in *N,N*-dimethylformamide (0.80 mL) was refluxed for 16 h. Cooled to ambient temperature, the reaction mixture was diluted with chloroform and the precipitate was collected by filtration. The solid was washed with chloroform/methanol (10/1) and hexane then dried to afford the titled compound as solid (0.019 g, y.

22%).

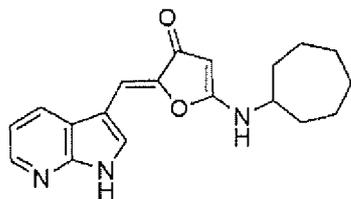
[0760]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.25 (br. s, 1H), 9.20 (t, *J* = 6.02 Hz, 1H), 8.41 (d, *J* = 7.53 Hz, 1H), 8.29 (dd, *J* = 1.26, 4.52 Hz, 1H), 7.99 (d, *J* = 2.01 Hz, 1H), 7.49 (dd, *J* = 1.00, 5.02 Hz, 1H), 7.12 - 7.20 (m, 2H), 7.02 (dd, *J* = 3.51, 5.02 Hz, 1H), 6.67 (s, 1H), 4.96 (br. s, 1H), 4.69 (br. s, 2H); LCMS (*m/z*): 324.0 [*M*+*H*]<sup>+</sup>.

Example 226

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-(cycloheptylamino)furan-3(2*H*)-one

[Chemical Formula 235]



[0761]

A solution of the compound (0.040g, 0.10mmol) of Example 59 in *N,N*-dimethylformamide (2.0 mL) was refluxed for 8 h. Cooled to ambient temperature, the reaction mixture was purified by preparative HPLC to afford the titled compound as solid (0.0040 g, y. 12%).

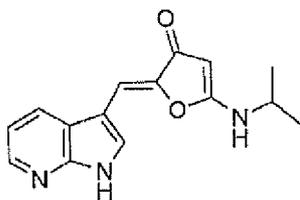
[0762]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.26 (br. s, 1H), 8.64 (d, *J* = 7.82 Hz, 1H), 8.39 (d, *J* = 7.34 Hz, 1H), 8.29 (d, *J* = 3.91 Hz, 1H), 8.00 (br. s, 1H), 7.17 (dd, *J* = 4.89, 7.82 Hz, 1H), 6.61 (s, 1H), 4.78 (br. s, 1H), 2.83 - 3.11 (m, 1H), 1.85 - 2.02 (m, 2H), 1.40 - 1.78 (m, 10H); LCMS (*m/z*): 324.2 [M+H]<sup>+</sup>.

15 Example 227

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-(isopropylamino)furan-3(2*H*)-one

[Chemical Formula 236]



[0763]

A solution of the compound (0.15g, 0.43mmol) of Example 56 in *N,N*-dimethylacetamide (1.5 mL) was refluxed for 12 h. Cooled to ambient temperature, the reaction mixture was diluted with water and the precipitate was collected by filtration. The solid was washed with diethyl ether then dried to afford the titled compound as solid (0.015 g, y. 12%).

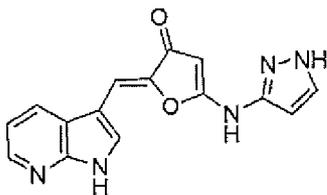
[0764]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.24 (br. s, 1H), 8.58 (d, *J* = 7.82 Hz, 1H), 8.38 (d, *J* = 7.83 Hz, 1H), 8.27 (d, *J* = 4.40 Hz, 1H), 7.97 (br. s, 1H), 7.15 (dd, *J* = 4.89, 7.82 Hz, 1H), 6.60 (s, 1H), 4.79 (br. s, 1H), 3.53 - 3.69 (m, 1H), 1.22 (d, *J* = 6.36 Hz, 6H); LCMS (*m/z*): 270.2 [M+H]<sup>+</sup>.

15 Example 228

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-[(3-pyrazolyl)amino]furan-3(2*H*)-one

[Chemical Formula 237]



20 The titled compound(solid) was similarly prepared according to the procedure described in the Example 227, using the compound of Example 67.

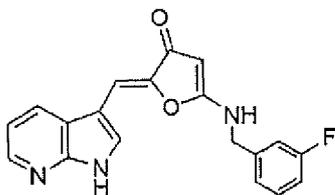
[0765]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.52 (br. s, 2H), 11.67 (br. s, 1H),  
8.45 (d, J = 6.85 Hz, 1H), 8.16 (d, J = 3.42 Hz, 1H), 7.72 (br.  
s, 2H), 7.56 (br. s, 1H), 7.13 - 7.25 (m, 1H), 6.98 - 7.09 (m,  
5 1H), 4.69 (s, 1H); LCMS (m/z): 294.2 [M+H]<sup>+</sup>.

Example 229

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-[(3-fluorobenz  
yl)amino]furan-3(2*H*)-one

10 [Chemical Formula 238]



[0766]

A solution of the compound (0.050g, 0.12mmol) of the Example 5  
8 in *N,N*-dimethylacetamide (1.5 mL) was refluxed for 12 h. Cool  
15 ed to ambient temperature, the reaction mixture was diluted wi  
th water and the precipitate was collected by filtration. The  
solid was purified by preparative HPLC to afford the titled co  
mpound as solid (0.012 g, y. 30%).

[0767]

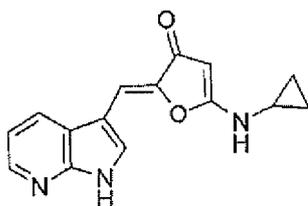
20 <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.26 (br. s, 1H), 9.13 - 9.23 (m, 1H),  
8.41 (br. s, 1H), 8.29 (d, J = 3.91 Hz, 1H), 7.98 (br. s, 1H),  
7.38 - 7.53 (m, 1H), 7.20 - 7.32 (m, 2H), 7.16 (d, J = 6.36 Hz,

2H), 6.66 (s, 1H), 4.91 (br. s, 1H), 4.41 - 4.60 (m, 2H); LCMS  
(m/z): 336.0 [M+H]<sup>+</sup>.

Example 230

5 2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-(cyclopropylamino) furan-3(2*H*)-one

[Chemical Formula 239]



[0768]

10 To a solution of the compound (0.25g, 0.76mmol) of Example 94 in ethanol (7.0 mL), 50% potassium hydroxide solution (4.0 mL, 0.071 mol) was added at ambient temperature. The mixture was refluxed for 2 h. Cooled to ambient temperature, the solvent was removed under reduced pressure. The residue was diluted with water, 1M hydrochloric acid was added to adjust pH to acidic, and then the solvent was removed under reduced pressure. The residue was purified by preparative HPLC to afford the titled compound as solid (0.0090 g, y. 4%).

[0769]

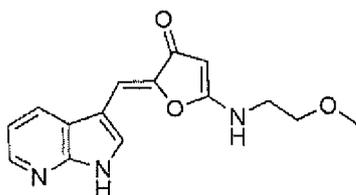
20 <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.26 (br. s, 1H), 8.88 (br. s, 1H), 8.44 (d, J = 6.85 Hz, 1H), 8.22 - 8.34 (m, 1H), 7.97 (br. s, 1H), 7.12 - 7.20 (m, 1H), 6.66 (br. s, 1H), 4.87 (br. s, 1H), 2.62

- 2.80 (m, 1H), 0.72 - 0.88 (m, 2H), 0.55 - 0.72 (m, 2H); LCMS  
(m/z): 268.0 [M+H]<sup>+</sup>.

Example 231

5 2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-[(2-methoxyeth  
yl)amino]furan-3(2*H*)-one

[Chemical Formula 240]



[0770]

10 To a solution of the compound (0.070g, 0.20mmol) of Example 98  
in ethanol (2.0 mL), 50% potassium hydroxide solution (1.0 mL,  
0.018 mol) was added at ambient temperature. The mixture was  
refluxed for 1 h. Cooled to ambient temperature, 1M hydrochlor  
ic acid was added to adjust pH to acidic, and then the solvent  
15 was removed under reduced pressure. To this residue, ethanol  
(2.0 mL) and water (2.0 mL) were added then refluxed for 1 h. C  
ooled to ambient temperature, the solvent was removed under re  
duced pressure, and the residue was purified by preparative HP  
LC to afford the titled compound as solid (0.0060 g, y. 12%).

20 [0771]

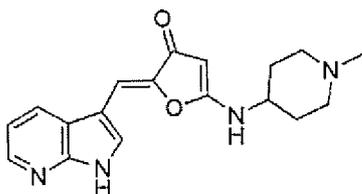
<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.24 (br. s, 1H), 8.65 - 8.90 (m, 1H),  
8.41 (d, J = 6.85 Hz, 1H), 8.29 (br. s, 1H), 8.01 (br. s, 1H),

7.08 - 7.32 (m, 1H), 6.53 - 6.70 (m, 1H), 4.72 - 4.97 (m, 1H),  
3.30 - 3.55 (m, 4H), 3.26 (br. s, 3H); LCMS (m/z): 286.2 [M+H]  
+.

5 Example 232

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-[(1-methyl-4-*p*-  
iperidinyl)amino]furan-3(2*H*)-one

[Chemical Formula 241]



10 The titled compound(solid) was similarly prepared according to  
the procedure described in the Example 231, using the compoun  
d of Example 65.

[0772]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.25 (br. s, 1H), 8.61 (d, *J* = 7.34 Hz,  
15 1H), 8.39 (d, *J* = 7.82 Hz, 1H), 8.23 - 8.34 (m, 1H), 8.17 (br.  
s, 1H), 7.99 (br. s, 1H), 7.06 - 7.24 (m, 1H), 6.62 (s, 1H), 4.  
77 - 4.99 (m, 1H), 2.73 - 2.85 (m, 2H), 2.22 (s, 3H), 2.00 - 2.  
14 (m, 2H), 1.82 - 1.97 (m, 2H), 1.49 - 1.67 (m, 2H); LCMS (m/  
z): 325.4 [M+H]<sup>+</sup>.

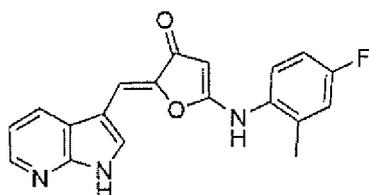
20

Example 233

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-[(4-fluoro-2-*m*

ethylphenyl) amino]furan-3(2H)-one

[Chemical Formula 242]



[0773]

5 To a solution of the compound (0.15g, 0.37mmol) of Example 97  
in ethanol (4.0 mL), 50% potassium hydroxide solution (2.0 mL,  
0.036 mol) was added at ambient temperature. The mixture was  
refluxed for 2 h. Cooled to ambient temperature, the solvent w  
as removed under reduced pressure. Water was added to this res  
10 idue, the mixture was washed with ethyl acetate then 1M hydroc  
hloric acid was added to adjust pH to acidic. The precipitate  
was collected by filtration, washed with water, diethyl ether,  
ethyl acetate and hexane then dried to afford the titled comp  
ound as solid (0.12 g, y. 93%).

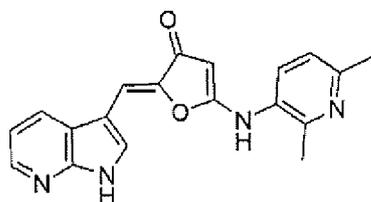
15 [0774]

$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 12.28 (br. s, 1H), 10.24 (s, 1H), 8.19  
- 8.32 (m, 2H), 7.97 (br. s, 1H), 7.43 (dd,  $J = 5.62, 8.56$  Hz,  
1H), 7.26 (d,  $J = 7.34$  Hz, 1H), 7.11 - 7.19 (m, 1H), 7.04 - 7.  
10 (m, 1H), 6.74 (s, 1H), 4.72 (s, 1H), 2.31 (s, 3H); LCMS (m/  
20 z): 335.8  $[\text{M}+\text{H}]^+$ .

Example 234

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-[(2,6-dimethyl-3-pyridinyl)amino]furan-3(2*H*)-one

[Chemical Formula 243]



5 [0775]

To a solution of the compound (0.090g, 0.20mmol) of Example 10  
7 in ethanol (4.0 mL), 50% potassium hydroxide solution (2.0 mL, 0.036 mol) was added at ambient temperature. The mixture was  
s refluxed for 2 h. Cooled to ambient temperature, the solvent  
10 was removed under reduced pressure. Water was added to this residue, the mixture was washed with ethyl acetate then 1M hydrochloric acid was added to adjust pH to acidic. The precipitate  
e was collected by filtration, washed with water and diethyl ether then dried to afford the titled compound (0.037 g, y. 5  
15 0%) as solid.

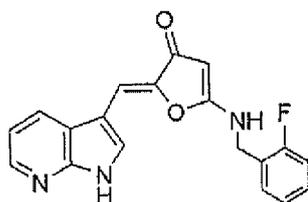
[0776]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.26 (br. s, 1H), 10.33 (br. s, 1H),  
8.28 (d, *J* = 4.40 Hz, 2H), 7.96 (br. s, 1H), 7.64 (d, *J* = 8.31  
Hz, 1H), 7.17 (d, *J* = 7.82 Hz, 1H), 7.02 - 7.12 (m, 1H), 6.70  
20 (br. s, 1H), 4.73 (br. s, 1H), 2.48 (br. s, 3H), 2.44 (br. s, 3H); LCMS (*m/z*): 333.3 [M+H]<sup>+</sup>.

Example 235

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-[(2-fluorobenzyl)amino]furan-3(2*H*)-one

[Chemical Formula 244]



5

[0777]

To a solution of the compound (0.10g, 0.25mmol) of Example 101 in ethanol (4.0 mL), 50% potassium hydroxide solution (2.0 mL, 0.036 mol) was added at ambient temperature. The mixture was refluxed for 2 h. Cooled to ambient temperature, the solvent was removed under reduced pressure. Water was added to this residue, the mixture was washed with ethyl acetate then 1M hydrochloric acid was added to adjust pH to acidic, and then extracted with ethyl acetate. The organic layer was dried over sodium sulfate and concentrate then purified by chromatography on silica gel (dichloromethane/methanol) to afford the titled compound as solid (0.012 g, y. 14%).

10

15

[0778]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.24 (br. s, 1H), 9.08 - 9.17 (m, 1H), 8.34 - 8.46 (m, 1H), 8.22 - 8.33 (m, 1H), 7.98 (br. s, 1H), 7.45 - 7.55 (m, 1H), 7.34 - 7.43 (m, 1H), 7.20 - 7.31 (m, 2H), 7.10 - 7.19 (m, 1H), 6.65 (s, 1H), 4.83 - 4.97 (m, 1H), 4.40-4.64

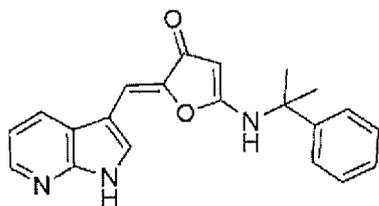
20

(m, 2H); LCMS (m/z): 335.8 [M+H]<sup>+</sup>.

Example 236

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-[(2-phenyl-2-propyl)amino]furan-3(2*H*)-one

[Chemical Formula 245]



[0779]

To a solution of the compound (0.060g, 0.14mmol) of Example 11  
 10 2 in ethanol (2.0 mL), 50% potassium hydroxide solution (1.0 mL, 0.018 mol) was added at ambient temperature. The mixture was refluxed for 2 h. Cooled to ambient temperature, the solvent was removed under reduced pressure. Water was added to this residue, the mixture was washed with ethyl acetate then 1M hydrochloric acid was added to adjust pH to acidic. The precipitate  
 15 was collected by filtration, washed with water and diethyl ether then dried to afford the titled compound as solid (0.010 g, y. 20%).

[0780]

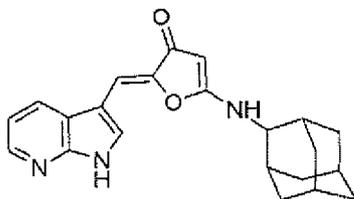
20 <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.26 (br. s, 1H), 9.05 (br. s, 1H), 8.24 - 8.38 (m, 2H), 8.0 (br, 1H), 7.36 - 7.50 (m, 4H), 7.25 - 7.32 (m, 1H), 7.12 - 7.18 (m, 1H), 6.57 (s, 1H), 4.06 (br. s, 1H),

1.70 (s, 6H); LCMS (m/z): 346.2 [M+H]<sup>+</sup>.

Example 237

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-(2-adamantylamino) furan-3(2*H*)-one

[Chemical Formula 246]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 236, using the compound of Example 113.

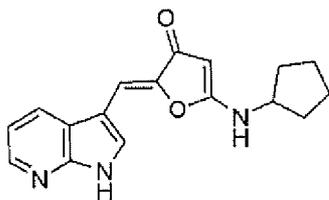
[0781]

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 12.29 (br. s, 1H), 8.55 (br. s, 1H), 8.37 (d, *J* = 7.82 Hz, 1H), 8.30 (d, *J* = 4.40 Hz, 1H), 8.14 (br. s, 1H), 7.17 (dd, *J* = 4.89, 7.83 Hz, 1H), 6.64 (s, 1H), 4.83 (s, 1H), 3.25 - 3.40 (m, 1H), 1.96 - 2.11 (m, 4H), 1.80 - 1.92 (m, 4H), 1.69 - 1.77 (m, 2H), 1.55 - 1.63 (m, 2H), 1.09 (t, *J* = 7.00 Hz, 2H); LCMS (m/z): 362.4 [M+H]<sup>+</sup>.

Example 238

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-(cyclopentylamino) furan-3(2*H*)-one

[Chemical Formula 247]



[0782]

To a solution of the compound (0.10g, 0.27mmol) of Example 103 in ethanol (4.0 mL), 50% potassium hydroxide solution (2.0 mL, 0.036 mol) was added at ambient temperature. The mixture was refluxed for 2 h. Cooled to ambient temperature, the solvent was removed under reduced pressure. Water was added to this residue, the mixture was washed with ethyl acetate then 1M hydrochloric acid was added to adjust pH to acidic, and then the solvent was removed under reduced pressure. The residue was purified by preparative HPLC to afford the titled compound as solid (0.0015 g, y. 5%).

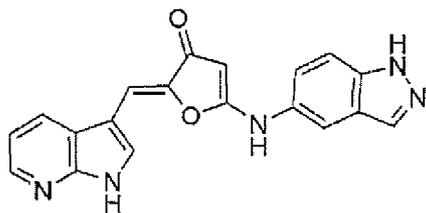
[0783]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.25 (br. s, 1H), 8.58 - 8.70 (m, 1H), 8.39 (d, J = 7.83 Hz, 1H), 8.22 - 8.32 (m, 1H), 7.99 (br. s, 1H), 7.17 (dd, J = 4.65, 7.58 Hz, 1H), 6.62 (s, 1H), 6.55 (s, 1H), 4.75 - 4.96 (m, 1H), 1.90 - 2.03 (m, 2H), 1.65 - 1.77 (m, 2H), 1.50 - 1.65 (m, 4H); LCMS (m/z): 296.2 [M+H]<sup>+</sup>.

20 Example 239

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-[(5-indazolyl)amino]furan-3(2*H*)-one

[Chemical Formula 248]



[0784]

To a solution of the compound (0.14g, 0.33mmol) of Example 118  
 5 in ethanol (4.0 mL), 50% potassium hydroxide solution (2.2 mL,  
 0.039 mol) was added at ambient temperature. The mixture was  
 refluxed for 2 h. Cooled to ambient temperature, 1M hydrochloric  
 acid was added to adjust pH to acidic, and the solvent was r  
 emoved under reduced pressure. The residue was purified by pre  
 10 parative HPLC to afford the titled compound as solid (0.010 g,  
 y. 9%).

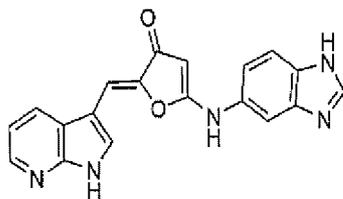
[0785]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 13.16 (br. s, 1H), 12.30 (br. s, 1H),  
 8.42 (br. s, 1H), 8.37 (d, J = 7.76 Hz, 1H), 8.28 (d, J = 3.91  
 15 Hz, 1H), 8.09 (br. s, 1H), 8.05 (br. s, 1H), 7.71 (s, 1H), 7.61  
 (d, J = 8.80 Hz, 1H), 7.35 (d, J = 8.80 Hz, 1H), 7.04 - 7.11  
 (m, 1H), 6.73 (s, 1H), 5.10 (s, 1H); LCMS (m/z): 344.2 [M+H]<sup>+</sup>.

Example 240

20 2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-[(5-benzimidaz  
 oyl)amino]furan-3(2*H*)-one

[Chemical Formula 249]



[0786]

To a solution of the compound (0.055g, 0.13mmol) of Example 119 in ethanol (6.0 mL), 50% potassium hydroxide solution (3.0 mL, 0.053 mol) was added at ambient temperature. The mixture was refluxed for 1.5 h. Cooled to ambient temperature, 1M hydrochloric acid was added to adjust pH to acidic, and the solvent was removed under reduced pressure. The residue was purified by preparative HPLC to afford the titled compound (0.0090 g, y. 20%) as solid.

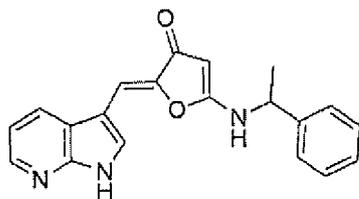
[0787]

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.28 (br. s, 1H), 12.10 (br. s, 1H), 8.34 (br. s, 1H), 8.22 - 8.29 (m, 1H), 8.10 - 8.20 (m, 1H), 7.95 (br. s, 1H), 7.50 - 7.62 (m, 1H), 7.25 - 7.38 (m, 1H), 6.98 - 7.15 (m, 2H), 6.34 - 6.67 (m, 2H), 4.84 (s, 1H); LCMS (m/z): 344.0 [M+H]<sup>+</sup>.

Example 241

2-[(1H-Pyrrolo[2,3-b]pyridin-3-yl)methylene]-5-[(1-phenylethyl)amino]furan-3(2H)-one

[Chemical Formula 250]



The titled compound(solid) was similarly prepared according to the procedure described in the Example 240, using the compound of Example 106.

5 [0788]

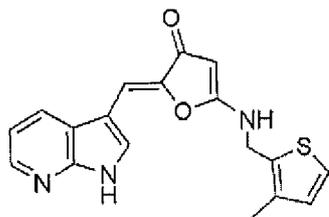
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.29 (br. s, 1H), 9.15 (d, J = 7.83 Hz, 1H), 8.23 - 8.43 (m, 2H), 7.80 (br. s, 1H), 7.11 - 7.49 (m, 6 H), 6.62 (s, 1H), 5.00 - 5.10 (m, 1H), 4.60 - 4.80 (m, 1H), 1.36 - 1.60 (m, 3H); LCMS (m/z): 332.2 [M+H]<sup>+</sup>.

10

Example 242

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-[[ (3-methyl-2-thienyl)methyl]amino]furan-3(2*H*)-one

[Chemical Formula 251]



15

[0789]

A solution of the compound (0.050g, 0.12mmol) of Example 124 in *N,N*-dimethylformamide (1.0 mL) was refluxed for 16 h. Cooled to ambient temperature, the reaction mixture was purified by

preparative HPLC to afford the titled compound as solid (0.012 g, y. 28%).

[0790]

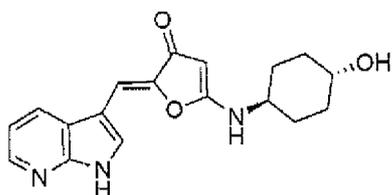
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.25 (br. s, 1H), 9.09 (t, J = 5.77 Hz, 1H), 8.40 (d, J = 7.78 Hz, 1H), 8.29 (dd, J = 1.38, 4.64 Hz, 1H), 7.99 (d, J = 2.26 Hz, 1H), 7.38 (d, J = 5.02 Hz, 1H), 7.15 (dd, J = 4.77, 8.03 Hz, 1H), 6.90 (d, J = 5.02 Hz, 1H), 6.66 (s, 1H), 4.92 (br. s, 1H), 4.59 (br. s, 2H), 2.25 (s, 3H); LCMS (m/z): 338.1 [M+H]<sup>+</sup>.

10

Example 243

2-[(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-5-[(*trans*-4-hydroxycyclohexyl)amino]furan-3(2*H*)-one

[Chemical Formula 252]



15

The titled compound (solid) was similarly prepared according to the procedure described in the Example 240, using the compound of Example 116.

[0791]

20

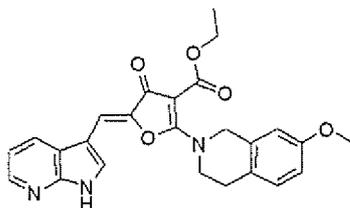
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.23 (br. s, 1H), 8.51 - 8.60 (m, 1H), 8.34 - 8.43 (m, 1H), 8.24 - 8.32 (m, 1H), 7.92 - 8.10 (m., 1H), 7.16 (dd, J = 4.64, 7.91 Hz, 1H), 6.61 (s, 1H), 4.85 (br. s, 1

H), 4.40 - 4.72 (m, 2H), 1.69 - 2.07 (m, 4H), 1.02 - 1.54 (m, 4H); LCMS (m/z): 326.1 [M+H]<sup>+</sup>.

Example 244

5 Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-(7-methoxy-3,4-dihydroisoquinolin-2(1*H*)-yl)-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 253]



10

First Step

To a suspension of 7-methoxy-1,2,3,4-tetrahydroisoquinoline hydrochloride (2.10 g, 10.5 mmol) in tetrahydrofuran, triethylamine (3.48 mL, 25.0 mmol) was added at ambient temperature and the mixture was stirred for 30 min. To this reaction mixture, ethyl 2-ethoxy-4-oxo-4,5-dihydrofuran-3-carboxylate (2.00 g, 10.0 mmol), which afforded in the Example 74, Third step was added and the mixture was stirred for 5 days. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulfate and concentrated. The residue was purified by

15

20

chromatography on silica gel (chloroform/methanol) to afford ethyl 2-[7-methoxy-3,4-dihydroisoquinolin-2(1H)-yl]-4-oxo-4,5-dihydrofuran-3-carboxylate as oil (2.85 g, y. 89%).

5  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  (ppm) 7.09 (d,  $J = 8.4$  Hz, 1H), 6.80 (dd,  $J = 8.4$ , 2.6 Hz, 1H), 6.64 (d,  $J = 2.4$  Hz, 1H), 4.78 (s, 2H), 4.54 (s, 2H), 4.33 (q,  $J = 7.1$  Hz, 2H), 3.89 (t,  $J = 5.9$  Hz, 2H), 3.79 (d,  $J = 2.9$  Hz, 3H), 2.86 - 3.04 (m, 2H), 1.38 (t,  $J = 7.1$  Hz, 3H); LCMS ( $m/z$ ): 318.2  $[\text{M}+\text{H}]^+$ .

10

#### Second Step

To a solution of ethyl 2-[7-methoxy-3,4-dihydroisoquinolin-2(1H)-yl]-4-oxo-4,5-dihydrofuran-3-carboxylate (2.58 g, 8.98 mmol) and 7-azaindole-3-carboxaldehyde (1.31 g, 8.98 mmol) in ethanol (12 mL), L-proline was added at ambient temperature. The mixture was refluxed for 24 h. The precipitate was collected by filtration, washed with ethanol and diisopropyl ether then dried to afford the titled compound as solid (1.20 g, y. 30%).

20

$^1\text{H}$  NMR ( $\text{DMSO}-d_6$ )  $\delta$  (ppm) 12.37 (s, 1H), 8.41 (dd,  $J = 7.9, 1.5$  Hz, 1H), 8.33 (dd,  $J = 4.7, 1.5$  Hz, 1H), 8.08 (s, 1H), 7.26 - 7.13 (m, 2H), 6.90 (s, 2H), 6.85 (dd,  $J = 8.3, 2.6$  Hz, 1H), 4.95 (br. s, 2H), 4.21 (q,  $J = 7.1$  Hz, 2H), 3.85 - 4.05 (m, 2H), 3.7

25

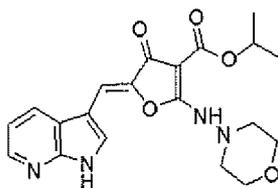
6 (s, 3H), 3.00 (t, J = 5.8 Hz, 2H), 1.26 (t, J = 7.1 Hz, 3H);  
LCMS (m/z): 446.2 [M+H]<sup>+</sup>.

[0792]

5 Example 245

Isopropyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-2-(mor-  
pholinoamino)-4-oxo-4,5-dihydrofuran-3-carboxylate

[Chemical Formula 254]



10 First Step

To a solution of isopropyl 2-isopropoxy-4-oxo-4,5-dihydrofuran-3-carboxylate (12.2 g, 53.6 mmol), which similarly prepared according to the procedure described in the Example 74, Third  
15 step using diisopropyl malonate and chloroacetyl chloride, in ethanol (45 mL), 4-aminomorpholine (5.7 mL, 59.2 mmol) was added at ambient temperature. The mixture was stirred for 18 h. The solvent was removed under reduced pressure, and the crude product was suspended in methyl *tert*-butyl ether, then the precipitate was collected by filtration, washed with methyl *tert*-  
20 butyl ether and hexane then dried to afford isopropyl 2-(morpholinoamino)-4-oxo-4,5-dihydrofuran-3-carboxylate as solid (11.

2 g, y. 75%).

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 9.60 (s, 1H), 4.95 - 5.05 (m, 1H), 4.5  
7 (s, 2H), 3.60 - 3.68 (m, 4H), 2.87 - 2.95 (m, 4H), 1.22 (d, J  
5 = 6.40 Hz, 6H); LCMS (m/z): 271.0 [M+H]<sup>+</sup>

#### Second Step

To a stirred solution of isopropyl 2-(morpholinoamino)-4-oxo-4,  
10 5-dihydrofuran-3-carboxylate (5.00 g, 18.5 mmol) and 7-azaindo  
le-3-carboxaldehyde (2.49 g, 17.1 mmol) in ethanol (25 mL), L-  
proline (0.24 g, 2.04 mmol) was added at ambient temperature.  
The mixture was refluxed for 3 days. The precipitate was colle  
cted by filtration, washed with hot ethanol then hexane, and t  
15 hen dried to afford the titled compound as solid (4.22 g, y. 6  
2%).

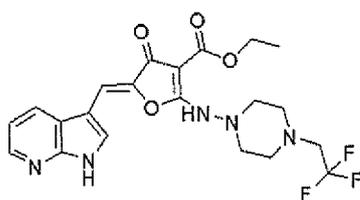
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.34 (br. s, 1H), 10.07 (s, 1H), 8.94  
(d, J = 7.78 Hz, 1H), 8.33 (dd, J = 1.38, 4.64 Hz, 1H), 8.12  
20 (d, J = 2.76 Hz, 1H), 7.22 (dd, J = 4.52, 8.03 Hz, 1H), 6.84 (s,  
1H), 4.99 - 5.12 (m, 1H), 3.75 - 3.86 (m, 4H), 3.03 - 3.13 (m,  
4H), 1.27 (d, J = 6.27 Hz, 6H); LCMS (m/z): 399.1 [M+H]<sup>+</sup>.

