

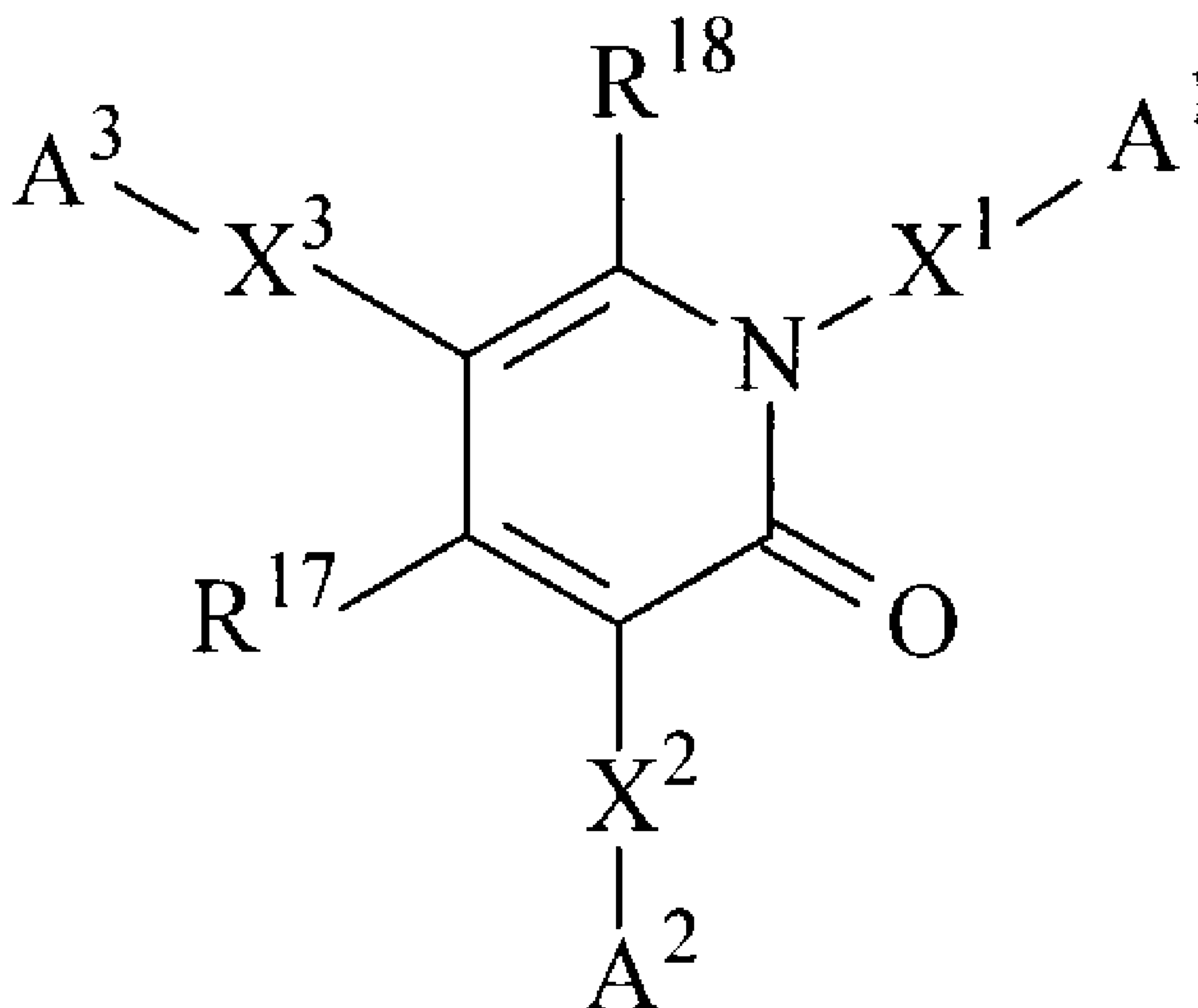


(86) Date de dépôt PCT/PCT Filing Date: 2001/06/08
(87) Date publication PCT/PCT Publication Date: 2001/12/20
(45) Date de délivrance/Issue Date: 2012/07/24
(85) Entrée phase nationale/National Entry: 2002/12/06
(86) N° demande PCT/PCT Application No.: JP 2001/004857
(87) N° publication PCT/PCT Publication No.: 2001/096308
(30) Priorités/Priorities: 2000/06/12 (JP2000-175966);
2000/09/13 (GB0022483.2)

(51) Cl.Int./Int.Cl. *C07D 213/64* (2006.01),
A61K 31/44 (2006.01), *A61K 31/443* (2006.01),
A61K 31/4433 (2006.01), *A61K 31/4436* (2006.01),
A61K 31/4439 (2006.01), *A61K 31/444* (2006.01),
A61K 31/4545 (2006.01), *A61K 31/4709* (2006.01),
A61K 31/4725 (2006.01), *A61K 31/496* (2006.01),
A61K 31/501 (2006.01), ...

(72) Inventeurs/Inventors:
NAGATO, SATOSHI, JP;
UENO, KOHSHI, JP;
KAWANO, KOKI, JP;
NORIMINE, YOSHIHIKO, JP;
ITO, KOICHI, JP; ...

(54) Titre : COMPOSES 1,2-DIHYDROPYRIDINE, LEUR PROCEDE DE PREPARATION ET LEUR UTILISATION
(54) Title: 1,2-DIHYDROPYRIDINE COMPOUNDS, MANUFACTURING METHOD THEREOF AND USE THEREOF



(57) Abrégé/Abstract:

The present invention provides a novel compound having an excellent AMPA receptor inhibitory action and/or kainate inhibitory action. A compound represented by the following formula, a salt thereof or hydrates thereof. (see formula I) In the formula, Q

(51) Cl.Int./Int.Cl. (suite/continued) *A61K 31/5377* (2006.01), *A61P 1/08* (2006.01), *A61P 13/02* (2006.01), *A61P 21/04* (2006.01), *A61P 25/00* (2006.01), *A61P 25/02* (2006.01), *A61P 25/04* (2006.01), *A61P 25/08* (2006.01), *A61P 25/14* (2006.01), *A61P 25/16* (2006.01), *A61P 25/18* (2006.01), *A61P 25/22* (2006.01), *A61P 25/28* (2006.01), *A61P 25/30* (2006.01), *A61P 43/00* (2006.01), *A61P 9/10* (2006.01), *C07D 213/65* (2006.01), *C07D 213/69* (2006.01), *C07D 213/70* (2006.01), *C07D 213/71* (2006.01), *C07D 213/73* (2006.01), *C07D 213/74* (2006.01), *C07D 213/75* (2006.01), *C07D 213/76* (2006.01), *C07D 213/81* (2006.01), *C07D 213/82* (2006.01), *C07D 213/84* (2006.01), *C07D 213/89* (2006.01), *C07D 401/04* (2006.01), *C07D 401/14* (2006.01), *C07D 405/04* (2006.01), *C07D 405/14* (2006.01), *C07D 409/04* (2006.01), *C07D 409/14* (2006.01), *C07D 413/04* (2006.01), *C07D 413/14* (2006.01), *C07D 417/04* (2006.01), *C07D 417/14* (2006.01), *C07D 471/04* (2006.01), *C07D 471/06* (2006.01), *C07F 7/18* (2006.01)

(72) Inventeurs(suite)/Inventors(continued): HANADA, TAKAHISA, JP; UENO, MASATAKA, JP; AMINO, HIROYUKI, JP; OGO, MAKOTO, JP; HATAKEYAMA, SHINJI, JP; URAWA, YOSHIO, JP; NAKA, HIROYUKI, JP; GROOM, ANTHONY JOHN, GB; RIVERS, LEANNE, GB; SMITH, TERENCE, GB

(73) Propriétaires(suite)/Owners(continued):EISAI R&D MANAGEMENT CO., LTD., JP

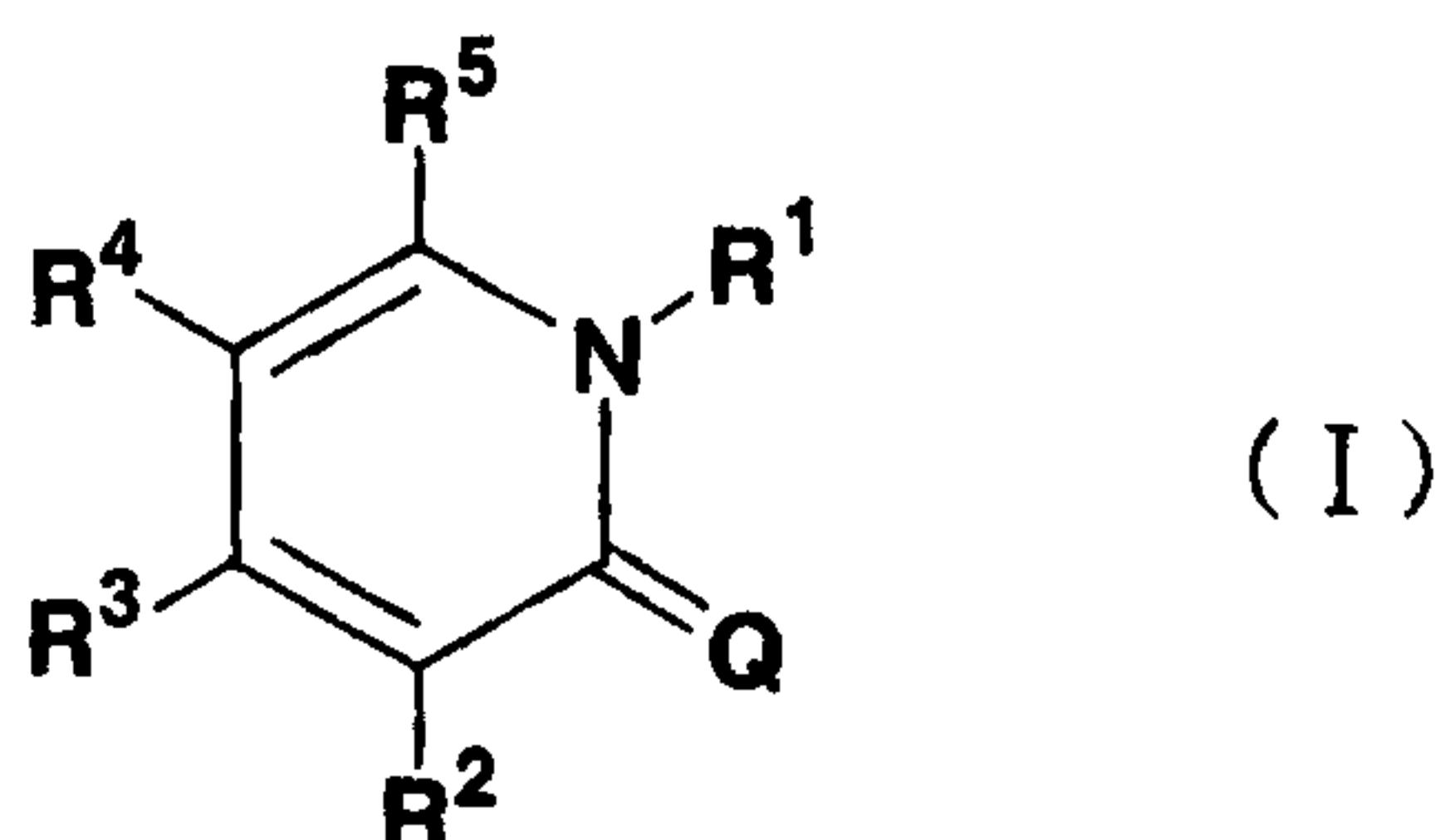
(74) Agent: SMART & BIGGAR

(57) Abrégé(suite)/Abstract(continued):

indicates NH, O or S; and R¹, R², R³, R⁴ and R⁵ are the same as or different from each other and each indicates hydrogen atom, a halogen atom, a C₁₋₆ alkyl group or a group represented by the formula -X-A (wherein X indicates a single bond, an optionally substituted C₁₋₆ alkylene group etc.; and A indicates an optionally substituted C₆₋₁₄ aromatic hydrocarbocyclic group or 5- to 14-membered aromatic heterocyclic group etc.).

Abstract

The present invention provides a novel compound having an excellent AMPA receptor inhibitory action and/or kainate inhibitory action. A compound represented by the following formula, a salt thereof or hydrates thereof.



In the formula, Q indicates NH, O or S; and R¹, R², R³, R⁴ and R⁵ are the same as or different from each other and each indicates hydrogen atom, a halogen atom, a C₁₋₆ alkyl group or a group represented by the formula -X-A (wherein X indicates a single bond, an optionally substituted C₁₋₆ alkylene group etc.; and A indicates an optionally substituted C₆₋₁₄ aromatic hydrocarbocyclic group or 5- to 14-membered aromatic heterocyclic group etc.).

DEMANDES OU BREVETS VOLUMINEUX

**LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVETS
COMPREND PLUS D'UN TOME.**

CECI EST LE TOME __1__ DE __2__

NOTE: Pour les tomes additionels, veuillez contacter le Bureau Canadien des Brevets.

JUMBO APPLICATIONS / PATENTS

**THIS SECTION OF THE APPLICATION / PATENT CONTAINS MORE
THAN ONE VOLUME.**

THIS IS VOLUME __1__ OF __2__

NOTE: For additional volumes please contact the Canadian Patent Office.

Description

1,2-Dihydropyridine compounds, manufacturing method thereof and use thereof

Field of the Invention

The present invention relates to a novel compound, a salt thereof and hydrates thereof, and to a method for manufacturing the same. More specifically, it relates to a pyridone compound, a salt thereof and hydrates thereof which are useful as inhibitors to non-NMDA receptors, particularly to AMPA receptor.

Prior Art

Glutamate and aspartate are important amino acids which participate in nerve functions such as recognition, memory, movement, respiration, cardiovascular adjustment and sensation and are called excitatory neurotransmitters as well. In the expression of their physiological activities, an interaction with a specific receptor is important and, generally, two types of receptors - an ion channel type and a G-protein coupled type - have been known. The former is further classified into N-methyl-D-aspartate (NMDA) receptor, α -amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) receptor, kainate receptor, etc. On the other hand, the amino acid as an excitatory neurotransmitter has been known to induce

neurotoxicity by, for example, abnormal excitation of central nerves. It has been noted that the said toxicity is as serious as being accompanied by the death of nerve cells causing various nervous diseases. Main nervous diseases which have been known are cerebral ischemia, head injury, spinal cord injury, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis (ALS), Huntington's chorea, AIDS nervous disturbance, epilepsy, neurodegeneration observed after the state of hypoxia, mental disorder, mobility disturbance, pain, spasticity, nervous disturbance by toxin in food, various neurodegenerative diseases, various mental diseases, chronic pain, migraine, cancer pain and pain caused by diabetic nervous disturbance. They are serious diseases where many mechanisms of onset, etc. have not been clarified yet and pharmaceutical agents which are effective for the therapy have not been found yet but it is believed that they are closely related to excessive release/accumulation of excitatory neurotransmitters, changes in expressing pattern of receptors, etc. For example, it has been reported that glutamate concentration in cerebrospinal fluid and plasma increases in stroke, cerebral ischemia, head injury and spinal cord injury (Castillo, J., Dazalos, A. and Noya, M., Lancet, 1997, 346:79-83; etc.). There is a report that neuropathy occurs when glutamate, NMDA, AMPA, kainate, etc. are excessively applied to nerve cells (Meldrum, B., Brain Res. Reviews, 18, 293, 1993). There are reports that, in Alzheimer's disease, β -amyloid protein enhances the neurotoxicity of

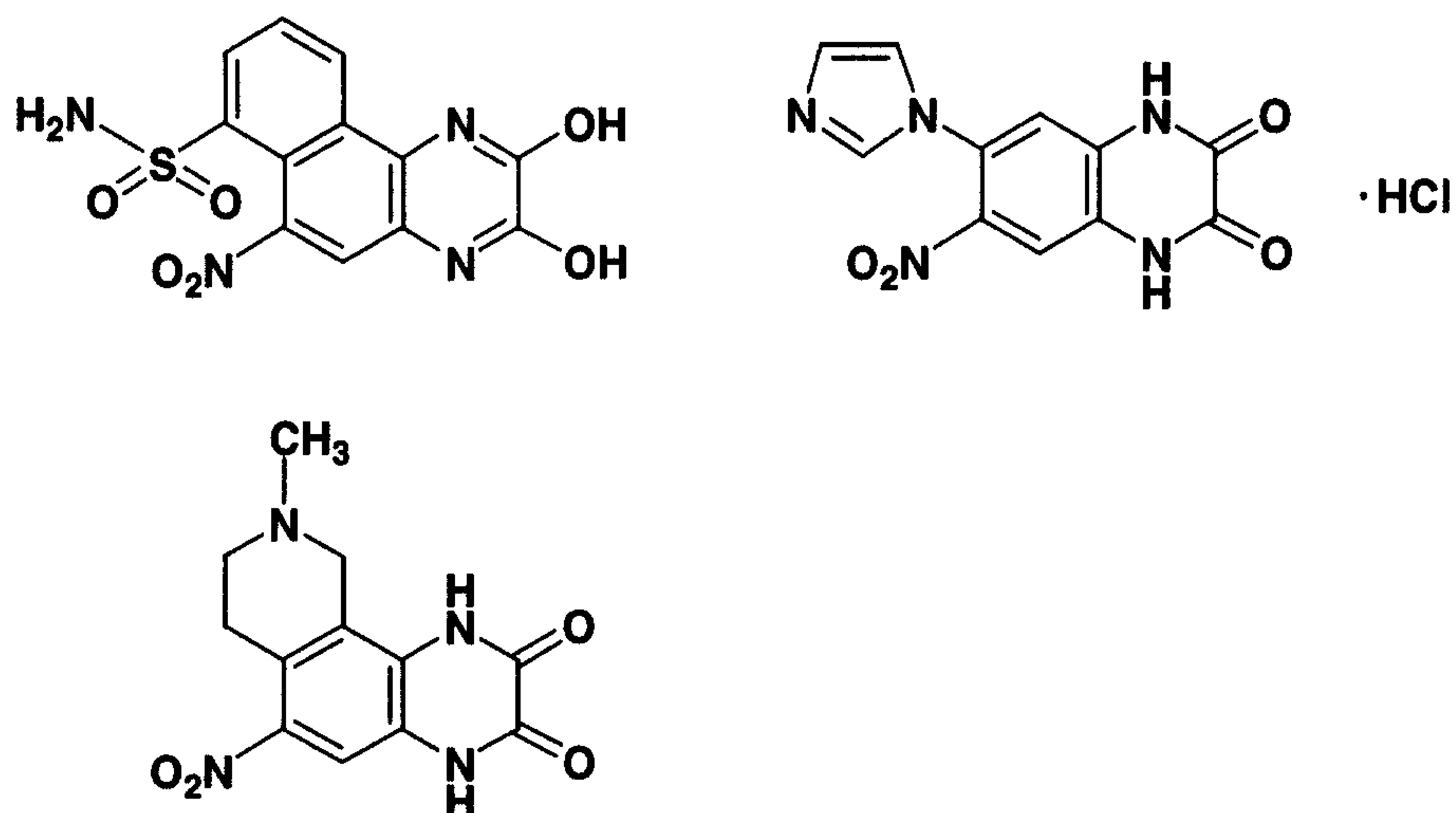
glutamate and that it promotes the release of glutamate (Arias, C., Arrieta, I. and Tapia, R., J. Neurosci. Res., 1995, 41:561-566; etc.). In the case of Parkinson's disease, there are reports that L-dopa hydroxide activates the AMPA receptor (Cha, J. J., et. al., Neurosci. Lett., 1991, 132:55-58) and enhances the neurotoxicity (Olney, J. W., et. al., 1990, 108:269-272; Rosenberg, P. A., et. al., Proc. Natl. Acad. Sci. USA, 1991, 88:4865-4869). There is another report that L-dopa promotes the generation of free radicals resulting in a rise of oxidative stress (Smith, T. S., et. al., Neuroreport, 1994, 5:1009-1011). In the case of Huntington's chorea, it is reported that a substance which inhibits the release of glutamate is effective in improving the symptoms. In the case of ALS, there are many reports showing the participation of glutamate in its pathology. There are some cases where the AIDS patients suffer from recognition nerve function deficiency and, even in such a nerve disease, participation of glutamate is suggested. For example, it is reported that gp 120 which is a glycoprotein in an envelope of HIV virus suppresses the uptake of glutamate by astrocytes (Dreyer, E. B., Eur. J. Neurosci., 1995, 7:2502-2507; Ushijima, H., et. al., Eur. J. Neurosci., 1995, 7:1353-1359) while a substance which inhibits the release of glutamate suppresses the neurodegeneration by gp 120 (Sindou, P., et. al., J. Neurosci. 1994, 126:133-137; Muller, W. E. G., et. al., Eur. J. Pharmacol. Molec. Pharmacol., 1992, 226:209-214; Lipton, S. A., Neurology, 1992, 42:1403-1405).

With regard to allergic encephalomyelitis, there is a report that, in the mice where the said inflammation takes place, enzyme which decomposes glutamate incorporated from outside of cells is deficient (Hardin-Pouzet, H., *Glia.*, 1997, 20:79-85). Olivopontocerebellar atrophy is a disease which is sometimes combined with Parkinson's disease and an antibody to GluR2 which is a subunit constituting the AMPA receptor has been found (Gahring, L. C., *Neurology*, 1997, 48:494-500) and the relation between olivopontocerebellar atrophy and AMPA receptor is suggested. With regard to a report for epilepsy, it is reported that, in the mice which are unable to construct the GluR2 in AMPA receptor, Ca^{2+} permeability of the AMPA receptor increases whereby it is apt to cause a sudden onset resulting in death (Brusa, R., *Science*, 1995, 270:1677-1680). Besides the above, it is reported that NBQX (2,3-dihydroxy-6-nitro-7-sulfamoylbenz[f]quinoxaline; Sheardown, et al., *Science*, 247, 571, 1990) and other inhibiting compounds to AMPA receptors have antianxiety and anticonvulsant action (*J. Pharmacol. Exp. Ther.*, 260, 742, 1992; *Pharmacol. Biochem. Behavior*, 1998, 60:119-124) and there are also reports for the connection of AMPA receptor/kainate receptor with urinary disturbance, drug abuse, pain, etc. (*J. Pharmacol. Exp. Ther.*, 280, 894-904, 1997; *Neuroscience Letters*, 268:127-130, 1999).

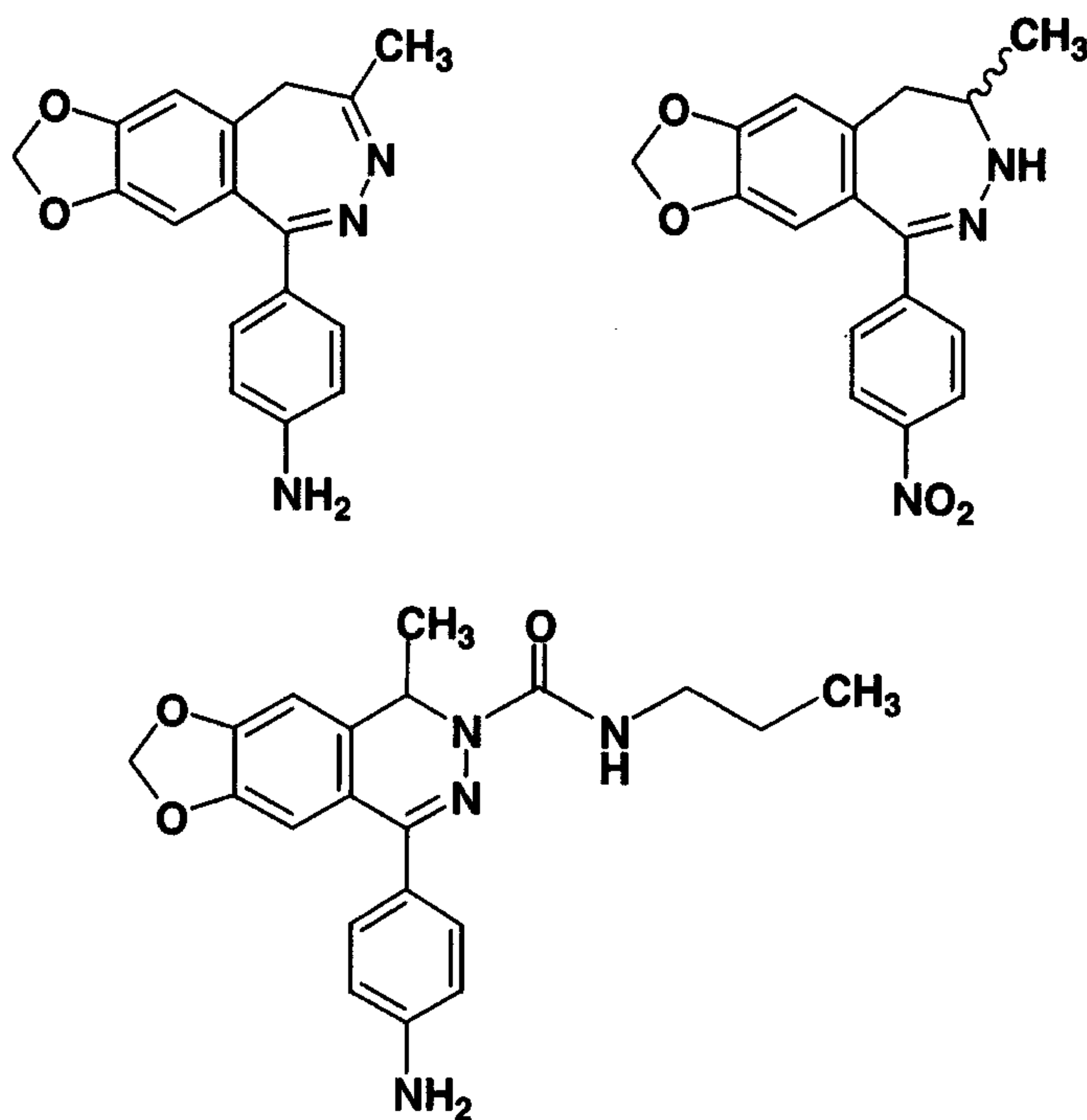
It can be expected that the substances showing an antagonistic action to excitatory neurotransmitter receptors are useful for the therapy of the above-mentioned nerve diseases.