[0793]

25 Example 246

Ethyl 5-[(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)methylene]-4-oxo-2-  
 {[4-(2,2,2-trifluoroethyl)piperazinyl]amino}-4,5-dihydrofuran  
 -3-carboxylate

[Chemical Formula 255]



5

#### First Step

To a solution of 1-(2,2,2-trifluoroethyl)piperazine (4.88 g, 2  
 9.0 mmol) in water (4.9 mL) that cooled with ice bath, a soluti  
 10 on of sodium nitrite (4.04 g, 58.6 mmol) in water (20 mL) and a  
 cetic acid (5.0 mL, 87.0 mmol) were added dropwise slowly, the  
 n the mixture was stirred for 1 h. The reaction mixture was all  
 owed to warm to ambient temperature, stirred for further 2 h.  
 The reaction mixture was adjusted to pH9 using sodium carbonat  
 15 e, diluted with ethyl acetate and washed with water and brine.

The organic layer was dried over magnesium sulfate and concen  
 trated to afford 1-nitroso-4-(2,2,2-trifluoroethyl)piperazine  
 as oil (5.57 g, y. 97%).

20 <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ (ppm) 4.18 - 4.22 (m, 2H), 3.72 - 3.76 (m, 2  
 H), 3.32 (q, *J* = 10.13 Hz, 2H), 2.84 - 2.89 (m, 2H), 2.59 - 2.6  
 4 (m, 2H).

## Second Step

To a suspension of lithium aluminum hydride (2.22 g, 58.5 mmol) in tetrahydrofuran (100 mL) that cooled with ice bath, a solution of 1-nitroso-4-(2,2,2-trifluoroethyl)piperazine (5.43 g, 27.5 mmol) in tetrahydrofuran (10 mL) was added dropwise and the reaction mixture was allowed to warm to ambient temperature, then stirred for 5 days. The reaction mixture was cooled with ice bath, ethyl acetate was added until cease bubbling up, and water (2.1 mL) was added then the mixture was stirred for 20 min. To this mixture, 15%w/v sodium hydroxide solution (2.1 mL) and water (6.3 mL) were added, then the suspension mixture was allowed to warm to ambient temperature and then the mixture was stirred vigorously for 1 h. Magnesium sulfate was added to the mixture and stirred for a while, then the suspension was filtered. The filtrate was concentrated to afford 4-(2,2,2-trifluoroethyl)piperazine-1-amine as oil (4.72 g, y. 94%).

$^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  (ppm) 3.12 (br. s, 1H), 2.98 (q,  $J$  = 9.6 Hz, 2H), 2.60 - 2.80 (m, 8H).

## Third Step

To a solution of 4-(2,2,2-trifluoroethyl)piperazine-1-amine (4.72 g, 25.8 mmol) in ethanol (43 mL), ethyl 2-ethoxy-4-oxo-4,

5-dihydrofuran-3-carboxylate (4.70 g, 23.5 mmol) which similarly prepared according to the procedure described in the Example 74, Third step was added at ambient temperature. The mixture was stirred for 2 h. The precipitate was collected by filtration, washed with diethyl ether and hexane then dried to afford ethyl 4-oxo-2-([4-(2,2,2-trifluoroethyl)piperazinyl]amino)-4,5-dihydrofuran-3-carboxylate as solid (5.64 g, y. 71%).

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 8.94 (s, 1H), 4.61 (s, 2H), 4.32 (q, J = 7.07 Hz, 2H), 3.03 (q, J = 9.47 Hz, 2H), 2.95 - 2.99 (m, 4H), 2.85 - 2.90 (m, 4H), 1.37 (t, J = 7.20 Hz, 3H); LCMS (m/z): 338.1 [M+H]<sup>+</sup>.

#### Fourth Step

To a solution of ethyl 4-oxo-2-([4-(2,2,2-trifluoroethyl)piperazinyl]amino)-4,5-dihydrofuran-3-carboxylate (3.01 g, 8.93 mmol) and 7-azaindole-3-carboxaldehyde (1.25 g, 8.55 mmol) in ethanol (25 mL), L-proline (99 mg, 0.86 mmol) was added at ambient temperature then the mixture was refluxed for 2 days. The precipitate was collected by filtration, washed with hot ethanol then hexane, and then dried to afford the titled compound as solid (2.64 g, y. 66%).

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ (ppm) 12.32 (s, 1H), 10.09 (s, 1H), 8.95 (d, J = 7.6 Hz, 1H), 8.33 (d, J = 4.1 Hz, 1H), 8.09 (s, 1H), 7.30

- 7.16 (m, 1H), 6.80 (s, 1H), 4.19 (q,  $J = 7.1$  Hz, 2H), 3.31 - 3.41 (m, 2H), 3.06 (s, 4H), 2.88 (s, 4H), 1.25 (t,  $J = 7.0$  Hz, 3H); LCMS ( $m/z$ ): 466.0  $[M+H]^+$ .

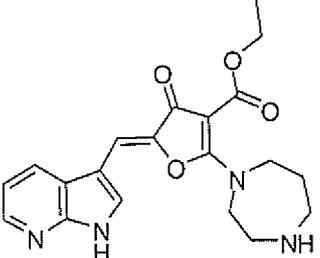
5 [0794]

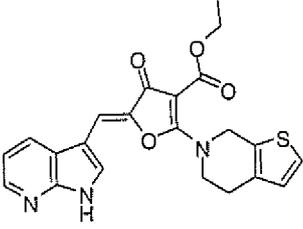
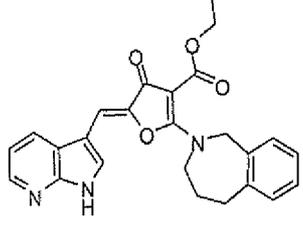
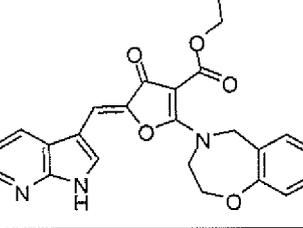
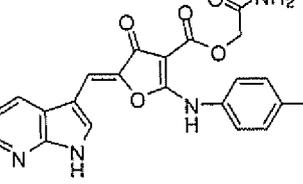
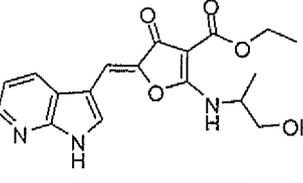
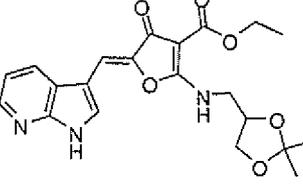
Each of the Example compounds shown in the following [Table 1-1] to [Table 1-10] were prepared according to the procedure described in the above Examples or modified procedure well known in the art of organic chemistry if needed, using appropriate starting materials (those materials which are commercially available, or which are derivatized by known methods or their modified methods from commercial compounds). The physicochemical data of each compound were shown in the following [Table 2-1] to [Table 2-6].

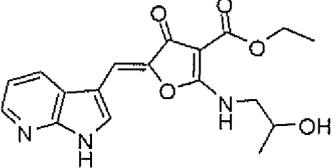
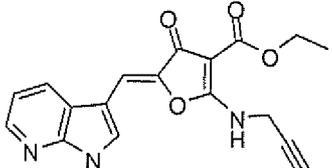
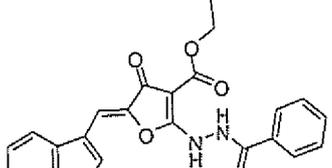
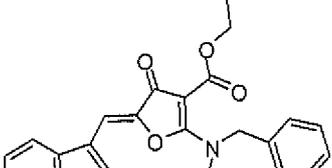
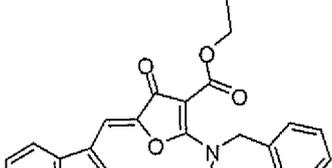
15

[0795]

[Table 1-1]

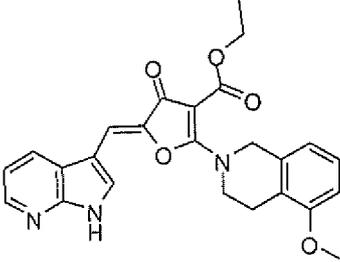
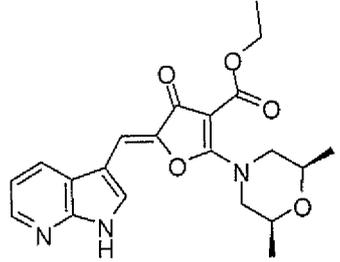
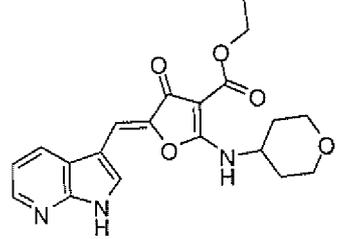
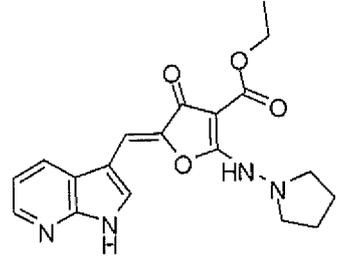
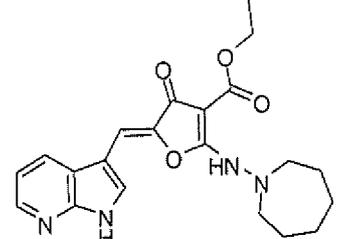
Example	Chemical Formula	Chemical Name
247		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(1,4-diazepan-1-yl)-4-oxo-4,5-dihydrofuran-3-carboxylate

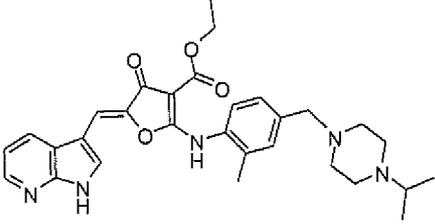
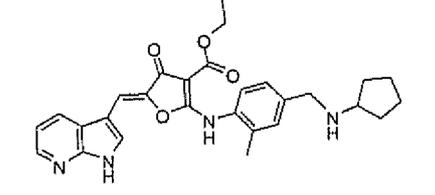
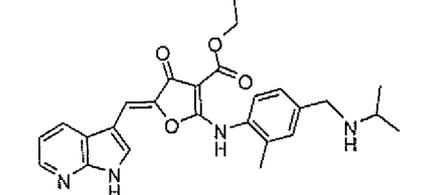
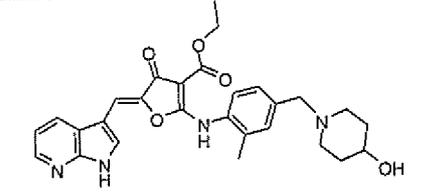
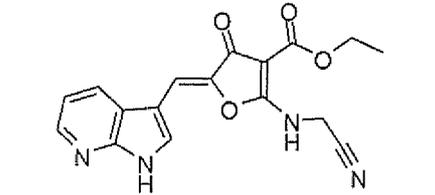
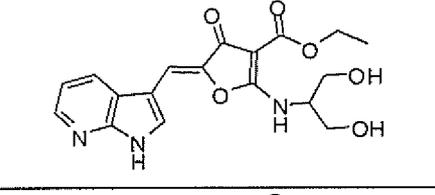
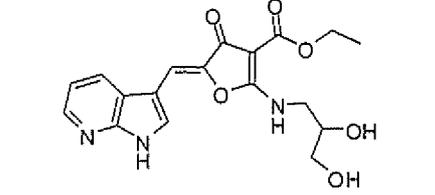
248		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(4,5-dihydrothieno[2,3- <i>c</i> ]pyridin-6(7 <i>H</i> )-yl)-4-oxo-4,5-dihydrofuran-3-carboxylate
249		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(4,5-dihydro-1 <i>H</i> -benzo[ <i>c</i> ]azepin-2(3 <i>H</i> )-yl)-4-oxo-4,5-dihydrofuran-3-carboxylate
250		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(2,3-dihydrobenzo[ <i>f</i> ][1,4]oxazepin-4(5 <i>H</i> )-yl)-4-oxo-4,5-dihydrofuran-3-carboxylate
251		Carbamoylmethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-[(4-fluorophenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate
252		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-[(1-hydroxypropan-2-yl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate
253		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-[(2,2-dimethyl-1,3-dioxolan-4-yl)methylamino]-4-oxo-4,5-dihydrofuran-3-carboxylate

254		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-[(2-hydroxypropyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate
255		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-4-oxo-2-(prop-2-yn-1-ylamino)-4,5-dihydrofuran-3-carboxylate
256		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(2-benzoylhydrazinyl)-4-oxo-4,5-dihydrofuran-3-carboxylate
257		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(2,3-dihydrobenzo[ <i>f</i> ][1,4]thiazepin-4(5 <i>H</i> )-yl)-4-oxo-4,5-dihydrofuran-3-carboxylate
258		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(2,3-dihydro-1 <i>H</i> -benzo[ <i>e</i> ][1,4]diazepin-4(5 <i>H</i> )-yl)-4-oxo-4,5-dihydrofuran-3-carboxylate

[0796]

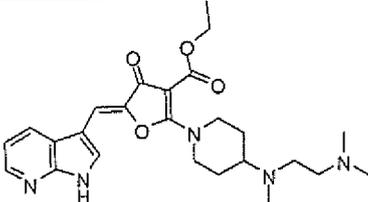
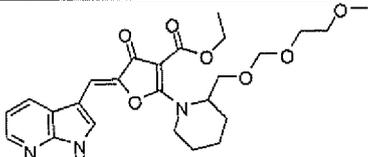
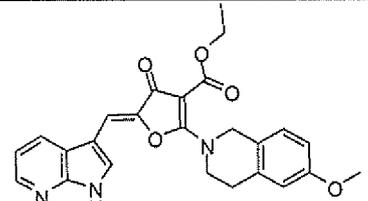
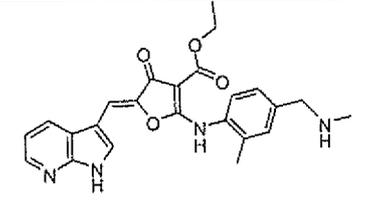
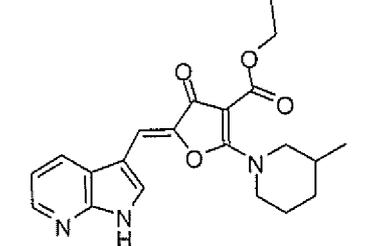
[Table 1-2]

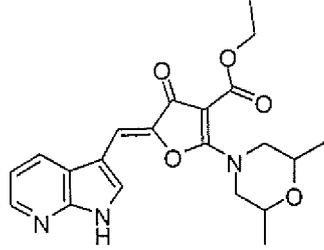
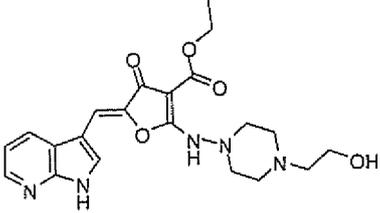
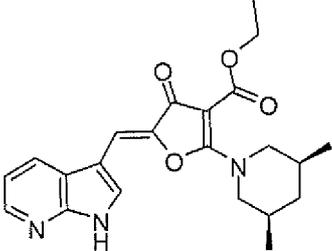
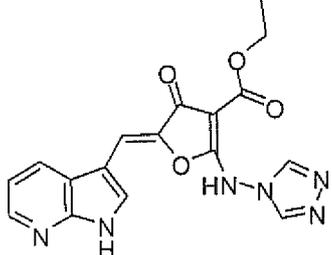
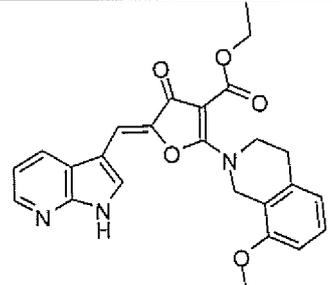
259		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(5-methoxy-3,4-dihydroisoquinolin-2(1 <i>H</i> )-yl)-4-oxo-4,5-dihydrofuran-3-carboxylate
260		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-[(2 <i>S</i> ,6 <i>R</i> )-2,6-dimethylmorpholino]-4-oxo-4,5-dihydrofuran-3-carboxylate
261		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-4-oxo-2-[(tetrahydro-2 <i>H</i> -pyran-4-yl)amino]-4,5-dihydrofuran-3-carboxylate
262		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-4-oxo-2-(pyrrolidin-1-ylamino)-4,5-dihydrofuran-3-carboxylate
263		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(azepan-1-ylamino)-4-oxo-4,5-dihydrofuran-3-carboxylate

264		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-[(4-[(4-isopropylpiperazinyl)methyl]-2-methylphenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate
265		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-[(4-[(cyclopentylamino)methyl]-2-methylphenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate
266		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-[(4-[(isopropylamino)methyl]-2-methylphenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate
267		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-[(4-[(4-hydroxypiperidinomethyl)-2-methylphenyl]amino)-4-oxo-4,5-dihydrofuran-3-carboxylate
268		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(cyanomethylamino)-4-oxo-4,5-dihydrofuran-3-carboxylate
269		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-[(1,3-dihydroxypropan-2-yl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate
270		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-[(2,3-dihydroxypropyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[0797]

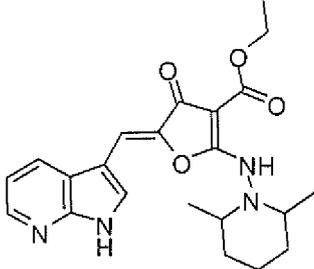
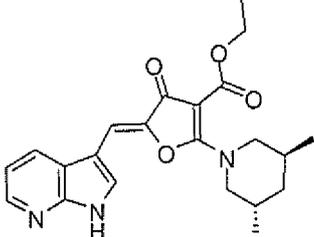
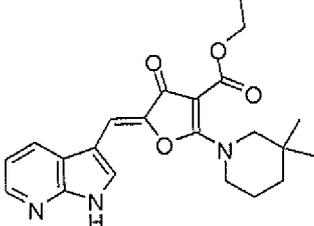
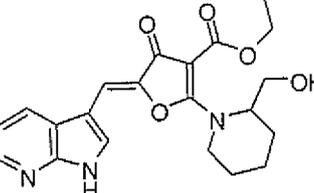
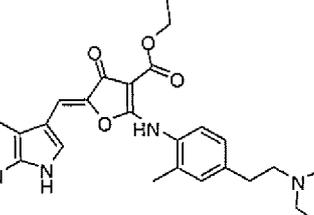
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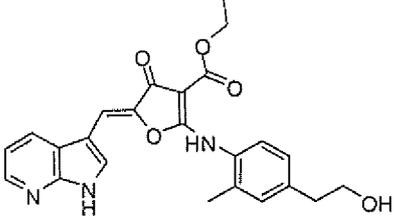
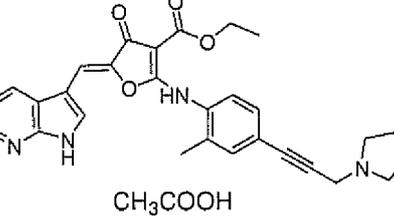
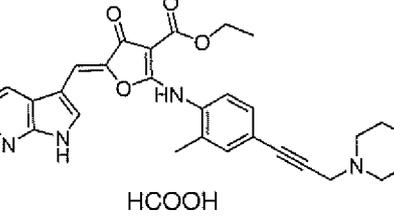
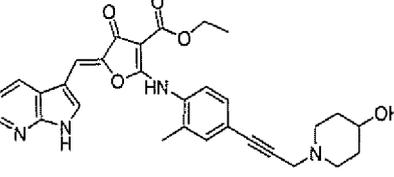
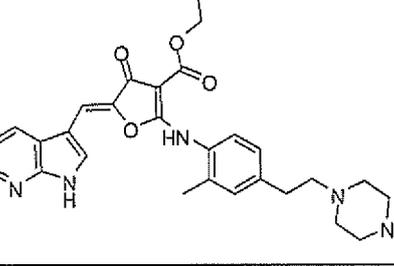
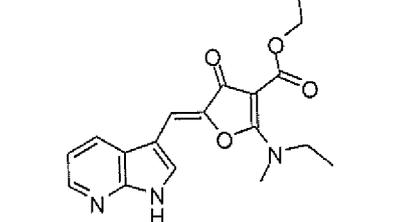
271		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(4-[[2-(dimethylamino)ethyl]( <i>N</i> -methyl)amino]piperidino)-4-oxo-4,5-dihydrofuran-3-carboxylate
272		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(2-[(2-methoxyethoxy)methoxy]methyl)piperidino)-4-oxo-4,5-dihydrofuran-3-carboxylate
273		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(6-methoxy-3,4-dihydroisoquinolin-2(1 <i>H</i> )-yl)-4-oxo-4,5-dihydrofuran-3-carboxylate
274		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-[(2-methyl-4-[(methylamino)methyl]phenyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate
275		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(3-methylpiperidino)-4-oxo-4,5-dihydrofuran-3-carboxylate

276		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(2,6-dimethylmorpholino)-4-oxo-4,5-dihydrofuran-3-carboxylate
277		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-[[4-(2-hydroxyethyl)piperazinyl]amino]-4-oxo-4,5-dihydrofuran-3-carboxylate
278		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-[(3 <i>R</i> ,5 <i>S</i> )-3,5-dimethylpiperidino]-4-oxo-4,5-dihydrofuran-3-carboxylate
279		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-[(4 <i>H</i> -1,2,4-triazol-4-yl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate
280		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-[8-methoxy-3,4-dihydroisoquinolin-2(1 <i>H</i> )-yl]-4-oxo-4,5-dihydrofuran-3-carboxylate

[0798]

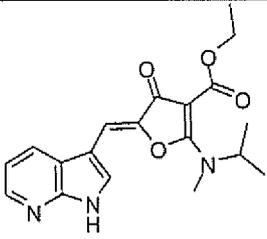
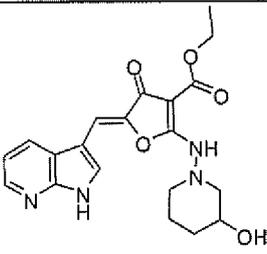
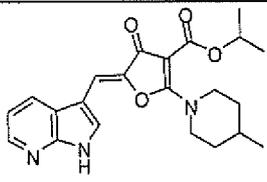
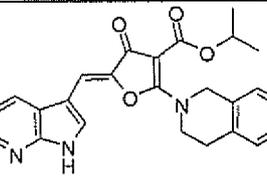
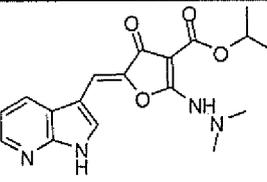
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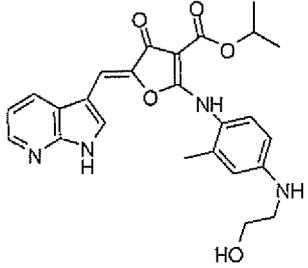
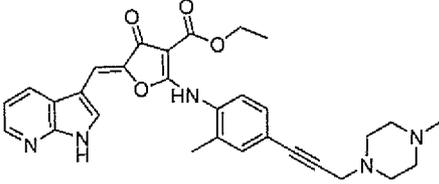
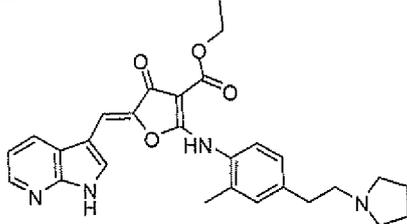
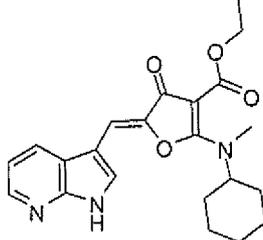
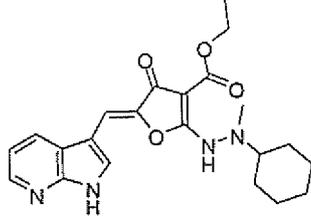
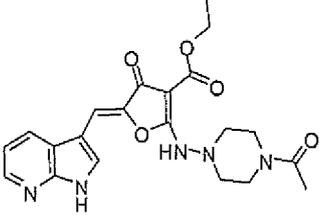
281		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(2,6-dimethylpiperidino)-4-oxo-4,5-dihydrofuran-3-carboxylate
282		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-[(3 <i>S</i> ,5 <i>S</i> )-3,5-dimethylpiperidino]-4-oxo-4,5-dihydrofuran-3-carboxylate
283		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(3,3-dimethylpiperidino)-4-oxo-4,5-dihydrofuran-3-carboxylate
284		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-[2-(hydroxymethyl)piperidino]-4-oxo-4,5-dihydrofuran-3-carboxylate
285		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-[[2-methyl-4-(2-morpholinoethyl)phenyl]amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

286		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-[[4-(2-hydroxyethyl)-2-methylphenyl]amino]-4-oxo-4,5-dihydrofuran-3-carboxylate
287	 <p>CH<sub>3</sub>COOH</p>	Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-((2-methyl-4-[(3-(pyrrolidinyl)prop-1-yn-1-yl]phenyl)amino)-4-oxo-4,5-dihydrofuran-3-carboxylate acetate
288	 <p>HCOOH</p>	Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-[[2-methyl-4-(3-morpholinoprop-1-yn-1-yl)phenyl]amino]-4-oxo-4,5-dihydrofuran-3-carboxylate formate
289		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-[[4-[3-(4-hydroxypiperidino)prop-1-yn-1-yl]-2-methylphenyl]amino]-4-oxo-4,5-dihydrofuran-3-carboxylate
290		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-[[2-methyl-4-[2-(4-methylpiperazinyl)ethyl]phenyl]amino]-4-oxo-4,5-dihydrofuran-3-carboxylate
291		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-[ethyl( <i>N</i> -methyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[0799]

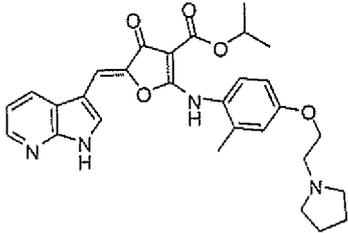
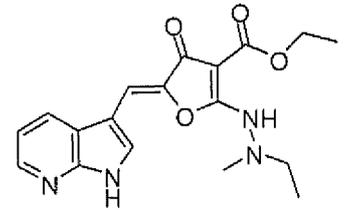
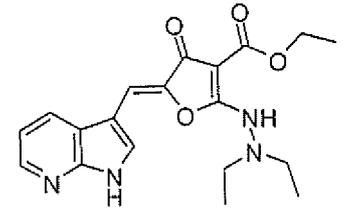
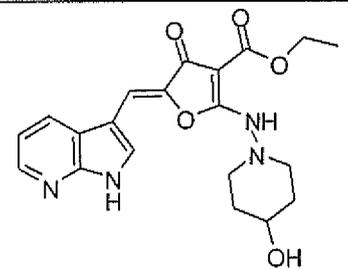
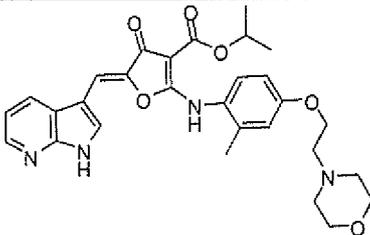
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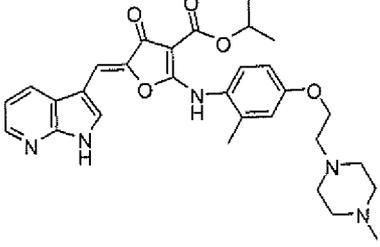
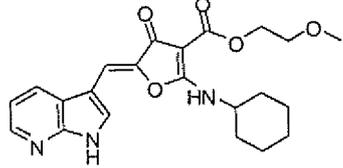
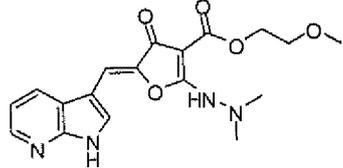
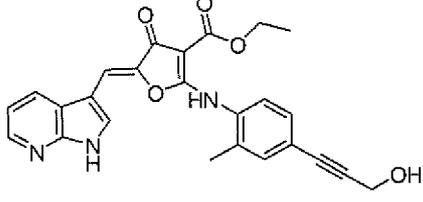
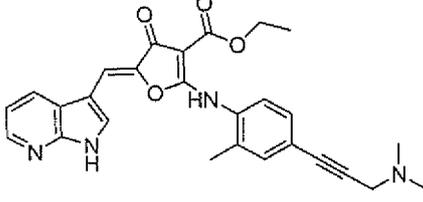
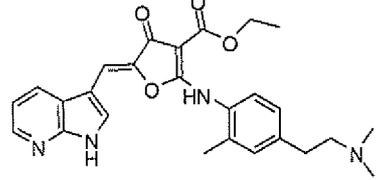
292		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-[isopropyl ( <i>N</i> -methyl) amino]-4-oxo-4,5-dihydrofuran-3-carboxylate
293		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(3-hydroxypiperidino)-4-oxo-4,5-dihydrofuran-3-carboxylate
294		Isopropyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(4-methylpiperidino)-4-oxo-4,5-dihydrofuran-3-carboxylate
295		Isopropyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(3,4-dihydroisoquinolin-2(1 <i>H</i> )-yl)-4-oxo-4,5-dihydrofuran-3-carboxylate
296		Isopropyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(2,2-dimethylhydrazinyl)-4-oxo-4,5-dihydrofuran-3-carboxylate

297		Isopropyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-({4-[(2-hydroxyethyl)amino]-2-methylphenyl}amino)-4-oxo-4,5-dihydrofuran-3-carboxylate
298		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-({2-methyl-4-[3-(4-methylpiperazinyl)prop-1-yn-1-yl]phenyl}amino)-4-oxo-4,5-dihydrofuran-3-carboxylate
299		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-({2-methyl-4-[2-(pyrrolidinyl)ethyl]phenyl}amino)-4-oxo-4,5-dihydrofuran-3-carboxylate
300		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-[(cyclohexyl( <i>N</i> -methyl)amino)-4-oxo-4,5-dihydrofuran-3-carboxylate
301		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(2-cyclohexyl-2-methylhydrazinyl)-4-oxo-4,5-dihydrofuran-3-carboxylate
302		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-[(4-acetylpiperazinyl)amino]-4-oxo-4,5-dihydrofuran-3-carboxylate

[0800]

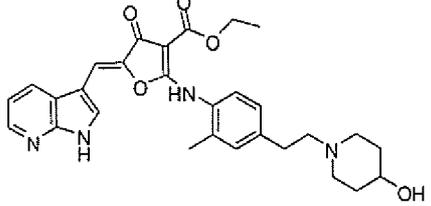
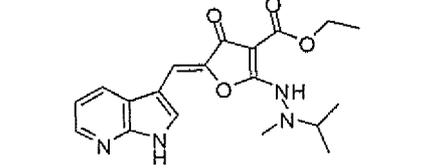
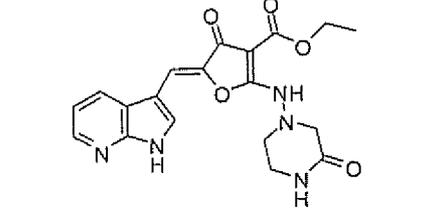
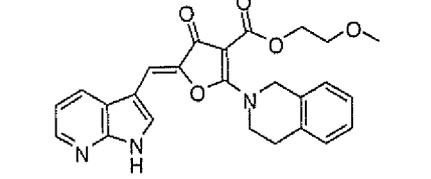
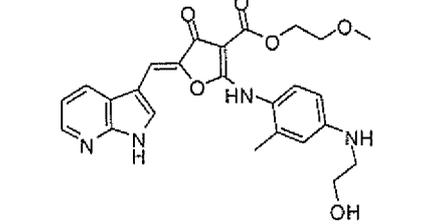
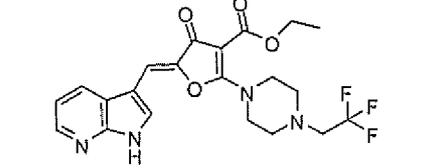
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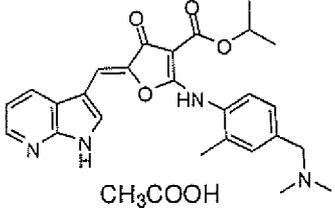
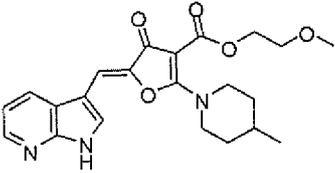
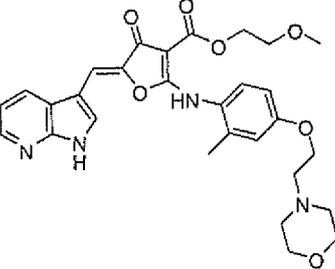
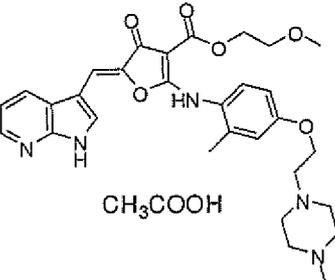
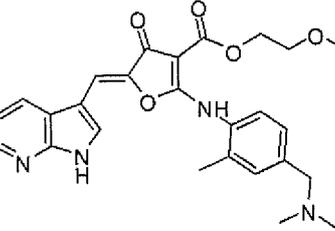
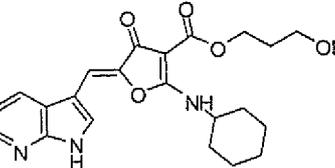
303		Isopropyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-({2-methyl-4-[2-(pyrrolidinyl)ethoxy]phenyl}amino)-4-oxo-4,5-dihydrofuran-3-carboxylate
304		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(2-ethyl-2-methylhydrazinyl)-4-oxo-4,5-dihydrofuran-3-carboxylate
305		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(2,2-diethylhydrazinyl)-4-oxo-4,5-dihydrofuran-3-carboxylate
306		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(4-hydroxypiperidinoamino)-4-oxo-4,5-dihydrofuran-3-carboxylate
307		Isopropyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-([2-methyl-4-(2-morpholinoethoxy)phenyl]amino)-4-oxo-4,5-dihydrofuran-3-carboxylate

308		Isopropyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-((2-methyl-4-[2-(4-methylpiperazinyl)ethoxy]phenyl)amino)-4-oxo-4,5-dihydrofuran-3-carboxylate
309		2-Methoxyethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(cyclohexylamino)-4-oxo-4,5-dihydrofuran-3-carboxylate
310		2-Methoxyethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(2,2-dimethylhydrazinyl)-4-oxo-4,5-dihydrofuran-3-carboxylate
311		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-([4-(3-hydroxyprop-1-yn-1-yl)-2-methylphenyl]amino)-4-oxo-4,5-dihydrofuran-3-carboxylate
312		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-([4-[3-(dimethylamino)prop-1-yn-1-yl]-2-methylphenyl]amino)-4-oxo-4,5-dihydrofuran-3-carboxylate
313		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-([4-[2-(dimethylamino)ethyl]-2-methylphenyl]amino)-4-oxo-4,5-dihydrofuran-3-carboxylate

[0801]

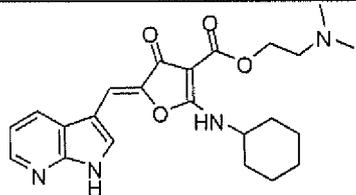
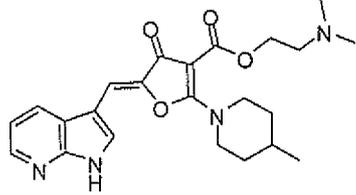
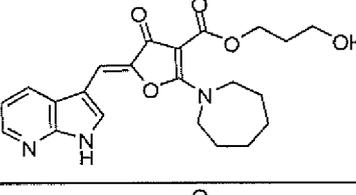
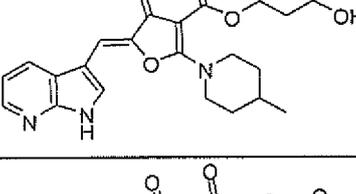
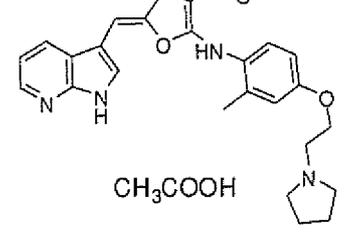
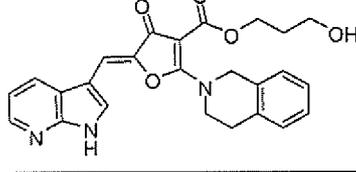
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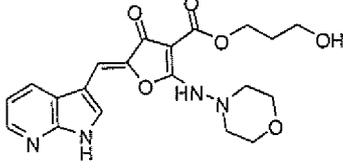
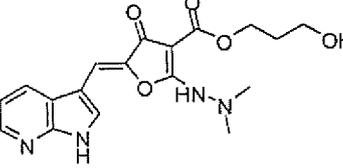
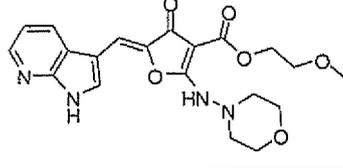
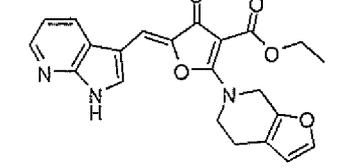
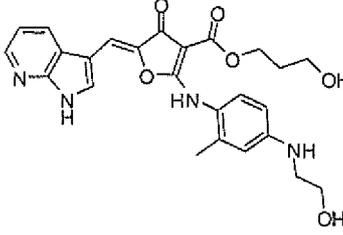
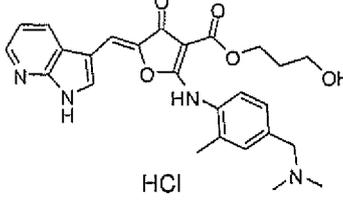
314		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-((4-[2-(4-hydroxypiperidino)ethyl]-2-methylphenyl)amino)-4-oxo-4,5-dihydrofuran-3-carboxylate
315		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(2-isopropyl-2-methylhydrazinyl)-4-oxo-4,5-dihydrofuran-3-carboxylate
316		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-4-oxo-2-[(3-oxopiperazinyl)amino]-4,5-dihydrofuran-3-carboxylate
317		2-Methoxyethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(3,4-dihydroisoquinolin-2(1 <i>H</i> )-yl)-4-oxo-4,5-dihydrofuran-3-carboxylate
318		2-Methoxyethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-((4-[(2-hydroxyethyl)amino]-2-methylphenyl)amino)-4-oxo-4,5-dihydrofuran-3-carboxylate
319		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-4-oxo-2-[4-(2,2,2-trifluoroethyl)piperazinyl]-4,5-dihydrofuran-3-carboxylate

320		Isopropyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-({4-[(dimethylamino)methyl]-2-methylphenyl}amino)-4-oxo-4,5-dihydrofuran-3-carboxylate acetate
321		2-Methoxyethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(4-methylpiperidino)-4-oxo-4,5-dihydrofuran-3-carboxylate
322		2-Methoxyethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-([2-methyl-4-(2-morpholinoethoxy)phenyl]amino)-4-oxo-4,5-dihydrofuran-3-carboxylate
323		2-Methoxyethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-([2-methyl-4-[2-(4-methylpiperazinyl)ethoxy]phenyl]amino)-4-oxo-4,5-dihydrofuran-3-carboxylate acetate
324		2-Methoxyethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-({4-[(dimethylamino)methyl]-2-methylphenyl}amino)-4-oxo-4,5-dihydrofuran-3-carboxylate
325		3-Hydroxypropyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(cyclohexylamino)-4-oxo-4,5-dihydrofuran-3-carboxylate

[0802]

[Table 1-8]

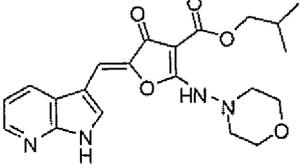
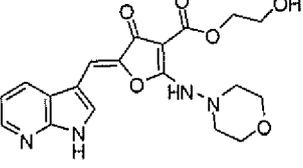
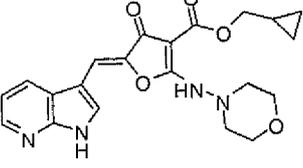
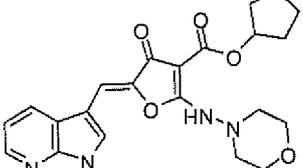
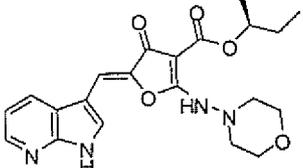
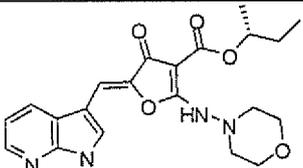
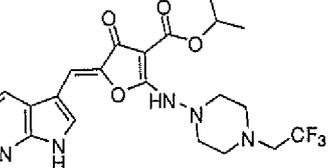
326		2-(Dimethylamino)ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(cyclohexylamino)-4-oxo-4,5-dihydrofuran-3-carboxylate
327		2-(Dimethylamino)ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(4-methylpiperidino)-4-oxo-4,5-dihydrofuran-3-carboxylate
328		3-Hydroxypropyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-azepinyl-4-oxo-4,5-dihydrofuran-3-carboxylate
329		3-Hydroxypropyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(4-methylpiperidino)-4-oxo-4,5-dihydrofuran-3-carboxylate
330		2-Methoxyethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-((2-methyl-4-[2-(pyrrolidinyl)ethoxy]phenyl)amino)-4-oxo-4,5-dihydrofuran-3-carboxylate acetate
331		3-Hydroxypropyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(3,4-dihydroisoquinolin-2(1 <i>H</i> )-yl)-4-oxo-4,5-dihydrofuran-3-carboxylate

332		3-Hydroxypropyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(morpholino)-4-oxo-4,5-dihydrofuran-3-carboxylate
333		3-Hydroxypropyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(2,2-dimethylhydrazinyl)-4-oxo-4,5-dihydrofuran-3-carboxylate
334		2-Methoxyethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(morpholino)-4-oxo-4,5-dihydrofuran-3-carboxylate
335		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(4,5-dihydrofuro[2,3- <i>c</i> ]pyridin-6(7 <i>H</i> )-yl)-4-oxo-4,5-dihydrofuran-3-carboxylate
336		3-Hydroxypropyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-((4-((2-hydroxyethyl)amino)-2-methylphenyl)amino)-4-oxo-4,5-dihydrofuran-3-carboxylate
337	 <p>HCl</p>	3-Hydroxypropyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-((4-((dimethylamino)methyl)-2-methylphenyl)amino)-4-oxo-4,5-dihydrofuran-3-carboxylate hydrochloride
338	 <p>CH<sub>3</sub>COOH</p>	2-(Dimethylamino)ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(2,2-dimethylhydrazinyl)-4-oxo-4,5-dihydrofuran-3-carboxylate acetate

[0803]

[Table 1-9]

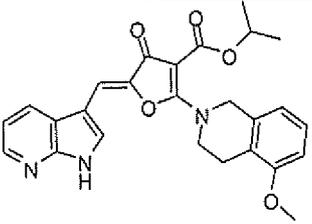
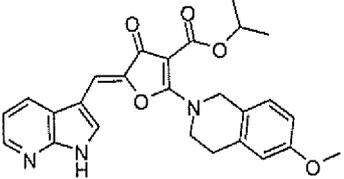
339		2-(Dimethylamino)ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(morpholinoamino)-4-oxo-4,5-dihydrofuran-3-carboxylate acetate
340		2-(Dimethylamino)ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-({4-[(2-hydroxyethyl)amino]-2-methylphenyl}amino)-4-oxo-4,5-dihydrofuran-3-carboxylate acetate
341		Ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-({4-(cyanomethyl)-2-methylphenyl}amino)-4-oxo-4,5-dihydrofuran-3-carboxylate
342		2-(Dimethylamino)ethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-({4-[(dimethylamino)methyl]-2-methylphenyl}amino)-4-oxo-4,5-dihydrofuran-3-carboxylate diformate
343		Isopropyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-({4-(2-hydroxyethoxy)-2-methylphenyl}amino)-4-oxo-4,5-dihydrofuran-3-carboxylate
344		Propyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(morpholinoamino)-4-oxo-4,5-dihydrofuran-3-carboxylate

345		Isobutyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(morpholinoamino)-4-oxo-4,5-dihydrofuran-3-carboxylate
346		2-Hydroxyethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(morpholinoamino)-4-oxo-4,5-dihydrofuran-3-carboxylate
347		Cyclopropylmethyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(morpholinoamino)-4-oxo-4,5-dihydrofuran-3-carboxylate
348		Cyclopentyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(morpholinoamino)-4-oxo-4,5-dihydrofuran-3-carboxylate
349		<i>(S)</i> - <i>sec</i> -Butyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(morpholinoamino)-4-oxo-4,5-dihydrofuran-3-carboxylate
350		<i>(R)</i> - <i>sec</i> -Butyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(morpholinoamino)-4-oxo-4,5-dihydrofuran-3-carboxylate
351		Isopropyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-4-oxo-2-[(4-(2,2,2-trifluoroethyl)piperazinyl)amino]-4,5-dihydrofuran-3-carboxylate

[0804]

[Table 1-10]

352		Isopropyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-4-oxo-2-[(tetrahydro-2 <i>H</i> -pyran-4-yl)amino]-4,5-dihydrofuran-3-carboxylate
353		Isopropyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-4-oxo-2-[(1,1-dioxidothiomorpholino)amino]-4,5-dihydrofuran-3-carboxylate
354		Isopropyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(7-methoxy-3,4-dihydroisoquinolin-2(1 <i>H</i> )-yl)-4-oxo-4,5-dihydrofuran-3-carboxylate
355	 CH <sub>3</sub> COOH	Isopropyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(7-methyl-3,4-dihydroisoquinolin-2(1 <i>H</i> )-yl)-4-oxo-4,5-dihydrofuran-3-carboxylate acetate
356	 CH <sub>3</sub> COOH	Isopropyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(7-chloro-3,4-dihydroisoquinolin-2(1 <i>H</i> )-yl)-4-oxo-4,5-dihydrofuran-3-carboxylate acetate
357		Isopropyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(7-fluoro-3,4-dihydroisoquinolin-2(1 <i>H</i> )-yl)-4-oxo-4,5-dihydrofuran-3-carboxylate

358		Isopropyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(5-methoxy-3,4-dihydroisoquinolin-2(1 <i>H</i> )-yl)-4-oxo-4,5-dihydrofuran-3-carboxylate
359		Isopropyl 5-[(1 <i>H</i> -pyrrolo[2,3- <i>b</i> ]pyridin-3-yl)methylene]-2-(6-methoxy-3,4-dihydroisoquinolin-2(1 <i>H</i> )-yl)-4-oxo-4,5-dihydrofuran-3-carboxylate

[0805]

[Table 2-1]

Examp le	<sup>1</sup> H-NMR δ (ppm)	LCMS m/z [M+H] <sup>+</sup>
247	(DMSO-d <sub>6</sub> ): 12.17 -12.43 (m, 1H), 8.18 - 8.41 (m, 3H), 7.94 (br. s, 1H), 7.12 - 7.23 (m, 1H), 6.85 (br. s, 1H), 4.10 - 4.23 (m, 2H), 3.65 - 3.93 (m, 2H), 2.93 - 3.13 (m, 2H), 2.77 - 2.93 (m, 2H), 1.80 - 1.98 (m, 2H), 1.10 - 1.35 (m, 5H).	383.2
248	(DMSO-d <sub>6</sub> ): 12.37 (s, 1H), 8.40 (d, J = 7.6 Hz, 1H), 8.33 (d, J = 3.7 Hz, 1H), 8.09 (s, 1H), 7.47 (d, J = 4.9 Hz, 1H), 7.21 (dd, J = 7.7, 4.7 Hz, 1H), 6.87 - 6.98 (m, 2H), 5.07 (s, 2H), 4.21 (q, J = 6.9 Hz, 2H), 3.98 - 4.08 (m, 2H), 2.92 - 3.03 (m, 2H), 1.26 (t, J = 7.0 Hz, 3H).	422.0
249	(DMSO-d <sub>6</sub> ): 12.37 (s, 1H), 8.28 - 8.39 (m, 2H), 8.02 (br. s, 1H), 7.10 - 7.29 (m, 5H), 6.81 (s, 1H), 5.13 (s, 2H), 4.18 - 4.30 (m, 2H), 4.00 - 4.18 (m, 2H), 2.99 - 3.12 (m, 2H), 1.92 - 2.07 (m, 2H), 1.28 (t, J = 6.6 Hz, 3H).	430.0
250	(DMSO-d <sub>6</sub> ): 12.42 (s, 1H), 8.27 - 8.38 (m, 2H), 7.97 (s, 1H), 7.30 - 7.43 (m, 1H), 7.15 - 7.27 (m, 2H), 7.03 - 7.13 (m, 1H), 6.96 (d, J = 7.7 Hz, 1H), 6.85 (s, 1H), 5.18 (s, 2H), 4.40 - 4.50 (m, 2H), 4.14 - 4.26 (m, 2H), 4.00 - 4.14 (m, 2H), 1.26 (t, J = 6.6 Hz, 3H).	432.3
251	(DMSO-d <sub>6</sub> ): 12.14 (s, 1H), 10.70 - 12.05 (m, 1H), 8.23 (d, J = 4.0 Hz, 1H), 8.00 (d, J = 7.8 Hz, 1H), 7.69 (s, 1H), 7.20 - 7.50 (m, 5H), 6.91 (dd, J = 7.7, 4.7 Hz, 1H), 4.51 (s, 2H).	423.2
252	(DMSO-d <sub>6</sub> ): 12.33 (br. s, 1H), 8.57 (d, J = 6.02 Hz, 1H), 8.42 (dd, J = 1.38, 7.91 Hz, 1H), 8.31 (dd, J = 1.25, 4.52 Hz, 1H), 8.01 (s, 1H), 7.20 (dd, J = 4.77, 8.03 Hz, 1H), 6.90 (s, 1H), 5.20 (t, J = 5.27 Hz, 1H), 4.16 - 4.34 (m, 3H), 3.52 - 3.68 (m, 2H), 1.32 (d, J = 6.53 Hz, 3H), 1.26 (t, J = 7.15 Hz, 3H).	358.0
253	(DMSO-d <sub>6</sub> ): 12.38 (br. s, 1H), 8.93 (br. s, 1H), 8.43 (dd, J = 1.38, 7.91 Hz, 1H), 8.31 (dd, J = 1.38, 4.64 Hz, 1H), 8.06 (s, 1H), 7.19 (dd, J = 4.64, 7.91 Hz, 1H), 6.90 (s, 1H), 4.37 - 4.46 (m, 1H), 4.22 (q, J = 7.03 Hz, 2H), 4.06 (dd, J = 6.53, 8.78 Hz, 1H), 3.68 - 3.89 (m, 3H), 1.32 (s, 3H), 1.23 - 1.29 (m, 6H).	414.0
254	(DMSO-d <sub>6</sub> ): 12.35 (br. s, 1H), 8.84 (br. s, 1H), 8.46 (dd, J = 1.38, 7.91 Hz, 1H), 8.31 (dd, J = 1.38, 4.64 Hz, 1H), 8.04 (s, 1H), 7.19 (dd, J = 4.77, 8.03 Hz, 1H), 6.89 (s, 1H), 5.17 (d, J = 4.52 Hz, 1H), 4.21 (q, J = 7.03 Hz, 2H), 3.89 - 4.00 (m, 1H), 3.57 - 3.67 (m, 1H), 3.45 - 3.56 (m, 1H), 1.26 (t, J = 7.15 Hz, 3H), 1.16 (d, J = 6.27 Hz, 3H).	358.0
255	(DMSO-d <sub>6</sub> ): 12.41 (br. s, 1H), 9.29 (br. s, 1H), 8.49 (d, J = 7.78 Hz, 1H), 8.32 (dd, J = 1.13, 4.64 Hz, 1H), 8.12 (s, 1H), 7.19 (dd, J = 4.64, 7.91 Hz, 1H), 6.96 (s, 1H), 4.43 (d, J = 1.51 Hz, 2H), 4.22 (q, J = 7.03 Hz, 2H), 3.42 (t, J	338.0

	= 2.26 Hz, 1H), 1.26 (t, J = 7.15 Hz, 3H).	
256	(DMSO-d6): 12.35 (s, 1H), 11.34 (s, 1H), 10.67 (s, 1H), 8.33 (d, J = 7.3 Hz, 1H), 8.10 (d, J = 4.4 Hz, 1H), 7.94 - 8.05 (m, 3H), 7.68 - 7.76 (m, 1H), 7.58 - 7.68 (m, 2H), 6.93 (s, 1H), 6.29 - 6.36 (m, 1H), 4.26 (q, J = 7.0 Hz, 2H), 1.29 (t, J = 7.0 Hz, 3H).	419.2
257	(DMSO-d6): 12.20 - 12.50 (m, 1H), 8.26 - 8.40 (m, 2H), 7.89 (s, 1H), 7.15 - 7.59 (m, 5H), 6.84 (s, 1H), 5.03 - 5.30 (m, 2H), 4.12 - 4.31 (m, 4H), 3.10 - 3.50 (m, 2H), 1.22 - 1.32 (m, 3H).	448.2
258	(DMSO-d6): 12.10 - 12.60 (m, 1H), 8.25 - 8.40 (m, 2H), 7.93 (s, 1H), 7.12 - 7.24 (m, 2H), 6.96 - 7.05 (m, 1H), 6.82 (s, 1H), 6.66 - 6.78 (m, 2H), 5.85 (s, 1H), 5.05 (s, 2H), 4.15 - 4.30 (m, 2H), 3.75 - 4.00 (m, 2H), 3.40 - 3.55 (m, 2H), 1.26 (t, J = 7.0 Hz, 3H).	431.2
259	(DMSO-d6): 12.33 (br. s, 1H), 8.40 (d, J = 7.8 Hz, 1H), 8.32 (d, J = 4.3 Hz, 1H), 8.07 (s, 1H), 7.17 - 7.29 (m, 2H), 6.80 - 6.95 (m, 3H), 4.96 (s, 2H), 4.21 (q, J = 7.0 Hz, 2H), 3.90 - 4.07 (m, 2H), 3.81 (s, 3H), 2.88 - 3.00 (m, 2H), 1.26 (t, J = 7.1 Hz, 3H).	446.2
260	(DMSO-d6): 12.32 (s, 1H), 8.37 (d, J = 7.9 Hz, 1H), 8.28 - 8.34 (m, 1H), 8.01 (s, 1H), 7.19 (dd, J = 8.0, 4.5 Hz, 1H), 6.88 (s, 1H), 4.08 - 4.24 (m, 4H), 3.73 - 3.87 (m, 2H), 2.95 - 3.06 (m, 2H), 1.24 (t, J = 7.0 Hz, 3H), 1.18 (d, J = 6.0 Hz, 6H).	398.2
261	(DMSO-d6): 12.35 (s, 1H), 8.66 (br. s, 1H), 8.41 (d, J = 7.9 Hz, 1H), 8.32 (d, J = 3.5 Hz, 1H), 8.01 (s, 1H), 7.21 (dd, J = 7.9, 4.7 Hz, 1H), 6.90 (s, 1H), 4.18 - 4.30 (m, 3H), 3.89 - 4.00 (m, 2H), 3.40 - 3.53 (m, 2H), 1.82 - 1.96 (m, 4H), 1.25 (q, J = 7.1 Hz, 3H).	384.2
262	(DMSO-d6): 12.31 (s, 1H), 9.87 (s, 1H), 8.93 (d, J = 7.8 Hz, 1H), 8.30 (d, J = 3.6 Hz, 1H), 8.06 (d, J = 2.2 Hz, 1H), 7.14 (dd, J = 8.0, 4.6 Hz, 1H), 6.85 (s, 1H), 4.20 (q, J = 7.0 Hz, 2H), 3.04 - 3.17 (m, 4H), 1.85 - 1.98 (m, 4H), 1.26 (t, J = 7.1 Hz, 3H).	369.2
263	(DMSO-d6): 12.39 (s, 1H), 10.05 (s, 1H), 8.85 (d, J = 7.8 Hz, 1H), 8.33 (d, J = 3.8 Hz, 1H), 8.12 (s, 1H), 7.17 (dd, J = 7.8, 4.6 Hz, 1H), 6.87 (s, 1H), 4.20 (q, J = 7.0 Hz, 2H), 3.08 - 3.20 (m, 4H), 1.63 - 1.84 (m, 8H), 1.26 (t, J = 7.0 Hz, 3H).	397.2
264	(DMSO-d6): 12.26 (s, 1H), 8.16 - 8.24 (m, 2H), 7.85 (d, J = 7.9 Hz, 1H), 7.62 (s, 1H), 7.38 (d, J = 7.5 Hz, 1H), 7.31 (s, 1H), 7.25 (d, J = 7.6 Hz, 1H), 6.82 (dd, J = 7.8, 4.7 Hz, 1H), 6.75 (s, 1H), 4.20 - 4.30 (m, 2H), 3.57 (s, 2H), 3.10 - 3.60 (m, 8H), 2.68 - 2.77 (m, 1H), 2.24 (s, 3H), 1.29 (t, J = 7.1 Hz, 3H), 0.99 (d, J = 6.5 Hz, 6H).	530.4
265	(DMSO-d6): 8.21 (s, 1H), 8.17 (d, J = 3.4 Hz, 1H), 7.83 (d, J = 7.7 Hz, 1H), 7.62 (s, 1H), 7.40 (s, 1H), 7.33 (s, 2H), 6.81 (dd, J = 8.0, 4.7 Hz, 1H), 6.63 (s, 1H), 4.15 - 4.30 (m, 3H), 3.95 (s, 2H), 2.43 - 2.56 (m, 2H), 2.22 (s, 3H), 1.81 - 1.94 (m, 2H), 1.63 - 1.75 (m, 2H), 1.43 - 1.60 (m, 4H), 1.22 - 1.33 (m, 3H).	487.2
266	(DMSO-d6): 8.16 (d, J = 3.8 Hz, 1H), 7.83 (d, J = 7.6 Hz, 1H), 7.60 (s, 1H), 7.18 - 7.39 (m, 3H), 6.87 (s, 1H), 6.75 - 6.84 (m, 1H), 6.54 (s, 1H), 4.10 - 4.25 (m, 2H), 3.93 (s, 2H), 2.95 - 3.10 (m, 1H), 2.15 - 2.20 (m, 3H), 1.20 - 1.30 (m, 3H), 1.10 - 1.20 (m, 6H).	461.2

[0806]

[Table 2-2]

267	(DMSO-d6): 12.26 (s, 1H), 10.32 (br. s, 1H), 8.20 (d, J = 3.5 Hz, 1H), 7.71 - 7.82 (m, 2H), 7.46 (d, J = 8.2 Hz, 1H), 7.35 (s, 1H), 7.29 (d, J = 8.5 Hz, 1H), 6.83 (s, 1H), 6.73 - 6.81 (m, 1H), 4.53 - 4.61 (m, 1H), 4.20 - 4.32 (m, 2H), 3.42 - 3.62 (m, 3H), 2.68 - 2.80 (m, 2H), 2.26 (s, 3H), 2.03 - 2.20 (m, 2H), 1.67 - 1.80 (m, 2H), 1.36 - 1.51 (m, 2H), 1.29 (t, J = 7.0 Hz, 3H).	503.2
268	(DMSO-d6): 12.49 (br. s, 1H), 9.38 (br. s, 1H), 8.44 (d, J = 7.53 Hz, 1H), 8.33 (dd, J = 1.25, 4.52 Hz, 1H), 8.17 (d, J = 2.51 Hz, 1H), 7.21 (dd, J = 4.77,	339.0