At present, the usefulness of the substances having an antagonistic action to non-NMDA receptors such as AMPA receptor and kainate receptor is particularly expected. For example, it is reported that inhibitors of the interaction of glutamate with the AMPA and/or kainate receptor complex are useful in treating demyelinating disorders such as encephalitis, acute disseminated encephalomyelitis, acute demyelinating polyneuropathy (Guillain Barre syndrome), chronic inflammatory demyelinating polyneuropathy, multiple sclerosis, Marchifava-Bignami disease, central pontine myelinolysis, Devic syndrome, Balo disease, HIV- or HTLV-myelopathy, progressive multifocal leucoencephalopathy, a secondary demyelinating disorder; for example, CNS lupus erythematoses, polyarteritis nodosa, Sjogren syndrome, sarcoidosis, isolated cerebral vasculitis, etc. as secondary demyelinating disorders, etc. in WO00/01376. With regard to the compound having an inhibitory action to AMPA receptor and kainate receptor, there are reports for the following compounds for example.

(1) Competitive AMPA receptor-inhibiting compounds represented by the following formulae.



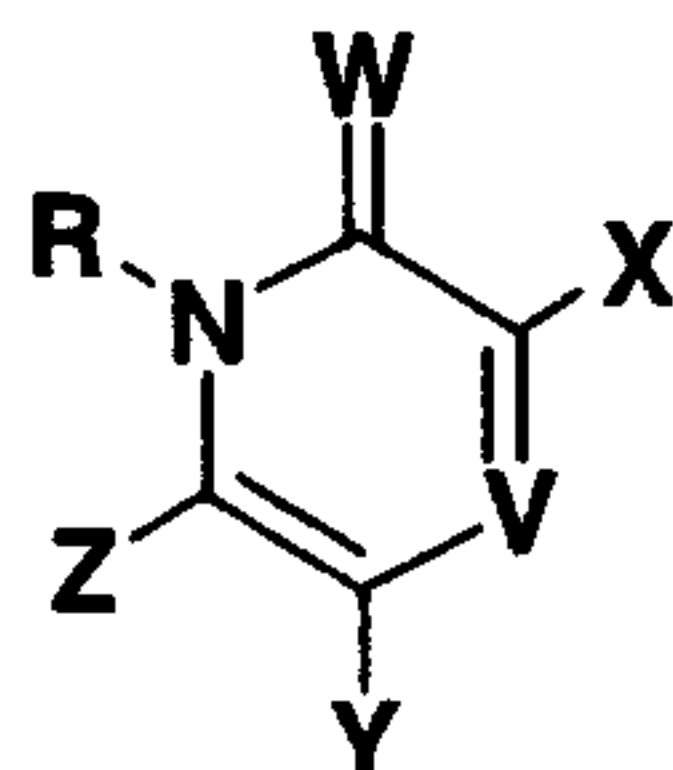
(2) Non-competitive AMPA receptor-inhibiting compounds represented by the following formulae.



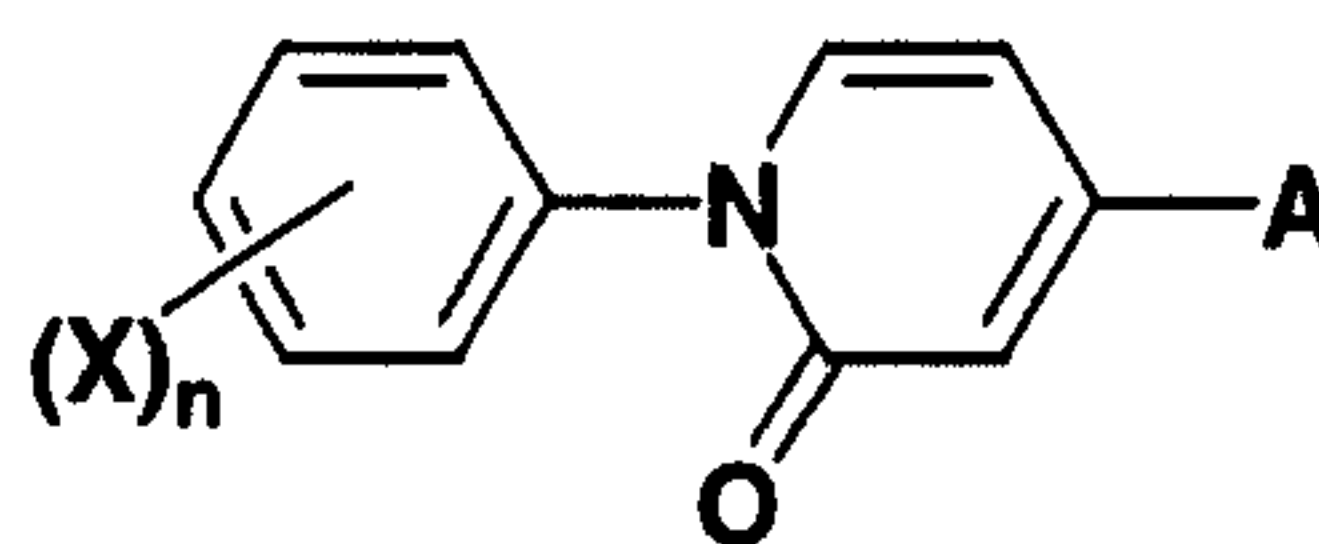
(3) Besides the above, there are reports on competitive AMPA receptor-inhibiting compounds having a quinoxalinedione skeleton in WO 94/25469, WO 96/10023, US 5356902, etc. and there are reports on non-competitive AMPA receptor-inhibiting compounds in WO 95/01357, WO 97/28135, WO 97/18163, WO 97/43276,

WO 97/34878, WO 98/38173, EP 802195, DE 19643037, etc.

On the other hand, with regard to 1,2-dihydropyridine compounds, there have been several reports for them such as the compounds represented by the formula



[in the formula, R is a hydrogen atom, a C₁₋₆ alkyl group, a C₂₋₆ alkenyl group, a C₂₋₆ alkynyl group, a C₁₋₆ alkoxy group, etc.; V is CH or N; W is O or S; X is a phenyl group which is unsubstituted or substituted with one or more group(s) selected from a C₁₋₆ alkyl group, CF₃, a cyano group, a nitro group, halogen, etc. or an aromatic hetero group which is substituted with one or more group(s) selected from a C₁₋₆ alkyl group, CF₃, halogen, etc.; Y is a hydrogen atom, a C₁₋₆ alkyl group, a C₂₋₆ alkenyl group, a C₂₋₆ alkynyl group, an aryl group, etc.; and Z is halogen, a C₃₋₆ cycloalkyl group, a C₁₋₆ alkylthio group, a C₂₋₆ alkenylthio group, an aryl group, etc.] or salts thereof as a ligand for GABA_Aα subunit in WO 98/55480 and the compounds represented by the formula



[in the formula, n is 0, 1, 2, 3, 4 or 5; X is a hydrogen atom, a C₁₋₄ alkyl group, a C₁₋₄ alkoxy group, a trifluoromethyl group, a trifluoromethoxy group or halogen; A is an amino group, a C₁₋₄

alkylamino group, a C₁₋₄ dialkylamino group, a morpholino group, a piperidino group or a pyrrolidino group] useful for therapy of epilepsy in WO 00/07988 but their connection with AMPA receptor and kainate receptor has not been known at all.

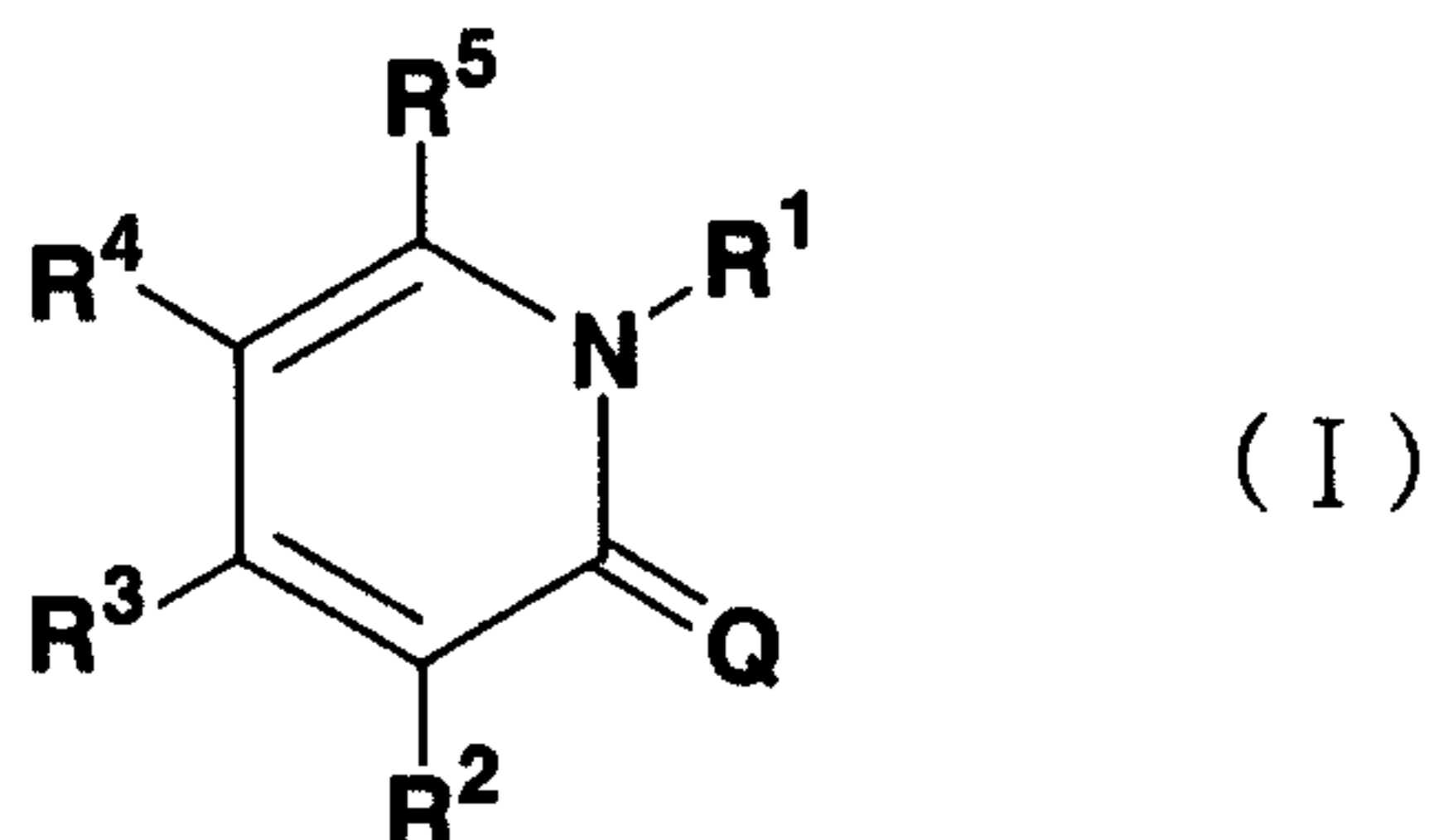
As such, there has been a brisk demand for the compounds which inhibit AMPA receptor/kainate receptor and are useful as pharmaceutical agents. However, the compounds which exhibit an excellent inhibiting action to AMPA receptor and/or kainate receptor and are highly useful as pharmaceutical agents effectively acting in clinical field have not been found yet. Thus, an object of the present invention is to investigate and find a compound which inhibits AMPA receptor and/or kainate receptor which suppresses the neurotoxicity of excitatory neurotransmitters and achieves an excellent neuroprotective action as pharmaceutical agents being useful as therapeutic/preventing/improving agents for various nerve diseases.

Disclosure of the Invention

Under such circumstances, the present inventors have carried out an intensive study and, as a result, they have succeeded in synthesizing a novel compound represented by the formula (I), a salt thereof or hydrates thereof, and have found an excellent method for producing the compound or a salt thereof, and useful intermediate in the method. Further, quite surprisingly, they have found that the above compound (I), a

salt or hydrates thereof shows an excellent antagonistic action to AMPA receptor, whereupon the present invention has been accomplished.

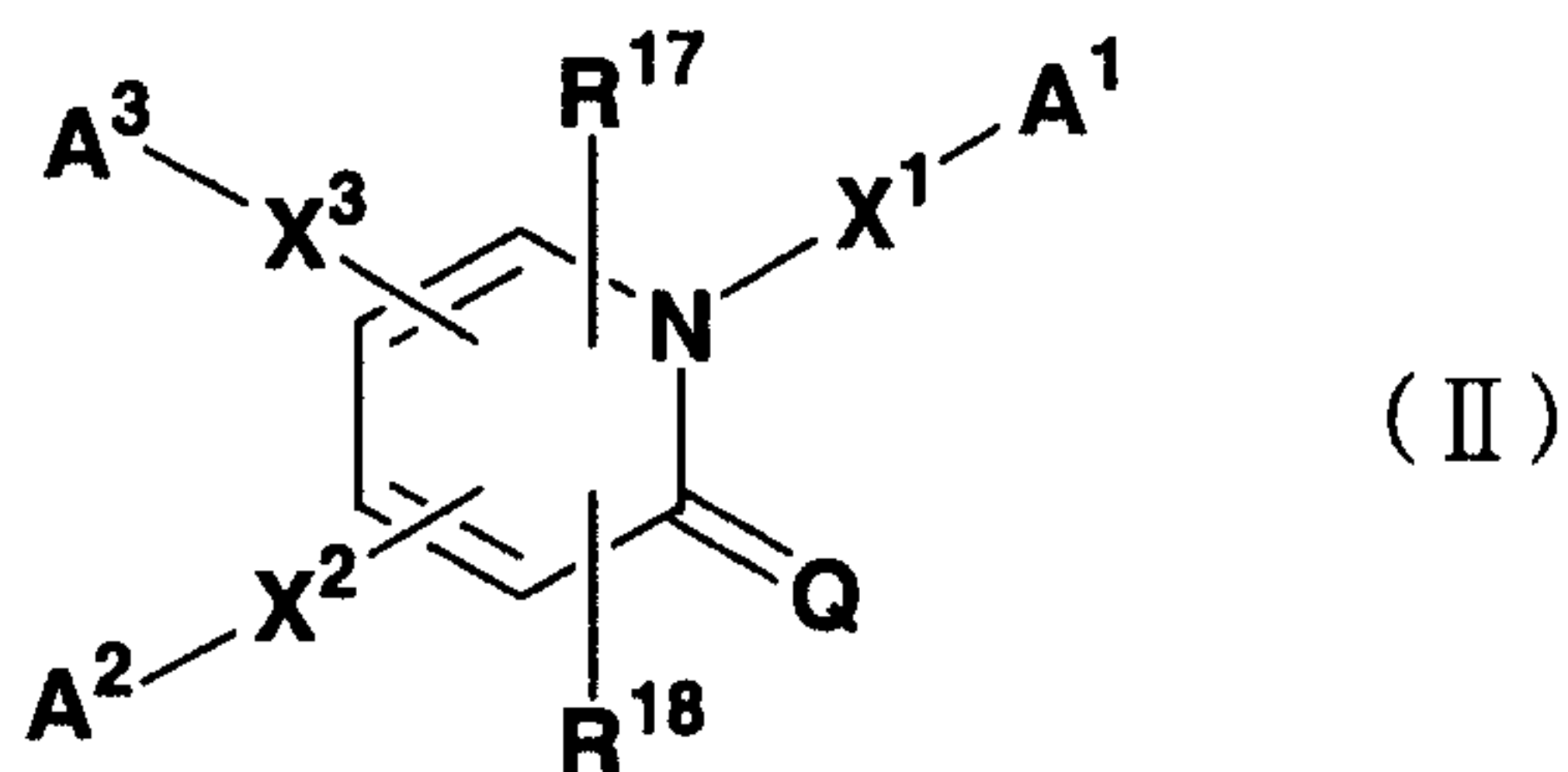
A compound represented by the following formula, a salt thereof or hydrates thereof.



In the formula, Q indicates NH, O or S; and R¹, R², R³, R⁴ and R⁵ are the same as or different from each other and each indicates hydrogen atom, a halogen atom, a C₁₋₆ alkyl group or a group represented by the formula -X-A (wherein X indicates a single bond, an optionally substituted C₁₋₆ alkylene group an optionally substituted C₂₋₆ alkenylene group, an optionally substituted C₂₋₆ alkynylene group, -O-, -S-, -CO-, -SO-, -SO₂-, -N(R⁶)-, -N(R⁷)-CO-, -CO-N(R⁸)-, -N(R⁹)-CH₂-, -CH₂-N(R¹⁰)-, -CH₂-CO-, -CO-CH₂-, -N(R¹¹)-S(O)_m-, -S(O)_n-N(R¹²)-, -CH₂-S(O)_p-, -S(O)_q-CH₂-, -CH₂-O-, -O-CH₂-, -N(R¹³)-CO-N(R¹⁴)- or -N(R¹⁵)-CS-N(R¹⁶)- (wherein R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹¹, R¹², R¹³, R¹⁴, R¹⁵ and R¹⁶ indicate hydrogen atom, a C₁₋₆ alkyl group or a C₁₋₆ alkoxy group; and m, n, p and q indicates an integer of 0, 1 or 2 independently); and A indicates a C₃₋₈ cycloalkyl group, a C₃₋₈ cycloalkenyl group, a 5 to 14 membered non-aromatic heterocyclic group, a C₆₋₁₄ aromatic hydrocarbocyclic group, or a 5 to 14 membered aromatic heterocyclic group which may be

substituted respectively, provided that 3 groups among R^1 , R^2 , R^3 , R^4 and R^5 are always the same as or different from each other and each indicates -X-A; and the residual 2 groups always indicate hydrogen atom, a halogen atom or a C_{1-6} alkyl group), provided that in the above-mentioned definition, the cases where (1) Q is O; R^1 and R^5 are hydrogen atoms; and R^2 , R^3 and R^4 are phenyl groups, (2) Q is O; R^1 and R^4 are hydrogen atoms; and R^2 , R^3 and R^5 are phenyl groups, and (3) Q is O; R^1 and R^2 are hydrogen atoms; and R^3 , R^4 and R^5 are phenyl groups, are excluded.

That is, the present invention relates to (1) the compound represented by the above formula (I), a salt thereof or hydrates thereof; (2) the compound according to the above (1), a salt thereof or hydrates thereof, which is represented by the formula:



wherein Q indicates NH, O or S; X^1 , X^2 and X^3 are the same as or different from each other and each indicates a single bond, an optionally substituted C_{1-6} alkylene group, an optionally substituted C_{2-6} alkenylene group, an optionally substituted C_{2-6} alkynylene group, -O-, -S-, -CO-, -SO-, -SO₂-, -N(R^6)-, -N(R^7)-CO-, -CO-N(R^8)-, -N(R^9)-CH₂-, -CH₂-N(R^{10})-, -CH₂-CO-, -CO-CH₂-, -N(R^{11})-S(O)_m-, -S(O)_n-N(R^{12})-, -CH₂-S(O)_p-, -S(O)_q-CH₂-,

65702-519

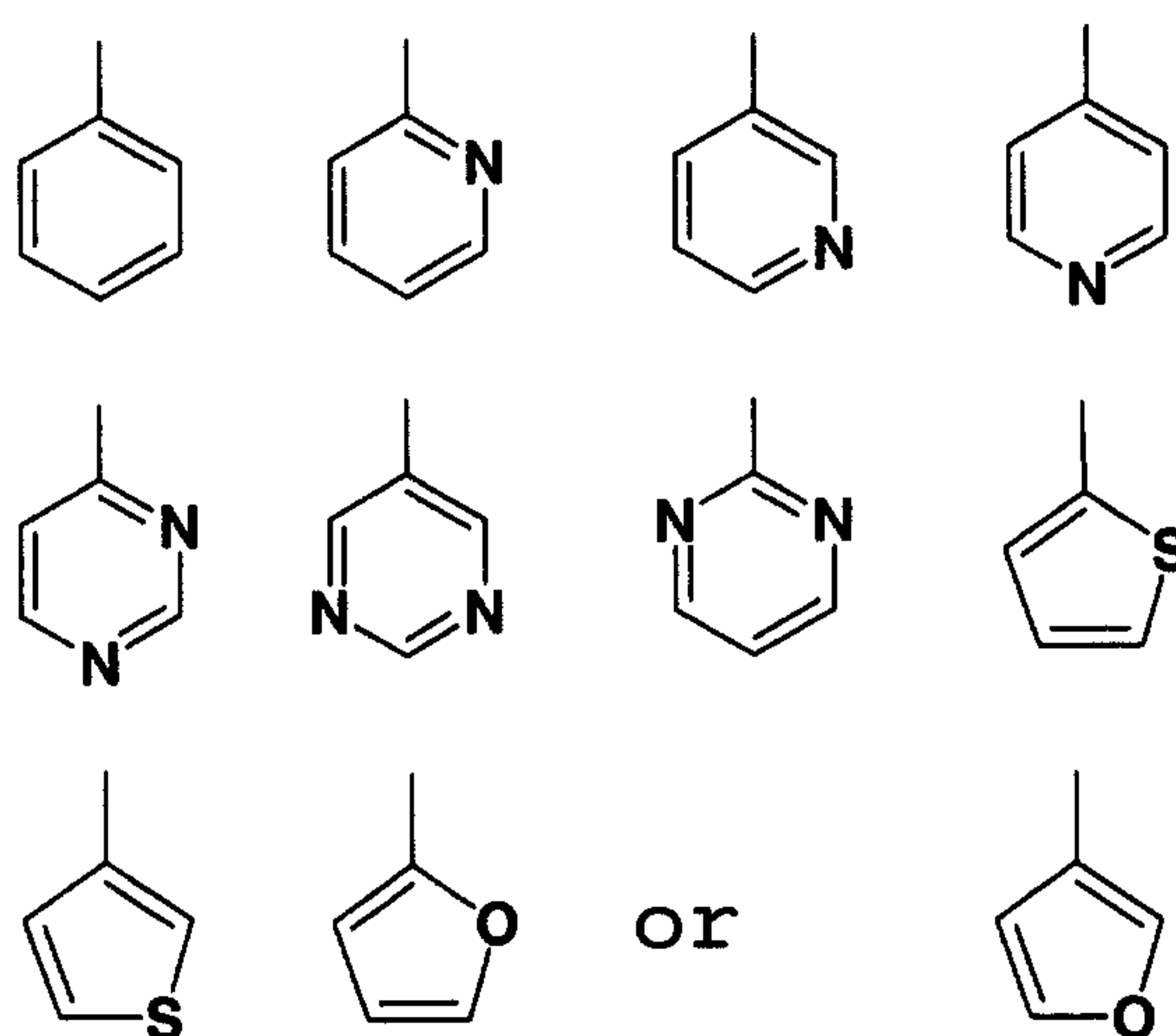
$-\text{CH}_2-\text{O}-$, $-\text{O}-\text{CH}_2-$, $-\text{N}(\text{R}^{13})-\text{CO}-\text{N}(\text{R}^{14})-$ or $-\text{N}(\text{R}^{15})-\text{CS}-\text{N}(\text{R}^{16})-$
 (wherein R^6 , R^7 , R^8 , R^9 , R^{10} , R^{11} , R^{12} , R^{13} , R^{14} , R^{15} and R^{16} indicate
 hydrogen atom, a C_{1-6} alkyl group or a C_{1-6} alkoxy group; and m ,
 n , p and q are independent of each other and each indicates an
 integer of 0, 1 or 2); A^1 , A^2 and A^3 are the same as or different
 from each other and each indicates an optionally substituted
 C_{3-8} cycloalkyl group, C_{3-8} cycloalkenyl group, 5 to 14-membered
 non-aromatic heterocyclic group, C_{6-14} aromatic
 hydrocarbocyclic group or 5 to 14-membered aromatic
 heterocyclic group; and R^{17} and R^{18} are the same as or different
 from each other and each indicates hydrogen atom, a halogen atom
 or a C_{1-6} alkyl group; (3) the compound according to the above
 (2), a salt thereof or hydrates thereof, wherein X^1 , X^2 and X^3
 are (1) single bond, (2) a C_{1-6} alkylene group, a C_{2-6} alkenylene
 group or a C_{2-6} alkynylene group which may be optionally
 substituted respectively with one or more groups selected from
 the following substituent group a, (3) $-\text{O}-$, (4) $-\text{S}-$, (5) $-\text{CO}-$,
 (6) $-\text{SO}-$, (7) $-\text{SO}_2-$, (8) $-\text{N}(\text{R}^6)-$, (9) $-\text{N}(\text{R}^7)-\text{CO}-$, (10) $-\text{CO}-\text{N}(\text{R}^8)-$,
 (11) $-\text{N}(\text{R}^9)-\text{CH}_2-$, (12) $-\text{CH}_2-\text{N}(\text{R}^{10})-$, (13) $-\text{CH}_2-\text{CO}-$, (14) $-\text{CO}-$
 CH_2- , (15) $-\text{N}(\text{R}^{11})-\text{S}(\text{O})_m-$, (16) $-\text{S}(\text{O})_n-\text{N}(\text{R}^{12})-$, (17) $-\text{CH}_2-\text{S}(\text{O})_p-$,
 (18) $-\text{S}(\text{O})_q-\text{CH}_2-$, (19) $-\text{CH}_2-\text{O}-$, (20) $-\text{O}-\text{CH}_2-$, (21) $-\text{N}(\text{R}^{13})-$
 $\text{CO}-\text{N}(\text{R}^{14})-$ or (22) $-\text{N}(\text{R}^{15})-\text{CS}-\text{N}(\text{R}^{16})-$ (wherein R^6 , R^7 , R^8 , R^9 , R^{10} ,
 R^{11} , R^{12} , R^{13} , R^{14} , R^{15} and R^{16} , m , n , p and q have the same meanings
 as defined in above); and A^1 , A^2 and A^3 are a C_{3-8}
 cycloalkyl group, a C_{3-8} cycloalkenyl group, a 5- to 14-membered
 non-aromatic heterocyclic group, a C_{6-14} aromatic