	8.03 Hz, 1H), 7.02 (s, 1H), 4.79 (s, 2H), 4.23 (q, J = 7.19 Hz, 2H), 1.26 (t, J = 7.03 Hz, 3H).	
269	(DMSO-d6): 12.35 (br. s, 1H), 8.60 (d, J = 8.78 Hz, 1H), 8.45 (dd, J = 1.26, 8.03 Hz, 1H), 8.31 (dd, J = 1.25, 4.52 Hz, 1H), 8.04 (s, 1H), 7.19 (dd, J = 4.77, 8.03 Hz, 1H), 6.90 (s, 1H), 5.18 (t, J = 5.14 Hz, 2H), 4.11 - 4.27 (m, 3H), 3.67 (t, J = 5.40 Hz, 4H), 1.26 (t, J = 7.15 Hz, 3H).	373.9
270	(DMSO-d6): 12.40 (br. s, 1H), 8.84 (t, J = 5.90 Hz, 1H), 8.49 (d, J = 8.03 Hz, 1H), 8.32 (dd, J = 1.38, 4.64 Hz, 1H), 8.06 (d, J = 2.51 Hz, 1H), 7.21 (dd, J = 4.77, 8.03 Hz, 1H), 6.90 (s, 1H), 4.21 (q, J = 7.03 Hz, 2H), 3.73 - 3.83 (m, 2H), 3.33 - 3.66 (m, 5H), 1.26 (t, J = 7.03 Hz, 3H).	374.0
271	(DMSO-d6): 12.10 - 12.20 (m, 1H), 8.20 - 8.42 (m, 2H), 7.98 (s, 1H), 7.19 (dd, J = 7.9, 4.6 Hz, 1H), 6.85 (s, 1H), 4.10 - 4.40 (m, 4H), 3.85 - 4.05 (m, 2H), 3.25 - 3.40 (m, 4H), 2.35 - 3.45 (m, 3H), 2.65 - 2.80 (m, 1H), 2.15 - 2.25 (m, 6H), 1.80 - 1.95 (m, 2H), 1.53 - 1.72 (m, 2H), 1.20 - 1.28 (m, 3H).	468.3
272	(DMSO-d6): 12.30 (s, 1H), 8.37 (d, J = 7.9 Hz, 1H), 8.31 (d, J = 4.2 Hz, 1H), 7.98 (s, 1H), 7.19 (dd, J = 7.8, 4.6 Hz, 1H), 6.84 (s, 1H), 4.58 - 4.73 (m, 3H), 4.16 (q, J = 7.0 Hz, 2H), 3.93 - 4.01 (m, 2H), 3.68 - 3.77 (m, 1H), 3.40 - 3.56 (m, 3H), 3.31 - 3.39 (m, 2H), 3.16 (s, 3H), 1.74 - 1.90 (m, 3H), 1.58 - 1.72 (m, 3H), 1.24 (t, J = 7.1 Hz, 3H).	486.2
273	(DMSO-d6): 12.35 (s, 1H), 8.41 (d, J = 6.8 Hz, 1H), 8.32 (d, J = 3.4 Hz, 1H), 8.06 (s, 1H), 7.22 (dd, J = 7.9, 4.6 Hz, 2H), 6.83 - 6.93 (m, 3H), 4.90 (s, 2H), 4.20 (q, J = 7.0 Hz, 2H), 3.84 - 4.00 (m, 2H), 3.76 (s, 3H), 3.01 - 3.09 (m, 2H), 1.26 (t, J = 7.1 Hz, 3H).	446.0
274	(DMSO-d6): 12.24 (s, 1H), 8.26 - 8.48 (m, 2H), 7.95 (s, 1H), 7.10 - 7.17 (m, 1H), 6.84 - 6.94 (m, 3H), 6.59 (d, J = 8.0 Hz, 1H), 4.90 (s, 2H), 4.77 (s, 2H), 4.15 (q, J = 7.1 Hz, 2H), 3.16 (s, 3H), 2.01 (s, 3H), 1.25 - 1.19 (m, 3H).	433.2
275	(DMSO-d6): 12.31 (s, 1H), 8.37 (d, J = 8.0 Hz, 1H), 8.31 (d, J = 3.6 Hz, 1H), 7.96 (s, 1H), 7.19 (dd, J = 7.9, 4.6 Hz, 1H), 6.84 (s, 1H), 4.00 - 4.25 (m, 4H), 3.22 - 3.32 (m, 1H), 3.05 - 2.95 (m, 1H), 1.75 - 1.91 (m, 3H), 1.60 - 1.74 (m, 1H), 1.17 - 1.33 (m, 4H), 0.95 (d, J = 6.2 Hz, 3H).	382.2
276	(DMSO-d6): 12.32 (s, 1H), 8.37 (d, J = 7.9 Hz, 1H), 8.31 (d, J = 4.6 Hz, 1H), 8.01 (s, 1H), 7.19 (dd, J = 7.9, 4.7 Hz, 1H), 6.88 (s, 1H), 4.12 - 4.22 (m, 4H), 3.76 - 3.86 (m, 2H), 2.96 - 3.06 (m, 2H), 1.24 (t, J = 7.1 Hz, 3H), 1.18 (d, J = 6.2 Hz, 6H).	398.2
277	(DMSO-d6): 12.37 (s, 1H), 9.96 (s, 1H), 8.99 (d, J = 7.8 Hz, 1H), 8.34 (d, J = 3.3 Hz, 1H), 8.11 (d, J = 2.5 Hz, 1H), 7.23 (dd, J = 8.0, 4.7 Hz, 1H), 6.85 (s, 1H), 4.49 (t, J = 5.2 Hz, 1H), 4.21 (q, J = 7.1 Hz, 2H), 3.56 (q, J = 6.0 Hz, 2H), 2.98 - 3.12 (m, 4H), 2.57 - 2.77 (m, 4H), 2.45 - 2.55 (m, 2H), 1.26 (t, J = 7.1 Hz, 3H).	428.4
278	(DMSO-d6): 12.21 (br. s, 1H), 8.28 - 8.42 (m, 2H), 7.96 (s, 1H), 7.18 (dd, J = 7.9, 4.7 Hz, 1H), 6.84 (s, 1H), 4.06 - 4.23 (m, 4H), 2.72 - 2.88 (m, 2H), 1.75 - 1.92 (m, 3H), 1.24 (t, J = 7.0 Hz, 3H), 0.86 - 1.00 (m, 7H).	396.2
279	(DMSO-d6): 12.27 (s, 1H), 9.22 (br. s, 1H), 6.4 - 8.6 (m, 7H), 4.15 - 4.25 (m, 2H), 1.18 - 1.30 (m, 3H).	367.2
280	(DMSO-d6): 12.10 - 12.65 (m, 1H), 8.25 - 8.53 (m, 2H), 8.01 (s, 1H), 7.14 - 7.29 (m, 2H), 6.80 - 6.95 (m, 3H), 4.68 - 4.93 (m, 2H), 4.15 - 4.27 (m, 2H), 3.93 - 4.05 (m, 2H), 3.80 - 3.92 (m, 3H), 2.98 - 3.10 (m, 2H), 1.23 - 1.32 (m, 3H).	446.0
281	(DMSO-d6): 12.34 (s, 1H), 9.51 (br. s, 1H), 9.17 (d, J = 7.3 Hz, 1H), 8.33 (d, J = 3.3 Hz, 1H), 8.12 (s, 1H), 7.18 (dd, J = 8.0, 4.6 Hz, 1H), 6.82 (s, 1H), 4.22 (q, J = 7.0 Hz, 2H), 2.95 - 3.10 (m, 2H), 1.70 - 1.85 (m, 3H), 1.37 - 1.53 (m, 3H), 1.27 (t, J = 7.1 Hz, 3H), 0.98 (d, J = 6.0 Hz, 6H).	411.2
282	(DMSO-d6): 12.25 (br. s, 1H), 8.34 - 8.39 (m, 1H), 8.32 (d, J = 4.6 Hz, 1H), 7.97 (s, 1H), 7.19 (dd, J = 7.9, 4.6 Hz, 1H), 6.84 (s, 1H), 4.10 - 4.27 (m, 2H), 3.73 (dd, J = 13.1, 3.5 Hz, 2H), 3.43 - 3.59 (m, 2H), 2.06 - 2.20 (m, 2H), 1.54 (t, J = 5.7 Hz, 2H), 1.25 (t, J = 6.7 Hz, 3H), 0.95 (d, J = 7.3 Hz, 6H).	396.2
283	(DMSO-d6): 12.30 (s, 1H), 8.37 (d, J = 7.9 Hz, 1H), 8.32 (d, J = 4.7 Hz, 1H), 7.97 (s, 1H), 7.19 (dd, J = 7.8, 4.7 Hz, 1H), 6.84 (s, 1H), 4.18 (q, J = 7.1 Hz, 2H), 3.62 - 3.71 (m, 2H), 3.54 (s, 2H), 1.71 - 1.82 (m, 2H), 1.45 - 1.56 (m, 2H), 1.25 (t, J = 7.1 Hz, 3H), 0.97 (s, 6H).	396.2
284	(DMSO-d6): 12.30 (s, 1H), 8.38 (d, J = 8.2 Hz, 1H), 8.31 (d, J = 4.2 Hz, 1H), 8.00 (s, 1H), 7.19 (dd, J = 8.0, 4.6 Hz, 1H), 6.83 (s, 1H), 4.97 - 5.10 (m, 1H), 4.42 - 4.56 (m, 1H), 4.10 - 4.23 (m, 2H), 3.80 - 3.95 (m, 2H), 3.57 - 3.72 (m, 2H), 1.70 - 1.90 (m, 3H), 1.55 - 1.70 (m, 3H), 1.24 (t, J = 7.0 Hz, 3H).	398.0

285	(DMSO-d6): 12.28 (br. s, 1H), 10.34 (br. s, 1H), 8.20 (dd, J = 1.38, 4.64 Hz, 1H), 7.73 - 7.79 (m, 2H), 7.42 (d, J = 7.78 Hz, 1H), 7.31 (s, 1H), 7.25 (d, J = 8.03 Hz, 1H), 6.84 (s, 1H), 6.76 (dd, J = 4.64, 7.91 Hz, 1H), 4.27 (q, J = 7.03 Hz, 2H), 3.61 (t, J = 4.52 Hz, 4H), 3.28 - 3.34 (m, 4H), 2.82 - 2.90 (m, 2H), 2.58 - 2.64 (m, 2H), 2.24 (s, 3H), 1.30 (t, J = 7.03 Hz, 3H).	503.3
286	(DMSO-d6): 12.25 (s, 1H), 10.37 (s, 1H), 8.20 (d, J = 3.7 Hz, 1H), 7.78 (d, J = 7.8 Hz, 1H), 7.72 (s, 1H), 7.42 (d, J = 8.0 Hz, 1H), 7.30 (s, 1H), 7.23 (d, J = 7.7 Hz, 1H), 6.85 (s, 1H), 6.80 (dd, J = 7.8, 4.7 Hz, 1H), 4.77 (t, J = 5.1 Hz, 1H), 4.27 (q, J = 6.9 Hz, 2H), 3.72 (q, J = 6.7 Hz, 2H), 2.85 (t, J = 6.9 Hz, 2H), 2.24 (s, 3H), 1.30 (t, J = 7.0 Hz, 3H).	434.0

[0807]

[Table 2-3]

287	(DMSO-d6): 12.11 (br. s, 1H), 8.15 (d, J = 3.8 Hz, 1H), 7.68 - 7.78 (m, 2H), 7.43 (s, 1H), 7.26 - 7.38 (m, 2H), 6.80 (dd, J = 7.7, 4.8 Hz, 1H), 6.60 (s, 1H), 4.15 - 4.25 (m, 2H), 3.66 (s, 2H), 2.60 - 2.70 (m, 4H), 2.19 (s, 3H), 1.91 (s, 3H), 1.70 - 1.82 (m, 4H), 1.27 (t, J = 7.0 Hz, 3H).	497.2
288	(DMSO-d6): 11.80 - 12.15 (m, 1H), 8.22 - 8.37 (m, 2H), 8.12 - 8.18 (m, 1H), 7.74 - 7.83 (m, 1H), 7.54 - 7.72 (m, 1H), 7.33 (s, 1H), 7.26 (d, J = 8.9 Hz, 1H), 6.91 - 7.05 (m, 1H), 6.77 - 6.84 (m, 1H), 6.27 - 6.39 (m, 1H), 4.04 - 4.23 (m, 2H), 3.60 - 3.70 (m, 4H), 3.56 (s, 2H), 2.53 - 2.62 (m, 4H), 2.10 (s, 3H), 1.20 - 1.30 (m, 3H).	513.0
289	(DMSO-d6): 8.05 - 8.15 (m, 1H), 7.82 (d, J = 7.4 Hz, 1H), 7.52 (s, 1H), 7.27 (s, 1H), 7.20 (d, J = 7.8 Hz, 1H), 6.91 (d, J = 7.9 Hz, 1H), 6.75 - 6.84 (m, 1H), 6.18 (s, 1H), 4.02 - 4.13 (m, 2H), 3.30 - 3.70 (m, 3H), 2.75 - 2.85 (m, 2H), 2.36 - 2.26 (m, 2H), 2.07 (s, 3H), 1.72 - 1.82 (m, 2H), 1.40 - 1.50 (m, 2H), 1.15 - 1.30 (m, 3H).	527.0
290	(DMSO-d6): 12.27 (br. s, 1H), 8.20 (dd, J = 1.25, 4.77 Hz, 1H), 7.72 - 7.80 (m, 2H), 7.40 (d, J = 8.03 Hz, 1H), 7.30 (s, 1H), 7.23 (d, J = 7.78 Hz, 1H), 6.82 (s, 1H), 6.76 (dd, J = 4.64, 7.91 Hz, 1H), 4.26 (q, J = 7.03 Hz, 2H), 3.25 - 3.50 (m, 4H), 2.79 - 2.89 (m, 2H), 2.56 - 2.66 (m, 2H), 2.31 - 3.47 (m, 4H), 2.23 (s, 3H), 2.20 (s, 3H), 1.29 (t, J = 7.15 Hz, 3H).	516.3
291	(DMSO-d6): 12.31 (s, 1H), 8.39 (d, J = 6.9 Hz, 1H), 8.31 (d, J = 4.6 Hz, 1H), 7.95 (s, 1H), 7.20 (dd, J = 7.9, 4.7 Hz, 1H), 6.84 (s, 1H), 4.17 (q, J = 7.1 Hz, 2H), 3.73 (q, J = 7.0 Hz, 2H), 3.26 (s, 3H), 1.20 - 1.33 (m, 6H).	342.2
292	(DMSO-d6): 8.38 (d, J = 7.9 Hz, 1H), 8.31 (d, J = 3.3 Hz, 1H), 7.95 (s, 1H), 7.19 (dd, J = 7.9, 4.7 Hz, 1H), 6.84 (s, 1H), 4.50 - 4.62 (m, 1H), 4.17 (d, J = 7.1 Hz, 2H), 3.09 (s, 3H), 1.36 - 1.20 (m, 9H).	356.0
293	(DMSO-d6): 12.31 (br. s, 1H), 10.01 (br. s, 1H), 8.92 (d, J = 7.8 Hz, 1H), 8.31 (d, J = 3.7 Hz, 1H), 8.08 (s, 1H), 7.18 (dd, J = 7.9, 4.7 Hz, 1H), 6.83 (s, 1H), 4.97 (br. s, 1H), 4.20 (q, J = 7.0 Hz, 2H), 3.72 - 3.83 (m, 1H), 3.12 - 3.20 (m, 1H), 2.97 - 3.06 (m, 1H), 2.71 - 2.91 (m, 2H), 1.80 - 1.93 (m, 2H), 1.56 - 1.68 (m, 1H), 1.18 - 1.31 (m, 4H).	399.2
294	(DMSO-d6): 12.29 (s, 1H), 8.29 - 8.38 (m, 2H), 7.96 (s, 1H), 7.19 (dd, J = 7.9, 4.7 Hz, 1H), 6.82 (s, 1H), 4.95 - 5.10 (m, 1H), 4.15 - 4.25 (m, 2H), 3.24 - 3.34 (m, 2H), 1.68 - 1.88 (m, 3H), 1.25 - 1.40 (m, 2H), 1.25 (d, J = 6.2 Hz, 6H), 0.97 (d, J = 6.3 Hz, 3H).	396.4
295	(DMSO-d6): 12.35 (s, 1H), 8.40 (d, J = 6.6 Hz, 1H), 8.33 (d, J = 4.6 Hz, 1H), 8.07 (s, 1H), 7.24 - 7.32 (m, 4H), 7.22 (dd, J = 7.9, 4.7 Hz, 1H), 6.87 (s, 1H), 5.00 - 5.12 (m, 1H), 4.97 (s, 2H), 3.90 - 4.02 (m, 2H), 3.03 - 3.13 (m, 2H), 1.27 (t, J = 8.9 Hz, 6H).	430.2
296	(DMSO-d6): 12.31 (s, 1H), 9.86 (s, 1H), 8.84 (d, J = 7.8 Hz, 1H), 8.30 (d, J = 3.3 Hz, 1H), 8.05 (d, J = 2.5 Hz, 1H), 7.20 (dd, J = 8.0, 4.6 Hz, 1H), 6.83 (s, 1H), 4.99 - 5.10 (m, 1H), 2.77 (s, 6H), 1.27 (d, J = 6.3 Hz, 6H).	357.2
297	(DMSO-d6): 12.26 (s, 1H), 10.07 (s, 1H), 8.17 (s, 1H), 7.85 (s, 1H), 7.69 (d, J = 7.4 Hz, 1H), 7.17 (d, J = 8.3 Hz, 1H), 6.72 - 6.88 (m, 2H), 6.52 - 6.67 (m, 2H), 5.	462.8

	80 - 5.92 (m, 1H), 5.07 - 5.18 (m, 1H), 4.71 - 4.81 (m, 1H), 3.58 - 3.69 (m, 2H), 3.15 - 3.25 (m, 2H), 2.13 (s, 3H), 1.30 (d, J = 5.9 Hz, 6H).	
298	(MeOD): 8.15 - 8.24 (m, 1H), 7.86 (d, J = 7.5 Hz, 1H), 7.65 (br. s, 1H), 7.40 - 7.55 (m, 3H), 6.90 - 7.03 (m, 2H), 6.61 (s, 1H), 4.34 - 4.43 (m, 2H), 3.66 (s, 2H), 2.70 - 2.98 (m, 8H), 2.49 (s, 3H), 2.32 (s, 3H), 1.35 - 1.42 (m, 3H).	526.4
299	(DMSO-d6): 12.31 (s, 1H), 10.42 (br. s, 1H), 8.23 (dd, J = 4.6, 1.4 Hz, 1H), 7.79 (d, J = 7.3 Hz, 1H), 7.72 (d, J = 2.7 Hz, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.37 (s, 1H), 7.30 (d, J = 7.9 Hz, 1H), 6.87 (s, 1H), 6.78 (dd, J = 7.9, 4.8 Hz, 1H), 4.27 (q, J = 7.1 Hz, 2H), 3.35 - 3.70 (m, 4H), 3.03 - 3.15 (m, 4H), 2.27 (s, 3H), 1.85 - 2.10 (s, 4H), 1.30 (t, J = 7.1 Hz, 3H).	487.0
300	(DMSO-d6): 12.30 (br. s, 1H), 8.39 (d, J = 7.6 Hz, 1H), 8.31 (d, J = 4.4 Hz, 1H), 7.93 (s, 1H), 7.19 (dd, J = 7.9, 4.7 Hz, 1H), 6.85 (s, 1H), 4.16 (q, J = 7.1 Hz, 3H), 3.11 (s, 3H), 1.79 - 1.92 (m, 4H), 1.60 - 1.75 (m, 3H), 1.28 - 1.44 (m, 2H), 1.11 - 1.28 (m, 4H).	396.0
301	(DMSO-d6): 12.30 (br. s, 1H), 9.62 (br. s, 1H), 8.91 (d, J = 8.0 Hz, 1H), 8.31 (d, J = 3.8 Hz, 1H), 8.07 (s, 1H), 7.16 (dd, J = 8.0, 4.6 Hz, 1H), 6.84 (s, 1H), 4.21 (q, J = 7.0 Hz, 2H), 2.78 - 2.88 (m, 1H), 2.77 (s, 3H), 1.88 - 2.00 (m, 2H), 1.68 - 1.80 (m, 2H), 1.48 - 1.59 (m, 1H), 1.16 - 1.31 (m, 7H), 1.00 - 1.12 (m, 1H).	411.0
302	(DMSO-d6): 12.31 (s, 1H), 10.07 (s, 1H), 8.94 (d, J = 7.5 Hz, 1H), 8.32 (d, J = 3.4 Hz, 1H), 8.12 (s, 1H), 7.21 (dd, J = 8.0, 4.7 Hz, 1H), 6.88 (s, 1H), 4.21 (q, J = 7.1 Hz, 2H), 3.57 - 3.76 (m, 4H), 2.97 - 3.12 (m, 4H), 2.08 (s, 3H), 1.26 (t, J = 7.1 Hz, 3H).	426.0
303	(DMSO-d6): 12.30 (br. s, 1H), 8.15 - 8.21 (m, 2H), 7.77 (s, 1H), 7.68 (d, J = 7.8 Hz, 1H), 7.42 (d, J = 8.7 Hz, 1H), 7.04 (s, 1H), 6.94 (d, J = 8.7 Hz, 1H), 6.73 - 6.81 (m, 2H), 5.08 - 5.19 (m, 1H), 4.19 (t, J = 5.6 Hz, 2H), 2.94 (t, J = 5.6 Hz, 2H), 2.62 - 2.71 (m, 4H), 2.23 (s, 3H), 1.70 - 1.80 (m, 4H), 1.31 (d, J = 6.2 Hz, 6H).	517.4
304	(DMSO-d6): 12.25 (br. s, 1H), 9.80 (br. s, 1H), 8.85 (d, J = 7.4 Hz, 1H), 8.29 (d, J = 3.6 Hz, 1H), 8.04 (s, 1H), 7.17 (dd, J = 8.0, 4.7 Hz, 1H), 6.78 (br. s, 1H), 4.19 (q, J = 6.9 Hz, 2H), 2.88 - 3.00 (m, 2H), 2.74 (s, 3H), 1.25 (t, J = 7.1 Hz, 3H), 1.05 (t, J = 7.1 Hz, 3H).	357.2
305	(DMSO-d6): 12.31 (br. s, 1H), 9.49 (br. s, 1H), 8.96 (d, J = 7.8 Hz, 1H), 8.31 (d, J = 3.3 Hz, 1H), 8.08 (s, 1H), 7.18 (dd, J = 8.0, 4.6 Hz, 1H), 6.86 (s, 1H), 4.22 (q, J = 7.1 Hz, 2H), 3.00 (q, J = 7.0 Hz, 4H), 1.27 (t, J = 7.1 Hz, 3H), 1.04 (t, J = 7.1 Hz, 6H).	371.2

[0808]

[Table 2-4]

306	(DMSO-d6): 12.09 (br. s, 1H), 8.98 (d, J = 7.6 Hz, 1H), 8.32 (d, J = 3.4 Hz, 1H), 8.05 (s, 1H), 7.21 (dd, J = 8.0, 4.7 Hz, 1H), 6.73 (s, 1H), 4.80 (s, 1H), 4.17 (q, J = 7.0 Hz, 2H), 3.54 - 3.69 (m, 1H), 3.04 - 3.15 (m, 2H), 2.82 - 2.95 (m, 2H), 1.83 - 1.94 (m, 2H), 1.63 - 1.77 (m, 2H), 1.24 (t, J = 7.0 Hz, 3H).	399.2
307	(DMSO-d6): 12.29 (s, 1H), 10.23 (s, 1H), 8.18 (d, J = 3.4 Hz, 1H), 7.78 (d, J = 2.5 Hz, 1H), 7.66 (d, J = 7.9 Hz, 1H), 7.42 (d, J = 8.6 Hz, 1H), 7.05 (d, J = 2.4 Hz, 1H), 6.94 (dd, J = 8.6, 2.7 Hz, 1H), 6.79 (s, 1H), 6.74 (dd, J = 7.9, 4.7 Hz, 1H), 5.09 - 5.18 (m, 1H), 4.19 (t, J = 5.6 Hz, 2H), 3.58 - 3.67 (m, 4H), 2.78 (t, J = 5.6 Hz, 2H), 2.49 - 2.57 (m, 4H), 2.23 (s, 3H), 1.31 (d, J = 6.3 Hz, 6H).	533.4
308	(DMSO-d6): 12.20 (br. s, 1H), 10.26 (br. s, 1H), 8.18 (d, J = 3.9 Hz, 1H), 7.66 - 7.77 (m, 2H), 7.26 - 7.39 (m, 1H), 7.00 (s, 1H), 6.86 - 6.93 (m, 1H), 6.61 - 6.78 (s, 2H), 5.06 - 5.17 (m, 1H), 4.11 - 4.18 (m, 2H), 2.76 (t, J = 5.5 Hz, 2H), 2.30 - 2.50 (m, 8H), 2.20 (s, 3H), 2.17 (s, 3H), 1.29 (d, J = 6.2 Hz, 6H).	546.6
309	(DMSO-d6): 12.30 (br. s, 1H), 8.42 (d, J = 8.0 Hz, 1H), 8.32 (d, J = 3.3 Hz, 1H), 7.98 (s, 1H), 7.20 (dd, J = 8.0, 4.7 Hz, 1H), 6.89 (s, 1H), 4.23 - 4.35 (m, 2H), 3.96 - 4.07 (m, 1H), 3.54 - 3.64 (m, 2H), 3.30 (s, 3H), 1.94 - 2.03 (m, 2H), 1.73 - 1.84 (m, 2H), 1.51 - 1.69 (m, 3H), 1.35 - 1.49 (m, 2H), 1.15 - 1.28 (m, 1H).	412.2
310	(DMSO-d6): 12.32 (s, 1H), 9.84 (s, 1H), 8.83 (d, J = 8.2 Hz, 1H), 8.30 (d, J = 3.4	373.4

	Hz, 1H), 8.05 (s, 1H), 7.20 (dd, J = 8.0, 4.5 Hz, 1H), 6.88 (s, 1H), 4.25 - 4.32 (m, 2H), 3.57 - 3.63 (m, 2H), 3.30 (s, 3H), 2.78 (s, 6H).	
311	(DMSO-d6): 12.31 (s, 1H), 10.43 (s, 1H), 8.23 (d, J = 3.8 Hz, 1H), 7.73 - 7.81 (m, 2H), 7.58 (d, J = 8.1 Hz, 1H), 7.53 (s, 1H), 7.44 (d, J = 7.9 Hz, 1H), 6.88 (s, 1H), 6.83 (dd, J = 7.9, 4.7 Hz, 1H), 5.42 (t, J = 5.9 Hz, 1H), 4.38 (d, J = 5.9 Hz, 2H), 4.27 (q, J = 7.0 Hz, 2H), 2.27 (s, 3H), 1.30 (t, J = 7.0 Hz, 3H).	444.4
312	(DMSO-d6): 12.27 (s, 1H), 10.41 (s, 1H), 8.16 (d, J = 3.4 Hz, 1H), 7.79 (d, J = 1.9 Hz, 1H), 7.64 (d, J = 7.5 Hz, 1H), 7.48 - 7.55 (m, 2H), 7.42 (d, J = 7.9 Hz, 1H), 6.82 (s, 1H), 6.79 (dd, J = 7.9, 4.6 Hz, 1H), 4.24 (q, J = 7.0 Hz, 2H), 3.53 (s, 2H), 2.30 (s, 6H), 2.23 (s, 3H), 1.27 (t, J = 7.0 Hz, 3H).	471.1
313	(DMSO-d6): 12.28 (s, 1H), 10.17 (br. s, 1H), 8.21 (d, J = 3.3 Hz, 1H), 7.71 - 7.80 (m, 2H), 7.44 (d, J = 8.1 Hz, 1H), 7.32 (s, 1H), 7.25 (d, J = 8.0 Hz, 1H), 6.84 (s, 1H), 6.75 - 6.81 (m, 1H), 4.23 - 4.32 (m, 2H), 2.85 - 2.95 (m, 2H), 2.75 - 2.85 (m, 2H), 2.42 (s, 6H), 2.24 (s, 3H), 1.30 (t, J = 7.1 Hz, 3H).	461.1
314	(DMSO-d6): 12.28 (s, 1H), 10.27 (br. s, 1H), 8.21 (d, J = 4.6 Hz, 1H), 7.72 - 7.78 (m, 2H), 7.42 (d, J = 8.0 Hz, 1H), 7.30 (s, 1H), 7.24 (d, J = 8.3 Hz, 1H), 6.84 (s, 1H), 6.76 (dd, J = 7.9, 4.6 Hz, 1H), 4.58 - 4.72 (m, 1H), 4.22 - 4.32 (m, 2H), 3.44 - 3.60 (m, 1H), 2.80 - 3.00 (m, 4H), 2.40 - 2.60 (m, 4H), 2.24 (s, 3H), 1.72 - 1.85 (m, 2H), 1.38 - 1.53 (m, 2H), 1.29 (t, J = 7.1 Hz, 3H).	517.1
315	(DMSO-d6): 12.26 (br. s, 1H), 9.72 (br. s, 1H), 8.91 (d, J = 7.6 Hz, 1H), 8.30 (d, J = 3.7 Hz, 1H), 8.05 (s, 1H), 7.16 (dd, J = 7.8, 4.6 Hz, 1H), 6.77 (br. s, 1H), 4.13 - 4.24 (m, 2H), 3.08 - 3.20 (m, 1H), 2.72 (s, 3H), 1.25 (t, J = 7.1 Hz, 3H), 1.10 (d, J = 6.3 Hz, 6H).	371.0
316	(DMSO-d6): 12.33 (br. s, 1H), 10.25 (br. s, 1H), 8.87 - 8.99 (m, 1H), 8.30 (d, J = 3.4 Hz, 1H), 8.01 - 8.18 (m, 2H), 7.07 (dd, J = 8.0, 4.6 Hz, 1H), 6.85 (br. s, 1H), 4.15 - 4.26 (m, 2H), 3.60 - 3.72 (m, 2H), 3.20 - 3.30 (m, 4H), 1.26 (t, J = 7.0 Hz, 3H).	398.0
317	(DMSO-d6): 12.36 (s, 1H), 8.42 (d, J = 7.3 Hz, 1H), 8.33 (d, J = 3.4 Hz, 1H), 8.07 (s, 1H), 7.24 - 7.32 (m, 4H), 7.22 (dd, J = 7.9, 4.7 Hz, 1H), 6.91 (s, 1H), 4.98 (br. s, 2H), 4.25 - 4.33 (m, 2H), 3.89 - 4.03 (m, 2H), 3.56 - 3.64 (m, 2H), 3.30 (s, 3H), 3.08 (t, J = 5.7 Hz, 2H).	446.1
318	(DMSO-d6): 12.26 (s, 1H), 10.09 (s, 1H), 8.18 (d, J = 3.3 Hz, 1H), 7.83 (s, 1H), 7.70 (d, J = 7.7 Hz, 1H), 7.16 (d, J = 8.5 Hz, 1H), 6.75 - 6.86 (m, 2H), 6.61 (s, 1H), 6.57 (d, J = 8.5 Hz, 1H), 5.81 - 5.89 (m, 1H), 4.76 (t, J = 5.4 Hz, 1H), 4.28 - 4.36 (m, 2H), 3.58 - 3.67 (m, 4H), 3.32 (s, 1H), 3.20 (q, J = 5.9 Hz, 2H), 2.13 (s, 3H).	479.1
319	(DMSO-d6): 12.24 (br. s, 1H), 8.36 (d, J = 8.0 Hz, 1H), 8.31 (d, J = 4.5 Hz, 1H), 8.00 (s, 1H), 7.20 (dd, J = 7.9, 4.6 Hz, 1H), 6.88 (s, 1H), 4.16 (q, J = 7.1 Hz, 2H), 3.76 - 3.86 (s, 4H), 3.26 - 3.32 (m, 2H), 2.82 - 2.90 (m, 4H), 1.25 (q, J = 7.0 Hz, 3H).	451.2
320	(DMSO-d6): 12.22 (br. s, 1H), 8.19 (s, 1H), 7.83 (d, J = 7.7 Hz, 1H), 7.72 (s, 1H), 7.21 - 7.47 (m, 3H), 6.70 - 6.85 (m, 2H), 5.06 - 5.18 (m, 1H), 3.49 (s, 2H), 2.25 (s, 3H), 2.22 (s, 6H), 1.91 (s, 3H), 1.30 (d, J = 5.8 Hz, 6H).	461.4
321	(DMSO-d6): 8.27 - 8.35 (m, 2H), 7.95 (s, 1H), 7.24 - 7.18 (m, 1H), 6.84 (s, 1H), 4.21 - 4.27 (m, 2H), 3.54 - 3.62 (m, 4H), 3.23 - 3.32 (m, 5H), 1.70 - 1.85 (m, 3H), 1.23 - 1.37 (m, 2H), 0.94 (d, J = 6.2 Hz, 3H).	412.1
322	(DMSO-d6): 12.27 (s, 1H), 10.24 (s, 1H), 8.16 - 8.23 (m, 1H), 7.76 (s, 1H), 7.68 (d, J = 7.9 Hz, 1H), 7.42 (d, J = 8.6 Hz, 1H), 7.05 (s, 1H), 6.95 (d, J = 8.1 Hz, 1H), 6.83 (s, 1H), 6.71 - 6.79 (m, 1H), 4.30 - 4.38 (m, 2H), 4.15 - 4.23 (m, 2H), 3.56 - 3.69 (m, 6H), 3.33 (s, 3H), 2.74 - 2.82 (m, 2H), 2.48 - 2.58 (m, 4H), 2.23 (s, 3H).	548.8
323	(DMSO-d6): 11.18 (br. s, 1H), 8.18 (d, J = 3.4 Hz, 1H), 7.66 - 7.75 (m, 2H), 7.32 (d, J = 8.6 Hz, 1H), 7.00 (s, 1H), 6.91 (d, J = 8.6 Hz, 1H), 6.70 - 6.78 (m, 2H), 4.27 - 4.35 (m, 2H), 4.16 (t, J = 5.7 Hz, 2H), 3.60 - 3.66 (m, 2H), 3.33 (s, 3H), 2.76 (t, J = 5.6 Hz, 2H), 2.48 - 2.58 (s, 4H), 2.31 - 2.42 (m, 4H), 2.20 (s, 3H), 2.17 (s, 3H), 1.90 (s, 3H).	562.2

[0809]

[Table 2-5]