hydrocarbocyclic group or a 5- to 14-membered aromatic heterocyclic group which may be optionally substituted with one or more groups selected from the following substituent group b (the substituent group a: the group consisting of hydroxy group, a halogen atom and nitrile group; and the substituent group b: the group consisting of (1) hydroxy group, (2) a halogen atom, (3) nitrile group, (4) nitro group, (5) a C₁₋₆ alkyl group, a C₂₋₆ alkenyl group or a C₂₋₆ alkynyl group which may be optionally substituted respectively with one or more groups selected from the group consisting of hydroxy group, nitrile group, a halogen atom, a C₁₋₆ alkylamino group, a di-(C₁₋₆ alkyl)amino group, a C₂₋₆ alkenylamino group, a di(C₂₋₆ alkenylamino) group, a C₂₋₆ alkynylamino group, a di(C₂₋₆ alkynylamino) group, an N-C₁₋₆ alkyl-N-C₂₋₆ alkenylamino group, an N-C₁₋₆ alkyl-N-C₂₋₆ alkynylamino group, an N-C₂₋₆ alkenyl-N-C₂₋₆ alkynylamino group, an aralkyloxy group, a TBDMS oxy group, a C₁₋₆ alkylsulfonylamino group, a C₁₋₆ alkylcarbonyloxy group, a C₂₋₆ alkenylcarbonyloxy group, a C₂₋₆ alkynylcarbonyloxy group, an N-C₁₋₆ alkylcarbamoyl group, an N-C₂₋₆ alkenylcarbamoyl group and an N-C₁₋₆ alkynylcarbamoyl group, (6) a C₁₋₆ alkoxy group, a C₂₋₆ alkenyloxy group or a C₂₋₆ alkynyloxy group which may be optionally substituted respectively with one or more groups selected from the group consisting of a C₁₋₆ alkylamino group, an aralkyloxy group and hydroxy group, (7) a C₁₋₆ alkylthio group, a C₂₋₆ alkenylthio group or a C₂₋₆ alkynylthio group which may be optionally substituted respectively with one or more groups

selected from the group consisting of hydroxy group, nitrile group, a halogen atom, a C₁₋₆ alkylamino group, an aralkyloxy group, a TBDMS oxy group, a C₁₋₆ alkylsulfonylamino group, a C₁₋₆ alkylcarbonyloxy group and a C₁₋₆ alkylcarbamoyl group, (8) a carbonyl group substituted with a group selected from the group consisting of a C₁₋₆ alkoxy group, amino group, a C₁₋₆ alkylamino group, a di(C₁₋₆ alkyl)amino group, a C₂₋₆ alkenylamino group, a di(C₂₋₆ alkenyl)amino group, a C₂₋₆ alkynylamino group, a di(C₂₋₆ alkynyl)amino group, an N-C₁₋₆ alkyl-N-C₂₋₆ alkenylamino group, an N-C₁₋₆ alkyl-N-C₂₋₆ alkynylamino group and an N-C₂₋₆ alkenyl-N-C₂₋₆ alkynylamino group, (9) amino group which may be optionally substituted with one or two groups selected from the group consisting of a C₁₋₆ alkyl group, a C₂₋₆ alkenyl group, a C₂₋₆ alkynyl group, a C₁₋₆ alkylsulfonyl group, a C₂₋₆ alkenylsulfonyl group, a C₂₋₆ alkynylsulfonyl group, a C₁₋₆ alkylcarbonyl group, a C₂₋₆ alkenylcarbonyl group and a C₂₋₆ alkynylcarbonyl group, (10) a C₁₋₆ alkylsulfonyl group, (11) a C₂₋₆ alkenylsulfonyl group, (12) a C₂₋₆ alkynylsulfonyl group, (13) a C₁₋₆ alkylsulfinyl group, (14) a C₂₋₆ alkenylsulfinyl group, (15) a C₂₋₆ alkynylsulfinyl group, (16) a formyl group, (17) a C₃₋₈ cycloalkyl group or a C₃₋₈ cycloalkenyl group which may be optionally substituted respectively with one or more groups selected from the group consisting of hydroxy group, a halogen atom, nitrile group, a C₁₋₆ alkyl group, a C₁₋₆ alkyloxy group, a C₁₋₆ alkyloxy C₁₋₆ alkyl group and an aralkyl group, (18) a 5- to 14-membered non-aromatic heterocyclic group which may be

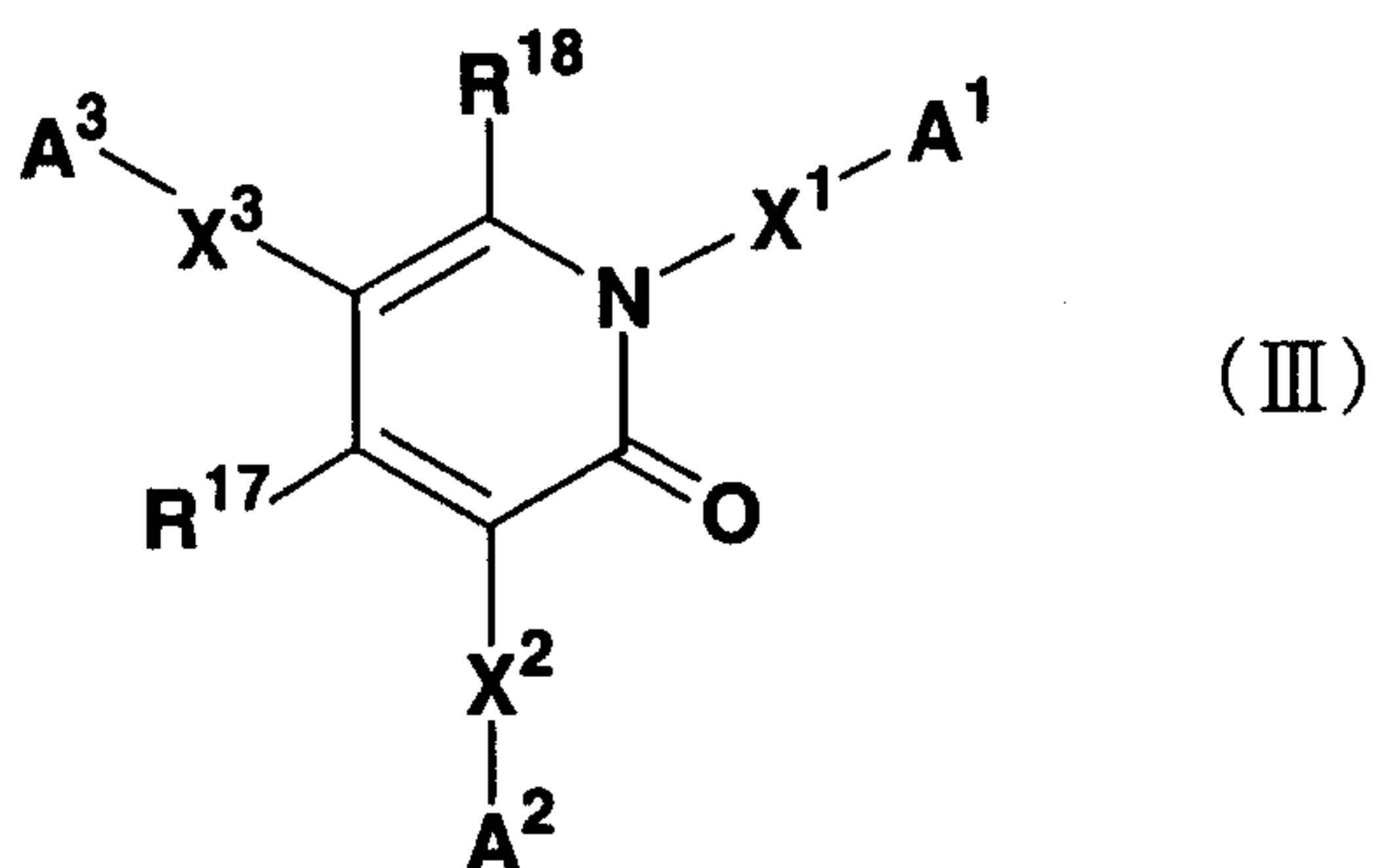
optionally substituted with one or more groups selected from the group consisting of hydroxy group, a halogen atom, nitrile group, a C₁₋₆ alkyl group, a C₁₋₆ alkyloxy group, a C₁₋₆ alkyloxy C₁₋₆ alkyl group and an aralkyl group, (19) a C₆₋₁₄ aromatic hydrocarbocyclic group which may be optionally substituted with one or more groups selected from the group consisting of hydroxy group, a halogen atom, nitrile group, a C₁₋₆ alkyl group, a C₁₋₆ alkyloxy group, a C₁₋₆ alkyloxy C₁₋₆ alkyl group and an aralkyl group, and (20) a 5- to 14-membered aromatic heterocyclic group which may be optionally substituted with one or more groups selected from the group consisting of hydroxy group, a halogen atom, nitrile group, a C₁₋₆ alkyl group, a C₁₋₆ alkyloxy group, a C₁₋₆ alkyloxy C₁₋₆ alkyl group and an aralkyl group); (4) the compound according to the above (2), a salt thereof or hydrates thereof, wherein A¹, A² and/or A³ are the same as or different from each other and each is an optionally substituted C₃₋₈ cycloalkyl, C₃₋₈ cycloalkenyl or 5- to 14-membered non-aromatic heteroring; (5) the compound according to the above (2), a salt thereof or hydrates thereof, wherein A¹, A² and/or A³ are the same as or different from each other and each is an optionally substituted C₆₋₁₄ aromatic hydrocarbon ring or a 5- to 14-membered aromatic heteroring; (6) the compound according to the above (2), a salt thereof or hydrates thereof, wherein A¹, A² and A³ are the same as or different from each other and each represents phenyl group, pyrrolyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, thienyl

group, thiazolyl group, furyl group, naphthyl group, quinolyl group, iso-quinolyl group, indolyl group, benzimidazolyl group, benzothiazolyl group, benzoxazolyl group, imidazopyridyl group, carbazolyl group, cyclopentyl group, cyclohexyl group, cyclohexenyl group, dioxinyl group, adamantyl group, pyrrolidinyl group, piperidinyl group, piperazinyl group or morpholyl group which may optionally have substituents, respectively; (7) the compound according to the above (2), a salt thereof or hydrates thereof, wherein A^1 , A^2 and A^3 are the same as or different from each other and each is a group represented by the formula:



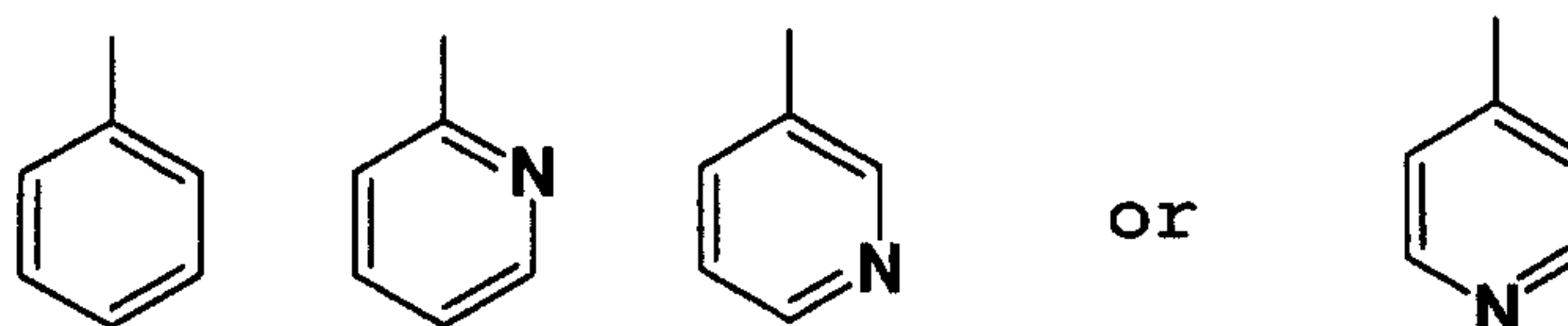
which may be substituted; (8) the compound according to the above (2), a salt thereof or hydrates thereof, wherein A^1 , A^2 and A^3 are the same as or different from each other and each is optionally substituted with hydroxyl group, a halogen atom, amino group or nitrile group; (9) the compound according to the above (7), a salt thereof or hydrates thereof, wherein the substituents of A^1 , A^2 and A^3 are the same as or different from

each other and each is hydroxyl group, a halogen atom or, amino group, nitrile group or nitro group; (10) the compound according to the above (1) or (2), a salt thereof or hydrates thereof, wherein Q is oxygen; (11) the compound according to the above (1) or (2), a salt thereof, hydrates thereof, wherein X^1 , X^2 and X^3 are the same as or different from each other and each represents single bond, $-CH_2-$, $-CH(OH)-$, $-CH_2-CH_2-$, $-CH=CH-$, $-C\equiv C-$, $-O-$ or $-CO-$; (12) the compound according to the above (2), a salt thereof or hydrates thereof, wherein X^1 , X^2 and X^3 are single bonds; (13) the compound according to the above (2), a salt thereof or hydrates thereof, wherein R^{17} and R^{18} are the same as or different from each other and each represents hydrogen atom, fluorine, chlorine, bromine, iodine, methyl group, ethyl group, n-propyl group or iso-propyl group; (14) the compound according to the above (2), a salt thereof or hydrates thereof, wherein R^{17} and R^{18} represent hydrogen atom; (15) the compound according to the above (1) or (2), a salt thereof or hydrates thereof, which is represented by the formula:



wherein X^1 , X^2 , X^3 , A^1 , A^2 , A^3 , R^{17} and R^{18} have the same meanings as defined in the above (2); (16) the compound according to the

above (15), a salt thereof or hydrates thereof, wherein A^1 , A^2 and A^3 are same as or different from each other and each represents optionally substituted C_{6-14} aromatic hydrocarbon ring or 5- to 14-membered aromatic heteroring; (16) the compound according to the above (15), a salt thereof or hydrates thereof, wherein A^1 , A^2 and A^3 are same as or different from each other and each represents optionally substituted C_{6-14} aromatic hydrocarbon ring or 5- to 14-membered aromatic heteroring; (17) the compound according to the above (15), a salt thereof or hydrates thereof, wherein A^1 , A^2 and A^3 are the same as or different from each other and each represents optionally substituted phenyl group, pyrrolyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, thienyl group, thiazolyl group, furyl group, naphthyl group, quinolyl group, iso-quinolyl group, indolyl group, benzimidazolyl group, benzothiazolyl group, benzoxazolyl group, imidazopyridyl group, carbazolyl group, cyclopentyl group, cyclohexyl group, cyclohexenyl group, dioxinyl group, adamantyl group, pyrrolidinyl group, piperidinyl group, piperazinyl group or morpholyl group; (18) the compound according to the above (15), a salt thereof or hydrates thereof, wherein A^1 , A^2 and A^3 are the same as or different from each other and each represents a group represented by the following formula:



which may be substituted; (19) the compound according to the above (15), a salt thereof or hydrates thereof, wherein the bonding site of the substituent at A¹, A² and/or A³ are α -position of the carbon atom bonding to the group X¹, X² and X³, respectively; (20) the compound according to the above (15), a salt thereof or hydrates thereof, wherein X¹, X² and X³ are single bonds; (21) the compound according to the above (15), a salt thereof or hydrates thereof, wherein R¹⁷ and R¹⁸ are hydrogen atoms; (22) the compound according to the above (1), a salt thereof or hydrates thereof, which is any one of compounds selected from: 3-(2-cyanophenyl)-5-(2-methylsulfonylaminophenyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-chloro-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-nitrophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-aminophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-methylsulfonylaminophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-methylaminophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-dimethylaminophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-[3-(5-methoxymethyl-2-oxazolidinon-3-yl)-phenyl]-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-methoxycarbonylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-

methylaminocarbonylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyano-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-chlorophenyl)-5-(2-pyridyl)-1-(4-hydroxyphenyl)-1,2-dihydropyridin-2-one; 3-(2-chlorophenyl)-5-(2-pyridyl)-1-(4-dimethylaminoethoxyphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-formylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-hydroxymethylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-cyanomethylphenyl)-1,2-dihydropyridine-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-acetylaminomethylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-methylsulfonylaminomethylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-acetoxymethylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-methylthiophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-methylsulfonylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-formylthiophen-3-yl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-diethylaminomethylthiophen-3-yl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-hydroxymethylthiophen-3-yl)-1-phenyl-1,2-dihydropyridine-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-benzyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-

55702-519

phenyl-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1,5-diphenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-methoxyphenyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(3,4-dimethoxyphenyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(thiophen-3-yl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-fluorophenyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(thiophen-2-yl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(3-furyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-furyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-chlorophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-on, 3-(2-methoxycarbonylphenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-phenyl-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-fluorophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-chlorophenyl)-5-(2-pyridyl)-1-(3-methoxyphenyl)-1,2-dihydropyridin-2-one; 3-(2-fluoro-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-methoxy-5-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-fluoro-3-pyridyl)-5-(2-pyridyl)-1-(3-methoxyphenyl)-1,2-dihydropyridin-2-one; 3-(2-fluoro-3-pyridyl)-5-(2-pyridyl)-1-(3-fluorophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-fluorophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-fluorophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-

65702-519

5-(2-pyridyl)-1-(4-methoxyphenyl)-1,2-dihydropyridin-2-one;
3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-methoxyphenyl)-1,2-
dihydropyridin-2-one; 3-phenyl-5-(2-pyridyl)-1-(3-
fluorophenyl)-1,2-dihydropyridin-2-one; 3-(2-chlorophenyl)-
5-(2-pyridyl)-1-(4-fluorophenyl)-1,2-dihydropyridin-2-one;
3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-formylphenyl)-1,2-
dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-
formylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-
5-(2-pyridyl)-1-(3-chlorophenyl)-1,2-dihydropyridin-2-one;
3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-tolyl)-1,2-
dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-
trifluoromethylphenyl)-1,2-dihydropyridin-2-one; 3-(2-
cyanophenyl)-5-(2-pyridyl)-1-(thiophen-3-yl)-1,2-
dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-
furyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-
pyridyl)-1-(4-tolyl)-1,2-dihydropyridin-2-one; 3-(2-
cyanophenyl)-5-(2-pyridyl)-1-(4-trifluoromethylphenyl)-1,2-
dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-
methoxypyridin-5-yl)-1,2-dihydropyridin-2-one; 3-(2-
cyanophenyl)-5-(2-pyridyl)-1-(pyrimidin-5-yl)-1,2-
dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-
benzyloxymethylpyridin-5-yl)-1,2-dihydropyridin-2-one; 3-
(2-cyanophenyl)-5-(2-pyridyl)-1-(2-ethylthiopyridin-5-yl)-
1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-
1-(4-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-
5-(2-pyridyl)-1-(3-methoxypyridin-5-yl)-1,2-dihydropyridin-

2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-chloropyridin-5-yl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-fluoropyridin-5-yl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-methoxyphenyl)-1,2-dihydropyridin-2-one; 3-phenyl-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-chlorophenyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one; 3-(thiophen-3-yl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one; 3-(2,6-dimethylphenyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanothiophen-3-yl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-fluoro-3-pyridyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-chlorophenyl)-5-(2-pyridyl)-1-(3-hydroxyphenyl)-1,2-dihydropyridin-2-one; 3-(2-chlorophenyl)-5-(2-pyridyl)-1-(3-dimethylaminoethoxyphenyl)-1,2-dihydropyridin-2-one; 3-(2-chlorophenyl)-5-(2-pyridyl)-1-(3-dimethylaminopropoxyphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-hydroxymethylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-cyanomethylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-cyanomethylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(6-diethylaminomethyl-2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-phenyl-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one; 3-(2-hydroxypyridin-6-yl)-1-phenyl-5-

65702-519

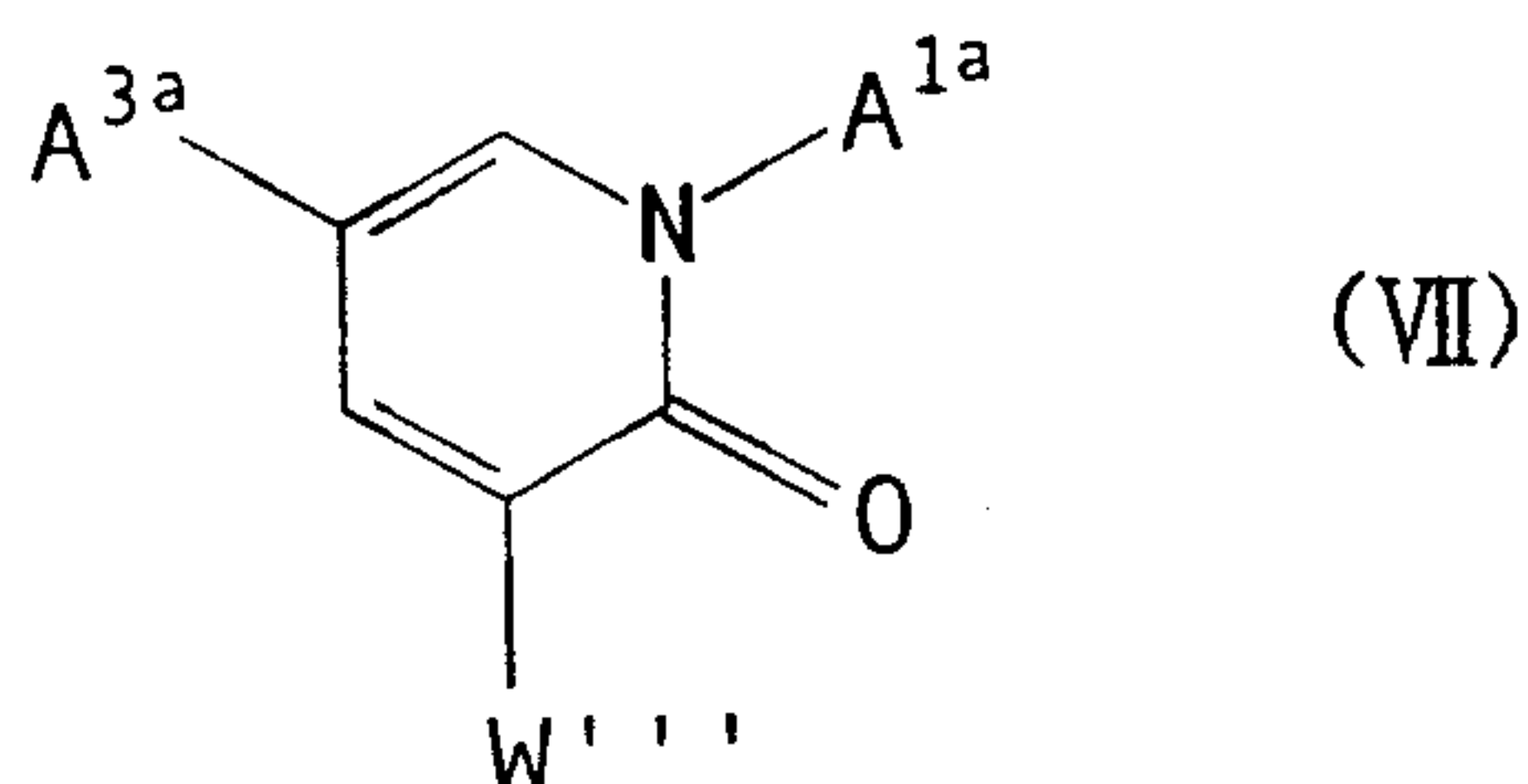
(2-pyridyl)-1,2-dihydropyridin-2-one; 1-(2-aminobenzothiazol-6-yl)-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(1-benzyl-1,2,5,6-tetrahydropyridin-3-yl)-1,2-dihydropyridin-2-one; 3-[2-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl]-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(6-methylpyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(5-methylpyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(3-hydroxypyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-phenyl-5-(2-thiazolyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(6-methoxypyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one; 1-(4-aminophenyl)-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 1-(3-aminophenyl)-3-(2-cyanophenyl)-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-amino-4-methylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-(3-dimethylaminoethoxyphenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-(3-piperidinoethoxyphenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-(3-pyrrolidinoethoxyphenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-(3-diisopropylaminoethoxyphenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-[3-(4-piperidinobutoxy)phenyl]-5-(2-pyridyl)-1,2-