324	(MeOD): 8.16 - 8.23 (m, 1H), 7.97 (d, $J = 7.7$ Hz, 1H), 7.30 - 7.60 (m, 4H), 6.90 - 6.71 (m, 2H), 6.60 (s, 1H), 4.42 - 4.53 (m, 2H), 3.65 - 3.80 (m, 4H), 3.41 (s, 3H), 2.41 (s, 6H), 2.35 (s, 3H).	477.0
325	(DMSO-d6): 12.39 (s, 1H), 8.59 (d, $J = 8.4$ Hz, 1H), 8.44 (d, $J = 7.8$ Hz, 1H), 8.34 (d, $J = 4.6$ Hz, 1H), 7.98 (d, $J = 2.4$ Hz, 1H), 7.22 (dd, $J = 7.9, 4.7$ Hz, 1H), 6.89 (s, 1H), 4.21 (t, $J = 6.3$ Hz, 2H), 3.94 - 4.06 (m, 1H), 3.56 (t, $J = 5.9$ Hz, 3H), 1.93 - 2.03 (m, 2H), 1.74 - 1.84 (m, 4H), 1.53 - 1.70 (m, 3H), 1.34 - 1.48 (m, 2H), 1.15 - 1.28 (m, 1H).	412.2
326	(DMSO-d6): 12.35 (s, 1H), 8.50 (br. s, 1H), 8.41 (d, $J = 7.0$ Hz, 1H), 8.30 - 8.35 (m, 1H), 7.98 (s, 1H), 7.20 (dd, $J = 7.9, 4.7$ Hz, 1H), 6.89 (s, 1H), 4.22 (t, $J = 5.8$ Hz, 2H), 3.94 - 4.06 (m, 1H), 2.51 - 2.58 (m, 2H), 2.23 (s, 6H), 1.96 - 2.05 (m, 2H), 1.75 - 1.86 (m, 2H), 1.62 - 1.72 (m, 1H), 1.34 - 1.59 (m, 4H), 1.16 - 1.29 (m, 1H).	425.2
327	(DMSO-d6): 12.30 (s, 1H), 8.37 (d, $J = 7.8$ Hz, 1H), 8.31 (d, $J = 4.2$ Hz, 1H), 7.96 (s, 1H), 7.19 (dd, $J = 7.9, 4.4$ Hz, 1H), 6.85 (s, 1H), 4.21 (t, $J = 5.7$ Hz, 2H), 2.40 - 2.60 (m, 6H), 2.22 (s, 6H), 1.73 - 1.87 (m, 2H), 1.15 - 1.42 (m, 3H), 0.97 (d, $J = 6.1$ Hz, 3H).	425.2
328	(DMSO-d6): 8.37 (d, $J = 7.8$ Hz, 1H), 8.31 (d, $J = 3.6$ Hz, 1H), 7.93 (s, 1H), 7.20 - 7.27 (m, 1H), 6.85 (s, 1H), 4.17 (t, $J = 6.2$ Hz, 2H), 3.70 - 3.90 (m, 4H), 3.50 - 3.56 (m, 2H), 1.70 - 1.88 (m, 6H), 1.50 - 1.60 (m, 4H).	412.2
329	(DMSO-d6): 12.42 (s, 1H), 8.43 (d, $J = 7.9$ Hz, 1H), 8.34 (d, $J = 4.2$ Hz, 1H), 7.98 (s, 1H), 7.24 (dd, $J = 7.9, 4.8$ Hz, 1H), 6.88 (s, 1H), 4.35 - 4.13 (m, 5H), 3.56 (t, $J = 6.0$ Hz, 2H), 3.25 - 3.37 (m, 2H), 1.70 - 1.88 (m, 5H), 1.26 - 1.40 (m, 2H), 0.96 (d, $J = 6.2$ Hz, 3H).	412.2
330	(DMSO-d6): 8.12 - 8.17 (m, 1H), 7.72 - 7.79 (m, 1H), 7.65 (s, 1H), 7.14 - 7.22 (m, 1H), 6.94 (s, 1H), 6.82 - 6.88 (m, 1H), 6.73 - 6.80 (m, 1H), 6.55 (s, 1H), 4.21 - 4.30 (m, 2H), 4.09 - 4.16 (m, 2H), 3.55 - 3.66 (m, 2H), 3.32 (s, 3H), 2.85 (t, $J = 5.7$ Hz, 2H), 2.54 - 2.61 (m, 4H), 2.16 (s, 3H), 1.90 (s, 3H), 1.68 - 1.76 (m, 4H).	533.6
331	(DMSO-d6): 12.47 (s, 1H), 8.47 (d, $J = 7.9$ Hz, 1H), 8.36 (br. s, 1H), 8.09 (s, 1H), 7.16 - 7.32 (m, 6H), 6.93 (s, 1H), 5.00 (br. s, 2H), 4.22 (t, $J = 6.4$ Hz, 2H), 3.80 - 4.10 (m, 2H), 3.57 (t, $J = 6.0$ Hz, 2H), 3.08 (t, $J = 5.6$ Hz, 2H), 1.75 - 1.85 (m, 2H).	446.0
332	(DMSO-d6): 12.39 (s, 1H), 10.14 (s, 1H), 8.95 (d, $J = 8.0$ Hz, 1H), 8.34 (d, $J = 4.5$ Hz, 1H), 8.12 (d, $J = 2.6$ Hz, 1H), 7.24 (dd, $J = 8.0, 4.7$ Hz, 1H), 6.88 (s, 1H), 4.21 (t, $J = 6.3$ Hz, 2H), 3.76 - 3.86 (m, 4H), 3.53 - 3.61 (m, 3H), 3.02 - 3.12 (m, 4H), 1.87 - 1.74 (m, 2H).	415.1
333	(DMSO-d6): 12.38 (s, 1H), 9.95 (br. s, 1H), 8.87 (d, $J = 7.7$ Hz, 1H), 8.32 (d, $J = 3.4$ Hz, 1H), 8.03 - 8.09 (m, 1H), 7.23 (dd, $J = 8.0, 4.7$ Hz, 1H), 6.88 (s, 1H), 4.21 (t, $J = 6.3$ Hz, 2H), 3.57 (t, $J = 5.8$ Hz, 2H), 3.39 (s, 1H), 2.77 (s, 6H), 1.75 - 1.85 (m, 2H).	373.2
334	(DMSO-d6): 12.31 (br. s, 1H), 8.91 (d, $J = 7.53$ Hz, 1H), 8.33 (d, $J = 3.51$ Hz, 1H), 8.09 (br. s, 1H), 7.22 (dd, $J = 4.64, 7.91$ Hz, 1H), 6.83 (br. s, 1H), 4.27 (t, $J = 4.64$ Hz, 2H), 3.77 - 3.85 (m, 4H), 3.56 - 3.62 (m, 2H), 3.30 (s, 3H), 3.00 - 3.10 (m, 4H).	415.2
335	(DMSO-d6): 12.37 (br. s, 1H), 8.40 (dd, $J = 1.26, 8.03$ Hz, 1H), 8.33 (dd, $J = 1.38, 4.64$ Hz, 1H), 8.06 (s, 1H), 7.63 (d, $J = 1.51$ Hz, 1H), 7.21 (dd, $J = 4.64, 7.91$ Hz, 1H), 6.92 (s, 1H), 6.47 (d, $J = 1.76$ Hz, 1H), 4.90 (br. s, 2H), 4.21 (q, $J = 7.19$ Hz, 2H), 3.95 - 4.05 (m, 2H), 2.74 - 2.83 (m, 2H), 1.26 (t, $J = 7.03$ Hz, 3H).	406.2
336	(DMSO-d6): 12.27 (s, 1H), 10.19 (s, 1H), 8.18 (d, $J = 3.5$ Hz, 1H), 7.80 - 7.86 (m, 1H), 7.68 (d, $J = 7.8$ Hz, 1H), 7.16 (d, $J = 8.4$ Hz, 1H), 6.76 - 6.84 (m, 2H), 6.62 (s, 1H), 6.58 (d, $J = 8.5$ Hz, 1H), 4.26 (t, $J = 6.3$ Hz, 2H), 3.54 - 3.66 (m, 4H), 3.20 (t, $J = 6.2$ Hz, 3H), 2.13 (s, 3H), 1.78 - 1.87 (m, 2H).	479.2
337	(DMSO-d6): 12.36 (s, 1H), 10.61 (br. s, 1H), 10.54 (s, 1H), 8.24 (d, $J = 3.8$ Hz, 1H), 7.97 (d, $J = 8.6$ Hz, 1H), 7.55 - 7.70 (m, 4H), 6.89 - 6.95 (m, 2H), 4.38 (d, $J = 4.8$ Hz, 2H), 4.29 (t, $J = 6.3$ Hz, 2H), 3.62 - 3.55 (m, 2H), 3.39 (s, 1H), 2.76 (d, $J = 4.6$ Hz, 6H), 2.32 (s, 3H), 1.80 - 1.89 (m, 2H).	477.4
338	(DMSO-d6): 12.23 (s, 1H), 8.78 (d, $J = 7.5$ Hz, 1H), 8.29 (d, $J = 4.1$ Hz, 1H), 8.01 (s, 1H), 7.19 (dd, $J = 7.9, 4.7$ Hz, 1H), 6.77 (s, 1H), 4.20 (t, $J = 5.8$ Hz, 2H), 2.73 (s, 6H), 2.53 - 2.58 (m, 2H), 2.24 (s, 6H), 1.90 (s, 3H).	386.4
339	(DMSO-d6): 8.71 (d, $J = 7.1$ Hz, 1H), 8.27 (d, $J = 4.6$ Hz, 1H), 7.89 (s, 1H), 7.15	428.4

	(dd, $J = 7.8, 4.6$ Hz, 1H), 6.37 (s, 1H), 4.10 (t, $J = 5.9$ Hz, 3H), 3.76 - 3.82 (m, 4H), 2.81 - 2.88 (m, 4H), 2.45 - 2.55 (m, 2H), 2.24 (s, 6H), 1.88 (s, 3H).	
340	(DMSO-d6): 12.23 (br. s, 1H), 8.17 (d, $J = 3.7$ Hz, 1H), 7.80 (s, 1H), 7.67 - 7.74 (m, 1H), 7.08 - 7.17 (m, 1H), 6.78 - 6.84 (m, 1H), 6.70 - 6.78 (m, 1H), 6.60 (s, 1H), 6.53 - 6.58 (m, 1H), 5.81 (br. s, 1H), 4.71 - 4.79 (m, 1H), 4.21 - 4.30 (m, 2H), 3.59 - 3.67 (m, 2H), 3.15 - 3.25 (m, 2H), 2.55 - 2.60 (m, 2H), 2.21 (s, 6H), 2.12 (s, 3H), 1.90 (s, 3H).	492.4
341	(DMSO-d6): 12.28 (br. s, 1H), 10.45 (s, 1H), 8.18 (dd, $J = 1.38, 4.64$ Hz, 1H), 7.70 - 7.76 (m, 2H), 7.55 (d, $J = 8.03$ Hz, 1H), 7.43 (s, 1H), 7.36 (d, $J = 7.78$ Hz, 1H), 6.85 (s, 1H), 6.77 (dd, $J = 4.64, 7.91$ Hz, 1H), 4.27 (q, $J = 7.03$ Hz, 2H), 4.17 (s, 2H), 2.28 (s, 3H), 1.30 (t, $J = 7.15$ Hz, 3H).	429.1
342	(DMSO-d6): 12.19 (br. s., 1H), 9.17 (s, 1H), 8.12 - 8.24 (m, 3H), 7.82 (d, $J = 8.03$ Hz, 1H), 7.66 (s, 1H), 7.21 - 7.40 (m, 3H), 6.78 (dd, $J = 4.64, 7.91$ Hz, 1H), 6.72 (s, 1H), 4.29 (t, $J = 5.77$ Hz, 2H), 3.52 (s, 2H), 2.65 - 2.73 (m, 2H), 2.30 (s, 6H), 2.23 (s, 9H).	490.2
343	(DMSO-d6): 12.39 (br. s, 1H), 9.93 (br. s, 1H), 8.28 (dd, $J = 1.26, 4.52$ Hz, 1H), 7.86 (s, 1H), 7.33 (d, $J = 8.53$ Hz, 2H), 7.10 - 7.19 (m, 2H), 7.00 (dd, $J = 2.76, 8.53$ Hz, 1H), 5.49 (br. s, 1H), 5.04 - 5.17 (m, 1H), 4.99 (t, $J = 5.40$ Hz, 1H), 4.12 (t, $J = 4.89$ Hz, 2H), 3.81 (q, $J = 4.94$ Hz, 2H), 2.23 (s, 3H), 1.28 (d, $J = 6.27$ Hz, 6H).	463.9

[0810]

[Table 2-6]

344	(DMSO-d6): 12.33 (s, 1H), 10.07 (s, 1H), 8.93 (d, $J = 7.8$ Hz, 1H), 8.33 (d, $J = 3.6$ Hz, 1H), 8.11 (s, 1H), 7.22 (dd, $J = 8.0, 4.6$ Hz, 1H), 6.86 (s, 1H), 4.11 (t, $J = 6.7$ Hz, 2H), 3.76 - 3.86 (s, 4H), 3.02 - 3.13 (s, 4H), 1.60 - 1.72 (m, 2H), 0.94 (t, $J = 7.4$ Hz, 3H).	399.0
345	(DMSO-d6): 12.34 (s, 1H), 10.07 (s, 1H), 8.92 (d, $J = 7.5$ Hz, 1H), 8.33 (d, $J = 3.3$ Hz, 1H), 8.11 (d, $J = 2.5$ Hz, 1H), 7.22 (dd, $J = 8.0, 4.7$ Hz, 1H), 6.86 (s, 1H), 3.94 (d, $J = 6.6$ Hz, 2H), 3.75 - 3.87 (m, 4H), 3.00 - 3.15 (m, 4H), 1.88 - 2.02 (m, 1H), 0.95 (d, $J = 6.7$ Hz, 6H).	413.4
346	(DMSO-d6): 12.02 (br. s, 1H), 8.89 (d, $J = 7.7$ Hz, 1H), 8.32 (d, $J = 3.4$ Hz, 1H), 8.07 (s, 1H), 7.21 (dd, $J = 8.0, 4.7$ Hz, 1H), 6.77 (s, 1H), 4.15 (t, $J = 5.4$ Hz, 2H), 3.73 - 3.87 (m, 4H), 3.63 (t, $J = 5.4$ Hz, 2H), 3.17 (s, 1H), 2.95 - 3.07 (m, 4H).	401.4
347	(DMSO-d6): 12.35 (s, 1H), 10.09 (s, 1H), 8.94 (d, $J = 7.9$ Hz, 1H), 8.33 (d, $J = 3.5$ Hz, 1H), 8.12 (d, $J = 2.4$ Hz, 1H), 7.22 (dd, $J = 8.0, 4.7$ Hz, 1H), 6.87 (s, 1H), 4.02 (d, $J = 7.1$ Hz, 2H), 3.72 - 3.90 (m, 4H), 3.00 - 3.16 (m, 4H), 1.12 - 1.23 (m, 1H), 0.48 - 0.58 (m, 2H), 0.26 - 0.37 (m, 2H).	411.3
348	(DMSO-d6): 12.34 (s, 1H), 10.08 (s, 1H), 8.93 (d, $J = 7.7$ Hz, 1H), 8.33 (d, $J = 4.5$ Hz, 1H), 8.12 (d, $J = 2.6$ Hz, 1H), 7.22 (dd, $J = 8.0, 4.7$ Hz, 1H), 6.82 (s, 1H), 5.15 - 5.22 (m, 1H), 3.75 - 3.87 (m, 4H), 3.02 - 3.13 (m, 4H), 1.83 - 1.96 (m, 2H), 1.63 - 1.78 (m, 4H), 1.50 - 1.62 (m, 2H).	425.4
349	(DMSO-d6): 12.24 (br. s, 1H), 10.20 (br. s, 1H), 8.88 (d, $J = 7.9$ Hz, 1H), 8.32 (d, $J = 3.5$ Hz, 1H), 8.07 (s, 1H), 7.21 (dd, $J = 8.0, 4.7$ Hz, 1H), 6.72 (s, 1H), 4.94 - 4.79 (m, 1H), 3.74 - 3.88 (m, 4H), 2.90 - 3.14 (m, 4H), 1.48 - 1.70 (m, 2H), 1.23 (d, $J = 6.2$ Hz, 3H), 0.91 (t, $J = 7.4$ Hz, 3H).	413.6
350	(DMSO-d6): 12.48 - 12.19 (m, 1H), 10.04 (br. s, 1H), 8.93 (s, 1H), 8.33 (d, $J = 3.7$ Hz, 1H), 8.10 (s, 1H), 7.22 (dd, $J = 7.9, 4.7$ Hz, 1H), 6.81 (s, 1H), 4.80 - 4.96 (m, 1H), 3.74 - 3.87 (m, 4H), 3.01 - 3.14 (m, 4H), 1.50 - 1.68 (m, 2H), 1.24 (d, $J = 6.2$ Hz, 3H), 0.91 (t, $J = 7.3$ Hz, 3H).	413.4
351	(DMSO-d6): 12.34 (br. s, 1H), 9.86 (br. s, 1H), 8.97 (d, $J = 7.8$ Hz, 1H), 8.33 (d, $J = 3.4$ Hz, 1H), 8.11 (s, 1H), 7.25 (dd, $J = 8.0, 4.7$ Hz, 1H), 6.80 (s, 1H), 5.00 - 5.09 (m, 1H), 3.30 - 3.40 (m, 2H), 3.01 - 3.13 (m, 4H), 2.81 - 2.94 (m, 4H), 1.27 (d, $J = 6.3$ Hz, 6H).	480.2
352	(DMSO-d6): 12.35 (br. s, 1H), 8.62 (br. s, 1H), 8.40 (dd, $J = 8.0, 1.3$ Hz, 1H), 8.	398.0

	32 (d, J = 4.6 Hz, 1H), 8.01 (s, 1H), 7.21 (dd, J = 7.9, 4.7 Hz, 1H), 6.86 (s, 1H), 4.99 - 5.13 (m, 1H), 4.18 - 4.31 (m, 1H), 3.87 - 3.99 (m, 2H), 3.39 - 3.54 (m, 2H), 1.80 - 1.97 (m, 4H), 1.27 (d, J = 6.3 Hz, 6H).	
353	(DMSO-d6): 12.36 (s, 1H), 10.43 (br. s, 1H), 8.88 (d, J = 6.5 Hz, 1H), 8.35 (d, J = 3.5 Hz, 1H), 8.14 (s, 1H), 7.17 (dd, J = 8.0, 4.7 Hz, 1H), 6.86 (s, 1H), 4.99 - 5.11 (m, 1H), 3.47 - 3.62 (m, 4H), 3.35 - 3.42 (m, 4H), 1.27 (d, J = 6.2 Hz, 6H).	447.2
354	(DMSO-d6): 12.36 (br. s, 1H), 8.39 (d, J = 7.9 Hz, 1H), 8.33 (d, J = 4.7 Hz, 1H), 8.07 (s, 1H), 7.16 - 7.26 (m, 2H), 6.80 - 6.92 (m, 3H), 5.01 - 5.12 (m, 1H), 4.94 (br. s, 2H), 3.83 - 4.02 (m, 2H), 3.76 (s, 3H), 3.00 (t, J = 5.7 Hz, 2H), 1.27 (d, J = 6.2 Hz, 6H).	460.2
355	(DMSO-d6): 13.04 (br. s, 1H), 8.40 (dd, J = 7.9, 1.4 Hz, 1H), 8.33 (dd, J = 4.6, 1.3 Hz, 1H), 8.07 (s, 1H), 7.22 (dd, J = 7.9, 4.7 Hz, 1H), 7.16 (d, J = 7.7 Hz, 1H), 7.08 (d, J = 7.1 Hz, 2H), 6.87 (s, 1H), 5.00 - 5.12 (m, 1H), 4.93 (br. s, 2H), 3.88 - 3.98 (m, 2H), 3.03 (t, J = 5.5 Hz, 2H), 2.30 (s, 3H), 1.89 (s, 3H), 1.28 (d, J = 6.2 Hz, 6H).	444.2
356	(DMSO-d6): 11.33 (br. s, 1H), 8.39 (dd, J = 7.9, 1.4 Hz, 1H), 8.33 (dd, J = 4.6, 1.3 Hz, 1H), 8.09 (s, 1H), 7.42 (s, 1H), 7.32 (s, 2H), 7.22 (dd, J = 7.9, 4.7 Hz, 1H), 6.88 (s, 1H), 4.94 - 5.11 (m, 3H), 3.87 - 4.00 (m, 2H), 3.07 (t, J = 5.7 Hz, 2H), 1.89 (s, 3H), 1.27 (t, J = 6.0 Hz, 6H).	464.2
357	(MeOD): 9.17 (s, 1H), 8.16 - 8.34 (m, 3H), 7.19 - 7.27 (m, 3H), 6.94 - 7.04 (m, 2H), 5.14 - 5.28 (m, 1H), 4.93 (br. s, 2H), 3.99 (t, J = 5.8 Hz, 2H), 3.05 (t, J = 5.5 Hz, 2H), 1.37 (d, J = 6.3 Hz, 6H).	448.0
358	(DMSO-d6): 12.36 (s, 1H), 8.39 (d, J = 7.9 Hz, 1H), 8.33 (d, J = 4.6 Hz, 1H), 8.06 (s, 1H), 7.18 - 7.28 (m, 2H), 6.81 - 6.94 (m, 3H), 5.00 - 5.11 (m, 1H), 4.96 (s, 2H), 3.91 - 4.06 (m, 2H), 3.81 (s, 3H), 2.94 (t, J = 5.7 Hz, 2H), 1.28 (d, J = 6.2 Hz, 6H).	460.2
359	(DMSO-d6): 12.34 (br. s, 1H), 8.39 (dd, J = 7.9, 1.1 Hz, 1H), 8.33 (dd, J = 4.6, 1.1 Hz, 1H), 8.06 (s, 1H), 7.17 - 7.25 (m, 2H), 6.82 - 6.90 (m, 3H), 5.00 - 5.10 (m, 1H), 4.89 (br. s, 2H), 3.84 - 4.00 (m, 2H), 3.76 (s, 3H), 3.05 (t, J = 5.7 Hz, 2H), 1.27 (d, J = 6.2 Hz, 6H).	460.4

[0811]

Biological activities of several compounds of the present invention were measured according to the methods mentioned blow.

5

[Preparation and Storage of Solutions of Test Compounds]

A test compound was dissolved or suspended in DMSO so as to be at 10 mM or 1 mM, thereby making a stock solution, which was stored at -20°C in the dark before being tested.

10

[0812]

Test Example 1

[Inhibitory Effect on Cdc7 Protein Kinase]

[0813]

Measurement of kinase activity was carried out using an MSA assay kit (QuickScout Screening Assist™ Kit, Carna Biosciences, Inc.).

[0814]

5 Assay buffer (20 mM HEPES, 0.01% Triton X-100(TM), 2 mM dithiothreitol, pH 7.5) was used to prepare a substrate mixture solution comprising 4  $\mu$ M of a kinase-reaction substrate (FITC-labeled MCM2 peptide), 40 mM MgCl<sub>2</sub>, and 20  $\mu$ M ATP.

10 The enzyme supplied in the kit (human Cdc7/human ASK complex protein) was diluted in the assay buffer so as to be at 7 nM, thereby preparing an enzyme solution.

[0815]

15 The stock solution of each test compound was diluted in DMSO to prepare diluted DMSO solutions of 10 concentrations (0.00003 mM, 0.0001 mM, 0.0003 mM, 0.001 mM, 0.003 mM, 0.01 mM, 0.03 mM, 0.1 mM, 0.3 mM, 1 mM), each of which was further diluted 25 times in the assay buffer to make a drug solution (a solution containing 4% DMSO).

20 [0816]

25 The kinase reaction was performed in wells of a polypropylene 384-well plate in which 5  $\mu$ l of each of the drug solutions or of a solvent (assay buffer containing 4% DMSO), 5  $\mu$ l of the substrate mixture solution, and 10  $\mu$ l of the enzyme solution were mixed. The assay buffer, instead of

the enzyme solution, was added to blank wells. After the reaction at room temperature for 5 hours, 60  $\mu$ l of the termination buffer supplied in the kit was added to each well to stop the reaction. The percent inhibition of each reaction was determined using a LabChip EZ Reader II system (manufactured by Caliper Life Sciences), according to the protocol provided with the assay kit. In this case, the peak heights of the separated substrate and the phosphorylated substrate were represented as S and P, respectively, and the percent inhibition (%) by a tested compound was calculated according to the following formula:

$$\text{Percent inhibition (\%)} = (1 - (C - A)/(B - A)) \times 100$$

wherein A denotes P/(P + S) for a blank well, B denotes P/(P + S) for a solvent well, and C denotes P/(P + S) for a compound-added well.

The IC<sub>50</sub> value of a tested compound was calculated by regression analysis of the percent inhibition values versus the (logarithmic) concentrations of the tested compound.

The IC<sub>50</sub> values of several compounds of the present invention against Cdc7 were all less than 1  $\mu$ M, as shown in Table 4 below.

[0817]

Test Example 2

[Inhibitory Effect on Phosphorylation using Cells]

Cultured cells

[0818]

COLO205 cells derived from human colon adenocarcinoma (RCB2127, RIKEN BRC) were cultured in 10cm dishes using RPMI-1640 medium (SIGMA, R8758) supplemented with 10% FCS (Equitech-bio) and 5% penicillin/streptomycin (GIBCO, 15140). After the cells were cultured to a confluence of 70 to 90%, the medium was removed, and the cells were treated with trypsin (2 mL, TrypLE Express, GIBCO, 12604-021) and then harvested using a new medium.

10 Addition of Drugs to Cultured Cells

[0819]

COLO205 cells were seeded in 6-well plates (FALCON, 35046) to  $2.5 \times 10^5$  cells (1 ml) per well and cultured overnight in a 5% CO<sub>2</sub> incubator. A drug solution, which was prepared by adding 1.5 µl of a 0.1-mM stock solution in DMSO of a test compound to 500 µl of medium, was added to each well (to a final drug concentration of 0.1 µM), and then cultured for another 24 hours.

Determination of Inhibitory Effect on MCM2 Phosphorylation

20 [0820]

Cells were cultured for 24 hours in the presence of a test compound, harvested using a similar way as described above, washed with PBS, and then pelletized and stored at -80°C. The frozen cells were thawed, subsequently suspended immediately in 2 × SDS-PAGE electrophoresis buffer ( $1 \times 10^5$

cells per 10  $\mu$ l), and heated at 95°C for 10 minutes, leading to the dissolution and denaturation of the proteins. The resulting sample solutions were subjected to SDS-PAGE using a 5-20% gradient acrylamide gel (e-PAGEL (5-20%), ATTO, E-T520L). After the electrophoresis was completed, the gel was immersed in tris-glycine buffer supplemented with 20% methanol, and the proteins in the gel were transferred onto a PVDF membrane (MILLIPORE, Immobilon-P, IPVH00010) using a semi-dry transfer apparatus (TRNS-BLOT SD SEMI-DRY TRANSFER CELL, BIO RAD).

[0821]

The transferred PVDF membrane was blocked with 5% skim milk (Difco Skim Milk, BD, 232100), and then subjected to reaction with an anti-MCM2 goat antibody (N-19, Santa Cruz, sc-9839) or anti-phosphorylated MCM2 rabbit antibody (S53) (Bethyl, A300-756A) as a primary antibody and additionally with an anti- $\alpha$  tubulin mouse antibody (Clone DM 1A, SIGMA, 9026) as an internal control. Each band was detected by chemiluminescence using an HRP-labeled anti-goat IgG donkey antibody (Santa Cruz, sc2020), anti-rabbit IgG sheep antibody (Roche, 12015218001), or anti-mouse IgG donkey antibody (Jackson ImmunoResearch, 715-035-151) as a secondary antibody. The combinations of and the diluted concentrations of the primary and secondary antibodies were as indicated below.

[0822]

[Table 3]

	Primary antibody(diluted concentration)	Secondary antibody(diluted concentration)
1	Anti-MCM2 goat antibody (1/500)	Anti-goat IgG donkey antibody (1/10000)
2	Anti-phosphorylated MCM2 rabbit antibody (S53) (1/500)	Anti-rabbit IgG sheep antibody (1/5000)
3	Anti- $\alpha$ -tubulin mouse antibody (1/1000)	Anti-mouse IgG donkey antibody (1/100000)

[0823]

The bands which were detected were normalized using the amount of endogenous  $\alpha$ -tubulin as a reference, and the percent phosphorylation of MCM2 was calculated for each of the tested compounds. Their inhibitory effects on MCM2 phosphorylation were indicated by a triple asterisk (\*\*\*) in the case where the percent phosphorylation of MCM2 was less than 20%, by a dual asterisk (\*\*) in the case where the percent phosphorylation of MCM2 was not less than 20% and less than 50%, and by a single asterisk (\*) in the case where the percent phosphorylation of MCM2 was not less than 50% and less than 70%.

It was found from this testing that as shown in Table 4, the tested compounds of the present invention inhibited the phosphorylation of MCM2 at a concentration of 0.1  $\mu$ M.

[0824]

[Table 4]

Example	Test Example 1 Cdc7 IC <sub>50</sub> value (μM)	Test Example 2 Inhibitory effect on MCM2 phosphorylation
15	0.002	**
22	0.010	*
63	0.006	***
68	0.004	***
78	0.011	***
81	0.005	***
89	0.003	***
91	0.004	***
102	0.004	***
126	0.003	***
129	0.009	***
142	0.003	**
157	0.003	**
173	0.003	***
226	0.004	***
233	0.002	**
239	0.001	**
242	0.001	***
244	0.004	***
245	0.008	***
246	0.008	***

[Industrial Applicability]

[0825]

5           The compounds provided by the present invention are capable of controlling the growth of cells through their inhibitory effects on Cdc7. Therefore, the compounds of the present invention which have an inhibitory effect on Cdc7 will be useful as a medicine, especially an agent for the

10 treatment of diseases derived from abnormal growth of cells, such as cancers.

	3 - 3.87 (m, 2H), 2.95 - 3.06 (m, 2H), 1.24 (t, J = 7.0 Hz, 3H), 1.18 (d, J = 6.0 Hz, 6H).	
261	(DMSO-d6): 12.35 (s, 1H), 8.66 (br. s, 1H), 8.41 (d, J = 7.9 Hz, 1H), 8.32 (d, J = 3.5 Hz, 1H), 8.01 (s, 1H), 7.21 (dd, J = 7.9, 4.7 Hz, 1H), 6.90 (s, 1H), 4.18 - 4.30 (m, 3H), 3.89 - 4.00 (m, 2H), 3.40 - 3.53 (m, 2H), 1.82 - 1.96 (m, 4H), 1.25 (q, J = 7.1 Hz, 3H).	384.2
262	(DMSO-d6): 12.31 (s, 1H), 9.87 (s, 1H), 8.93 (d, J = 7.8 Hz, 1H), 8.30 (d, J = 3.6 Hz, 1H), 8.06 (d, J = 2.2 Hz, 1H), 7.14 (dd, J = 8.0, 4.6 Hz, 1H), 6.85 (s, 1H), 4.20 (q, J = 7.0 Hz, 2H), 3.04 - 3.17 (m, 4H), 1.85 - 1.98 (m, 4H), 1.26 (t, J = 7.1 Hz, 3H).	369.2
263	(DMSO-d6): 12.39 (s, 1H), 10.05 (s, 1H), 8.85 (d, J = 7.8 Hz, 1H), 8.33 (d, J = 3.8 Hz, 1H), 8.12 (s, 1H), 7.17 (dd, J = 7.8, 4.6 Hz, 1H), 6.87 (s, 1H), 4.20 (q, J = 7.0 Hz, 2H), 3.08 - 3.20 (m, 4H), 1.63 - 1.84 (m, 8H), 1.26 (t, J = 7.0 Hz, 3H).	397.2
264	(DMSO-d6): 12.26 (s, 1H), 8.16 - 8.24 (m, 2H), 7.85 (d, J = 7.9 Hz, 1H), 7.62 (s, 1H), 7.38 (d, J = 7.5 Hz, 1H), 7.31 (s, 1H), 7.25 (d, J = 7.6 Hz, 1H), 6.82 (dd, J = 7.8, 4.7 Hz, 1H), 6.75 (s, 1H), 4.20 - 4.30 (m, 2H), 3.57 (s, 2H), 3.10 - 3.60 (m, 8H), 2.68 - 2.77 (m, 1H), 2.24 (s, 3H), 1.29 (t, J = 7.1 Hz, 3H), 0.99 (d, J = 6.5 Hz, 6H).	530.4
265	(DMSO-d6): 8.21 (s, 1H), 8.17 (d, J = 3.4 Hz, 1H), 7.83 (d, J = 7.7 Hz, 1H), 7.62 (s, 1H), 7.40 (s, 1H), 7.33 (s, 2H), 6.81 (dd, J = 8.0, 4.7 Hz, 1H), 6.63 (s, 1H), 4.15 - 4.30 (m, 3H), 3.95 (s, 2H), 2.43 - 2.56 (m, 2H), 2.22 (s, 3H), 1.81 - 1.94 (m, 2H), 1.63 - 1.75 (m, 2H), 1.43 - 1.60 (m, 4H), 1.22 - 1.33 (m, 3H).	487.2
266	(DMSO-d6): 8.16 (d, J = 3.8 Hz, 1H), 7.83 (d, J = 7.6 Hz, 1H), 7.60 (s, 1H), 7.18 - 7.39 (m, 3H), 6.87 (s, 1H), 6.75 - 6.84 (m, 1H), 6.54 (s, 1H), 4.10 - 4.25 (m, 2H), 3.93 (s, 2H), 2.95 - 3.10 (m, 1H), 2.15 - 2.20 (m, 3H), 1.20 - 1.30 (m, 3H), 1.10 - 1.20 (m, 6H).	461.2

[0806]

[Table 2-2]

267	(DMSO-d6): 12.26 (s, 1H), 10.32 (br. s, 1H), 8.20 (d, J = 3.5 Hz, 1H), 7.71 - 7.82 (m, 2H), 7.46 (d, J = 8.2 Hz, 1H), 7.35 (s, 1H), 7.29 (d, J = 8.5 Hz, 1H), 6.83 (s, 1H), 6.73 - 6.81 (m, 1H), 4.53 - 4.61 (m, 1H), 4.20 - 4.32 (m, 2H), 3.42 - 3.62 (m, 3H), 2.68 - 2.80 (m, 2H), 2.26 (s, 3H), 2.03 - 2.20 (m, 2H), 1.67 - 1.80 (m, 2H), 1.36 - 1.51 (m, 2H), 1.29 (t, J = 7.0 Hz, 3H).	503.2
268	(DMSO-d6): 12.49 (br. s, 1H), 9.38 (br. s, 1H), 8.44 (d, J = 7.53 Hz, 1H), 8.33 (dd, J = 1.25, 4.52 Hz, 1H), 8.17 (d, J = 2.51 Hz, 1H), 7.21 (dd, J = 4.77, 8.03 Hz, 1H), 7.02 (s, 1H), 4.79 (s, 2H), 4.23 (q, J = 7.19 Hz, 2H), 1.26 (t, J = 7.03 Hz, 3H).	339.0
269	(DMSO-d6): 12.35 (br. s, 1H), 8.60 (d, J = 8.78 Hz, 1H), 8.45 (dd, J = 1.26, 8.03 Hz, 1H), 8.31 (dd, J = 1.25, 4.52 Hz, 1H), 8.04 (s, 1H), 7.19 (dd, J = 4.77, 8.03 Hz, 1H), 6.90 (s, 1H), 5.18 (t, J = 5.14 Hz, 2H), 4.11 - 4.27 (m, 3H), 3.67 (t, J = 5.40 Hz, 4H), 1.26 (t, J = 7.15 Hz, 3H).	373.9
270	(DMSO-d6): 12.40 (br. s, 1H), 8.84 (t, J = 5.90 Hz, 1H), 8.49 (d, J = 8.03 Hz, 1H), 8.32 (dd, J = 1.38, 4.64 Hz, 1H), 8.06 (d, J = 2.51 Hz, 1H), 7.21 (dd, J = 4.77, 8.03 Hz, 1H), 6.90 (s, 1H), 4.21 (q, J = 7.03 Hz, 2H), 3.73 - 3.83 (m, 2H), 3.33 - 3.66 (m, 5H), 1.26 (t, J = 7.03 Hz, 3H).	374.0
271	(DMSO-d6): 12.10 - 12.20 (m, 1H), 8.20 - 8.42 (m, 2H), 7.98 (s, 1H), 7.19 (dd, J = 7.9, 4.6 Hz, 1H), 6.85 (s, 1H), 4.10 - 4.40 (m, 4H), 3.85 - 4.05 (m, 2H), 3.25 - 3.40 (m, 4H), 2.35 - 3.45 (m, 3H), 2.65 - 2.80 (m, 1H), 2.15 - 2.25 (m, 6H), 1.80 - 1.95 (m, 2H), 1.53 - 1.72 (m, 2H), 1.20 - 1.28 (m, 3H).	468.3
272	(DMSO-d6): 12.30 (s, 1H), 8.37 (d, J = 7.9 Hz, 1H), 8.31 (d, J = 4.2 Hz, 1H), 7.98 (s, 1H), 7.19 (dd, J = 7.8, 4.6 Hz, 1H), 6.84 (s, 1H), 4.58 - 4.73 (m, 3H), 4.16 (q, J = 7.0 Hz, 2H), 3.93 - 4.01 (m, 2H), 3.68 - 3.77 (m, 1H), 3.40 - 3.56 (m, 3H), 3.31 - 3.39 (m, 2H), 3.16 (s, 3H), 1.74 - 1.90 (m, 3H), 1.58 -	486.2

	1.72 (m, 3H), 1.24 (t, J = 7.1 Hz, 3H).	
273	(DMSO-d6): 12.35 (s, 1H), 8.41 (d, J = 6.8 Hz, 1H), 8.32 (d, J = 3.4 Hz, 1H), 8.06 (s, 1H), 7.22 (dd, J = 7.9, 4.6 Hz, 2H), 6.83 - 6.93 (m, 3H), 4.90 (s, 2H), 4.20 (q, J = 7.0 Hz, 2H), 3.84 - 4.00 (m, 2H), 3.76 (s, 3H), 3.01 - 3.09 (m, 2H), 1.26 (t, J = 7.1 Hz, 3H).	446.0
274	(DMSO-d6): 12.24 (s, 1H), 8.26 - 8.48 (m, 2H), 7.95 (s, 1H), 7.10 - 7.17 (m, 1H), 6.84 - 6.94 (m, 3H), 6.59 (d, J = 8.0 Hz, 1H), 4.90 (s, 2H), 4.77 (s, 2H), 4.15 (q, J = 7.1 Hz, 2H), 3.16 (s, 3H), 2.01 (s, 3H), 1.25 - 1.19 (m, 3H).	433.2
275	(DMSO-d6): 12.31 (s, 1H), 8.37 (d, J = 8.0 Hz, 1H), 8.31 (d, J = 3.6 Hz, 1H), 7.96 (s, 1H), 7.19 (dd, J = 7.9, 4.6 Hz, 1H), 6.84 (s, 1H), 4.00 - 4.25 (m, 4H), 3.22 - 3.32 (m, 1H), 3.05 - 2.95 (m, 1H), 1.75 - 1.91 (m, 3H), 1.60 - 1.74 (m, 1H), 1.17 - 1.33 (m, 4H), 0.95 (d, J = 6.2 Hz, 3H).	382.2
276	(DMSO-d6): 12.32 (s, 1H), 8.37 (d, J = 7.9 Hz, 1H), 8.31 (d, J = 4.6 Hz, 1H), 8.01 (s, 1H), 7.19 (dd, J = 7.9, 4.7 Hz, 1H), 6.88 (s, 1H), 4.12 - 4.22 (m, 4H), 3.76 - 3.86 (m, 2H), 2.96 - 3.06 (m, 2H), 1.24 (t, J = 7.1 Hz, 3H), 1.18 (d, J = 6.2 Hz, 6H).	398.2
277	(DMSO-d6): 12.37 (s, 1H), 9.96 (s, 1H), 8.99 (d, J = 7.8 Hz, 1H), 8.34 (d, J = 3.3 Hz, 1H), 8.11 (d, J = 2.5 Hz, 1H), 7.23 (dd, J = 8.0, 4.7 Hz, 1H), 6.85 (s, 1H), 4.49 (t, J = 5.2 Hz, 1H), 4.21 (q, J = 7.1 Hz, 2H), 3.56 (q, J = 6.0 Hz, 2H), 2.98 - 3.12 (m, 4H), 2.57 - 2.77 (m, 4H), 2.45 - 2.55 (m, 2H), 1.26 (t, J = 7.1 Hz, 3H).	428.4
278	(DMSO-d6): 12.21 (br. s, 1H), 8.28 - 8.42 (m, 2H), 7.96 (s, 1H), 7.18 (dd, J = 7.9, 4.7 Hz, 1H), 6.84 (s, 1H), 4.06 - 4.23 (m, 4H), 2.72 - 2.88 (m, 2H), 1.75 - 1.92 (m, 3H), 1.24 (t, J = 7.0 Hz, 3H), 0.86 - 1.00 (m, 7H).	396.2
279	(DMSO-d6): 12.27 (s, 1H), 9.22 (br. s, 1H), 6.4 - 8.6 (m, 7H), 4.15 - 4.25 (m, 2H), 1.18 - 1.30 (m, 3H).	367.2
280	(DMSO-d6): 12.10 - 12.65 (m, 1H), 8.25 - 8.53 (m, 2H), 8.01 (s, 1H), 7.14 - 7.29 (m, 2H), 6.80 - 6.95 (m, 3H), 4.68 - 4.93 (m, 2H), 4.15 - 4.27 (m, 2H), 3.93 - 4.05 (m, 2H), 3.80 - 3.92 (m, 3H), 2.98 - 3.10 (m, 2H), 1.23 - 1.32 (m, 3H).	446.0
281	(DMSO-d6): 12.34 (s, 1H), 9.51 (br. s, 1H), 9.17 (d, J = 7.3 Hz, 1H), 8.33 (d, J = 3.3 Hz, 1H), 8.12 (s, 1H), 7.18 (dd, J = 8.0, 4.6 Hz, 1H), 6.82 (s, 1H), 4.22 (q, J = 7.0 Hz, 2H), 2.95 - 3.10 (m, 2H), 1.70 - 1.85 (m, 3H), 1.37 - 1.53 (m, 3H), 1.27 (t, J = 7.1 Hz, 3H), 0.98 (d, J = 6.0 Hz, 6H).	411.2
282	(DMSO-d6): 12.25 (br. s, 1H), 8.34 - 8.39 (m, 1H), 8.32 (d, J = 4.6 Hz, 1H), 7.97 (s, 1H), 7.19 (dd, J = 7.9, 4.6 Hz, 1H), 6.84 (s, 1H), 4.10 - 4.27 (m, 2H), 3.73 (dd, J = 13.1, 3.5 Hz, 2H), 3.43 - 3.59 (m, 2H), 2.06 - 2.20 (m, 2H), 1.54 (t, J = 5.7 Hz, 2H), 1.25 (t, J = 6.7 Hz, 3H), 0.95 (d, J = 7.3 Hz, 6H).	396.2
283	(DMSO-d6): 12.30 (s, 1H), 8.37 (d, J = 7.9 Hz, 1H), 8.32 (d, J = 4.7 Hz, 1H), 7.97 (s, 1H), 7.19 (dd, J = 7.8, 4.7 Hz, 1H), 6.84 (s, 1H), 4.18 (q, J = 7.1 Hz, 2H), 3.62 - 3.71 (m, 2H), 3.54 (s, 2H), 1.71 - 1.82 (m, 2H), 1.45 - 1.56 (m, 2H), 1.25 (t, J = 7.1 Hz, 3H), 0.97 (s, 6H).	396.2
284	(DMSO-d6): 12.30 (s, 1H), 8.38 (d, J = 8.2 Hz, 1H), 8.31 (d, J = 4.2 Hz, 1H), 8.00 (s, 1H), 7.19 (dd, J = 8.0, 4.6 Hz, 1H), 6.83 (s, 1H), 4.97 - 5.10 (m, 1H), 4.42 - 4.56 (m, 1H), 4.10 - 4.23 (m, 2H), 3.80 - 3.95 (m, 2H), 3.57 - 3.72 (m, 2H), 1.70 - 1.90 (m, 3H), 1.55 - 1.70 (m, 3H), 1.24 (t, J = 7.0 Hz, 3H).	398.0
285	(DMSO-d6): 12.28 (br. s, 1H), 10.34 (br. s, 1H), 8.20 (dd, J = 1.38, 4.64 Hz, 1H), 7.73 - 7.79 (m, 2H), 7.42 (d, J = 7.78 Hz, 1H), 7.31 (s, 1H), 7.25 (d, J = 8.03 Hz, 1H), 6.84 (s, 1H), 6.76 (dd, J = 4.64, 7.91 Hz, 1H), 4.27 (q, J = 7.03 Hz, 2H), 3.61 (t, J = 4.52 Hz, 4H), 3.28 - 3.34 (m, 4H), 2.82 - 2.90 (m, 2H), 2.58 - 2.64 (m, 2H), 2.24 (s, 3H), 1.30 (t, J = 7.03 Hz, 3H).	503.3
286	(DMSO-d6): 12.25 (s, 1H), 10.37 (s, 1H), 8.20 (d, J = 3.7 Hz, 1H), 7.78 (d, J = 7.8 Hz, 1H), 7.72 (s, 1H), 7.42 (d, J = 8.0 Hz, 1H), 7.30 (s, 1H), 7.23 (d, J = 7.7 Hz, 1H), 6.85 (s, 1H), 6.80 (dd, J = 7.8, 4.7 Hz, 1H), 4.77 (t, J = 5.1 Hz, 1H), 4.27 (q, J = 6.9 Hz, 2H), 3.72 (q, J = 6.7 Hz, 2H), 2.85 (t, J = 6.9 Hz, 2H), 2.24 (s, 3H), 1.30 (t, J = 7.0 Hz, 3H).	434.0

[0807]

[Table 2-3]

287	(DMSO-d6): 12.11 (br. s, 1H), 8.15 (d, J = 3.8 Hz, 1H), 7.68 - 7.78 (m, 2H), 7.43 (s, 1H), 7.26 - 7.38 (m, 2H), 6.80 (dd, J = 7.7, 4.8 Hz, 1H), 6.60 (s, 1H), 4.15 - 4.25 (m, 2H), 3.66 (s, 2H), 2.60 - 2.70 (m, 4H), 2.19 (s, 3H), 1.91 (s, 3H), 1.70 - 1.82 (m, 4H), 1.27 (t, J = 7.0 Hz, 3H).	497.2
288	(DMSO-d6): 11.80 - 12.15 (m, 1H), 8.22 - 8.37 (m, 2H), 8.12 - 8.18 (m, 1H), 7.74 - 7.83 (m, 1H), 7.54 - 7.72 (m, 1H), 7.33 (s, 1H), 7.26 (d, J = 8.9 Hz, 1H), 6.91 - 7.05 (m, 1H), 6.77 - 6.84 (m, 1H), 6.27 - 6.39 (m, 1H), 4.04 - 4.23 (m, 2H), 3.60 - 3.70 (m, 4H), 3.56 (s, 2H), 2.53 - 2.62 (m, 4H), 2.10 (s, 3H), 1.20 - 1.30 (m, 3H).	513.0
289	(DMSO-d6): 8.05 - 8.15 (m, 1H), 7.82 (d, J = 7.4 Hz, 1H), 7.52 (s, 1H), 7.27 (s, 1H), 7.20 (d, J = 7.8 Hz, 1H), 6.91 (d, J = 7.9 Hz, 1H), 6.75 - 6.84 (m, 1H), 6.18 (s, 1H), 4.02 - 4.13 (m, 2H), 3.30 - 3.70 (m, 3H), 2.75 - 2.85 (m, 2H), 2.36 - 2.26 (m, 2H), 2.07 (s, 3H), 1.72 - 1.82 (m, 2H), 1.40 - 1.50 (m, 2H), 1.15 - 1.30 (m, 3H).	527.0
290	(DMSO-d6): 12.27 (br. s, 1H), 8.20 (dd, J = 1.25, 4.77 Hz, 1H), 7.72 - 7.80 (m, 2H), 7.40 (d, J = 8.03 Hz, 1H), 7.30 (s, 1H), 7.23 (d, J = 7.78 Hz, 1H), 6.82 (s, 1H), 6.76 (dd, J = 4.64, 7.91 Hz, 1H), 4.26 (q, J = 7.03 Hz, 2H), 3.25 - 3.50 (m, 4H), 2.79 - 2.89 (m, 2H), 2.56 - 2.66 (m, 2H), 2.31 - 3.47 (m, 4H), 2.23 (s, 3H), 2.20 (s, 3H), 1.29 (t, J = 7.15 Hz, 3H).	516.3
291	(DMSO-d6): 12.31 (s, 1H), 8.39 (d, J = 6.9 Hz, 1H), 8.31 (d, J = 4.6 Hz, 1H), 7.95 (s, 1H), 7.20 (dd, J = 7.9, 4.7 Hz, 1H), 6.84 (s, 1H), 4.17 (q, J = 7.1 Hz, 2H), 3.73 (q, J = 7.0 Hz, 2H), 3.26 (s, 3H), 1.20 - 1.33 (m, 6H).	342.2
292	(DMSO-d6): 8.38 (d, J = 7.9 Hz, 1H), 8.31 (d, J = 3.3 Hz, 1H), 7.95 (s, 1H), 7.19 (dd, J = 7.9, 4.7 Hz, 1H), 6.84 (s, 1H), 4.50 - 4.62 (m, 1H), 4.17 (d, J = 7.1 Hz, 2H), 3.09 (s, 3H), 1.36 - 1.20 (m, 9H).	356.0
293	(DMSO-d6): 12.31 (br. s, 1H), 10.01 (br. s, 1H), 8.92 (d, J = 7.8 Hz, 1H), 8.31 (d, J = 3.7 Hz, 1H), 8.08 (s, 1H), 7.18 (dd, J = 7.9, 4.7 Hz, 1H), 6.83 (s, 1H), 4.97 (br. s, 1H), 4.20 (q, J = 7.0 Hz, 2H), 3.72 - 3.83 (m, 1H), 3.12 - 3.20 (m, 1H), 2.97 - 3.06 (m, 1H), 2.71 - 2.91 (m, 2H), 1.80 - 1.93 (m, 2H), 1.56 - 1.68 (m, 1H), 1.18 - 1.31 (m, 4H).	399.2
294	(DMSO-d6): 12.29 (s, 1H), 8.29 - 8.38 (m, 2H), 7.96 (s, 1H), 7.19 (dd, J = 7.9, 4.7 Hz, 1H), 6.82 (s, 1H), 4.95 - 5.10 (m, 1H), 4.15 - 4.25 (m, 2H), 3.24 - 3.34 (m, 2H), 1.68 - 1.88 (m, 3H), 1.25 - 1.40 (m, 2H), 1.25 (d, J = 6.2 Hz, 6H), 0.97 (d, J = 6.3 Hz, 3H).	396.4
295	(DMSO-d6): 12.35 (s, 1H), 8.40 (d, J = 6.6 Hz, 1H), 8.33 (d, J = 4.6 Hz, 1H), 8.07 (s, 1H), 7.24 - 7.32 (m, 4H), 7.22 (dd, J = 7.9, 4.7 Hz, 1H), 6.87 (s, 1H), 5.00 - 5.12 (m, 1H), 4.97 (s, 2H), 3.90 - 4.02 (m, 2H), 3.03 - 3.13 (m, 2H), 1.27 (t, J = 8.9 Hz, 6H).	430.2
296	(DMSO-d6): 12.31 (s, 1H), 9.86 (s, 1H), 8.84 (d, J = 7.8 Hz, 1H), 8.30 (d, J = 3.3 Hz, 1H), 8.05 (d, J = 2.5 Hz, 1H), 7.20 (dd, J = 8.0, 4.6 Hz, 1H), 6.83 (s, 1H), 4.99 - 5.10 (m, 1H), 2.77 (s, 6H), 1.27 (d, J = 6.3 Hz, 6H).	357.2
297	(DMSO-d6): 12.26 (s, 1H), 10.07 (s, 1H), 8.17 (s, 1H), 7.85 (s, 1H), 7.69 (d, J = 7.4 Hz, 1H), 7.17 (d, J = 8.3 Hz, 1H), 6.72 - 6.88 (m, 2H), 6.52 - 6.67 (m, 2H), 5.80 - 5.92 (m, 1H), 5.07 - 5.18 (m, 1H), 4.71 - 4.81 (m, 1H), 3.58 - 3.69 (m, 2H), 3.15 - 3.25 (m, 2H), 2.13 (s, 3H), 1.30 (d, J = 5.9 Hz, 6H).	462.8
298	(MeOD): 8.15 - 8.24 (m, 1H), 7.86 (d, J = 7.5 Hz, 1H), 7.65 (br. s, 1H), 7.40 - 7.55 (m, 3H), 6.90 - 7.03 (m, 2H), 6.61 (s, 1H), 4.34 - 4.43 (m, 2H), 3.66 (s, 2H), 2.70 - 2.98 (m, 8H), 2.49 (s, 3H), 2.32 (s, 3H), 1.35 - 1.42 (m, 3H).	526.4
299	(DMSO-d6): 12.31 (s, 1H), 10.42 (br. s, 1H), 8.23 (dd, J = 4.6, 1.4 Hz, 1H), 7.79 (d, J = 7.3 Hz, 1H), 7.72 (d, J = 2.7 Hz, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.37 (s, 1H), 7.30 (d, J = 7.9 Hz, 1H), 6.87 (s, 1H), 6.78 (dd, J = 7.9, 4.8 Hz, 1H), 4.27 (q, J = 7.1 Hz, 2H), 3.35 - 3.70 (m, 4H), 3.03 - 3.15 (m, 4H), 2.27 (s, 3H), 1.85 - 2.10 (s, 4H), 1.30 (t, J = 7.1 Hz, 3H).	487.0
300	(DMSO-d6): 12.30 (br. s, 1H), 8.39 (d, J = 7.6 Hz, 1H), 8.31 (d, J = 4.4 Hz, 1H), 7.93 (s, 1H), 7.19 (dd, J = 7.9, 4.7 Hz, 1H), 6.85 (s, 1H), 4.16 (q, J = 7.1 Hz, 3H), 3.11 (s, 3H), 1.79 - 1.92 (m, 4H), 1.60 - 1.75 (m, 3H), 1.28 - 1.44 (m, 2H), 1.11 - 1.28 (m, 4H).	396.0
301	(DMSO-d6): 12.30 (br. s, 1H), 9.62 (br. s, 1H), 8.91 (d, J = 8.0 Hz, 1H), 8.31 (d, J = 3.8 Hz, 1H), 8.07 (s, 1H), 7.16 (dd, J = 8.0, 4.6 Hz, 1H), 6.84 (s, 1H), 4.21 (q, J = 7.0 Hz, 2H), 2.78 - 2.88 (m, 1H), 2.77 (s, 3H), 1.88 - 2.00 (m, 2H), 1.68 -	411.0

	1.80 (m, 2H), 1.48 - 1.59 (m, 1H), 1.16 - 1.31 (m, 7H), 1.00 - 1.12 (m, 1H).	
302	(DMSO-d6): 12.31 (s, 1H), 10.07 (s, 1H), 8.94 (d, J = 7.5 Hz, 1H), 8.32 (d, J = 3.4 Hz, 1H), 8.12 (s, 1H), 7.21 (dd, J = 8.0, 4.7 Hz, 1H), 6.88 (s, 1H), 4.21 (q, J = 7.1 Hz, 2H), 3.57 - 3.76 (m, 4H), 2.97 - 3.12 (m, 4H), 2.08 (s, 3H), 1.26 (t, J = 7.1 Hz, 3H).	426.0
303	(DMSO-d6): 12.30 (br. s, 1H), 8.15 - 8.21 (m, 2H), 7.77 (s, 1H), 7.68 (d, J = 7.8 Hz, 1H), 7.42 (d, J = 8.7 Hz, 1H), 7.04 (s, 1H), 6.94 (d, J = 8.7 Hz, 1H), 6.73 - 6.81 (m, 2H), 5.08 - 5.19 (m, 1H), 4.19 (t, J = 5.6 Hz, 2H), 2.94 (t, J = 5.6 Hz, 2H), 2.62 - 2.71 (m, 4H), 2.23 (s, 3H), 1.70 - 1.80 (m, 4H), 1.31 (d, J = 6.2 Hz, 6H).	517.4
304	(DMSO-d6): 12.25 (br. s, 1H), 9.80 (br. s, 1H), 8.85 (d, J = 7.4 Hz, 1H), 8.29 (d, J = 3.6 Hz, 1H), 8.04 (s, 1H), 7.17 (dd, J = 8.0, 4.7 Hz, 1H), 6.78 (br. s, 1H), 4.19 (q, J = 6.9 Hz, 2H), 2.88 - 3.00 (m, 2H), 2.74 (s, 3H), 1.25 (t, J = 7.1 Hz, 3H), 1.05 (t, J = 7.1 Hz, 3H).	357.2
305	(DMSO-d6): 12.31 (br. s, 1H), 9.49 (br. s, 1H), 8.96 (d, J = 7.8 Hz, 1H), 8.31 (d, J = 3.3 Hz, 1H), 8.08 (s, 1H), 7.18 (dd, J = 8.0, 4.6 Hz, 1H), 6.86 (s, 1H), 4.22 (q, J = 7.1 Hz, 2H), 3.00 (q, J = 7.0 Hz, 4H), 1.27 (t, J = 7.1 Hz, 3H), 1.04 (t, J = 7.1 Hz, 6H).	371.2

[0808]

[Table 2-4]

306	(DMSO-d6): 12.09 (br. s, 1H), 8.98 (d, J = 7.6 Hz, 1H), 8.32 (d, J = 3.4 Hz, 1H), 8.05 (s, 1H), 7.21 (dd, J = 8.0, 4.7 Hz, 1H), 6.73 (s, 1H), 4.80 (s, 1H), 4.17 (q, J = 7.0 Hz, 2H), 3.54 - 3.69 (m, 1H), 3.04 - 3.15 (m, 2H), 2.82 - 2.95 (m, 2H), 1.83 - 1.94 (m, 2H), 1.63 - 1.77 (m, 2H), 1.24 (t, J = 7.0 Hz, 3H).	399.2
307	(DMSO-d6): 12.29 (s, 1H), 10.23 (s, 1H), 8.18 (d, J = 3.4 Hz, 1H), 7.78 (d, J = 2.5 Hz, 1H), 7.66 (d, J = 7.9 Hz, 1H), 7.42 (d, J = 8.6 Hz, 1H), 7.05 (d, J = 2.4 Hz, 1H), 6.94 (dd, J = 8.6, 2.7 Hz, 1H), 6.79 (s, 1H), 6.74 (dd, J = 7.9, 4.7 Hz, 1H), 5.09 - 5.18 (m, 1H), 4.19 (t, J = 5.6 Hz, 2H), 3.58 - 3.67 (m, 4H), 2.78 (t, J = 5.6 Hz, 2H), 2.49 - 2.57 (m, 4H), 2.23 (s, 3H), 1.31 (d, J = 6.3 Hz, 6H).	533.4
308	(DMSO-d6): 12.20 (br. s, 1H), 10.26 (br. s, 1H), 8.18 (d, J = 3.9 Hz, 1H), 7.66 - 7.77 (m, 2H), 7.26 - 7.39 (m, 1H), 7.00 (s, 1H), 6.86 - 6.93 (m, 1H), 6.61 - 6.78 (s, 2H), 5.06 - 5.17 (m, 1H), 4.11 - 4.18 (m, 2H), 2.76 (t, J = 5.5 Hz, 2H), 2.30 - 2.50 (m, 8H), 2.20 (s, 3H), 2.17 (s, 3H), 1.29 (d, J = 6.2 Hz, 6H).	546.6
309	(DMSO-d6): 12.30 (br. s, 1H), 8.42 (d, J = 8.0 Hz, 1H), 8.32 (d, J = 3.3 Hz, 1H), 7.98 (s, 1H), 7.20 (dd, J = 8.0, 4.7 Hz, 1H), 6.89 (s, 1H), 4.23 - 4.35 (m, 2H), 3.96 - 4.07 (m, 1H), 3.54 - 3.64 (m, 2H), 3.30 (s, 3H), 1.94 - 2.03 (m, 2H), 1.73 - 1.84 (m, 2H), 1.51 - 1.69 (m, 3H), 1.35 - 1.49 (m, 2H), 1.15 - 1.28 (m, 1H).	412.2
310	(DMSO-d6): 12.32 (s, 1H), 9.84 (s, 1H), 8.83 (d, J = 8.2 Hz, 1H), 8.30 (d, J = 3.4 Hz, 1H), 8.05 (s, 1H), 7.20 (dd, J = 8.0, 4.5 Hz, 1H), 6.88 (s, 1H), 4.25 - 4.32 (m, 2H), 3.57 - 3.63 (m, 2H), 3.30 (s, 3H), 2.78 (s, 6H).	373.4
311	(DMSO-d6): 12.31 (s, 1H), 10.43 (s, 1H), 8.23 (d, J = 3.8 Hz, 1H), 7.73 - 7.81 (m, 2H), 7.58 (d, J = 8.1 Hz, 1H), 7.53 (s, 1H), 7.44 (d, J = 7.9 Hz, 1H), 6.88 (s, 1H), 6.83 (dd, J = 7.9, 4.7 Hz, 1H), 5.42 (t, J = 5.9 Hz, 1H), 4.38 (d, J = 5.9 Hz, 2H), 4.27 (q, J = 7.0 Hz, 2H), 2.27 (s, 3H), 1.30 (t, J = 7.0 Hz, 3H).	444.4
312	(DMSO-d6): 12.27 (s, 1H), 10.41 (s, 1H), 8.16 (d, J = 3.4 Hz, 1H), 7.79 (d, J = 1.9 Hz, 1H), 7.64 (d, J = 7.5 Hz, 1H), 7.48 - 7.55 (m, 2H), 7.42 (d, J = 7.9 Hz, 1H), 6.82 (s, 1H), 6.79 (dd, J = 7.9, 4.6 Hz, 1H), 4.24 (q, J = 7.0 Hz, 2H), 3.53 (s, 2H), 2.30 (s, 6H), 2.23 (s, 3H), 1.27 (t, J = 7.0 Hz, 3H).	471.1
313	(DMSO-d6): 12.28 (s, 1H), 10.17 (br. s, 1H), 8.21 (d, J = 3.3 Hz, 1H), 7.71 - 7.80 (m, 2H), 7.44 (d, J = 8.1 Hz, 1H), 7.32 (s, 1H), 7.25 (d, J = 8.0 Hz, 1H), 6.84 (s, 1H), 6.75 - 6.81 (m, 1H), 4.23 - 4.32 (m, 2H), 2.85 - 2.95 (m, 2H), 2.75 - 2.85 (m, 2H), 2.42 (s, 6H), 2.24 (s, 3H), 1.30 (t, J = 7.1 Hz, 3H).	461.1
314	(DMSO-d6): 12.28 (s, 1H), 10.27 (br. s, 1H), 8.21 (d, J = 4.6 Hz, 1H), 7.72 - 7.78 (m, 2H), 7.42 (d, J = 8.0 Hz, 1H), 7.30 (s, 1H), 7.24 (d, J = 8.3 Hz, 1H), 6.84 (s, 1H), 6.76 (dd, J = 7.9, 4.6 Hz, 1H), 4.58 - 4.72 (m, 1H), 4.22 - 4.32 (m, 2H),	517.1