65702-519

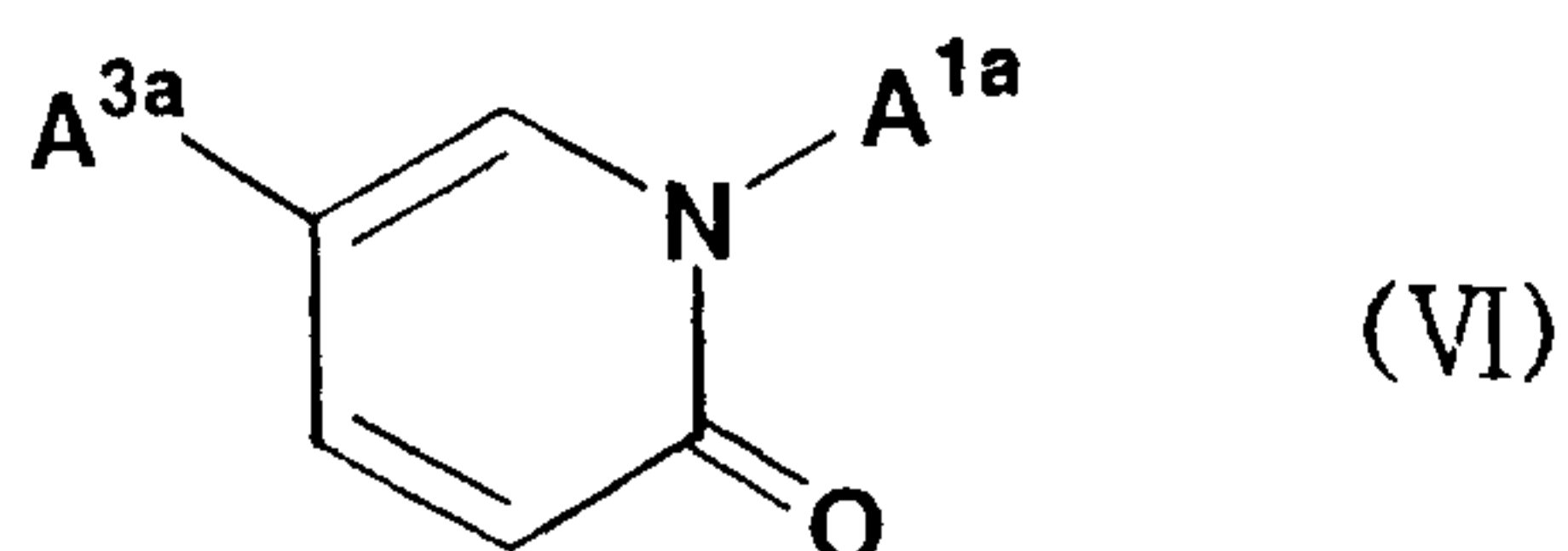
dihydropyridin-2-one; 3-(2-cyanophenyl)-1-(4-nitrophenyl)-
 5-(2-pyridyl)-1,2-dihydropyridin-2-one; 1-phenyl-5-(2-
 pyridyl)-3-(2-thiazolyl)-1,2-dihydropyridin-2-one; 3-(2-
 cyanophenyl)-1-(3-pyridyl)-5-(2-pyrimidinyl)-1,2-
 dihydropyridin-2-one; 3-(2-fluoropyridin-3-yl)-1-phenyl-5-
 (2-pyrimidinyl)-1,2-dihydropyridin-2-one; 3-(2-
 cyanopyridin-3-yl)-1-phenyl-5-(2-pyrimidinyl)-1,2-
 dihydropyridin-2-one; 3-(2-cyanophenyl)-1-(3-nitrophenyl)-
 5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one; 3-(2-
 nitrophenyl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-
 one; 3-(2-formylthiophen-3-yl)-5-(2-pyridyl)-1-phenyl-1,2-
 dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-
 naphthyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-
 pyridyl)-1-(1-naphthyl)-1,2-dihydropyridin-2-one; 5-(2-
 aminopyridin-6-yl)-3-(2-cyanophenyl)-1-phenyl-1,2-
 dihydropyridin-2-one; 5-(6-bromopyridin-2-yl)-3-(2-
 cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-
 cyanophenyl)-5-(2-morpholinopyridin-6-yl)-1-phenyl-1,2-
 dihydropyridin-2-one; 3-(2-cyanophenyl)-1-(3-hydroxyphenyl)-
 5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-
 1-[3-(4-piperidyloxy)]phenyl-5-(2-pyridyl)-1,2-
 dihydropyridin-2-one; 1-[3-(N-acetylpiperidin-4-yl-
 oxy)phenyl]-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-
 dihydropyridin-2-one; 3-(2-cyanophenyl)-1-[3-(1-
 methylsulfonylpiperidin-4-yl-oxy)phenyl]-5-(2-pyridyl)-
 1,2-dihydropyridin-2-one; 1-[3-(N-methylpiperidin-4-yl-

65702-519

oxy)phenyl]-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(6-chloro-1H-benzimidazol-2-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-nitro-4-methylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanothiophen-3-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-[2-(5-oxazolyl)phenyl]-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-[2-(5-oxazolyl)thiophen-3-yl]-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one; and 3-(2-ethoxycarbonylvinylthiophen-3-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; (23) a process for producing a compound represented by the formula:



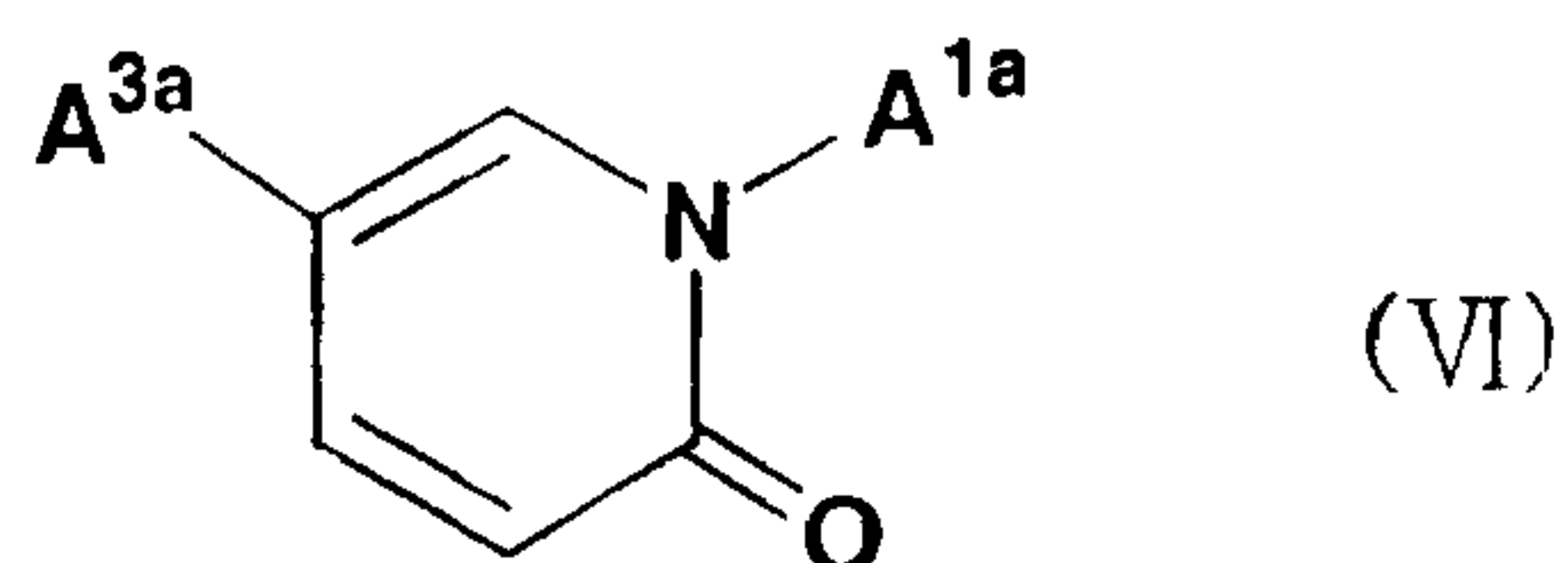
(wherein, each A^{1a} and A^{3a} are the same as or different from each other and each indicates an optionally substituted C₆₋₁₄ aromatic hydrocarbocyclic group or 5 to 14-membered aromatic heterocyclic group; and W' ' ' represents a halogen atom) or a salt thereof, which comprises subjecting the compound represented by the formula:



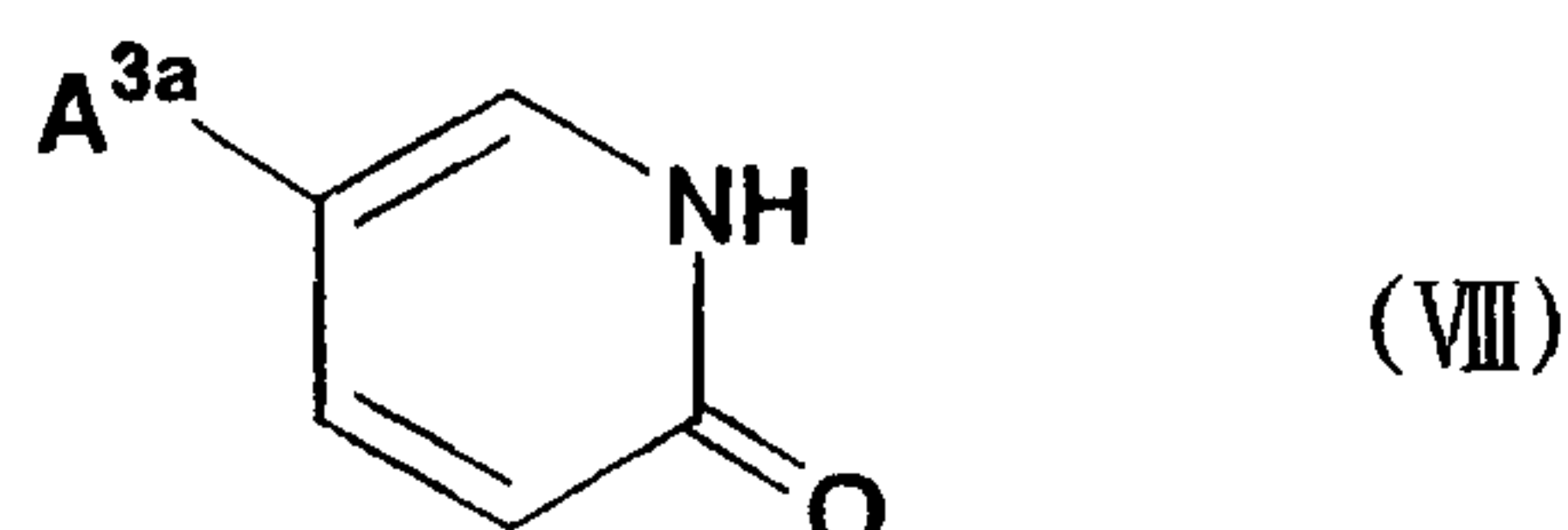
(wherein A^{1a} and A^{3a} have the same meanings as defined above) or a salt thereof to a halogenation

65702-519

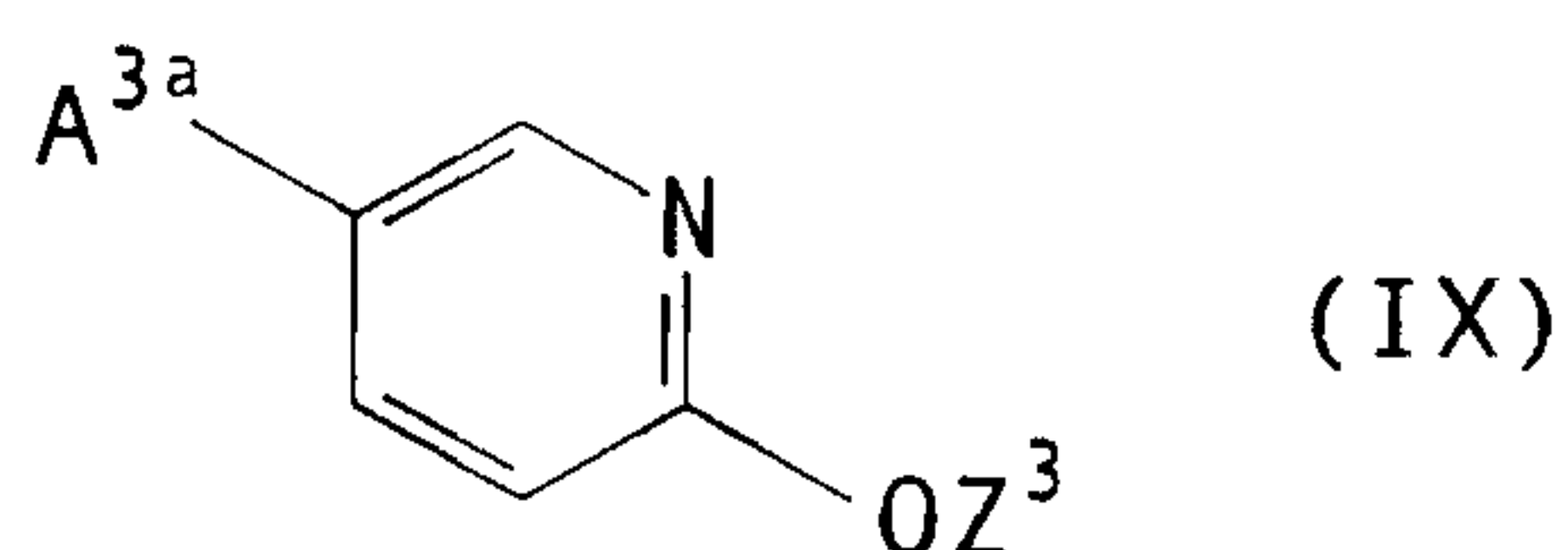
reaction; (24) a process for producing a compound represented by the formula:



(wherein A^{1a} and A^{3a} have the same meanings as defined above) or a salt thereof, which comprises subjecting the compound represented by the formula:



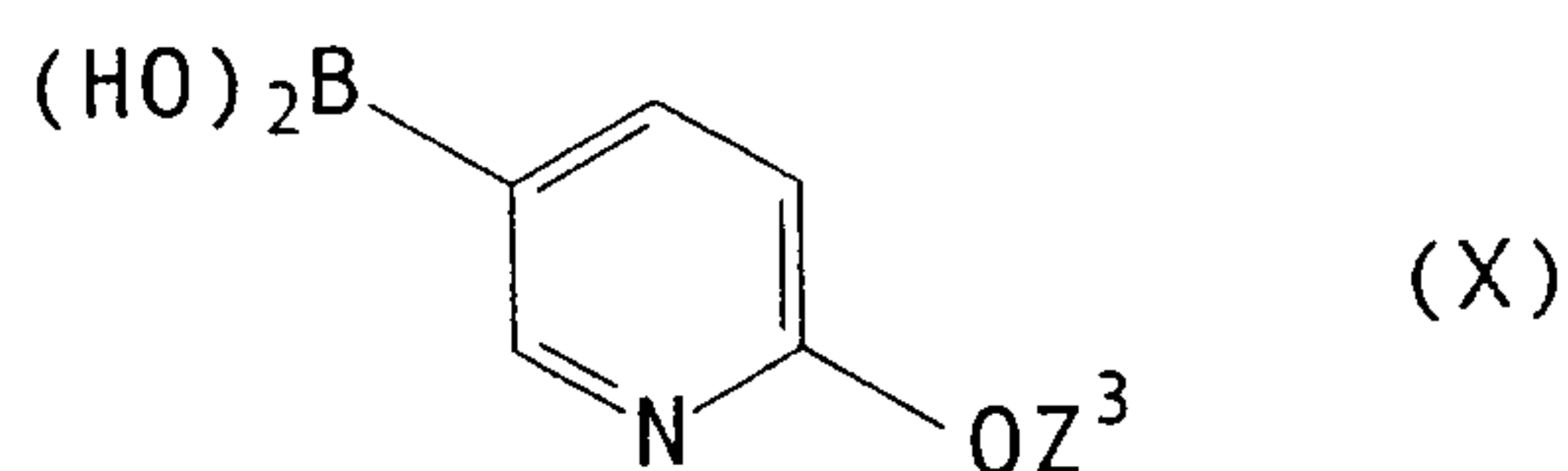
(wherein A^{3a} has the same meaning as defined above) or a salt thereof and a boronic acid derivative represented by the formula A^{1a}B(OH)₂ (wherein A^{1a} represents an optionally substituted C₆₋₁₄ aromatic hydrocarbon ring or 5- to 14-membered aromatic heteroring) to a coupling reaction in the presence of a copper compound; (25) the production process according to the above (24), which comprises subjecting the compound represented by the above formula (VIII) or a salt thereof produced by subjecting the compound represented by the formula:



(wherein A^{3a} has the same meaning as defined above; and Z³ indicates a protecting group of an alcoholic hydroxy group) to de-protecting reaction and a boronic acid derivative

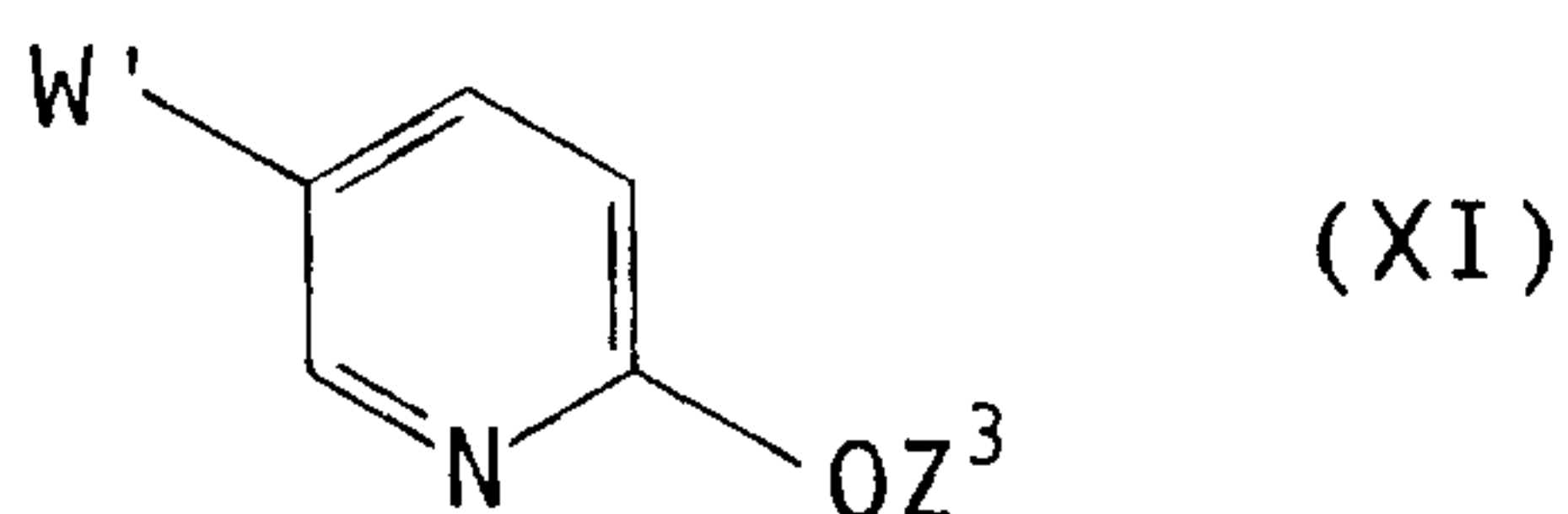
65702-519

represented by the formula $A^{1a}B(OH)_2$ (wherein A^{1a} has the same meaning as defined above) to a coupling reaction in the presence of a copper compound; (26) the production process according to the above (24), which comprises producing the compound represented by the above formula (VIII) or a salt thereof by subjecting the compound represented by the above formula (IX) or a salt thereof produced by subjecting a boronic acid derivative represented by the formula:

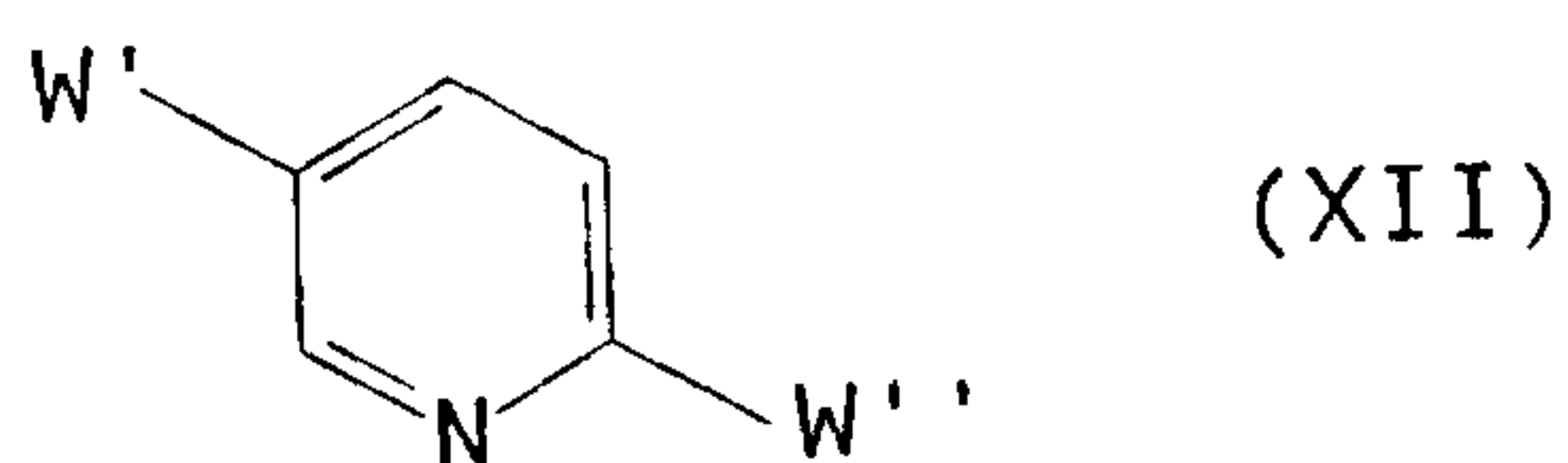


(wherein Z^3 has the same meaning as defined above) or a salt thereof and the compound represented by the formula $A^{3a}-Z^1$ (wherein A^{3a} has the same meaning as defined above; and Z^1 represents a halogen atom) or a salt thereof to a coupling reaction in the presence of a palladium catalyst, to a de-protecting reaction; and then subjecting the compound (VIII) or a salt thereof and a boronic acid derivative represented by the formula $A^{1a}B(OH)_2$ (wherein A^{1a} has the same meaning as defined above) to a coupling reaction in the presence of a copper compound; (27) the production process according to the above (24), which comprises producing the compound represented by the above formula (X) or a salt thereof by reacting the compound represented by the formula:

65702-519



(wherein Z^3 has the same meaning as defined above; and W' represents a halogen atom) or a salt thereof and trimethoxyborane in the presence of a base; producing the compound represented by the above formula (IX) or a salt thereof by subjecting the compound (X) or a salt and the compound represented by the formula $A^{3a}-Z^1$ (wherein A^{3a} and Z^1 have the same meanings as defined above) or a salt thereof to a coupling reaction in the presence of a palladium catalyst; producing the compound represented by the above formula (VIII) or a salt thereof by subjecting the compound (IX) or a salt thereof to a de-protecting reaction; and then subjecting the compound (VIII) and a boronic acid derivative represented by the formula $A^{1a}B(OH)_2$ (wherein A^{1a} has the same meaning as defined above) to a coupling reaction in the presence of a copper compound; (28) the production process according to the above (24), which comprises producing the compound represented by the above formula (X) or a salt thereof by reacting the compound represented by the above formula (XI) or a salt thereof produced by reacting the compound represented by the formula:



(wherein W' and W'' are the same as or different from each other

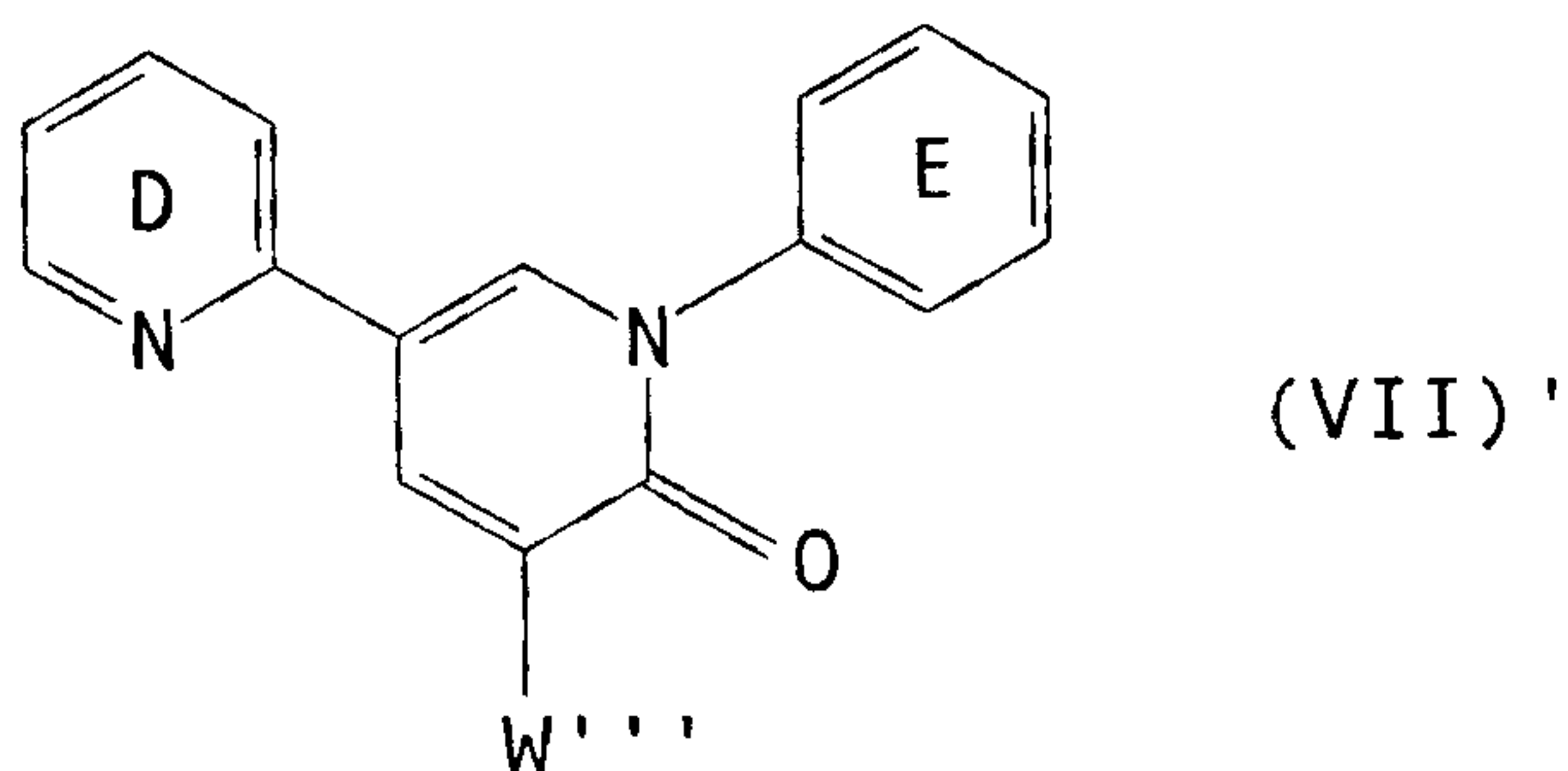
and each represents halogen atoms) or a salt thereof and the compound represented by the formula Z^3OM (wherein Z^3 has the same meaning as defined above; and M represents an alkali metal atom) and trimethoxyborane in the presence of a base; producing the compound represented by the above formula (IX) or a salt thereof by subjecting the compound (X) or a salt thereof and the compound represented by the formula $A^{3a}-Z^1$ (wherein A^{3a} and Z^1 have the same meanings as defined above) or a salt thereof to a coupling reaction in the presence of a palladium catalyst; producing the compound represented by the above formula (VIII) or a salt thereof by subjecting the compound (IX) or a salt thereof to a de-protecting reaction; and then subjecting the compound (VIII) and a boronic acid derivative represented by the formula $A^{1a}B(OH)_2$ (wherein A^{1a} has the same meaning as defined above) to a coupling reaction in the presence of a copper compound; (29) the production process according to the above (23), which comprises subjecting the compound represented by the above formula (VI) and produced by the production process according to any of the above (24) to (28) or a salt thereof to a halogenation reaction; (30) the production process according to the above (23) or (29), wherein W is bromine or iodine; (31) the production process according to the above (23) or (29), wherein the halogenation reaction for producing the compound (VII) or a salt thereof is (1) a bromination reaction using N-bromosuccinimide or acetic acid-bromine or (2) an iodination reaction using N-iodosuccinimide or iodine; (32) the

production process according to the above (23) or (29), wherein the halogenation reaction for producing the compound (VII) or a salt thereof is carried out using N,N-dimethylformamide as a solvent; (33) the production process according to the above (23) or (29), wherein A^{1a} and A^{3a} are the same as or different from each other and each represents an optionally substituted phenyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, thienyl group, thiazolyl group, furyl group, naphthyl group, quinolyl group, iso-quinolyl group, indolyl group, benzimidazolyl group, benzothiazolyl group, benzoxazolyl group, imidazopyridyl group or carbazolyl group; (34) the production process according to any of the above (24) to (28), wherein A^{1a} and A^{3a} are the same as or different from each other and each represents an optionally substituted phenyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, thienyl group, thiazolyl group, furyl group, naphthyl group, quinolyl group, iso-quinolyl group, indolyl group, benzimidazolyl group, benzothiazolyl group, benzoxazolyl group, imidazopyridyl group or carbazolyl group; (35) the production process according to any of the above (24) to (29), wherein the copper compound used for a coupling reaction using the compound (VIII) or a salt thereof is copper acetate or di- μ -hydroxo-bis[(N,N,N',N'-tetramethylethylenediamine)copper (II)] chloride; (36) the production process according to any of the above (24) to (29), wherein the coupling reaction using the compound (VIII) or a

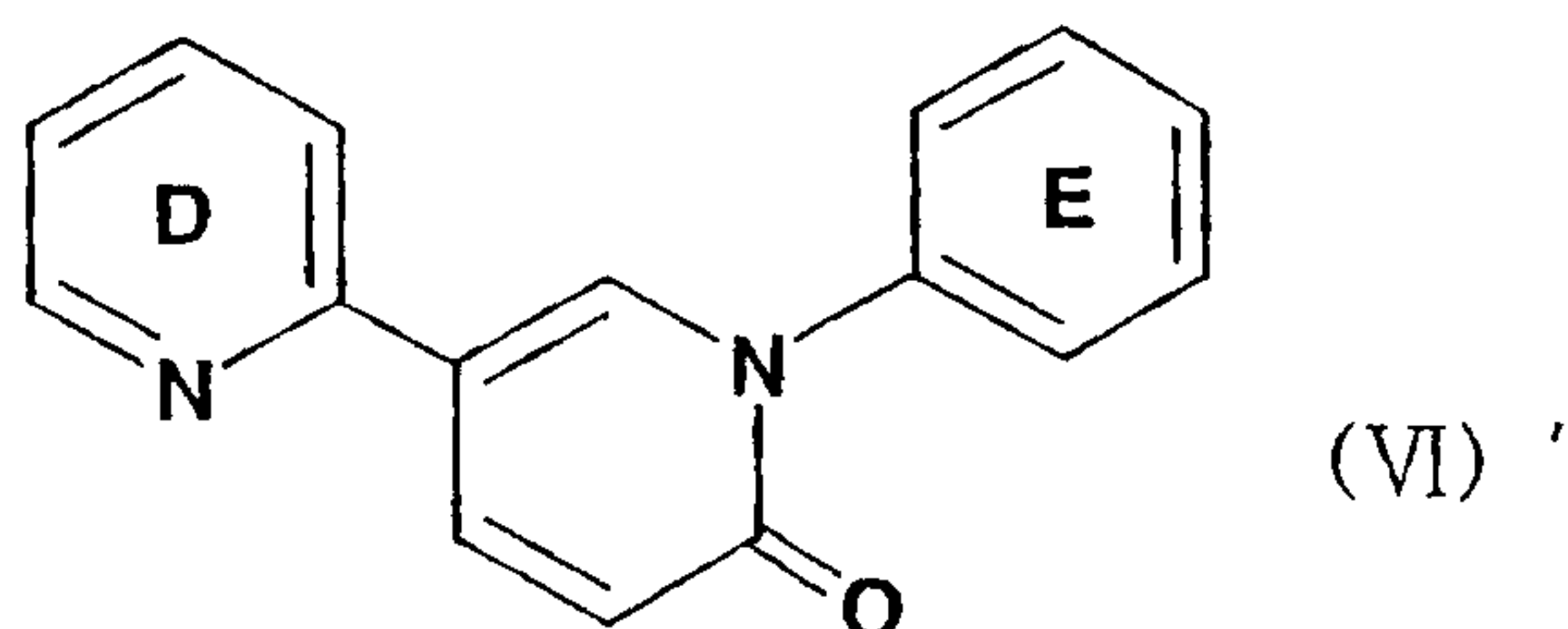
salt thereof is carried out in the presence of a base; (37) the production process according to the above (36), wherein the base is triethylamine, pyridine or tetramethylethylenediamine; (38) the production process according to any of the above (24) to (29), wherein the coupling reaction using the compound (VIII) or a salt thereof is carried out using N,N-dimethylformamide as a solvent; (39) the production process according to any of the above (25) to (29), wherein Z^3 is a C_{1-6} alkyl group or a C_{1-6} aralkyl group; (40) the production process according to the above (25) to (29), wherein the reaction of de-protection of the compound (IX) or a salt thereof is carried out in the presence of an acid; (41) the production process according to the above (40), wherein the acid is hydrochloric acid; (42) the production process according to the above (26) to (29), wherein a catalyst in the coupling reaction using the compound (X) or a salt thereof is palladium acetate and triphenylphosphine; (43) the production process according to the above (26) to (29), wherein the coupling reaction using the compound (X) or a salt thereof is carried out in the presence of a base; (44) the production process according to the above (43), wherein the base is cesium carbonate, sodium carbonate or potassium carbonate; (45) the production process according to any of the above (27) to (29), wherein W' is bromine; (46) the production process according to the above (27) to (29), wherein the base used for the reaction of the compound (XI) or a salt thereof with trimethoxyborane is n-butyllithium; (47) the production process according to the

65702-519

above (28) or (29), wherein W' and W'' are bromine; (48) the production process according to the above (28) or (29), wherein the compound represented by the formula Z³OM is sodium methoxide or sodium ethoxide; (49) a process for producing a compound represented by the formula:

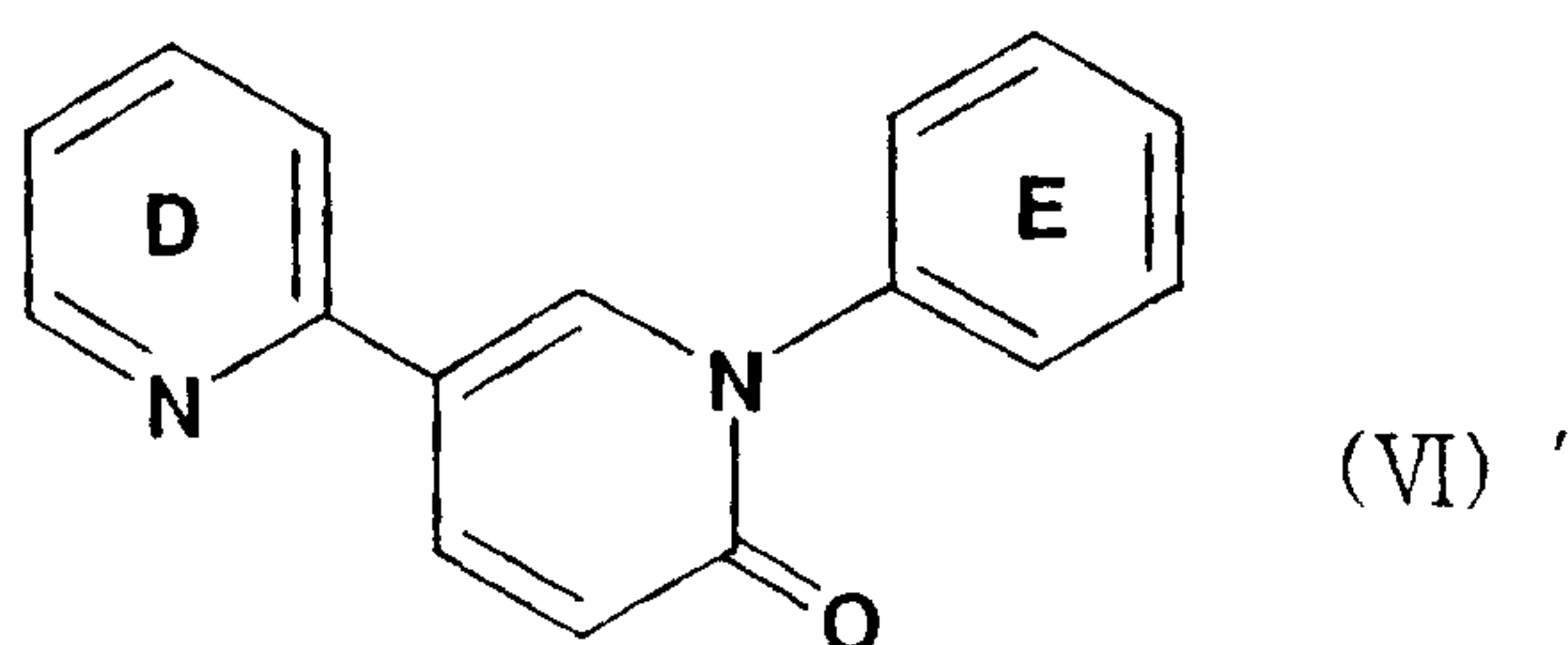


(wherein, the ring D indicates an optionally substituted pyridine ring; and the ring E represents an optionally substituted benzene ring; and W''' has the same meaning as defined above) or a salt thereof, which comprises subjecting a compound represented by the formula:

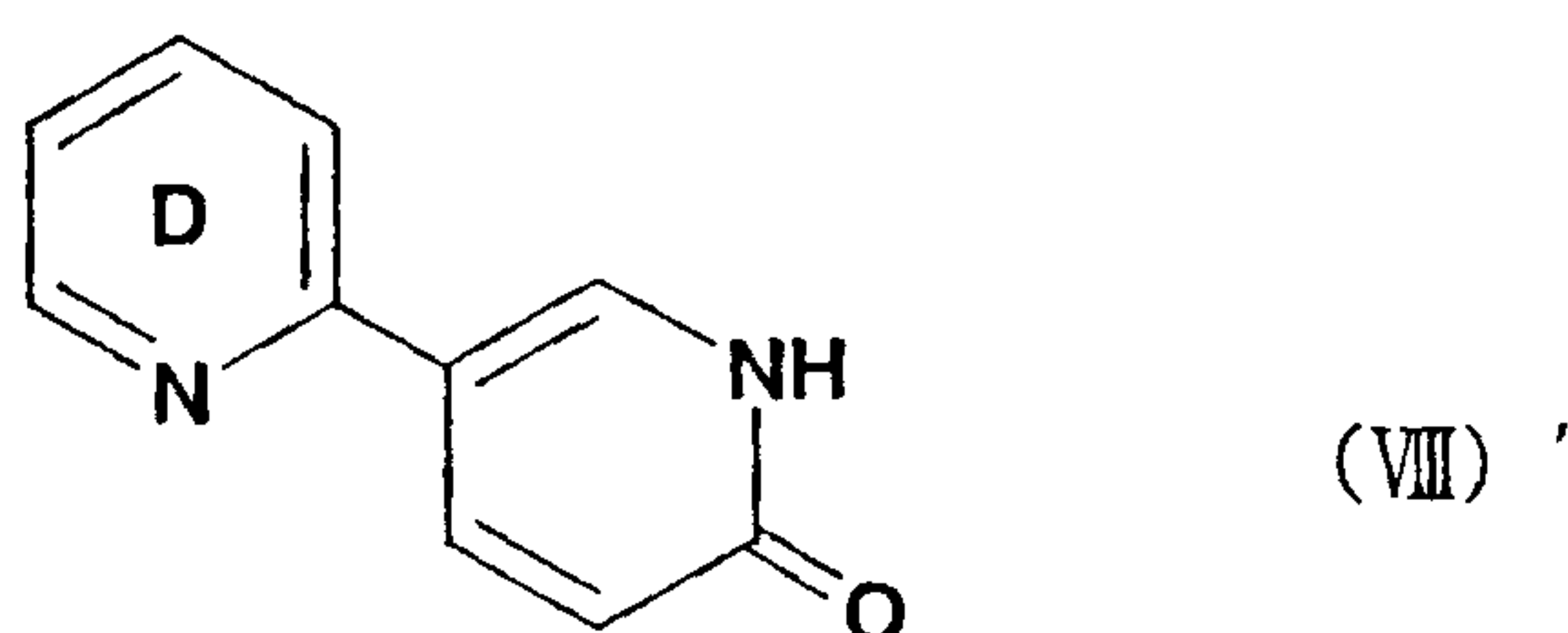


(wherein, the ring D and E have the same meanings as defined above) or a salt thereof to a halogenation reaction; (50) a process for producing a compound represented by the formula:

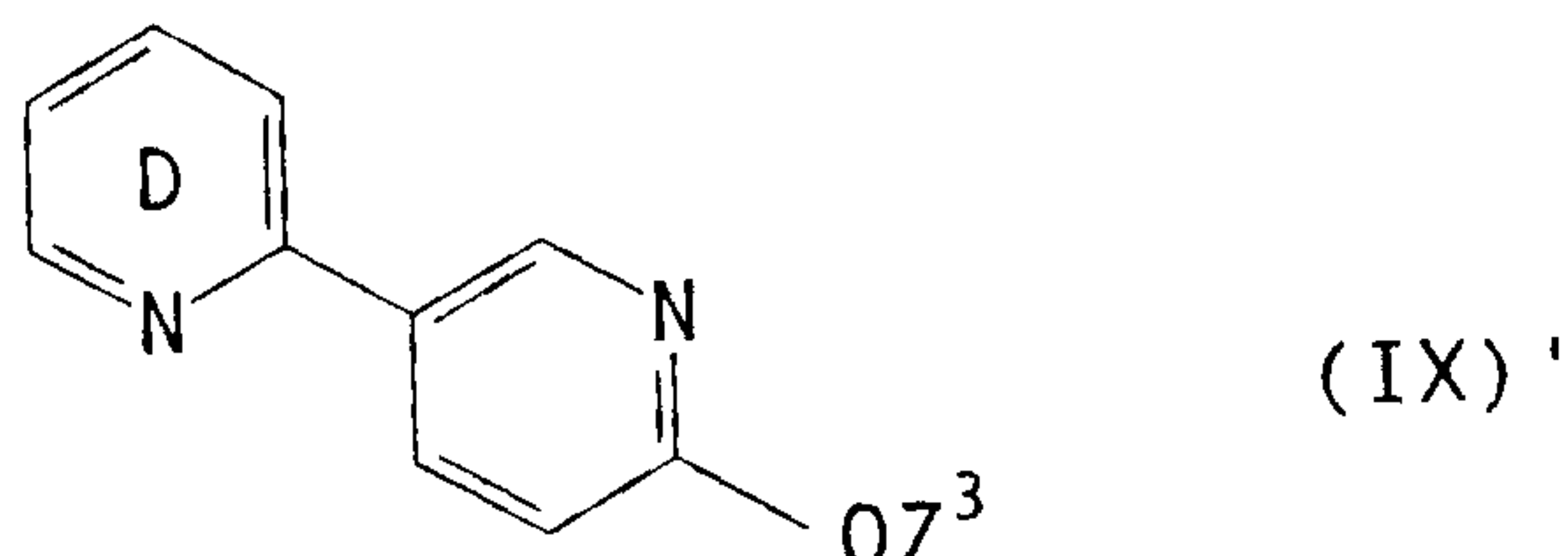
65702-519



(wherein, the ring D and the ring E have the same meanings as defined above) or a salt thereof, which comprises subjecting the compound represented by the formula:



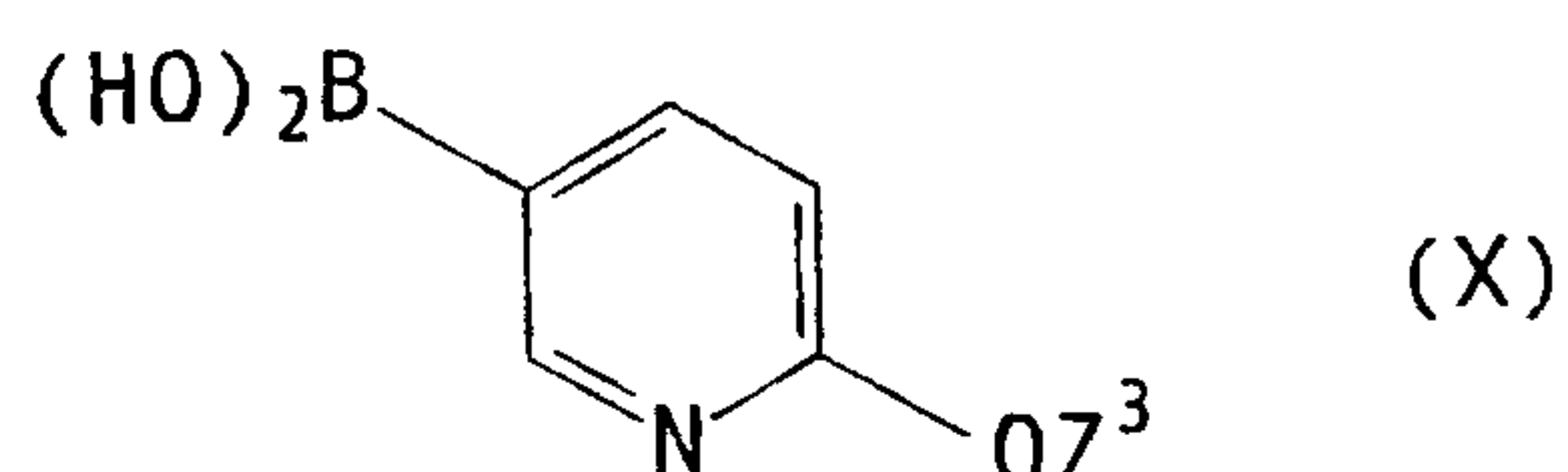
(wherein the ring D has the same meaning as defined above) or a salt thereof and a boronic acid derivative represented by the formula $\text{PhB}(\text{OH})_2$ (wherein Ph indicates an optionally substituted phenyl group) to a coupling reaction in the presence of a copper compound; (51) the production process according to the above (50), which comprises subjecting the compound represented by the above formula (VIII)' or a salt thereof produced by subjecting the compound represented by the formula:



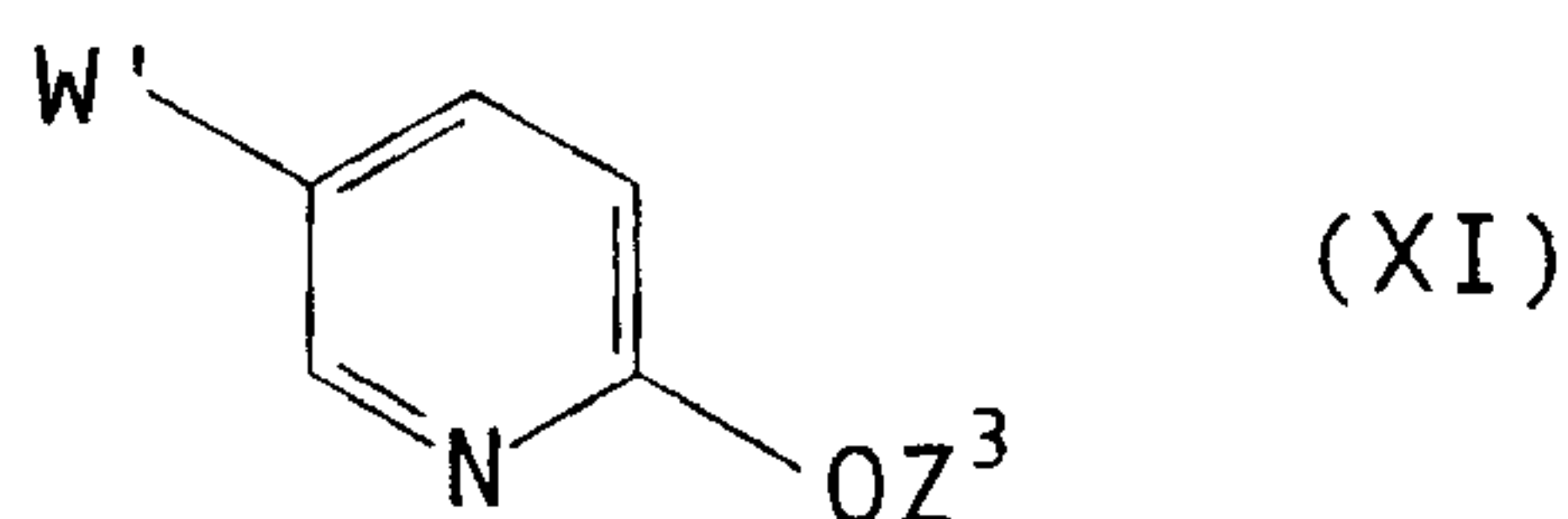
(wherein the ring D and Z^3 have the same meanings as defined above) or a salt thereof to a de-protecting reaction, and a boronic acid derivative represented by the formula $\text{PhB}(\text{OH})_2$

65702-519

(wherein Ph has the same meaning as defined above) to a coupling reaction in the presence of a copper compound; (52) the production process according to the above (50), which comprises producing the compound represented by the above formula (VII)' or a salt thereof by subjecting the compound represented by the above formula (IX)' or a salt thereof produced by subjecting a boronic acid derivative represented by the formula:



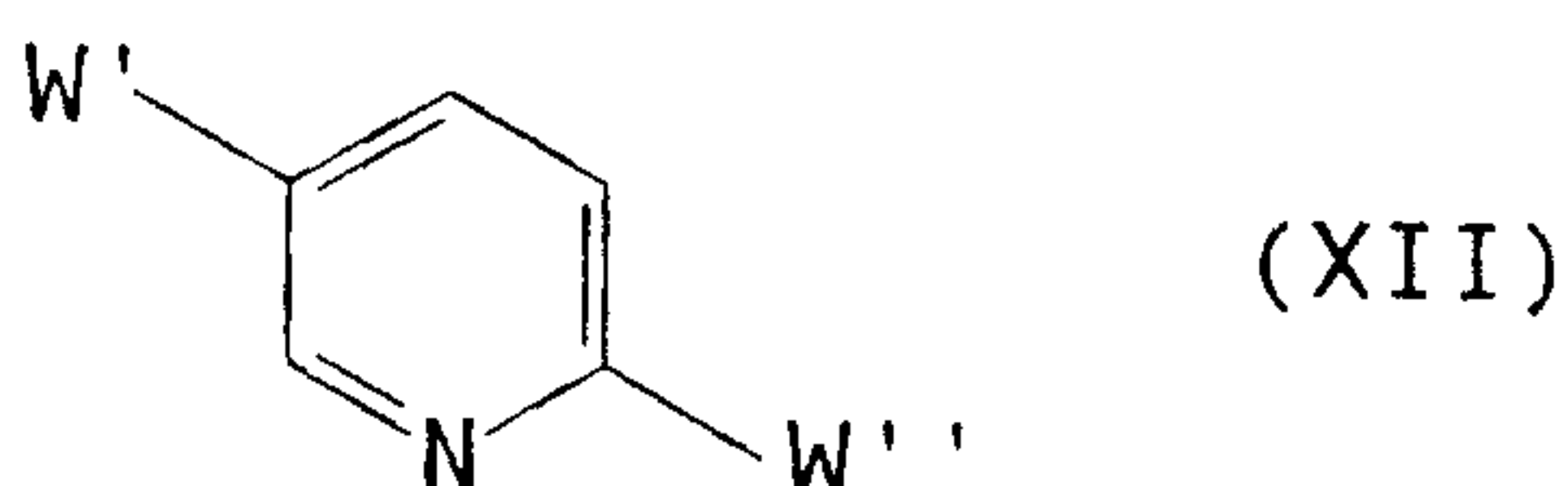
(wherein Z³ has the same meaning as defined above) or a salt thereof and an optionally substituted 2-halogenopyridine or a salt thereof to a coupling reaction in the presence of a palladium catalyst to a de-protecting reaction; and then subjecting the compound (VIII)' or a salt thereof and a boronic acid derivative represented by the formula PhB(OH)₂ (wherein Ph has the same meaning as defined above) to a coupling reaction in the presence of a copper compound; (53) the production process according to the above (50), which comprises producing the compound represented by the above formula (X) or a salt thereof by reacting the compound represented by the formula:



(wherein Z³ has the same meaning as defined above; and W' represents a halogen atom) or a salt thereof and

65702-519

trimethoxyborane in the presence of a base; producing the compound represented by the above formula (IX)' or a salt thereof by subjecting the compound (X) or a salt thereof and an optionally substituted 2-halogenopyridine or a salt thereof to a coupling reaction in the presence of a palladium catalyst; producing the compound represented by the above formula (VIII)' or a salt thereof by subjecting the compound (IX)' or a salt to a de-protecting reaction; and then subjecting the compound (VIII)' and a boronic acid derivative represented by the formula $\text{PhB}(\text{OH})_2$ (wherein Ph has the same meaning as defined above) in the presence of a copper compound; (54) the production process according to the above (50), which comprises producing the compound represented by the above formula (X) or a salt thereof by reacting the compound represented by the above formula (XI) or a salt thereof produced by reacting the compound represented by the formula:



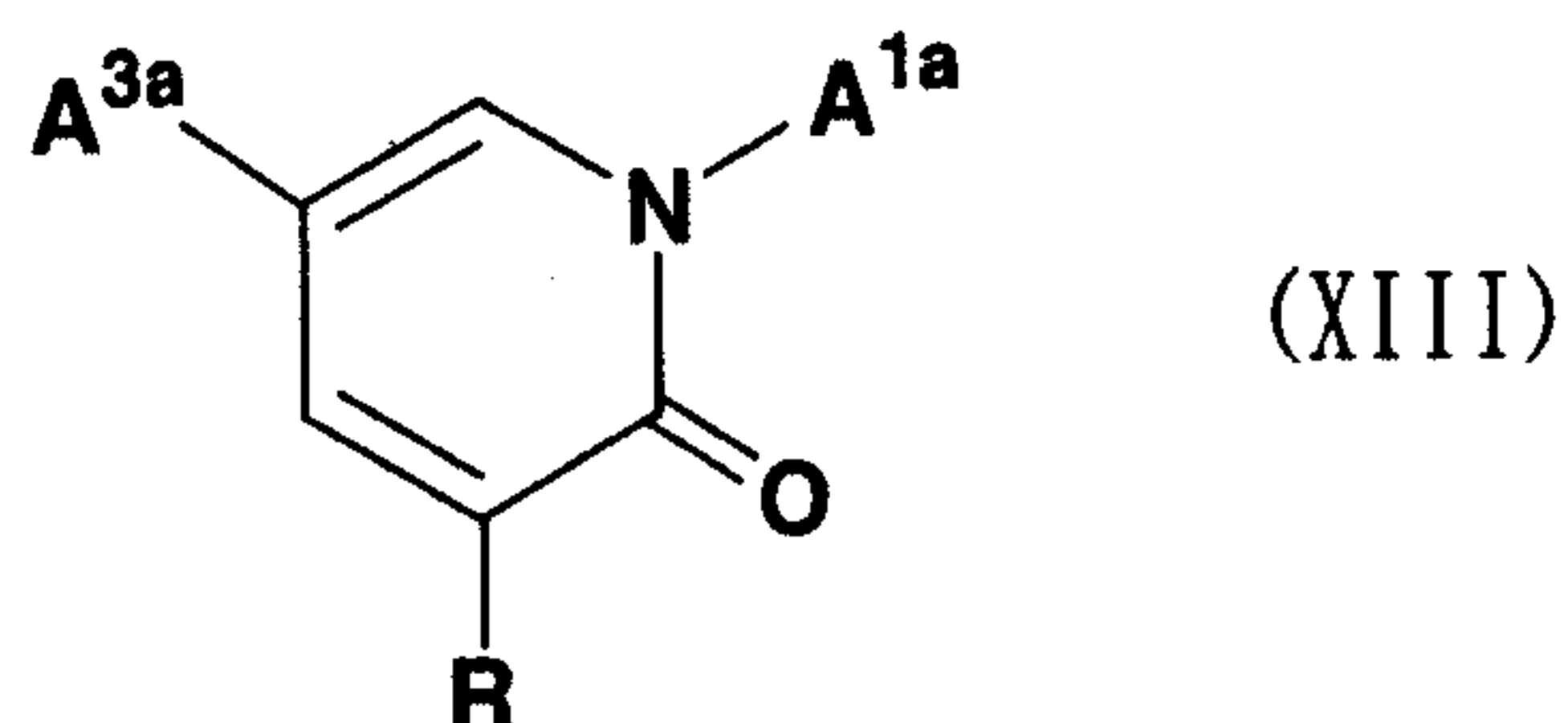
(wherein W' and W'' are the same as or different from each other and each represents halogen atoms) or a salt thereof and the compound represented by the formula Z^3OM (wherein Z^3 and M have the same meanings as defined above), and trimethoxyborane in the presence of a base; producing the compound represented by the above formula (IX)' or a salt thereof by subjecting the compound (X) or a salt and an optionally substituted 2-

halogenopyridine or a salt thereof to a coupling reaction in the presence of a palladium catalyst; producing the compound represented by the above formula (VIII) or a salt thereof by subjecting the compound (IX)' or a salt to a de-protecting reaction; and then subjecting the compound (VIII)' and a boronic acid derivative represented by the formula PhB(OH)_2 (wherein Ph has the same meaning as defined above) to a coupling reaction in the presence of a copper compound; (55) the production process according to the above (25), which comprises subjecting the compound represented by the above formula (VI)' and produced by the production process according to any of the above (29) to (32) or a salt thereof to a halogenation reaction; (56) the production process according to the above (49) or (55), wherein W is bromine or iodine; (57) the production process according to the above (49) or (55), wherein the halogenation reaction for producing the compound (VII) or a salt thereof is (1) a bromination reaction using N-bromosuccinimide or acetic acid-bromine, or (2) an iodination reaction using N-iodosuccinimide or iodine; (58) the production process according to the above (49) or (55), wherein the halogenation reaction for producing the compound (VII) or a salt thereof is carried out using N,N-dimethylformamide as a solvent; (59) the production process according to the above (49) or (55), wherein A^{1a} and A^{3a} are the same as or different from each other and each represents an optionally substituted phenyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group,

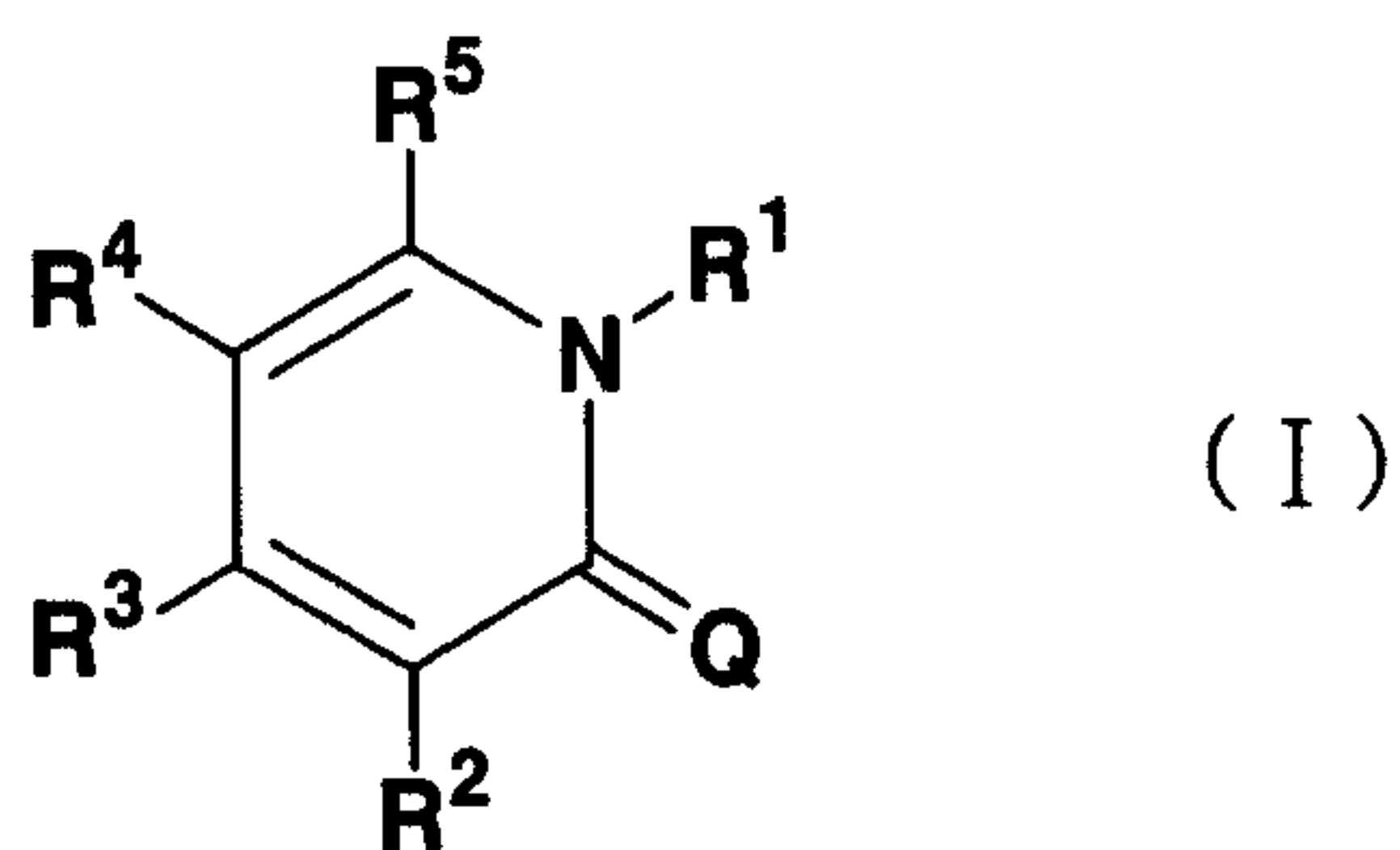
thienyl group, thiazolyl group, furyl group, naphthyl group, quinolyl group, iso-quinolyl group, indolyl group, benzimidazolyl group, benzothiazolyl group, benzoxazolyl group, imidazopyridyl group or carbazolyl group; (60) the production process according to any of the above (50) to (54), wherein A^{1a} and A^{3a} are the same as or different from each other and each represents an optionally substituted phenyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, thienyl group, thiazolyl group, furyl group, naphthyl group, quinolyl group, iso-quinolyl group, indolyl group, benzimidazolyl group, benzothiazolyl group, benzoxazolyl group, imidazopyridyl group or carbazolyl group; (61) the production process according to any of the above (50) to (55), wherein the copper compound used for the coupling reaction using the compound (VIII) or a salt thereof is copper acetate or di- μ -hydroxo-bis[(N,N,N',N'-tetramethylethylenediamine)copper (II)] chloride; (62) the production process according to any of the above (50) to (55), wherein the coupling reaction using the compound (VIII) or a salt thereof is carried out in the presence of a base; (63) the production process according to the above (62), wherein the base is triethylamine, pyridine or tetramethylethylenediamine; (64) the production process according to any of the above (50) to (55), wherein the coupling reaction using the compound (VIII) or a salt thereof is carried out using N,N-dimethylformamide as a solvent; (65) the production process according to any of the above (51) to (55),

wherein Z^3 is a C_{1-6} alkyl group or an aralkyl group; (66) the production process according to the above (51) to (55), wherein the de-protection reaction of the compound (IX) or a salt thereof is carried out in the presence of an acid; (67) the production process according to the above (66), wherein the acid is hydrochloric acid; (68) the production process according to the above (52) to (55), wherein a catalyst in the coupling reaction using the compound (X) or a salt thereof is palladium acetate and triphenylphosphine; (69) the production process according to the above (52) to (55), wherein the coupling reaction using the compound (X) or a salt thereof is carried out in the presence of a base; (70) the production process according to the above (69), wherein the base is cesium carbonate, sodium carbonate or potassium carbonate; (71) the production process according to any of the above (53) to (55), wherein W' is bromine; (72) the production process according to the above (53) to (55), wherein the base used for the reaction of the compound (XI) or a salt thereof with trimethoxyborane is n-butyllithium; (73) the production process according to the above (54) or (55), wherein W' and W'' are bromine; (74) the production process according to the above (54) or (55), wherein the compound represented by the formula Z^3OM is sodium methoxide or sodium ethoxide; (75) the production process according to any of the above (52) to (55), wherein the optionally substituted 2-halogenopyridine is an optionally substituted 2-bromopyridine; (76) a compound represented by the following

formula or a salt thereof:



wherein A^{1a} and A^{3a} are the same as or different from each other and each indicates an optionally substituted C₆₋₁₄ aromatic hydrocarbocyclic group or 5 to 14-membered aromatic heterocyclic group; and R indicates hydrogen atom or a halogen atom; (77) the compound according to the above (76) or a salt thereof, wherein A^{1a} and A^{3a} are the same as or different from each other and each represents an optionally substituted phenyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, thienyl group, thiazolyl group, furyl group, naphthyl group, quinolyl group, iso-quinolyl group, indolyl group, benzimidazolyl group, benzothiazolyl group, benzoxazolyl group, imidazopyridyl group or carbazolyl group; (78) the compound according to the above (76) or a salt thereof, wherein A^{1a} and A^{3a} are the same as or different from each other and each represents an optionally substituted phenyl group, pyridyl group, pyrimidinyl group, thienyl group or furyl group; (79) the compound according to the above (76) or a salt thereof, wherein R is hydrogen atom or bromine; (80) a pharmaceutical composition comprising a compound represented by the following formula, a salt thereof or hydrates thereof:



in the formula, Q indicates NH, O or S; and R^1 , R^2 , R^3 , R^4 and R^5 are the same as or different from each other and each indicates hydrogen atom, a halogen atom, a C_{1-6} alkyl group or the formula -X-A (wherein X indicates a single bond, a C_{1-6} alkylene group which may optionally have a substituent, a C_{2-6} alkenylene group which may optionally have a substituent, a C_{2-6} alkynylene group which may optionally have a substituent, -O-, -S-, -CO-, -SO-, -SO₂-, -N(R^6)-, -N(R^7)-CO-, -CO-N(R^8)-, -N(R^9)-CH₂-, -CH₂-N(R^{10})-, -CH₂-CO-, -CO-CH₂-, -N(R^{11})-S(O)_m-, -S(O)_n-N(R^{12})-, -CH₂-S(O)_p-, -S(O)_q-CH₂-, -CH₂-O-, -O-CH₂-, -N(R^{13})-CO-N(R^{14})- or -N(R^{15})-CS-N(R^{16})- (wherein R^6 , R^7 , R^8 , R^9 , R^{10} , R^{11} , R^{12} , R^{13} , R^{14} , R^{15} and R^{16} indicates hydrogen atom, a C_{1-6} alkyl group or a C_{1-6} alkoxy group; and m, n, p and q are independent of each other and each indicates an integer of 0, 1 or 2); and A indicates an optionally substituted C_{3-8} cycloalkyl group, C_{3-8} cycloalkenyl group, 5- to 14-membered non-aromatic heterocyclic group, C_{6-14} aromatic hydrocarbocyclic group or 5- to 14-membered aromatic heterocyclic group), provided that 3 groups among R^1 , R^2 , R^3 , R^4 and R^5 are always the same as or different from each other and each indicates -X-A; and the residual 2 groups always indicate hydrogen atom, a halogen atom or a C_{1-6} alkyl group;

(81) the pharmaceutical composition according to the above (80),

65702-519

wherein it is an inhibitor to an α -amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (hereinafter, referred to as "AMPA") receptor and/or a kainate receptor; (82) the pharmaceutical composition according to the above (80), wherein it is an inhibitor to an AMPA receptor; (83) the pharmaceutical composition according to the above (80), wherein it is an inhibitor to an kainate receptor; (84) the pharmaceutical composition according to the above (80), which is a therapeutic or preventive agent for the diseases in which an AMPA receptor or a kainate receptor is participated; (85) the pharmaceutical composition according to the above (80), which is a therapeutic or preventive agent for the diseases in which an AMPA receptor is participated; (86) the pharmaceutical composition according to the above (80), which is a therapeutic or preventive agent for acute neurodegenerative disease; (87) the pharmaceutical composition according to the above (80), which is a therapeutic or preventive agent for cerebrovascular disorders at acute stage, head injury, spinal cord injury, neuropathies due to hypoxia or hypoglycemia; (88) the pharmaceutical composition according to the above (80), which is a therapeutic or preventive agent for chronic neurodegenerative disease; (89) the pharmaceutical composition according to the above (80), which is a therapeutic or preventive agent for Alzheimer's disease, Parkinson's disease, Huntington's chorea, amyotrophic lateral sclerosis or spinocerebellar degeneration; (90) the pharmaceutical composition according to

the above (80), which is an agent for treating or preventing epilepsy, hepatic encephalopathy, peripheral neuropathy, Parkinson's syndrome, spasticity, pain, neuralgia, schizophrenia, anxiety, drug abuse, nausea, emesis, dysuria, paropsia caused by glaucoma, paraculis caused by antibiotics or food poisoning; (91) the pharmaceutical composition according to the above (80), which is an agent for treating or preventing infectious encephalomyelitis, cerebrovascular senile dementia or dementia or neurosis caused by cerebrospinal meningitis; (92) the pharmaceutical composition according to the above (91), wherein the infectious encephalomyelitis is HIV encephalomyelitis; (93) the pharmaceutical composition according to the above (80), which is an agent for treating or preventing demyelinating disease; (94) the pharmaceutical composition according to the above (93), wherein the demyelinating disease is encephalitis, acute disseminated encephalomyelitis, multiple sclerosis, acute polyradiculoneuritis, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy, Marchifava-Bignami disease, central pontine myelinolysis, neuromyelitis optica, Devic disease, Balo disease, HIV myelopathy, HTLV myelopathy, progressive multifocal leukoencephalopathy or secondary demyelinating disease; (95) the pharmaceutical composition according to the above (94), wherein the secondary demyelinating disease is CNS erythematodes, polyarteritis nodosa, Sjogren's syndrome, sarcoidosis or isolated cerebral

65702-519

vasculitis; and the like.

The present invention also relates to a pharmaceutical composition comprising a compound as described herein, or a pharmaceutically acceptable salt thereof or a hydrate thereof, and a pharmaceutically acceptable carrier.

5 The present invention further relates to a use of a compound of the invention as described herein, or a pharmaceutically acceptable salt thereof or a hydrate thereof, for the manufacture of a medicament.

 The present invention provides in an embodiment a process for preventing or treating diseases in which AMPA receptor or kainate receptor is
10 participated, by dosing a pharmacologically effective dose of the compound represented by the formula (I), a salt thereof or hydrates thereof to a patient.

Compounds represented by the formula (I), a salt thereof or hydrates thereof may be used for producing a therapeutic or preventive agent for diseases in which AMPA receptor or kainate receptor is participated.