	3.44 - 3.60 (m, 1H), 2.80 - 3.00 (m, 4H), 2.40 - 2.60 (m, 4H), 2.24 (s, 3H), 1.72 - 1.85 (m, 2H), 1.38 - 1.53 (m, 2H), 1.29 (t, J = 7.1 Hz, 3H).	
315	(DMSO-d6): 12.26 (br. s, 1H), 9.72 (br. s, 1H), 8.91 (d, J = 7.6 Hz, 1H), 8.30 (d, J = 3.7 Hz, 1H), 8.05 (s, 1H), 7.16 (dd, J = 7.8, 4.6 Hz, 1H), 6.77 (br. s, 1H), 4.13 - 4.24 (m, 2H), 3.08 - 3.20 (m, 1H), 2.72 (s, 3H), 1.25 (t, J = 7.1 Hz, 3H), 1.10 (d, J = 6.3 Hz, 6H).	371.0
316	(DMSO-d6): 12.33 (br. s, 1H), 10.25 (br. s, 1H), 8.87 - 8.99 (m, 1H), 8.30 (d, J = 3.4 Hz, 1H), 8.01 - 8.18 (m, 2H), 7.07 (dd, J = 8.0, 4.6 Hz, 1H), 6.85 (br. s, 1H), 4.15 - 4.26 (m, 2H), 3.60 - 3.72 (m, 2H), 3.20 - 3.30 (m, 4H), 1.26 (t, J = 7.0 Hz, 3H).	398.0
317	(DMSO-d6): 12.36 (s, 1H), 8.42 (d, J = 7.3 Hz, 1H), 8.33 (d, J = 3.4 Hz, 1H), 8.07 (s, 1H), 7.24 - 7.32 (m, 4H), 7.22 (dd, J = 7.9, 4.7 Hz, 1H), 6.91 (s, 1H), 4.98 (br. s, 2H), 4.25 - 4.33 (m, 2H), 3.89 - 4.03 (m, 2H), 3.56 - 3.64 (m, 2H), 3.30 (s, 3H), 3.08 (t, J = 5.7 Hz, 2H).	446.1
318	(DMSO-d6): 12.26 (s, 1H), 10.09 (s, 1H), 8.18 (d, J = 3.3 Hz, 1H), 7.83 (s, 1H), 7.70 (d, J = 7.7 Hz, 1H), 7.16 (d, J = 8.5 Hz, 1H), 6.75 - 6.86 (m, 2H), 6.61 (s, 1H), 6.57 (d, J = 8.5 Hz, 1H), 5.81 - 5.89 (m, 1H), 4.76 (t, J = 5.4 Hz, 1H), 4.28 - 4.36 (m, 2H), 3.58 - 3.67 (m, 4H), 3.32 (s, 1H), 3.20 (q, J = 5.9 Hz, 2H), 2.13 (s, 3H).	479.1
319	(DMSO-d6): 12.24 (br. s, 1H), 8.36 (d, J = 8.0 Hz, 1H), 8.31 (d, J = 4.5 Hz, 1H), 8.00 (s, 1H), 7.20 (dd, J = 7.9, 4.6 Hz, 1H), 6.88 (s, 1H), 4.16 (q, J = 7.1 Hz, 2H), 3.76 - 3.86 (s, 4H), 3.26 - 3.32 (m, 2H), 2.82 - 2.90 (m, 4H), 1.25 (q, J = 7.0 Hz, 3H).	451.2
320	(DMSO-d6): 12.22 (br. s, 1H), 8.19 (s, 1H), 7.83 (d, J = 7.7 Hz, 1H), 7.72 (s, 1H), 7.21 - 7.47 (m, 3H), 6.70 - 6.85 (m, 2H), 5.06 - 5.18 (m, 1H), 3.49 (s, 2H), 2.25 (s, 3H), 2.22 (s, 6H), 1.91 (s, 3H), 1.30 (d, J = 5.8 Hz, 6H).	461.4
321	(DMSO-d6): 8.27 - 8.35 (m, 2H), 7.95 (s, 1H), 7.24 - 7.18 (m, 1H), 6.84 (s, 1H), 4.21 - 4.27 (m, 2H), 3.54 - 3.62 (m, 4H), 3.23 - 3.32 (m, 5H), 1.70 - 1.85 (m, 3H), 1.23 - 1.37 (m, 2H), 0.94 (d, J = 6.2 Hz, 3H).	412.1
322	(DMSO-d6): 12.27 (s, 1H), 10.24 (s, 1H), 8.16 - 8.23 (m, 1H), 7.76 (s, 1H), 7.68 (d, J = 7.9 Hz, 1H), 7.42 (d, J = 8.6 Hz, 1H), 7.05 (s, 1H), 6.95 (d, J = 8.1 Hz, 1H), 6.83 (s, 1H), 6.71 - 6.79 (m, 1H), 4.30 - 4.38 (m, 2H), 4.15 - 4.23 (m, 2H), 3.56 - 3.69 (m, 6H), 3.33 (s, 3H), 2.74 - 2.82 (m, 2H), 2.48 - 2.58 (m, 4H), 2.23 (s, 3H).	548.8
323	(DMSO-d6): 11.18 (br. s, 1H), 8.18 (d, J = 3.4 Hz, 1H), 7.66 - 7.75 (m, 2H), 7.32 (d, J = 8.6 Hz, 1H), 7.00 (s, 1H), 6.91 (d, J = 8.6 Hz, 1H), 6.70 - 6.78 (m, 2H), 4.27 - 4.35 (m, 2H), 4.16 (t, J = 5.7 Hz, 2H), 3.60 - 3.66 (m, 2H), 3.33 (s, 3H), 2.76 (t, J = 5.6 Hz, 2H), 2.48 - 2.58 (s, 4H), 2.31 - 2.42 (m, 4H), 2.20 (s, 3H), 2.17 (s, 3H), 1.90 (s, 3H).	562.2

[0809]

[Table 2-5]

324	(MeOD): 8.16 - 8.23 (m, 1H), 7.97 (d, J = 7.7 Hz, 1H), 7.30 - 7.60 (m, 4H), 6.90 - 6.71 (m, 2H), 6.60 (s, 1H), 4.42 - 4.53 (m, 2H), 3.65 - 3.80 (m, 4H), 3.41 (s, 3H), 2.41 (s, 6H), 2.35 (s, 3H).	477.0
325	(DMSO-d6): 12.39 (s, 1H), 8.59 (d, J = 8.4 Hz, 1H), 8.44 (d, J = 7.8 Hz, 1H), 8.34 (d, J = 4.6 Hz, 1H), 7.98 (d, J = 2.4 Hz, 1H), 7.22 (dd, J = 7.9, 4.7 Hz, 1H), 6.89 (s, 1H), 4.21 (t, J = 6.3 Hz, 2H), 3.94 - 4.06 (m, 1H), 3.56 (t, J = 5.9 Hz, 3H), 1.93 - 2.03 (m, 2H), 1.74 - 1.84 (m, 4H), 1.53 - 1.70 (m, 3H), 1.34 - 1.48 (m, 2H), 1.15 - 1.28 (m, 1H).	412.2
326	(DMSO-d6): 12.35 (s, 1H), 8.50 (br. s, 1H), 8.41 (d, J = 7.0 Hz, 1H), 8.30 - 8.35 (m, 1H), 7.98 (s, 1H), 7.20 (dd, J = 7.9, 4.7 Hz, 1H), 6.89 (s, 1H), 4.22 (t, J = 5.8 Hz, 2H), 3.94 - 4.06 (m, 1H), 2.51 - 2.58 (m, 2H), 2.23 (s, 6H), 1.96 - 2.05 (m, 2H), 1.75 - 1.86 (m, 2H), 1.62 - 1.72 (m, 1H), 1.34 - 1.59 (m, 4H), 1.16 - 1.29 (m, 1H).	425.2
327	(DMSO-d6): 12.30 (s, 1H), 8.37 (d, J = 7.8 Hz, 1H), 8.31 (d, J = 4.2 Hz, 1H), 7.96	425.2

	(s, 1H), 7.19 (dd, J = 7.9, 4.4 Hz, 1H), 6.85 (s, 1H), 4.21 (t, J = 5.7 Hz, 2H), 2.40 - 2.60 (m, 6H), 2.22 (s, 6H), 1.73 - 1.87 (m, 2H), 1.15 - 1.42 (m, 3H), 0.97 (d, J = 6.1 Hz, 3H).	
328	(DMSO-d6): 8.37 (d, J = 7.8 Hz, 1H), 8.31 (d, J = 3.6 Hz, 1H), 7.93 (s, 1H), 7.20 - 7.27 (m, 1H), 6.85 (s, 1H), 4.17 (t, J = 6.2 Hz, 2H), 3.70 - 3.90 (m, 4H), 3.50 - 3.56 (m, 2H), 1.70 - 1.88 (m, 6H), 1.50 - 1.60 (m, 4H).	412.2
329	(DMSO-d6): 12.42 (s, 1H), 8.43 (d, J = 7.9 Hz, 1H), 8.34 (d, J = 4.2 Hz, 1H), 7.98 (s, 1H), 7.24 (dd, J = 7.9, 4.8 Hz, 1H), 6.98 (s, 1H), 4.35 - 4.13 (m, 5H), 3.56 (t, J = 6.0 Hz, 2H), 3.25 - 3.37 (m, 2H), 1.70 - 1.88 (m, 5H), 1.26 - 1.40 (m, 2H), 0.96 (d, J = 6.2 Hz, 3H).	412.2
330	(DMSO-d6): 8.12 - 8.17 (m, 1H), 7.72 - 7.79 (m, 1H), 7.65 (s, 1H), 7.14 - 7.22 (m, 1H), 6.94 (s, 1H), 6.82 - 6.88 (m, 1H), 6.73 - 6.80 (m, 1H), 6.55 (s, 1H), 4.21 - 4.30 (m, 2H), 4.09 - 4.16 (m, 2H), 3.55 - 3.66 (m, 2H), 3.32 (s, 3H), 2.85 (t, J = 5.7 Hz, 2H), 2.54 - 2.61 (m, 4H), 2.16 (s, 3H), 1.90 (s, 3H), 1.68 - 1.76 (m, 4H).	533.6
331	(DMSO-d6): 12.47 (s, 1H), 8.47 (d, J = 7.9 Hz, 1H), 8.36 (br. s, 1H), 8.09 (s, 1H), 7.16 - 7.32 (m, 6H), 6.93 (s, 1H), 5.00 (br. s, 2H), 4.22 (t, J = 6.4 Hz, 2H), 3.80 - 4.10 (m, 2H), 3.57 (t, J = 6.0 Hz, 2H), 3.08 (t, J = 5.6 Hz, 2H), 1.75 - 1.85 (m, 2H).	446.0
332	(DMSO-d6): 12.39 (s, 1H), 10.14 (s, 1H), 8.95 (d, J = 8.0 Hz, 1H), 8.34 (d, J = 4.5 Hz, 1H), 8.12 (d, J = 2.6 Hz, 1H), 7.24 (dd, J = 8.0, 4.7 Hz, 1H), 6.88 (s, 1H), 4.21 (t, J = 6.3 Hz, 2H), 3.76 - 3.86 (m, 4H), 3.53 - 3.61 (m, 3H), 3.02 - 3.12 (m, 4H), 1.87 - 1.74 (m, 2H).	415.1
333	(DMSO-d6): 12.38 (s, 1H), 9.95 (br. s, 1H), 8.87 (d, J = 7.7 Hz, 1H), 8.32 (d, J = 3.4 Hz, 1H), 8.03 - 8.09 (m, 1H), 7.23 (dd, J = 8.0, 4.7 Hz, 1H), 6.88 (s, 1H), 4.21 (t, J = 6.3 Hz, 2H), 3.57 (t, J = 5.8 Hz, 2H), 3.39 (s, 1H), 2.77 (s, 6H), 1.75 - 1.85 (m, 2H).	373.2
334	(DMSO-d6): 12.31 (br. s, 1H), 8.91 (d, J = 7.53 Hz, 1H), 8.33 (d, J = 3.51 Hz, 1H), 8.09 (br. s, 1H), 7.22 (dd, J = 4.64, 7.91 Hz, 1H), 6.83 (br. s, 1H), 4.27 (t, J = 4.64 Hz, 2H), 3.77 - 3.85 (m, 4H), 3.56 - 3.62 (m, 2H), 3.30 (s, 3H), 3.00 - 3.10 (m, 4H).	415.2
335	(DMSO-d6): 12.37 (br. s, 1H), 8.40 (dd, J = 1.26, 8.03 Hz, 1H), 8.33 (dd, J = 1.38, 4.64 Hz, 1H), 8.06 (s, 1H), 7.63 (d, J = 1.51 Hz, 1H), 7.21 (dd, J = 4.64, 7.91 Hz, 1H), 6.92 (s, 1H), 6.47 (d, J = 1.76 Hz, 1H), 4.90 (br. s, 2H), 4.21 (q, J = 7.19 Hz, 2H), 3.95 - 4.05 (m, 2H), 2.74 - 2.83 (m, 2H), 1.26 (t, J = 7.03 Hz, 3H).	406.2
336	(DMSO-d6): 12.27 (s, 1H), 10.19 (s, 1H), 8.18 (d, J = 3.5 Hz, 1H), 7.80 - 7.86 (m, 1H), 7.68 (d, J = 7.8 Hz, 1H), 7.16 (d, J = 8.4 Hz, 1H), 6.76 - 6.84 (m, 2H), 6.62 (s, 1H), 6.58 (d, J = 8.5 Hz, 1H), 4.26 (t, J = 6.3 Hz, 2H), 3.54 - 3.66 (m, 4H), 3.20 (t, J = 6.2 Hz, 3H), 2.13 (s, 3H), 1.78 - 1.87 (m, 2H).	479.2
337	(DMSO-d6): 12.36 (s, 1H), 10.61 (br. s, 1H), 10.54 (s, 1H), 8.24 (d, J = 3.8 Hz, 1H), 7.97 (d, J = 8.6 Hz, 1H), 7.55 - 7.70 (m, 4H), 6.89 - 6.95 (m, 2H), 4.38 (d, J = 4.8 Hz, 2H), 4.29 (t, J = 6.3 Hz, 2H), 3.62 - 3.55 (m, 2H), 3.39 (s, 1H), 2.76 (d, J = 4.6 Hz, 6H), 2.32 (s, 3H), 1.80 - 1.89 (m, 2H).	477.4
338	(DMSO-d6): 12.23 (s, 1H), 8.78 (d, J = 7.5 Hz, 1H), 8.29 (d, J = 4.1 Hz, 1H), 8.01 (s, 1H), 7.19 (dd, J = 7.9, 4.7 Hz, 1H), 6.77 (s, 1H), 4.20 (t, J = 5.8 Hz, 2H), 2.73 (s, 6H), 2.53 - 2.58 (m, 2H), 2.24 (s, 6H), 1.90 (s, 3H).	386.4
339	(DMSO-d6): 8.71 (d, J = 7.1 Hz, 1H), 8.27 (d, J = 4.6 Hz, 1H), 7.89 (s, 1H), 7.15 (dd, J = 7.8, 4.6 Hz, 1H), 6.37 (s, 1H), 4.10 (t, J = 5.9 Hz, 3H), 3.76 - 3.82 (m, 4H), 2.81 - 2.88 (m, 4H), 2.45 - 2.55 (m, 2H), 2.24 (s, 6H), 1.88 (s, 3H).	428.4
340	(DMSO-d6): 12.23 (br. s, 1H), 8.17 (d, J = 3.7 Hz, 1H), 7.80 (s, 1H), 7.67 - 7.74 (m, 1H), 7.08 - 7.17 (m, 1H), 6.78 - 6.84 (m, 1H), 6.70 - 6.78 (m, 1H), 6.60 (s, 1H), 6.53 - 6.58 (m, 1H), 5.81 (br. s, 1H), 4.71 - 4.79 (m, 1H), 4.21 - 4.30 (m, 2H), 3.59 - 3.67 (m, 2H), 3.15 - 3.25 (m, 2H), 2.55 - 2.60 (m, 2H), 2.21 (s, 6H), 2.12 (s, 3H), 1.90 (s, 3H).	492.4
341	(DMSO-d6): 12.28 (br. s, 1H), 10.45 (s, 1H), 8.18 (dd, J = 1.38, 4.64 Hz, 1H), 7.70 - 7.76 (m, 2H), 7.55 (d, J = 8.03 Hz, 1H), 7.43 (s, 1H), 7.36 (d, J = 7.78 Hz, 1H), 6.85 (s, 1H), 6.77 (dd, J = 4.64, 7.91 Hz, 1H), 4.27 (q, J = 7.03 Hz, 2H), 4.17 (s, 2H), 2.28 (s, 3H), 1.30 (t, J = 7.15 Hz, 3H).	429.1
342	(DMSO-d6): 12.19 (br. s, 1H), 9.17 (s, 1H), 8.12 - 8.24 (m, 3H), 7.82 (d, J = 8.03 Hz, 1H), 7.66 (s, 1H), 7.21 - 7.40 (m, 3H), 6.78 (dd, J = 4.64, 7.91 Hz, 1H), 6.72 (s, 1H), 4.29 (t, J = 5.77 Hz, 2H), 3.52 (s, 2H), 2.65 - 2.73 (m, 2H), 2.30 (s, 6H), 2.23 (s, 9H).	490.2
343	(DMSO-d6): 12.39 (br. s, 1H), 9.93 (br. s, 1H), 8.28 (dd, J = 1.26, 4.52 Hz, 1H), 7.86 (s, 1H), 7.33 (d, J = 8.53 Hz, 2H), 7.10 - 7.19 (m, 2H), 7.00 (dd, J = 2.75,	463.9

	8.53 Hz, 1H), 5.49 (br. s, 1H), 5.04 - 5.17 (m, 1H), 4.99 (t, J = 5.40 Hz, 1H), 4.12 (t, J = 4.89 Hz, 2H), 3.81 (q, J = 4.94 Hz, 2H), 2.23 (s, 3H), 1.28 (d, J = 6.27 Hz, 6H)	
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[0810]

[Table 2-6]

344	(DMSO-d6): 12.33 (s, 1H), 10.07 (s, 1H), 8.93 (d, J = 7.8 Hz, 1H), 8.33 (d, J = 3.6 Hz, 1H), 8.11 (s, 1H), 7.22 (dd, J = 8.0, 4.6 Hz, 1H), 6.86 (s, 1H), 4.11 (t, J = 6.7 Hz, 2H), 3.76 - 3.86 (s, 4H), 3.02 - 3.13 (s, 4H), 1.60 - 1.72 (m, 2H), 0.94 (t, J = 7.4 Hz, 3H).	399.0
345	(DMSO-d6): 12.34 (s, 1H), 10.07 (s, 1H), 8.92 (d, J = 7.5 Hz, 1H), 8.33 (d, J = 3.3 Hz, 1H), 8.11 (d, J = 2.5 Hz, 1H), 7.22 (dd, J = 8.0, 4.7 Hz, 1H), 6.86 (s, 1H), 3.94 (d, J = 6.6 Hz, 2H), 3.75 - 3.87 (m, 4H), 3.00 - 3.15 (m, 4H), 1.88 - 2.02 (m, 1H), 0.95 (d, J = 6.7 Hz, 6H).	413.4
346	(DMSO-d6): 12.02 (br. s, 1H), 8.89 (d, J = 7.7 Hz, 1H), 8.32 (d, J = 3.4 Hz, 1H), 8.07 (s, 1H), 7.21 (dd, J = 8.0, 4.7 Hz, 1H), 6.77 (s, 1H), 4.15 (t, J = 5.4 Hz, 2H), 3.73 - 3.87 (m, 4H), 3.63 (t, J = 5.4 Hz, 2H), 3.17 (s, 1H), 2.95 - 3.07 (m, 4H).	401.4
347	(DMSO-d6): 12.35 (s, 1H), 10.09 (s, 1H), 8.94 (d, J = 7.9 Hz, 1H), 8.33 (d, J = 3.5 Hz, 1H), 8.12 (d, J = 2.4 Hz, 1H), 7.22 (dd, J = 8.0, 4.7 Hz, 1H), 6.87 (s, 1H), 4.02 (d, J = 7.1 Hz, 2H), 3.72 - 3.90 (m, 4H), 3.00 - 3.16 (m, 4H), 1.12 - 1.23 (m, 1H), 0.48 - 0.58 (m, 2H), 0.26 - 0.37 (m, 2H).	411.3
348	(DMSO-d6): 12.34 (s, 1H), 10.08 (s, 1H), 8.93 (d, J = 7.7 Hz, 1H), 8.33 (d, J = 4.5 Hz, 1H), 8.12 (d, J = 2.6 Hz, 1H), 7.22 (dd, J = 8.0, 4.7 Hz, 1H), 6.82 (s, 1H), 5.15 - 5.22 (m, 1H), 3.75 - 3.87 (m, 4H), 3.02 - 3.13 (m, 4H), 1.83 - 1.96 (m, 2H), 1.63 - 1.78 (m, 4H), 1.50 - 1.62 (m, 2H).	425.4
349	(DMSO-d6): 12.24 (br. s, 1H), 10.20 (br. s, 1H), 8.88 (d, J = 7.9 Hz, 1H), 8.32 (d, J = 3.5 Hz, 1H), 8.07 (s, 1H), 7.21 (dd, J = 8.0, 4.7 Hz, 1H), 6.72 (s, 1H), 4.94 - 4.79 (m, 1H), 3.74 - 3.88 (m, 4H), 2.90 - 3.14 (m, 4H), 1.48 - 1.70 (m, 2H), 1.23 (d, J = 6.2 Hz, 3H), 0.91 (t, J = 7.4 Hz, 3H).	413.6
350	(DMSO-d6): 12.48 - 12.19 (m, 1H), 10.04 (br. s, 1H), 8.93 (s, 1H), 8.33 (d, J = 3.7 Hz, 1H), 8.10 (s, 1H), 7.22 (dd, J = 7.9, 4.7 Hz, 1H), 6.81 (s, 1H), 4.80 - 4.96 (m, 1H), 3.74 - 3.87 (m, 4H), 3.01 - 3.14 (m, 4H), 1.50 - 1.68 (m, 2H), 1.24 (d, J = 6.2 Hz, 3H), 0.91 (t, J = 7.3 Hz, 3H).	413.4
351	(DMSO-d6): 12.34 (br. s, 1H), 9.86 (br. s, 1H), 8.97 (d, J = 7.8 Hz, 1H), 8.33 (d, J = 3.4 Hz, 1H), 8.11 (s, 1H), 7.25 (dd, J = 8.0, 4.7 Hz, 1H), 6.80 (s, 1H), 5.00 - 5.09 (m, 1H), 3.30 - 3.40 (m, 2H), 3.01 - 3.13 (m, 4H), 2.81 - 2.94 (m, 4H), 1.27 (d, J = 6.3 Hz, 6H).	480.2
352	(DMSO-d6): 12.35 (br. s, 1H), 8.62 (br. s, 1H), 8.40 (dd, J = 8.0, 1.3 Hz, 1H), 8.32 (d, J = 4.6 Hz, 1H), 8.01 (s, 1H), 7.21 (dd, J = 7.9, 4.7 Hz, 1H), 6.86 (s, 1H), 4.99 - 5.13 (m, 1H), 4.18 - 4.31 (m, 1H), 3.87 - 3.99 (m, 2H), 3.39 - 3.54 (m, 2H), 1.80 - 1.97 (m, 4H), 1.27 (d, J = 6.3 Hz, 6H).	398.0
353	(DMSO-d6): 12.36 (s, 1H), 10.43 (br. s, 1H), 8.88 (d, J = 6.5 Hz, 1H), 8.35 (d, J = 3.5 Hz, 1H), 8.14 (s, 1H), 7.17 (dd, J = 8.0, 4.7 Hz, 1H), 6.86 (s, 1H), 4.99 - 5.11 (m, 1H), 3.47 - 3.62 (m, 4H), 3.35 - 3.42 (m, 4H), 1.27 (d, J = 6.2 Hz, 6H).	447.2
354	(DMSO-d6): 12.36 (br. s, 1H), 8.39 (d, J = 7.9 Hz, 1H), 8.33 (d, J = 4.7 Hz, 1H), 8.07 (s, 1H), 7.16 - 7.26 (m, 2H), 6.80 - 6.92 (m, 3H), 5.01 - 5.12 (m, 1H), 4.94 (br. s, 2H), 3.83 - 4.02 (m, 2H), 3.76 (s, 3H), 3.00 (t, J = 5.7 Hz, 2H), 1.27 (d, J = 6.2 Hz, 6H).	460.2
355	(DMSO-d6): 13.04 (br. s, 1H), 8.40 (dd, J = 7.9, 1.4 Hz, 1H), 8.33 (dd, J = 4.6, 1.3 Hz, 1H), 8.07 (s, 1H), 7.22 (dd, J = 7.9, 4.7 Hz, 1H), 7.16 (d, J = 7.7 Hz, 1H), 7.08 (d, J = 7.1 Hz, 2H), 6.87 (s, 1H), 5.00 - 5.12 (m, 1H), 4.93 (br. s, 2H), 3.88 - 3.98 (m, 2H), 3.03 (t, J = 5.5 Hz, 2H), 2.30 (s, 3H), 1.89 (s, 3H), 1.28 (d, J = 6.2 Hz, 6H).	444.2
356	(DMSO-d6): 11.33 (br. s, 1H), 8.39 (dd, J = 7.9, 1.4 Hz, 1H), 8.33 (dd, J = 4.6, 1.3 Hz, 1H), 8.09 (s, 1H), 7.42 (s, 1H), 7.32 (s, 2H), 7.22 (dd, J = 7.9, 4.7 Hz,	464.2

	1H), 6.88 (s, 1H), 4.94 - 5.11 (m, 3H), 3.87 - 4.00 (m, 2H), 3.07 (t, J = 5.7 Hz, 2H), 1.89 (s, 3H), 1.27 (t, J = 6.0 Hz, 6H).	
357	(MeOD): 9.17 (s, 1H), 8.16 - 8.34 (m, 3H), 7.19 - 7.27 (m, 3H), 6.94 - 7.04 (m, 2H), 5.14 - 5.28 (m, 1H), 4.93 (br. s, 2H), 3.99 (t, J = 5.8 Hz, 2H), 3.05 (t, J = 5.5 Hz, 2H), 1.37 (d, J = 6.3 Hz, 6H).	448.0
358	(DMSO-d6): 12.36 (s, 1H), 8.39 (d, J = 7.9 Hz, 1H), 8.33 (d, J = 4.6 Hz, 1H), 8.06 (s, 1H), 7.18 - 7.28 (m, 2H), 6.81 - 6.94 (m, 3H), 5.00 - 5.11 (m, 1H), 4.96 (s, 2H), 3.91 - 4.06 (m, 2H), 3.81 (s, 3H), 2.94 (t, J = 5.7 Hz, 2H), 1.28 (d, J = 6.2 Hz, 6H).	460.2
359	(DMSO-d6): 12.34 (br. s, 1H), 8.39 (dd, J = 7.9, 1.1 Hz, 1H), 8.33 (dd, J = 4.6, 1.1 Hz, 1H), 8.06 (s, 1H), 7.17 - 7.25 (m, 2H), 6.82 - 6.90 (m, 3H), 5.00 - 5.10 (m, 1H), 4.89 (br. s, 2H), 3.84 - 4.00 (m, 2H), 3.76 (s, 3H), 3.05 (t, J = 5.7 Hz, 2H), 1.27 (d, J = 6.2 Hz, 6H).	460.4

[0811]

Biological activities of several compounds of the present invention were measured according to the methods mentioned blow.

[Preparation and Storage of Solutions of Test Compounds]

A test compound was dissolved or suspended in DMSO so as to be at 10 mM or 1 mM, thereby making a stock solution, which was stored at -20°C in the dark before being tested.

[0812]

Test Example 1

[Inhibitory Effect on Cdc7 Protein Kinase]

[0813]

Measurement of kinase activity was carried out using an MSA assay kit (QuickScout Screening Assist™ Kit, Carna Biosciences, Inc.).

[0814]

Assay buffer (20 mM HEPES, 0.01% Triton X-100(TM), 2 mM dithiothreitol, pH 7.5) was used to prepare a substrate mixture solution comprising 4 μM of a kinase-reaction

substrate (FITC-labeled MCM2 peptide), 40 mM MgCl<sub>2</sub>, and 20 μM ATP.

The enzyme supplied in the kit (human Cdc7/human ASK complex protein) was diluted in the assay buffer so as to be at 7 nM, thereby preparing an enzyme solution.

[0815]

The stock solution of each test compound was diluted in DMSO to prepare diluted DMSO solutions of 10 concentrations (0.00003 mM, 0.0001 mM, 0.0003 mM, 0.001 mM, 0.003 mM, 0.01 mM, 0.03 mM, 0.1 mM, 0.3 mM, 1 mM), each of which was further diluted 25 times in the assay buffer to make a drug solution (a solution containing 4% DMSO).

[0816]

The kinase reaction was performed in wells of a polypropylene 384-well plate in which 5 μl of each of the drug solutions or of a solvent (assay buffer containing 4% DMSO), 5 μl of the substrate mixture solution, and 10 μl of the enzyme solution were mixed. The assay buffer, instead of the enzyme solution, was added to blank wells. After the reaction at room temperature for 5 hours, 60 μl of the termination buffer supplied in the kit was added to each well to stop the reaction. The percent inhibition of each reaction was determined using a LabChip EZ Reader II system (manufactured by Caliper Life Sciences), according to the protocol provided with the assay kit. In this case, the peak

heights of the separated substrate and the phosphorylated substrate were represented as S and P, respectively, and the percent inhibition (%) by a tested compound was calculated according to the following formula:

5           Percent inhibition (%) =  $(1 - (C - A)/(B - A)) \times 100$

wherein A denotes P/(P + S) for a blank well, B denotes P/(P + S) for a solvent well, and C denotes P/(P + S) for a compound-added well.

10           The IC<sub>50</sub> value of a tested compound was calculated by regression analysis of the percent inhibition values versus the (logarithmic) concentrations of the tested compound.

The IC<sub>50</sub> values of several compounds of the present invention against Cdc7 were all less than 1 μM, as shown in Table 4 below.