15 In the present invention, "the disease(s) in which AMPA receptor or kainate receptor is participated" may include acute neurodegenerative disease; cerebrovascular disorders at acute stage; head injury; spinal cord injury; and neuropathies due to hypoxia or hypoglycemia; chronic neurodegenerative disease; Alzheimer's disease; Parkinson's disease; Huntington's chorea; amyotrophic lateral
20 sclerosis; spinocerebellar degeneration; epilepsy; hepatic encephalopathy; peripheral neuropathy; Parkinson's syndrome; spasticity; pain; neuralgia; schizophrenia; anxiety; drug abuse; nausea; emesis; dysuria; paropsia caused by glaucoma; paraculis caused by antibiotics; food poisoning; infectious encephalomyelitis; cerebrovascular dementia; dementia or neurosis caused by meningitis; and
25 demyelinating diseases.

Detailed Description of the Invention

As hereunder, meanings of the symbols, terms, etc. mentioned in the specification of this application will be explained, whereby the present invention will be illustrated in detail.

As "acute neurodegenerative disease" in the present invention, for example, cerebrovascular disorders at acute stage (subarachnoid hemorrhage, cerebral infarction and the like), head injury, spinal cord injury, and neuropathies due to hypoxia or hypoglycemia; and the like are mentioned. As "chronic neurodegenerative disease", for example, Alzheimer's disease, Parkinson's disease, Huntington's chorea, amyotrophic lateral sclerosis, spinocerebellar degeneration and the like are mentioned. As "infectious encephalomyelitis", for example, HIV encephalomyelitis is mentioned, and as "demyelinating disease", for example, encephalitis, acute disseminated encephalomyelitis, multiple sclerosis, acute polyradiculoneuritis, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy, Marchifava-Bignami disease, central pontine myelinolysis, neuromyelitis optica, Devic disease, Balo disease, HIV myelopathy, HTLV myelopathy, progressive multifocal leukoencephalopathy, secondary demyelinating disease and the like are mentioned. As "the secondary demyelinating disease" mentioned above, for example, CNS lupus erythematoses, polyarteritis nodosa, Sjogren's syndrome, sarcoidosis, isolated cerebral

vasculitis and the like are mentioned.

The term "and/or" used in the present invention is used in the meaning that both cases in case of "and" and in case of "or" are included.

Incidentally, in the specification of this application, although structural formula of a compound may express a certain isomer for the sake of convenience, the present invention covers all isomers such as geometrical isomers resulted from the structure of the compound, optical isomers due to asymmetric carbon, rotamers, stereo isomers and tautomers as well as a mixture of isomers and the present invention is not limited to the description of the formula given for the sake of convenience but may be another isomer or may be a mixture. Accordingly, although it is possible that an asymmetric carbon atom is present in a molecule and accordingly that optically active substance and racemic substance may be present, the present invention is not limited thereto but covers any of them. Further, crystal polymorphism may be present but, again, there is no limitation but any of single crystal form or a mixture will do. The compound (I) or its salt related to the present invention may be an anhydride or a hydrate, and either of them are included in the scope of claim for patent in the present invention. The metabolite which is generated by decomposing the compound (I) related to the present invention *in vivo*, and the prodrug of the compound (I) or its salt related to the present invention produce are also included in the scope of claim for

patent in the present invention.

The "halogen atom" used in the present invention indicates fluorine, chlorine, bromine, iodine and the like, and the preferable atom include fluorine, chlorine and bromine.

The " C_{1-6} alkyl group" used in the present invention indicates an alkyl group having 1 to 6 carbons, and examples include linear chain or branched chain alkyl groups such as methyl group, ethyl group, n-propyl group, iso-propyl group, n-butyl group, iso-butyl group, sec-butyl group, tert-butyl group, n-pentyl group, 1,1-dimethylpropyl group, 1,2-dimethylpropyl group, 2,2-dimethylpropyl group, 1-ethylpropyl group, 2-ethylpropyl group, n-hexyl group, 1-methyl-2-ethylpropyl group, 1-ethyl-2-methylpropyl group, 1,1,2-trimethylpropyl group, 1-propylpropyl group, 1-methylbutyl group, 2-methylbutyl group, 1,1-dimethylbutyl group, 1,2-dimethylbutyl group, 2,2-dimethylbutyl group, 1,3-dimethylbutyl group, 2,3-dimethylbutyl group, 2-ethylbutyl group, 2-methylpentyl group, 3-methylpentyl group, and the like.

The " C_{2-6} alkenyl group" used in the present invention indicates an alkenyl group having 2 to 6 carbons, and examples of the preferable group include vinyl group, allyl group, 1-propenyl group, 2-propenyl group, iso-propenyl group, 2-methyl-1-propenyl group, 3-methyl-1-propenyl group, 2-methyl-2-propenyl group, 3-methyl-2-propenyl group, 1-butenyl group, 2-butenyl group, 3-butenyl group, 1-pentenyl group,

65702-519

1-hexenyl group, 1,3-hexadienyl group, 1,6-hexadienyl group, and the like.

The " C_{2-6} alkynyl group" used in the present invention indicates an alkynyl group having 2 to 6 carbons, and examples of the preferable group include ethynyl group, 1-propynyl group, 2-propynyl group, 1-butylnyl group, 2-butylnyl group, 3-butylnyl group, 3-methyl-1-propynyl group, 1-ethynyl-2-propynyl group, 2-methyl-3-propynyl group, 1-pentylnyl group, 1-hexynyl group, 1,3-hexadiynyl group, 1,6-hexadiynyl group, and the like.

The " C_{1-6} alkoxy group" used in the present invention indicates an alkoxy group having 1 to 6 carbons, and examples include methoxy group, ethoxy group, n-propoxy group, iso-propoxy group, sec-propoxy group, n-butoxy group, iso-butoxy group, sec-butoxy group, tert-butoxy group, n-pentyloxy group, iso-pentyloxy group, sec-pentyloxy group, n-hexoxy group, iso-hexoxy group, 1,1-dimethylpropoxy group, 1,2-dimethylpropoxy group, 2,2-dimethylpropoxy group, 2-ethylpropoxy group, 1-methyl-2-ethylpropoxy group, 1-ethyl-2-methylpropoxy group, 1,1,2-trimethylpropoxy group, 1,1-dimethylbutoxy group, 1,2-dimethylbutoxy group, 2,2-dimethylbutoxy group, 2,3-dimethylbutoxy group, 1,3-dimethylbutoxy group, 2-ethylbutoxy group, 1,3-dimethylbutoxy group, 2-methylpentoxy group, 3-methylpentoxy group, hexyloxy group, and the like.

The " C_{2-6} alkenyloxy group" used in the present invention indicates an alkenyloxy group having 2 to 6 carbons, and

examples of the preferable group include vinyloxy group, allyloxy group, 1-propenyloxy group, 2-propenyloxy group, iso-propenyloxy group, 2-methyl-1-propenyloxy group, 3-methyl-1-propenyloxy group, 2-methyl-2-propenyloxy group, 3-methyl-2-propenyloxy group, 1-butenyloxy group, 2-butenyloxy group, 3-butenyloxy group, 1-pentenyloxy group, 1-hexenyloxy group, 1,3-hexadienyloxy group, 1,6-hexadienyloxy group, and the like.

The "C₃₋₈ cycloalkyl group" used in the present invention indicates a cycloalkyl group composed of 3 to 8 carbon atoms, and examples include cyclopropyl group, cyclobutyl group, cyclopentyl group, cyclohexyl group, cycloheptyl group, cyclooctyl group, and the like.

The "C₃₋₈ cycloalkenyl group" used in the present invention indicates a C₃₋₈ cycloalkenyl group composed of 3 to 8 carbon atoms, and examples include cyclopropen-1-yl, cyclopropen-3-yl, cyclobuten-1-yl, cyclobuten-3-yl, 1,3-cyclobutadien-1-yl, cyclopenten-1-yl, cyclopenten-3-yl, cyclopenten-4-yl, 1,3-cyclopentadien-1-yl, 1,3-cyclopentadien-2-yl, 1,3-cyclopentadien-5-yl, cyclohexen-1-yl, cyclohexen-3-yl, cyclohexen-4-yl, 1,3-cyclohexadien-1-yl, 1,3-cyclohexadien-2-yl, 1,3-cyclohexadien-5-yl, 1,4-cyclohexadien-3-yl, 1,4-cyclohexadien-1-yl, cyclohepten-1-yl, cyclohepten-3-yl, cyclohepten-4-yl, cyclohepten-5-yl, 1,3-cyclohepten-2-yl, 1,3-cyclohepten-1-yl, 1,3-cycloheptadien-5-yl, 1,3-cycloheptadien-6-yl, 1,4-cycloheptadien-3-yl, 1,4-

65702-519

cycloheptadien-2-yl, 1,4-cycloheptadien-1-yl, 1,4-cycloheptadien-6-yl, 1,3,5-cycloheptatrien-3-yl, 1,3,5-cycloheptatrien-2-yl, 1,3,5-cycloheptatrien-1-yl, 1,3,5-cycloheptatrien-7-yl, cycloocten-1-yl, cycloocten-3-yl, cycloocten-4-yl, cycloocten-5-yl, 1,3-cyclooctadien-2-yl, 1,3-cyclooctadien-1-yl, 1,3-cyclooctadien-5-yl, 1,3-cyclooctadien-6-yl, 1,4-cyclooctadien-3-yl, 1,4-cyclooctadien-2-yl, 1,4-cyclooctadien-1-yl, 1,4-cyclooctadien-6-yl, 1,4-cyclooctadien-7-yl, 1,5-cyclooctadien-3-yl, 1,5-cyclooctadien-2-yl, 1,3,5-cyclooctatrien-3-yl, 1,3,5-cyclooctatrien-2-yl, 1,3,5-cyclooctatrien-1-yl, 1,3,5-cyclooctatrien-7-yl, 1,3,6-cyclooctatrien-2-yl, 1,3,6-cyclooctatrien-1-yl, 1,3,6-cyclooctatrien-5-yl, 1,3,6-cyclooctatrien-6-yl group, and the like.

The "5 to 14 membered non-aromatic heterocyclic group" used in the present invention means a mono-cyclic type, di-cyclic type, or tri-cyclic type 5 to 14 membered non-aromatic heterocyclic group which contains one or more of hetero atoms selected from a group which consists of nitrogen atom, sulfur atom and oxygen atom. Specific examples in the group include, for example, pyrrolidinyl group, pyrrolinyl group, piperidyl group, piperazinyl group, imidazolidinyl group, pyrazolidinyl group, morpholinyl group, tetrahydrofuryl group, tetrahydropyranyl group, dihydrofuryl group, dihydropyranyl group, imidazolinyl group, oxazolinyl group,

and the like. Further, a group derived from a pyridone ring and a non-aromatic condensed ring (for example, a group derived from a phthalimide ring, a succinimide ring, and the like) are also included in the non-aromatic heterocyclic group.

The "C₆₋₁₄ aromatic hydrocarbocyclic group" and the "aryl group" used in the present invention mean an aromatic hydrocarbocyclic group having which is composed of 6 to 14 carbon atoms, and a mono-cyclic group, and a condensed group of a di-cyclic group, a tri-cyclic group and the like are also included. Specific examples in the group include phenyl group, indenyl group, 1-naphthyl group, 2-naphthyl group, azulenyl group, heptalenyl group, biphenyl group, indathenyl group, acenaphthyl group, fluorenyl group, phenalenyl group, phenanthrenyl group, anthracenyl group, cyclopentacyclooctenyl group, benzocyclooctenyl group etc.

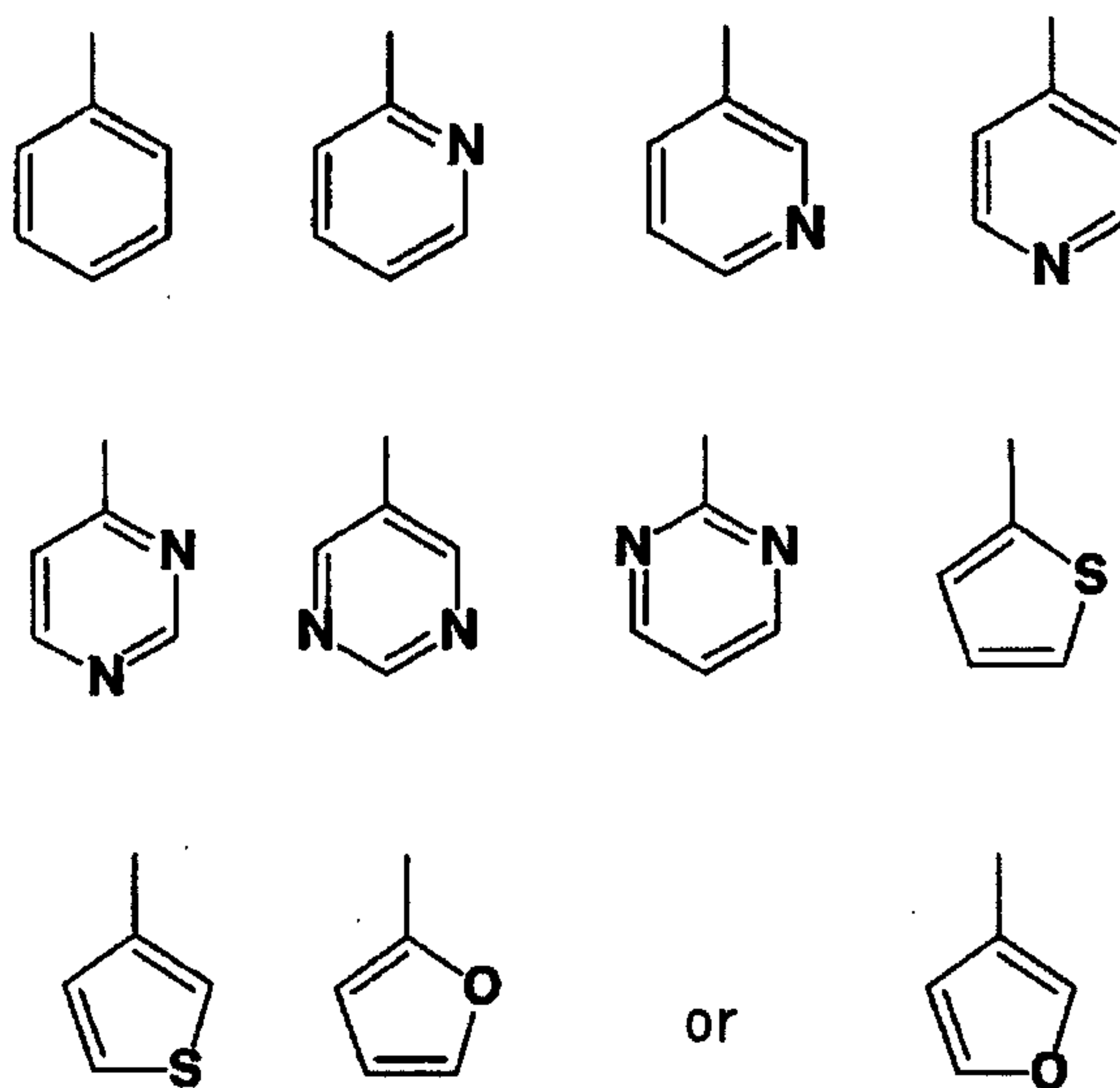
The "5 to 14 membered aromatic heterocyclic group" and the "heteroaryl group" used in the present invention mean a mono-cyclic type, di-cyclic type, or tri-cyclic type 5 to 14 membered aromatic heterocyclic group which contains one or more of hetero atoms selected from a group which consists of nitrogen atom, sulfur atom and oxygen atom. For example, specific examples in the group include 1) aromatic heterocyclic groups containing nitrogen such as pyrrolyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, triazolyl group, tetrazolyl group, benzotriazolyl group, pyrazolyl group, imidazolyl group, benzimidazolyl group,

65702-519

indolyl group, iso-indolyl group, indolizinyll group, prenyl group, indazolyl group, quinolyl group, iso-quinolyl group, quinoliziniyl group, phthalazyl group, naphthylidinyll group, quinoxalyl group, quinazolinyl group, cynnolinyll group, pteridinyl group, imidazotriazinyl group, pyrazinopyridazinyl group, acridinyl group, phenanthridinyl group, carbazolyl group, carbazolinyl group, perimidinyl group, phenanthrolinyl group, phenacinyll group, imidazopyridinyl group, imidazopyrimidinyl group, pyrazolopyridinyl group, pyrazolopyridinyl group etc; 2) aromatic heterocyclic groups containing sulfur such as thienyl group or benzothienyl group; 3) aromatic heterocyclic groups containing oxygen such as furyll group, pyranyl group, cyclopentapyranyl group, benzofuryll group or iso-benzofuryll group; and 4) aromatic heterocyclic groups containing 2 or more of different hetero atoms such as thiazolyl group, iso-thiazolyl group, benzothiazolyl group, benzthiadiazolyl group, phenothiazinyl group, isoxazolyl group, furazanyl group, phenoxazinyl group, oxazolyl group, isoxazolyl group, benzoxazolyl group, oxadiazolyl group, pyrazoloxadiazolyl group, imidazothiazolyl group, thienofuranyl group, furopyrrrolyl group or pyridoxadinyl group.

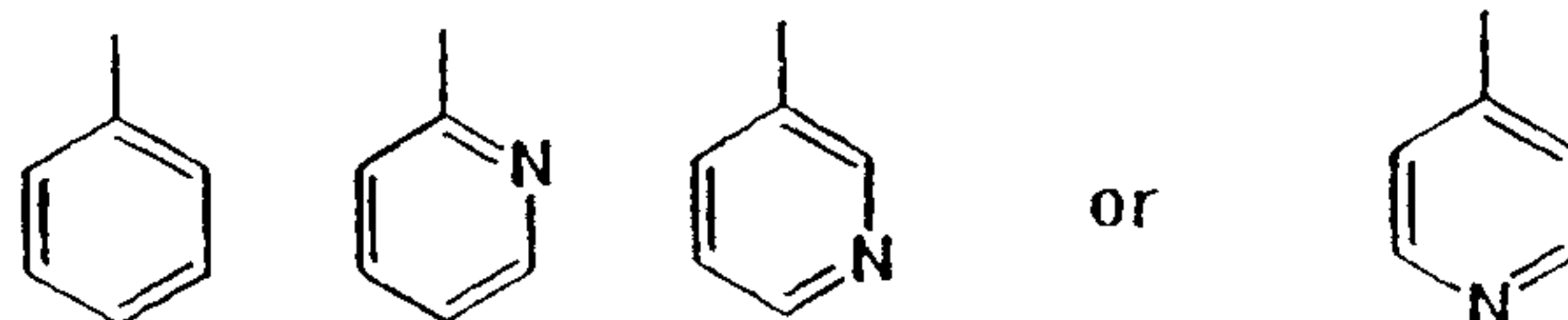
The groups indicated by A, A¹, A² and A³ in the formula (I) and (II) in the present invention indicate independently an optionally substituted C₃₋₈ cycloalkyl group, an optionally substituted C₃₋₈ cycloalkenyl group, an optionally substituted

5 to 14 membered non-aromatic heterocyclic group, an optionally substituted C_{6-14} aromatic hydrocarbocyclic group or an optionally substituted 5 to 14 membered aromatic heterocyclic group, and each of the groups has the same meanings as the above definitions, respectively. The preferable group in A, A¹, A² and A³ is not specifically limited, but the more preferable group includes phenyl group, pyrrolyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, thienyl group, thiazolyl group, furyl group, naphthyl group, quinolyl group, iso-quinolyl group, indolyl group, benzimidazolyl group, benzothiazolyl group, benzoxazolyl group, imidazopyridyl group, carbazolyl group, cyclopentyl group, cyclohexyl group, cyclohexenyl group, dioxinyl group, adamantyl group, pyrrolidinyl group, piperidinyl group, piperazinyl group and morpholinyl group which may be substituted, respectively, etc. The more preferable group includes a group represented by the formula:



65702-519

which may optionally have substituents respectively, etc., and the most preferable group includes a group represented by the formula:



which may optionally have substituents respectively, etc.

Examples of the preferable group in the "substituents" of the groups indicated by A, A¹, A² and A³ in the formula (I) and (II) include a group such as hydroxy group, a halogen atom, nitrile group, nitro group, a C₁₋₆ alkyl group, C₂₋₆ alkenyl group, C₂₋₆ alkynyl group, C₁₋₆ alkoxy group, C₂₋₆ alkenyloxy group, C₂₋₆ alkynyloxy group, C₁₋₆ alkylthio group, C₂₋₆ alkenylthio group, C₂₋₆ alkynylthio group, amino group, a substituted carbonyl group, C₁₋₆ alkylsulfonyl group, C₂₋₆ alkenylsulfonyl group, C₂₋₆ alkynylsulfonyl group, C₁₋₆ alkylsulfinyl group, C₂₋₆ alkenylsulfinyl group, C₂₋₆ alkynylsulfinyl group, formyl group, aralkyl group, heteroarylalkyl group, aralkyloxy group, heteroarylalkyloxy group, C₃₋₈ cycloalkyl group, C₃₋₈ cycloalkenyl group, 5 to 14 membered non-aromatic heterocyclic group, C₆₋₁₄ aromatic hydrocarbon group, 5 to 14 membered aromatic heterocyclic group etc., which may be substituted, respectively.

Also included within the scope are compounds wherein the bonding site of the substituent at A¹, A² and/or A³ are at the α position of the carbon atom bonding to the group X¹, X² and X³, respectively.

Examples of the preferable group in the "halogen atom" include fluorine atom, chlorine atom, bromine atom, iodine atom etc., and the more preferable example includes fluorine atom,

chlorine atom and bromine atom.

Examples of the preferable group in the "C₁₋₆ alkyl group which may optionally have substituents" include methyl group, ethyl group, n-propyl group, iso-propyl group, n-butyl group, iso-butyl group, tert-butyl group, n-pentyl group, iso-pentyl group, neopentyl group, n-hexyl group, 1-methylpropyl group, 1,2-dimethylpropyl group, 2-ethylpropyl group, 1-methyl-2-ethylpropyl group, 1-ethyl-2-methylpropyl group, 1,1,2-trimethylpropyl group, 1-methylbutyl group, 2-methylbutyl group, 1,1-dimethylbutyl group, 2,2-dimethylbutyl group, 2-ethylbutyl group, 1,3-dimethylbutyl group, 2-methylpentyl group, 3-methylpentyl group etc. Examples of the preferable group in the "C₂₋₆ alkenyl group which may optionally have substituents" include a vinyl group, allyl group, 1-propenyl group, iso-propenyl group, 1-buten-1-yl group, 1-buten-2-yl group, 1-buten-3-yl group, 2-buten-1-yl group, 2-buten-2-yl group etc., which may be substituted, respectively. Examples of the preferable group in the "C₂₋₆ alkynyl group which may optionally have substituents respectively" include an ethynyl group, 1-propynyl group, 2-propynyl group, butynyl group, pentynyl group, hexynyl group etc., which may be substituted, respectively. Further, preferable examples of the "substituents" in the "which may optionally have substituents" include 1 or more groups selected from hydroxy group, nitrile group, a halogen atom, an N-C₁₋₆ alkylamino group, an N,N-di-C₁₋₆ alkylamino group, an N-C₂₋₆ alkenylamino group, an N,N-di-C₂₋₆

65702-519

alkenylamino group, an N-C₂₋₆ alkynylamino group, an N,N-di-C₂₋₆ alkynylamino group, a C₆₋₁₄ aromatic hydrocarbocyclic group (for example, phenyl group etc.), a 5 to 14 membered aromatic heterocyclic group (for example, thienyl group, furyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group etc.), an aralkyloxy group, a heteroaryloxy group, a TBDMS-oxy group, a C₁₋₆ alkylsulfonylamino group, a C₂₋₆ alkenylsulfonylamino group, a C₂₋₆ alkynylsulfonylamino group, a C₁₋₆ alkylcarbonyloxy group, a C₂₋₆ alkenylcarbonyloxy group, a C₂₋₆ alkynylcarbonyloxy group, a C₁₋₆ alkylcarbamoyl group, a C₂₋₆ alkenylcarbamoyl group, a C₂₋₆ alkynylcarbamoyl group, and the like.