15    [0817]

Test Example 2

[Inhibitory Effect on Phosphorylation using Cells]

Cultured cells

[0818]

20           COLO205 cells derived from human colon adenocarcinoma (RCB2127, RIKEN BRC) were cultured in 10cm dishes using RPMI-1640 medium (SIGMA, R8758) supplemented with 10% FCS (Equitech-bio) and 5% penicillin/streptomycin (GIBCO, 15140). After the cells were cultured to a confluence of 70 to 90%,  
25    the medium was removed, and the cells were treated with

trypsin (2 mL, TrypLE Express, GIBCO, 12604-021) and then harvested using a new medium.

#### Addition of Drugs to Cultured Cells

[0819]

5            COLO205 cells were seeded in 6-well plates (FALCON, 35046) to  $2.5 \times 10^5$  cells (1 ml) per well and cultured overnight in a 5% CO<sub>2</sub> incubator. A drug solution, which was prepared by adding 1.5  $\mu$ l of a 0.1-mM stock solution in DMSO of a test compound to 500  $\mu$ l of medium, was added to each  
10 well (to a final drug concentration of 0.1  $\mu$ M), and then cultured for another 24 hours.

#### Determination of Inhibitory Effect on MCM2 Phosphorylation

[0820]

15            Cells were cultured for 24 hours in the presence of a test compound, harvested using a similar way as described above, washed with PBS, and then pelletized and stored at -80°C. The frozen cells were thawed, subsequently suspended immediately in 2  $\times$  SDS-PAGE electrophoresis buffer ( $1 \times 10^5$  cells per 10  $\mu$ l), and heated at 95°C for 10 minutes, leading  
20 to the dissolution and denaturation of the proteins. The resulting sample solutions were subjected to SDS-PAGE using a 5-20% gradient acrylamide gel (e-PAGEL (5-20%), ATTO, E-T520L). After the electrophoresis was completed, the gel was immersed in tris-glycine buffer supplemented with 20%  
25 methanol, and the proteins in the gel were transferred onto a

PVDF membrane (Immobilon-P, MILLIPORE, IPVH00010) using a semi-dry transfer apparatus (TRNS-BLOT SD SEMI-DRY TRANSFER CELL, BIO RAD).

[0821]

5           The transferred PVDF membrane was blocked with 5% skim milk (Difco Skim Milk, ED, 232100), and then subjected to reaction with an anti-MCM2 goat antibody (N-19, Santa Cruz, sc-9839) or anti-phosphorylated MCM2 rabbit antibody (S53) (Bethyl, A300-756A) as a primary antibody and additionally  
10 with an anti- $\alpha$  tubulin mouse antibody (Clone DM 1A, SIGMA, 9026) as an internal control. Each band was detected by chemiluminescence using an HRP-labeled anti-goat IgG donkey antibody (Santa Cruz, sc2020), anti-rabbit IgG sheep antibody (Roche, 12015218001), or anti-mouse IgG donkey antibody  
15 (Jackson ImmunoResearch, 715-035-151) as a secondary antibody. The combinations of and the diluted concentrations of the primary and secondary antibodies were as indicated below.

[0822]

[Table 3]

	Primary antibody (diluted concentration)	Secondary antibody (diluted concentration)
1	Anti-MCM2 goat antibody (1/500)	Anti-goat IgG donkey antibody (1/10000)
2	Anti-phosphorylated MCM2 rabbit antibody (S53) (1/500)	Anti-rabbit IgG sheep antibody (1/5000)

3	Anti- $\alpha$ -tubulin mouse antibody (1/1000)	Anti-mouse IgG donkey antibody (1/100000)
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[0823]

The bands which were detected were normalized using the amount of endogenous  $\alpha$ -tubulin as a reference, and the percent phosphorylation of MCM2 was calculated for each of the tested compounds. Their inhibitory effects on MCM2 phosphorylation were indicated by a triple asterisk (\*\*\*) in the case where the percent phosphorylation of MCM2 was less than 20%, by a dual asterisk (\*\*) in the case where the percent phosphorylation of MCM2 was not less than 20% and less than 50%, and by a single asterisk (\*) in the case where the percent phosphorylation of MCM2 was not less than 50% and less than 70%.

It was found from this testing that as shown in Table 4, the tested compounds of the present invention inhibited the phosphorylation of MCM2 at a concentration of 0.1  $\mu$ M.

[0824]

[Table 4]

Example	Test Example 1 Cdc7 IC <sub>50</sub> value ( $\mu$ M)	Test Example 2 Inhibitory effect on MCM2 phosphorylation
15	0.002	**
22	0.010	*
63	0.006	***
68	0.004	***
78	0.011	***
81	0.005	***

89	0.003	***
91	0.004	***
102	0.004	***
126	0.003	***
129	0.009	***
142	0.003	**
157	0.003	**
173	0.003	***
226	0.004	***
233	0.002	**
239	0.001	**
242	0.001	***
244	0.004	***
245	0.008	***
246	0.008	***

[Industrial Applicability]

[0825]

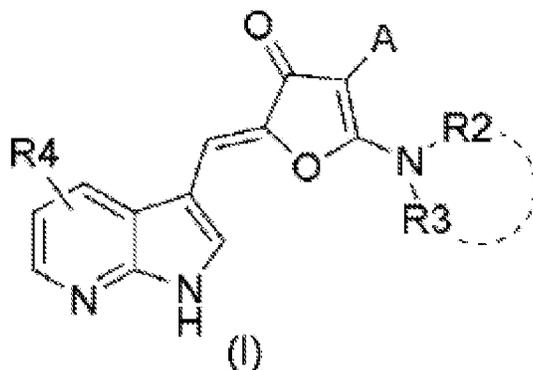
5 The compounds provided by the present invention are  
capable of controlling the growth of cells through their  
inhibitory effects on Cdc7. Therefore, the compounds of the  
present invention which have an inhibitory effect on Cdc7  
will be useful as a medicine, especially an agent for the  
treatment of diseases derived from abnormal growth of cells,  
10 such as cancers.

In the claims which follow and in the preceding description of the invention, except where the context requires otherwise due to express language or necessary implication, the word “comprise” or variations such as “comprises” or “comprising” is used in an inclusive sense, i.e. to specify the presence of the stated features but not to preclude the presence or addition of further features in various embodiments of the invention.

It is to be understood that, if any prior art publication is referred to herein, such reference does not constitute an admission that the publication forms a part of the common general knowledge in the art, in Australia or any other country.

## CLAIMS:

1. A furanone derivative or a pharmaceutically acceptable salt thereof, represented



by the formula (I):

wherein

A represents  $-\text{COOR}_1$  or a hydrogen atom;

R1 represents a hydrogen atom, an optionally substituted hydrocarbon group selected from a linear or branched alkyl group having 1 to 6 carbon atoms, a linear or branched alkenyl group having 2 to 6 carbon atoms, an alkynyl group having 2 to 6 carbon atoms, a cycloalkyl group having 3 to 8 carbon atoms, a cycloalkenyl group having 3 to 8 carbon atoms, or an aralkyl group the aryl moiety of which is an aryl group having 6 to 14 carbon atoms and the alkyl moiety of which having 1 to 6 carbon atoms; or an optionally substituted heterocycle wherein the heterocycle is selected from a 3-8 membered alicyclic heterocycle containing at least one heteroatom selected from N, S, and O, or a 5- or 6- membered monocyclic aromatic heterocycle containing at least one heteroatom selected from N, S, and O;

R2 and R3 are the same or different and each independently represent a hydrogen atom, a an optionally substituted hydrocarbon group selected from a linear or branched alkyl group having 1 to 6 carbon atoms, a linear or branched alkenyl group having 2 to 6 carbon atoms, an alkynyl group having 2 to 6 carbon atoms, a cycloalkyl group having 3 to 8 carbon atoms, a cycloalkenyl group having 3 to 8 carbon atoms, or an aralkyl group the aryl moiety of which is an aryl group having 6 to 14 carbon atoms and the alkyl moiety of which having 1 to 6 carbon atoms; an optionally substituted phenyl group; an optionally substituted heterocycle wherein the heterocycle is selected from a 3-8

membered alicyclic heterocycle containing at least one heteroatom selected from N, S, and O, or a 5- or 6- membered monocyclic aromatic heterocycle containing at least one heteroatom selected from N, S, and O; an optionally substituted heterocyclic fused ring wherein the heterocyclic fused ring moiety is bicyclic, formed by fusing 3-8 membered rings, and contains at least one heteroatom selected from N, S, and O; or an optionally substituted amino group in which the optional substituent group is selected from linear, branched, or cyclic alkyl, aryl, or heteroaryl having 1 to 6 carbon atoms, each of which may be optionally substituted with one or more groups selected from halogen, alkyl, alkenyl, alkynyl, alkoxy, amino, nitro, cyano, hydroxy, alkylamino, carbamoyl, carboxyl, formyl, acetyl, and benzoyl;

or alternatively, R2 and R3, taken together with the nitrogen atom to which they are attached, form an optionally substituted heterocycle wherein the heterocycle is selected from a 3-8 membered alicyclic heterocycle containing at least one heteroatom selected from N, S, and O, or a 5- or 6- membered monocyclic aromatic heterocycle containing at least one heteroatom selected from N, S, and O; or an optionally substituted heterocyclic fused ring wherein the heterocyclic fused ring moiety is bicyclic, formed by fusing 3-8 membered rings, and contains at least one heteroatom selected from N, S, and O; and

R4 represents a hydrogen atom or a halogen atom;

wherein the optional substituent(s) on the hydrocarbon group, heterocycle, phenyl, or heterocyclic fused ring is one or more groups selected from halogen, alkyl, alkoxy, amino, nitro, cyano, hydroxy, alkylamino, carbamoyl, carboxyl, formyl, acetyl, and benzoyl;

with the proviso that when A represents  $-\text{COOR}_1$ , R2 and R3 are not optionally substituted amino groups at the same time, and when A represents a hydrogen atom, R3 represents a hydrogen atom;

or the furanone derivative is selected from any one of examples 1-359 or pharmaceutically acceptable salts thereof.

2. The furanone derivative or a pharmaceutically acceptable salt thereof according to claim 1, wherein A is  $-\text{COOR}_1$ .

3. The furanone derivative or a pharmaceutically acceptable salt thereof according to claim 1, wherein A is a hydrogen atom.

4. The furanone derivative or a pharmaceutically acceptable salt thereof according to claim 1, wherein:

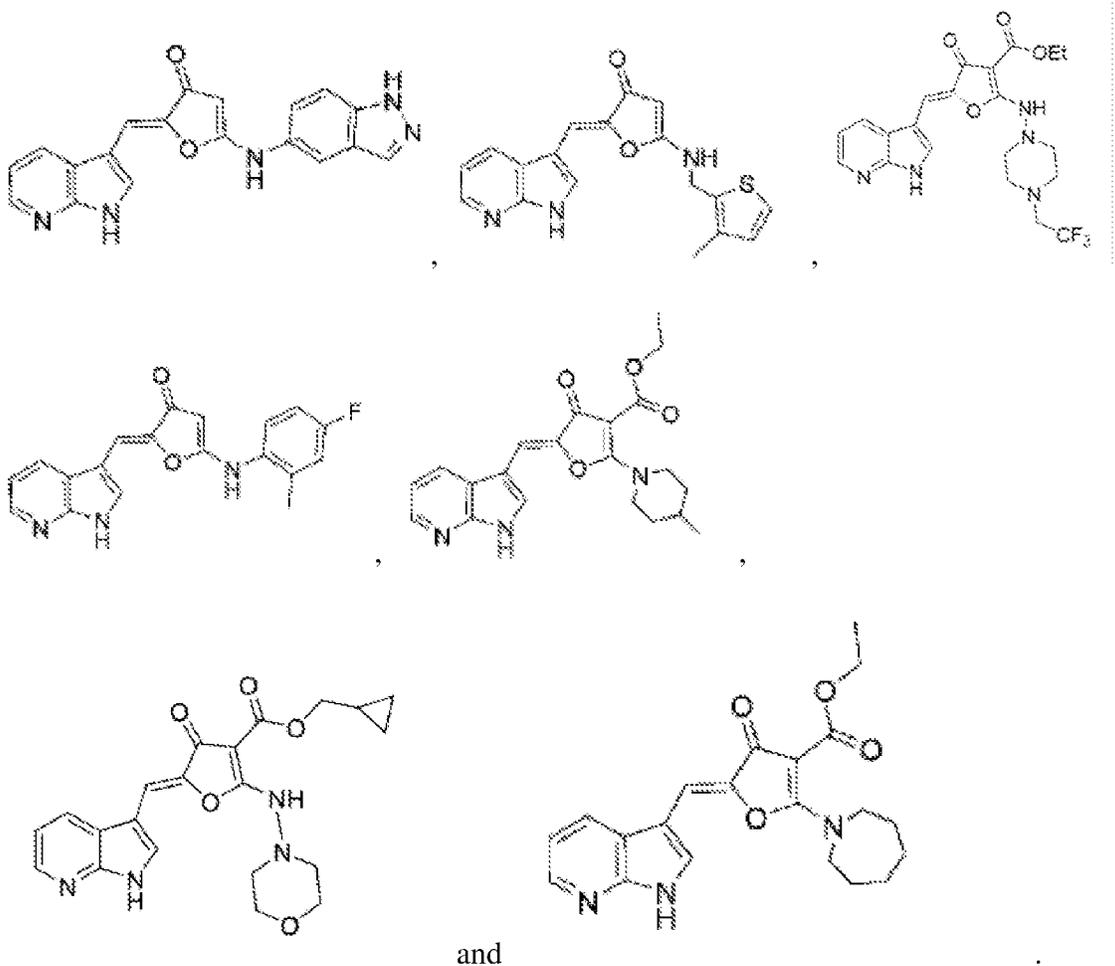
R1 is selected from a hydrogen atom, an optionally substituted hydrocarbon group having 1 to 6 carbon atoms, and an optionally substituted heterocycle wherein the heterocycle is selected from a 3-8 membered alicyclic heterocycle containing at least one heteroatom selected from N, S, and O;

R2 and R3 taken together with the nitrogen atom to which they are attached, form an optionally substituted heterocycle wherein the heterocycle is selected from a 3-8 membered alicyclic heterocycle containing at least one heteroatom selected from N, S, and O; or an optionally substituted heterocyclic fused ring wherein the heterocyclic fused ring moiety is bicyclic, formed by fusing 3-8 membered rings, and contains at least one heteroatom selected from N, S, and O

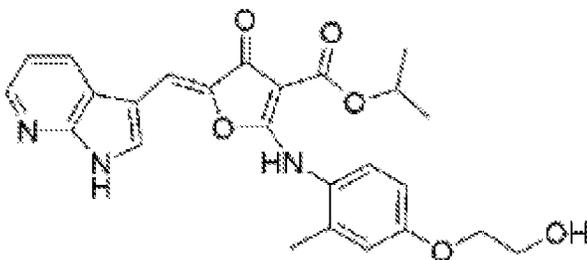
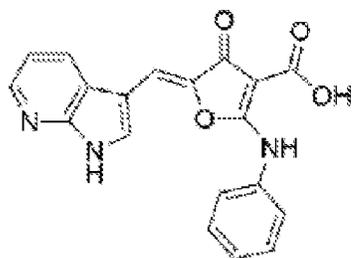
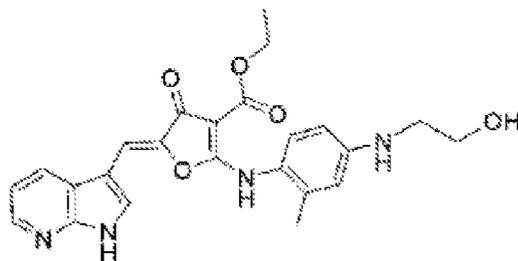
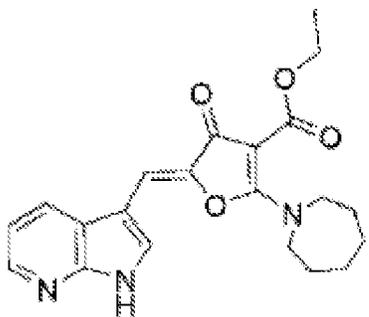
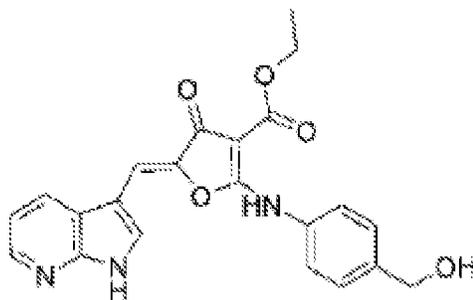
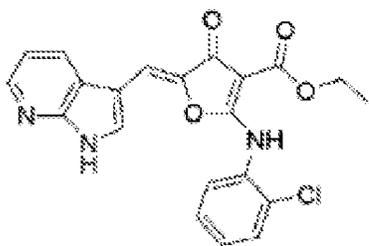
wherein the optional substituents are as defined in claim 1.

5. The furanone derivative or a pharmaceutically acceptable salt thereof according to claim 4, wherein A and R4 are both a hydrogen atom, and R2 and R3 taken together with the nitrogen atom to which they are attached, form an optionally substituted heterocycle wherein the heterocycle is selected from a 3-8 membered alicyclic heterocycle containing at least one heteroatom selected from N, S, and O.

6. The furanone derivative or a pharmaceutically acceptable salt thereof according to claim 1, wherein the furanone derivative or pharmaceutically acceptable salt thereof is selected from:

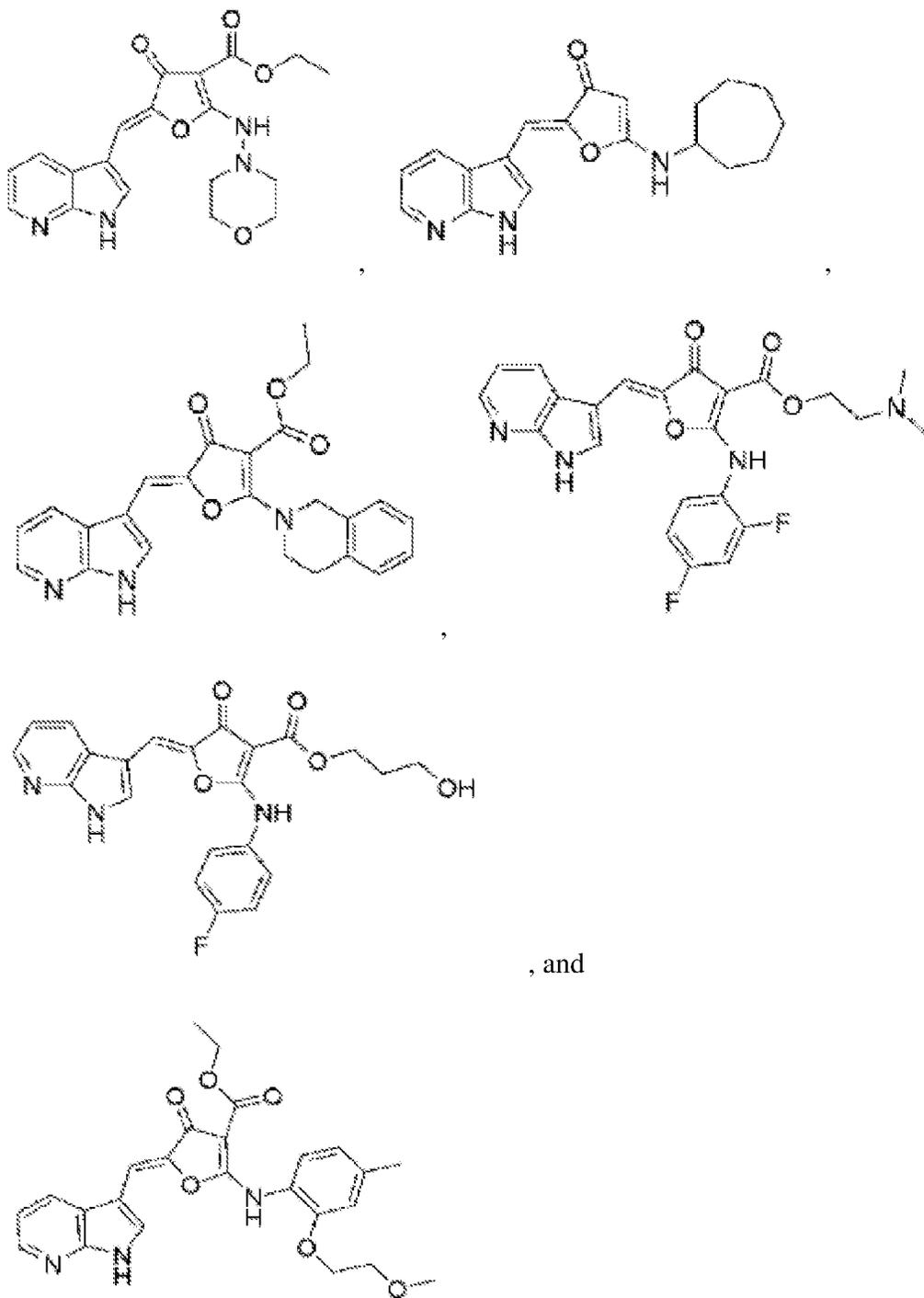


7. The furanone derivative or a pharmaceutically acceptable salt thereof according to claim 1, wherein the furanone derivative or pharmaceutically acceptable salt thereof is selected from:

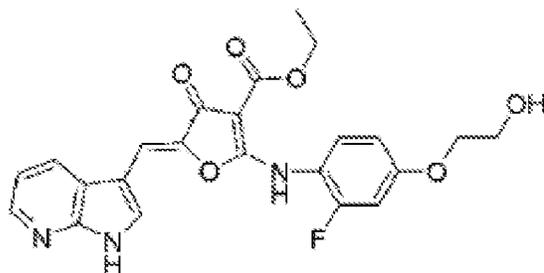
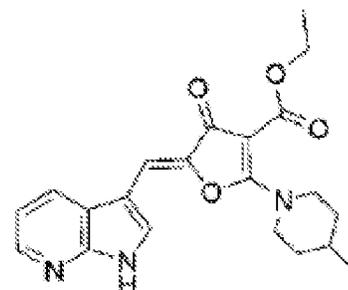
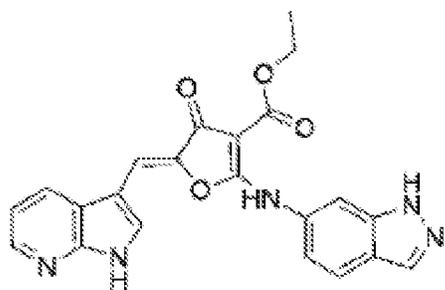
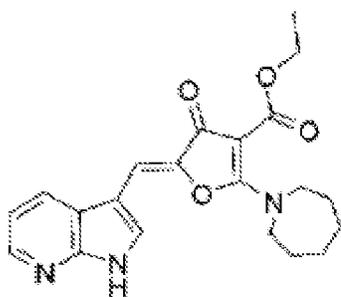
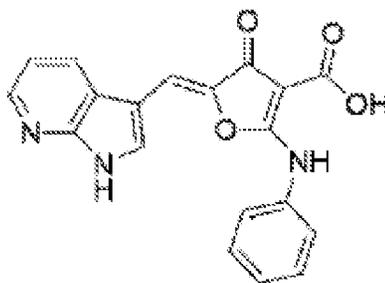
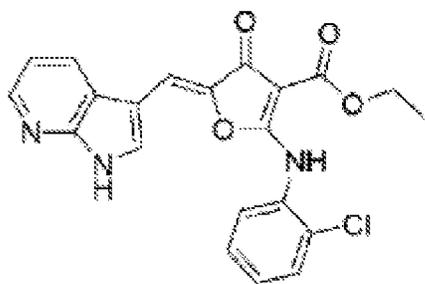


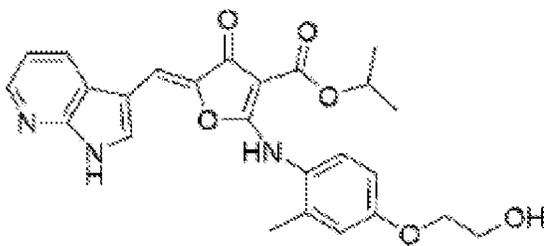
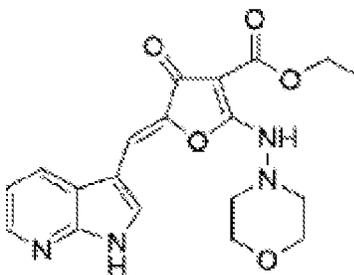
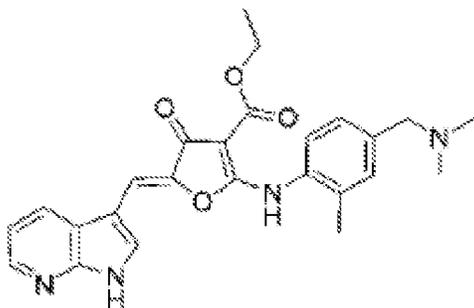
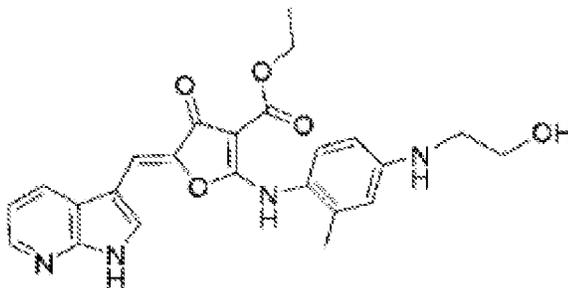
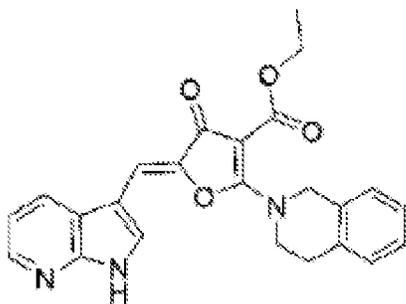
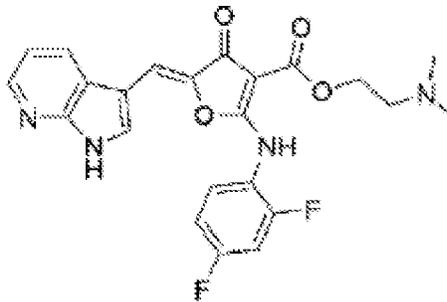
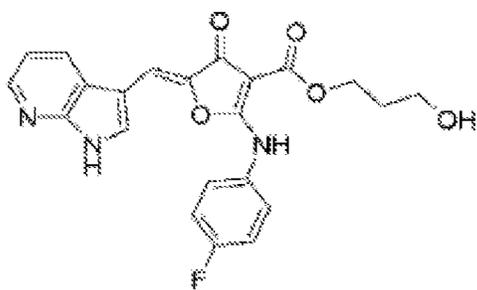
, and

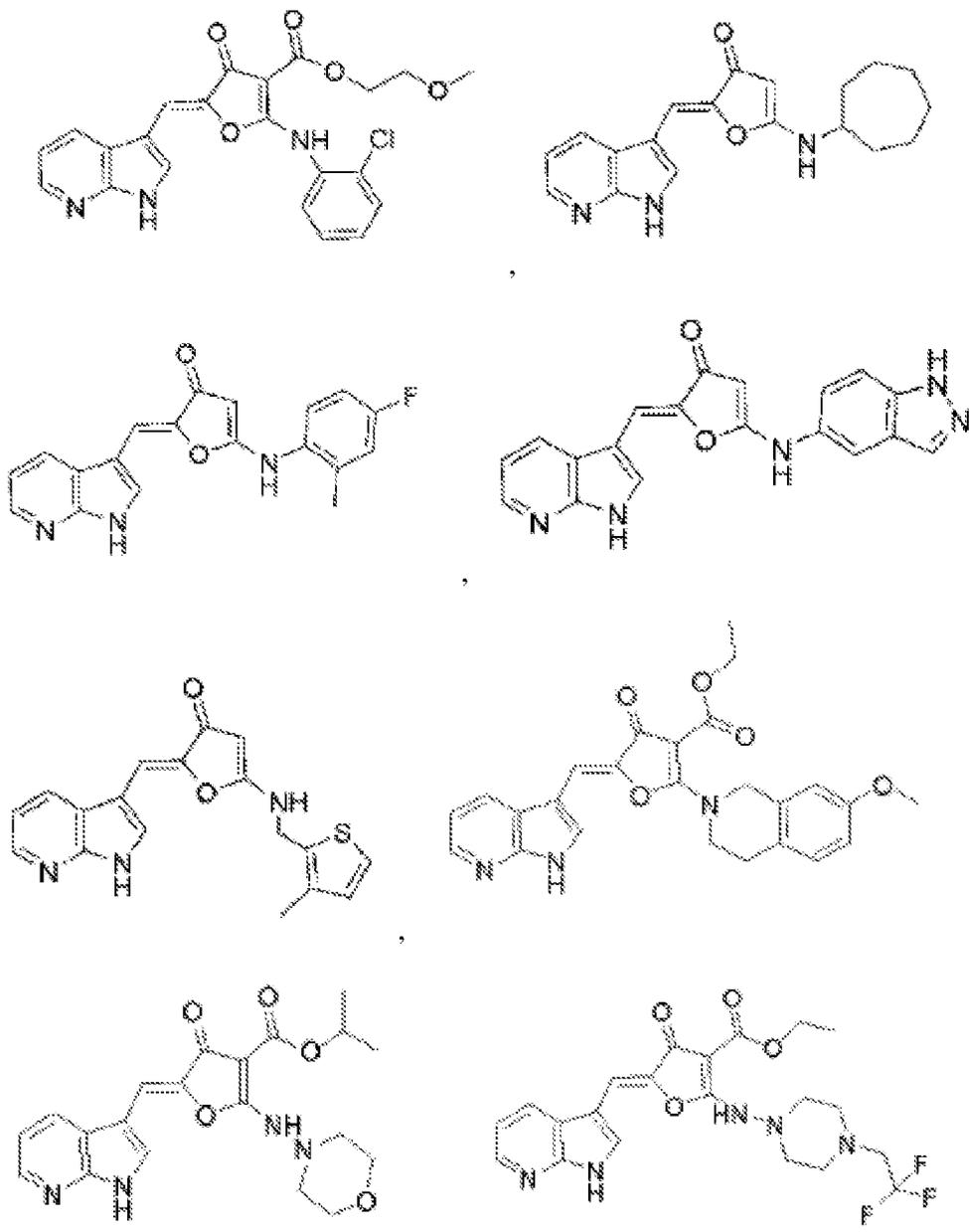
8. The furanone derivative or a pharmaceutically acceptable salt thereof according to claim 1, wherein the furanone derivative or pharmaceutically acceptable salt thereof is selected from:



9. The furanone derivative or a pharmaceutically acceptable salt thereof according to claim 1 selected from:







, and

10. The furanone derivative or a pharmaceutically acceptable salt thereof according to any one of the preceding claims, wherein the pharmaceutically acceptable salt is the hydrochloride or p-toluenesulfonate salt.

11. The furanone derivative or a pharmaceutically acceptable salt thereof according to any one of claims 1 to 10 for use in therapy.
  
12. The furanone derivative or a pharmaceutically acceptable salt thereof according to any one of claims 1 to 10 for use as an anti-tumour agent.
  
13. A pharmaceutical composition comprising the furanone derivative or a pharmaceutically acceptable salt thereof according to any one of claims 1 to 10.