Preferable examples in the "C₁₋₆ alkoxy group which may optionally have substituents" include methoxy group, ethoxy group, n-propoxy group, iso-propoxy group, sec-propoxy group, n-butoxy group, iso-butoxy group, sec-butoxy group, tert-butoxy group, n-pentoxy group, iso-pentoxy group, sec-pentoxy group, tert-pentoxy group, n-hexoxy group, iso-hexoxy group, 1,2-dimethylpropoxy group, 2-ethylpropoxy group, 1-methyl-2-ethylpropoxy group, 1-ethyl-2-methylpropoxy group, 1,1,2-trimethylpropoxy group, 1,1-dimethylbutoxy group, 2,2-dimethylbutoxy group, 2-ethylbutoxy group, 1,3-dimethylbutoxy group, 2-methylpentoxy group, 3-methylpentoxy group, hexyloxy group etc. Preferable examples in the "C₂₋₆ alkenyloxy group which may optionally have substituents" include vinyloxy group, allyloxy group, 1-propenyloxy group, iso-propenyloxy group,

1-buten-1-yloxy group, 1-buten-2-yloxy group, 1-buten-3-yloxy group, 2-buten-1-yloxy group, 2-buten-2-yloxy group etc. Preferable examples in the "C₂₋₆ alkynyloxy group which may optionally have substituents" include ethynyloxy group, 1-propynyloxy group, 2-propynyloxy group, butynyloxy group, pentynyloxy group, hexynyloxy group etc. Further, preferable examples of the "substituents" in the "which may optionally have substituents" include 1 or more groups selected from an C₁₋₆ alkylamino group, an aralkyloxy group, hydroxy group, and the like.

Respectively preferable examples in the "C₁₋₆ alkylthio group which may optionally have substituents", "C₂₋₆ alkenylthio group which may optionally have substituents" and "C₂₋₆ alkynylthio group which may optionally have substituents" include a C₁₋₆ alkylthio group (for example, methylthio group, ethylthio group, n-propylthio group, iso-propylthio group, n-butylthio group, iso-butylthio group, tert-butylthio group, n-pentylthio group, iso-pentylthio group, neopentylthio group, n-hexylthio group etc.), a C₂₋₆ alkenylthio group (for example, vinylthio group, allylthio group, 1-propenylthio group, iso-propenylthio group, 1-buten-1-ylthio group, 1-buten-2-ylthio group, 1-buten-3-ylthio group, 2-buten-1-ylthio group, 2-buten-2-ylthio group etc.) and a C₂₋₆ alkynylthio group (for example, ethynylthio group, 1-propynylthio group, 2-propynylthio group, butynylthio group, pentynylthio group, hexynylthio group etc.), which may be optionally substituted

by 1 or more groups selected from the group consisting of hydroxy group, a halogen atom, nitrile group and nitro group.

Preferable examples in the "carbonyl group which was substituted" include a group which is represented by the formula -CO-W (examples of W in the formula include a C₁₋₆ alkyl group, a C₂₋₆ alkenyl group, a C₂₋₆ alkynyl group, a C₁₋₆ alkoxy group, amino group, an N-C₁₋₆ alkylamino group, an N,N-di(C₁₋₆ alkyl)amino group, an N-C₂₋₆ alkenylamino group, an N,N-di(C₂₋₆ alkenyl)amino group, an N-C₂₋₆ alkynylamino group, an N,N-di(C₂₋₆ alkynyl)amino group, an N-C₁₋₆ alkyl-N-C₂₋₆ alkenylamino group, an N-C₁₋₆ alkyl-N-C₂₋₆ alkynylamino group, an N-C₂₋₆ alkenyl-N-C₂₋₆ alkynylamino group etc.).

Examples of the "substituents" in the "amino group which may optionally have substituents" include 1 or 2 groups selected from a C₁₋₆ alkyl group, C₂₋₆ alkenyl group, C₂₋₆ alkynyl group, C₁₋₆ alkylsulfonyl group, C₂₋₆ alkenylsulfonyl group, C₂₋₆ alkynylsulfonyl group, C₁₋₆ alkylcarbonyl group, C₂₋₆ alkenylcarbonyl group, C₂₋₆ alkynylcarbonyl group etc., which may be substituted, respectively. Preferable examples in the "substituents" of the C₁₋₆ alkyl group, C₂₋₆ alkenyl group, C₂₋₆ alkynyl group, C₁₋₆ alkylsulfonyl group, C₂₋₆ alkenylsulfonyl group, C₂₋₆ alkynylsulfonyl group, C₁₋₆ alkylcarbonyl group, C₂₋₆ alkenylcarbonyl group and C₂₋₆ alkynylcarbonyl group include hydroxy group, a halogen atom, nitrile group, a C₁₋₆ alkoxy group, a C₁₋₆ alkylthio group etc. Specifically preferable examples in the "amino group which may optionally have substituents" in

particular include methylamino group, ethylamino group, n-propylamino group, iso-propylamino group, n-butylamino group, iso-butylamino group, tert-butylamino group, n-pentylamino group, iso-pentylamino group, neopentylamino group, n-hexylamino group, 1-methylpropylamino group, 1,2-dimethylpropylamino group, 2-ethylpropylamino group, 1-methyl-2-ethylpropylamino group, 1-ethyl-2-methylpropylamino group, 1,1,2-trimethylpropylamino group, 1-methylbutylamino group, 2-methylbutylamino group, 1,1-dimethylbutylamino group, 2,2-dimethylbutylamino group, 2-ethylbutylamino group, 1,3-dimethylbutylamino group, 2-methylpentylamino group, 3-methylpentylamino group, N,N-dimethylamino group, N,N-diethylamino group, N,N-di(n-propyl)amino group, N,N-di(iso-propyl)amino group, N,N-di(n-butyl)amino group, N,N-di(iso-butyl)amino group, N,N-di(tert-butyl)amino group, N,N-di(n-pentyl)amino group, N,N-di(iso-pentyl)amino group, N,N-di(neopentyl)amino group, N,N-di(n-hexyl)amino group, N,N-di(1-methylpropyl)amino group, N,N-di(1,2-dimethylpropyl)amino group, N-methyl-N-ethylamino group, N-ethyl-N-(n-propyl)amino group, N-ethyl-N-(iso-propyl)amino group, vinylamino group, allylamino group, (1-propenyl)amino group, iso-propenylamino group, (1-buten-1-yl)amino group, (1-buten-2-yl)amino group, (1-buten-3-yl)amino group, (2-buten-1-yl)amino group, (2-buten-2-yl)amino group, N,N-divinylamino group, N,N-diallylamino group, N,N-di(1-propenyl)amino group, N,N-di(iso-propenyl)amino group, N-

vinyl-N-allylamino group, ethynylamino group, 1-propynylamino group, 2-propynylamino group, butynylamino group, pentynylamino group, hexynylamino group, N,N-diethynylamino group, N,N-di(1-propynyl)amino group, N,N-di(2-propynyl)amino group, N,N-dibutynylamino group, N,N-dipentynylamino group, N,N-dihexynylamino group, hydroxymethylamino group, 1-hydroxyethylamino group, 2-hydroxyethylamino group, 3-hydroxy-n-propylamino group, methylsulfonylamino group, ethylsulfonylamino group, n-propylsulfonylamino group, iso-propylsulfonylamino group, n-butylsulfonylamino group, tert-butylsulfonylamino group, vinylsulfonylamino group, allylsulfonylamino group, iso-propenylsulfonylamino group, iso-pentenylsulfonylamino group, ethynylsulfonylamino group, methylcarbonylamino group, ethylcarbonylamino group, n-propylcarbonylamino group, iso-propylcarbonylamino group, n-butylcarbonylamino group, tert-butylcarbonylamino group, vinylcarbonylamino group, allylcarbonylamino group, iso-propenylcarbonylamino group, iso-pentenylcarbonylamino group, ethynylcarbonylamino group etc.

Respectively preferable examples in the "C₁₋₆ alkylsulfonyl group which may optionally have substituents", "C₂₋₆ alkenylsulfonyl group which may optionally have substituents", "C₂₋₆ alkynylsulfonyl group which may optionally have substituents", "C₁₋₆ alkylsulfinyl group which may optionally have substituents", "C₂₋₆ alkenylsulfinyl group

which may optionally have substituents" and "C₂₋₆ alkynylsulfonyl group which may optionally have substituents" include methylsulfonyl group, ethylsulfonyl group, n-propylsulfonyl group, iso-propylsulfonyl group, n-butylsulfonyl group, tert-butylsulfonyl group, vinylsulfonyl group, allylsulfonyl group, iso-propenylsulfonyl group, iso-pentenylsulfonyl group, ethynylsulfonyl group, methylsulfinyl group, ethylsulfinyl group, n-propylsulfinyl group, iso-propylsulfinyl group, n-butylsulfinyl group, tert-butylsulfinyl group, vinylsulfinyl group, allylsulfinyl group, iso-propenylsulfinyl group, iso-pentenylsulfinyl group, ethynylsulfinyl group etc.

Preferable examples in the "aralkyl group" and "heteroarylalkyl group" include benzyl group, phenethyl group, naphthylmethyl group, naphthylethyl group, pyridylmethyl group, pyridylethyl group, thienylmethyl group, thienylethyl group etc., preferable examples in the "aralkyloxy group" include benzyloxy group, phenethyloxy group, phenylpropoxy group, naphthylmethyloxy group, naphthylethyloxy group, naphthylpropyloxy group etc., and preferable examples in the "heteroarylalkyloxy group" include pyridylmethyloxy group, pyrazinylmethyloxy group, pyrimidinylmethyloxy group, pyrrolylmethyloxy group, imidazolylmethyloxy group, pyrazolylmethyloxy group, quinolylmethyloxy group, iso-quinolylmethyloxy group, fulfuryloxy group, thienylmethyloxy group, thiazolylmethyloxy group etc.

Preferable examples in the "C₃₋₈ cycloalkyl group which may optionally have substituents" and "C₃₋₈ cycloalkenyl group which may optionally have a substituent" include a C₃₋₈ cycloalkyl group (for example, cyclopropyl group, cyclobutyl group, cyclopentyl group, cyclohexyl group, cycloheptyl group, and the like) and a C₃₋₈ cycloalkenyl group (for example, cyclopropenyl group, cyclopentenyl group, cyclohexenyl group, cycloheptenyl group, and the like) which may be optionally substituted respectively by 1 or more groups selected from hydroxy group, a halogen atom, nitrile group, a C₁₋₆ alkyl group (for example, methyl group, ethyl group, n-propyl group, iso-propyl group, n-butyl group, iso-butyl group, tert-butyl group, n-pentyl group, iso-pentyl group, neopentyl group, n-hexyl group etc.), a C₁₋₆ alkoxy group (for example, methoxy group, ethoxy group, n-propoxy group, iso-propoxy group, sec-propoxy group, n-butoxy group, iso-butoxy group, sec-butoxy group, tert-butoxy group, n-pentoxy group, iso-pentoxy group, sec-pentoxy group, tert-pentoxy group, n-hexoxy group etc.), a C₁₋₆ alkoxy C₁₋₆ alkyl group, an aralkyl group (for example, benzyl group, phenethyl group, naphthylmethyl group, naphthylethyl group etc.), and the like.

Preferable examples of the "5 to 14 membered non-aromatic heterocyclic group", "C₆₋₁₄ aromatic hydrocarbocyclic group" and "5 to 14 membered aromatic heterocyclic group" in "an optionally substituted 5 to 14 membered non-aromatic heterocyclic group", "an optionally substituted C₆₋₁₄ aromatic

65702-519

hydrocarbocyclic group" and "an optionally substituted 5 to 14 membered aromatic heterocyclic group" are not specifically limited, but the more preferable "5 to 14 membered non-aromatic heterocyclic group" includes pyrrolidinyl group, pyrrolinyl group, piperidyl group, piperazinyl group, imidazolidinyl group, pyrazolidinyl group, morpholinyl group, phthalimidoyl group, a succinimidoyl group etc.; the more preferable " C_{6-14} aromatic hydrocarbocyclic group" includes phenyl group, indenyl group, naphthyl group, azulenyl group, heptalenyl group, biphenyl group etc.; the more preferable "5 to 14 membered aromatic heterocyclic group" includes pyrrolyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, pyrazolyl group, imidazolyl group, thienyl group, furyl group, thiazolyl group, iso-thiazolyl group, quinolyl group, iso-quinolyl group, indolyl group, benzimidazolyl group, benzothiazolyl group, benzoxazolyl group, carbazolyl group, dioxinyl group etc., respectively. Further, preferable examples of the "substituents" in the "which may optionally have substituents" include 1 or more groups selected from hydroxy group, a halogen atom (for example, fluorine atom, chlorine atom, bromine atom, iodine atom etc.), nitrile group, a C_{1-6} alkyl group (for example, methyl group, ethyl group, n-propyl group, iso-propyl group, n-butyl group, iso-butyl group, tert-butyl group, n-pentyl group, iso-pentyl group, neopentyl group, n-hexyl group etc.), a C_{1-6} alkoxy group (methoxy group, ethoxy group, n-propoxy group, iso-propoxy

65702-519

group, sec-propoxy group, n-butoxy group, iso-butoxy group, sec-butoxy group, tert-butoxy group, n-pentoxy group, iso-pentoxy group, sec-pentoxy group, tert-pentoxy group, n-hexoxy group etc.), a C_{1-6} alkoxy C_{1-6} alkyl group (for example, methoxymethyl group, methoxyethyl group, ethoxymethyl group, ethoxyethyl group etc.), an aralkyl group (for example, benzyl group, phenethyl group, naphthylmethyl group, naphthylethyl group etc.), and the like. Further, an amino group, a cyclic amino group, and an alkoxyamino group which may optionally have substituents are also preferable as the substituents.

Q indicates NH, O or S in the formula (I) and (II), and is preferably O.

The groups indicated by X, X^1 , X^2 and X^3 in the present invention indicate the same or different single bonding, an optionally substituted C_{1-6} alkylene group, an optionally substituted C_{2-6} alkenylene group, an optionally substituted C_{2-6} alkynylene group, -O-, -S-, -CO-, -SO-, -SO₂-, -N(R⁶)-, -N(R⁷)-CO-, -CO-N(R⁸)-, -N(R⁹)-CH₂-, -CH₂-N(R¹⁰)-, -CH₂-CO-, -CO-CH₂-, -N(R¹¹)-S(O)_m-, -S(O)_n-N(R¹²)-, -CH₂-S(O)_p-, -S(O)_q-CH₂-, -CH₂-O-, -O-CH₂-, -N(R¹³)-CO-N(R¹⁴)- or -N(R¹⁵)-CS-N(R¹⁶)- (wherein R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹¹, R¹², R¹³, R¹⁴, R¹⁵ and R¹⁶ indicate hydrogen atom, a C_{1-6} alkyl group or a C_{1-6} alkoxy group; and m, n, p and q indicates an integer of 0, 1 or 2 independently).

Specifically preferable examples in the above " C_{1-6} alkylene group" is an alkenylene group having 1 to 3 carbons, and examples include -CH₂-, -(CH₂)₂-, -CH(CH₃)-, -(CH₂)₃-, -

65702-519

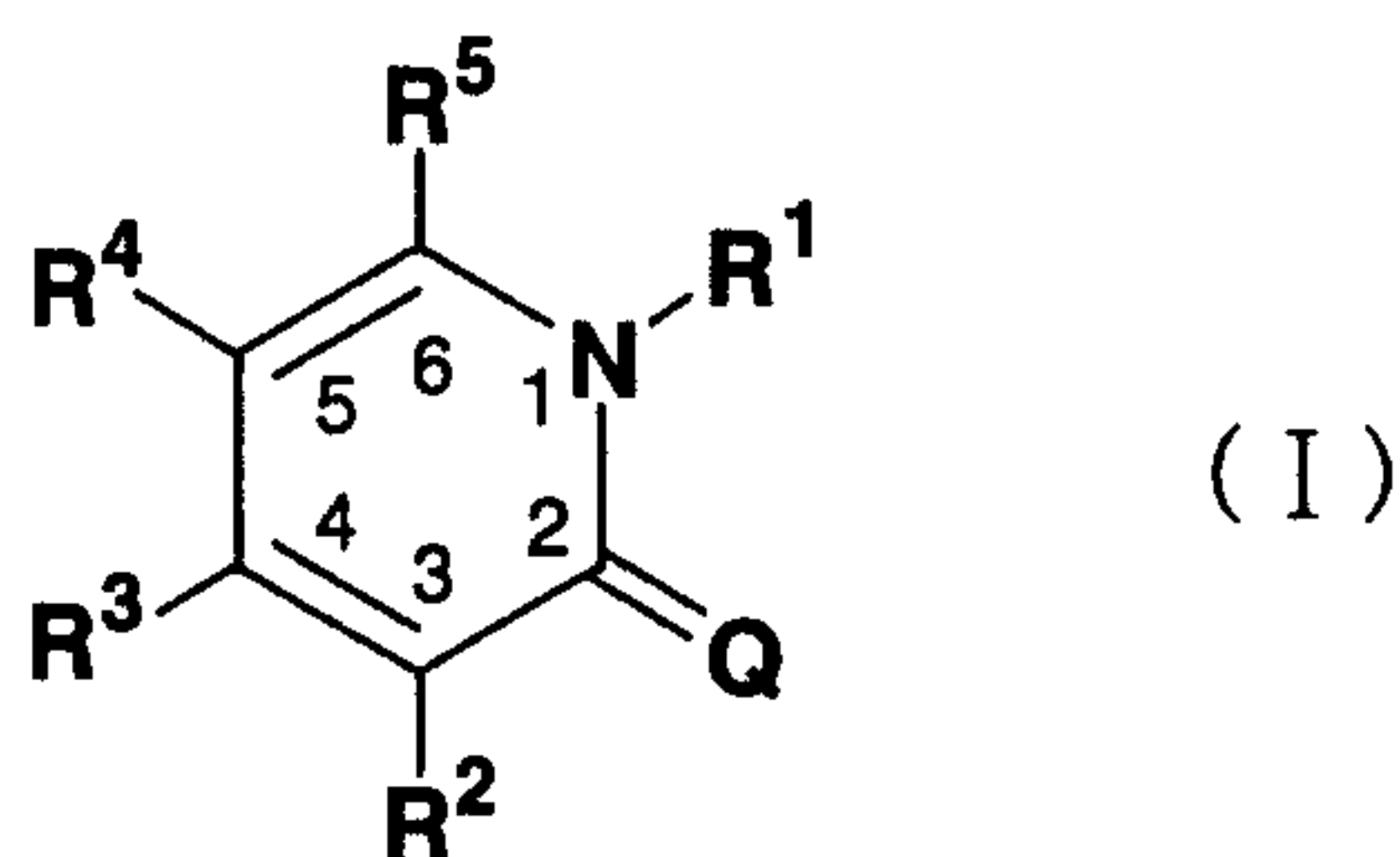
CH(CH₃)-CH₂-, -CH₂-CH(CH₃)- etc. Specifically preferable examples in the above "C₂₋₆ alkenylene group" is an alkenylene group having 2 or 3 carbons, and examples include -CH=CH-, -CH=CH-CH₂-, -CH₂-CH=CH-, -C(CH₃)=CH-, -CH=C(CH₃)- etc. Specifically preferable examples in the above "C₂₋₆ alkynylene group" is an alkynylene group having 2 or 3 carbons, and examples include -C≡C-, -C≡C-CH₂-, -CH₂-C≡C- etc. Preferable examples in the substituents indicated by X, X¹, X² and X³ in the "C₁₋₆ alkylene group which may optionally have substituents", "C₂₋₆ alkenylene group which may optionally have substituents" or "C₂₋₆ alkynylene group which may optionally have substituents" include a halogen atom (for example, fluorine atom, chlorine atom, bromine atom, iodine atom etc.), hydroxy group, nitrile group, nitro group etc.

The preferable C₁₋₆ alkyl group represented by the R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹¹, R¹², R¹³, R¹⁴, R¹⁵ and R¹⁶ includes methyl group, ethyl group, n-propyl group, iso-propyl group, n-butyl group, tert-butyl group etc., and the preferable C₂₋₆ alkoxy group includes methoxy group, ethoxy group, n-propoxy group, iso-propoxy group, n-butoxy group, tert-butoxy group etc.

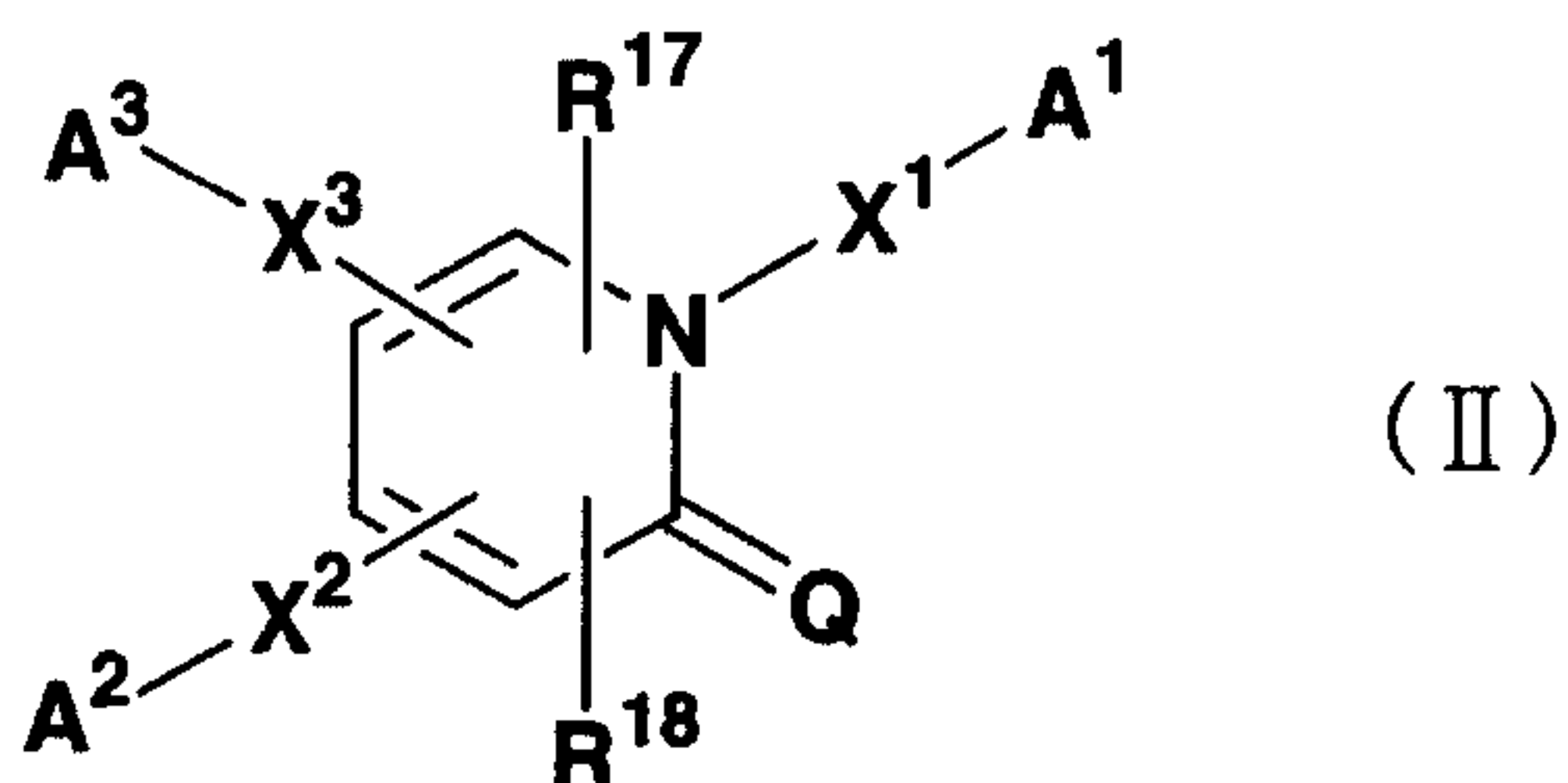
The preferable group in X, X¹, X² and X³ in the above formula (I) and (II) includes single bond, -CH₂-, -CH(OH)-, -CH(CN)-, -CH₂-CH₂-, -CH(OH)-CH₂-, -CH(CN)-CH₂-, -CH₂-CH(OH)-, -CH₂-CH(CN)-, -CH=CH-, -CH=CH-CH₂-, -CH=CH-CH(OH)-, -CH=CH-CH(CN)-, -CH(OH)-CH=CH-, -CH(CN)-CH=CH-, -C≡C-, -O-, -S-, -SO-, -SO₂-, -CO-, -NH-CO-NH-, -NH-CS-NH-, and the like; the more preferable group includes

single bond, $-\text{CH}_2-$, $-\text{CH}(\text{OH})-$, $-\text{CH}(\text{CN})-$, $-\text{CH}_2-\text{CH}_2-$, $-\text{CH}(\text{OH})-\text{CH}_2-$, $-\text{CH}(\text{CN})-\text{CH}_2-$, $-\text{CH}_2-\text{CH}(\text{OH})-$, $-\text{CH}_2-\text{CH}(\text{CN})-$, $-\text{CH}=\text{CH}-$, $-\text{C}\equiv\text{C}-$, $-\text{CO}-$, and the like; the further preferable group are $-\text{CH}_2-$, $-\text{CH}(\text{OH})-$, $-\text{CO}-$, and a single bond is most preferable.

The preferable mode of in the compound according to the present invention represented by the formula:

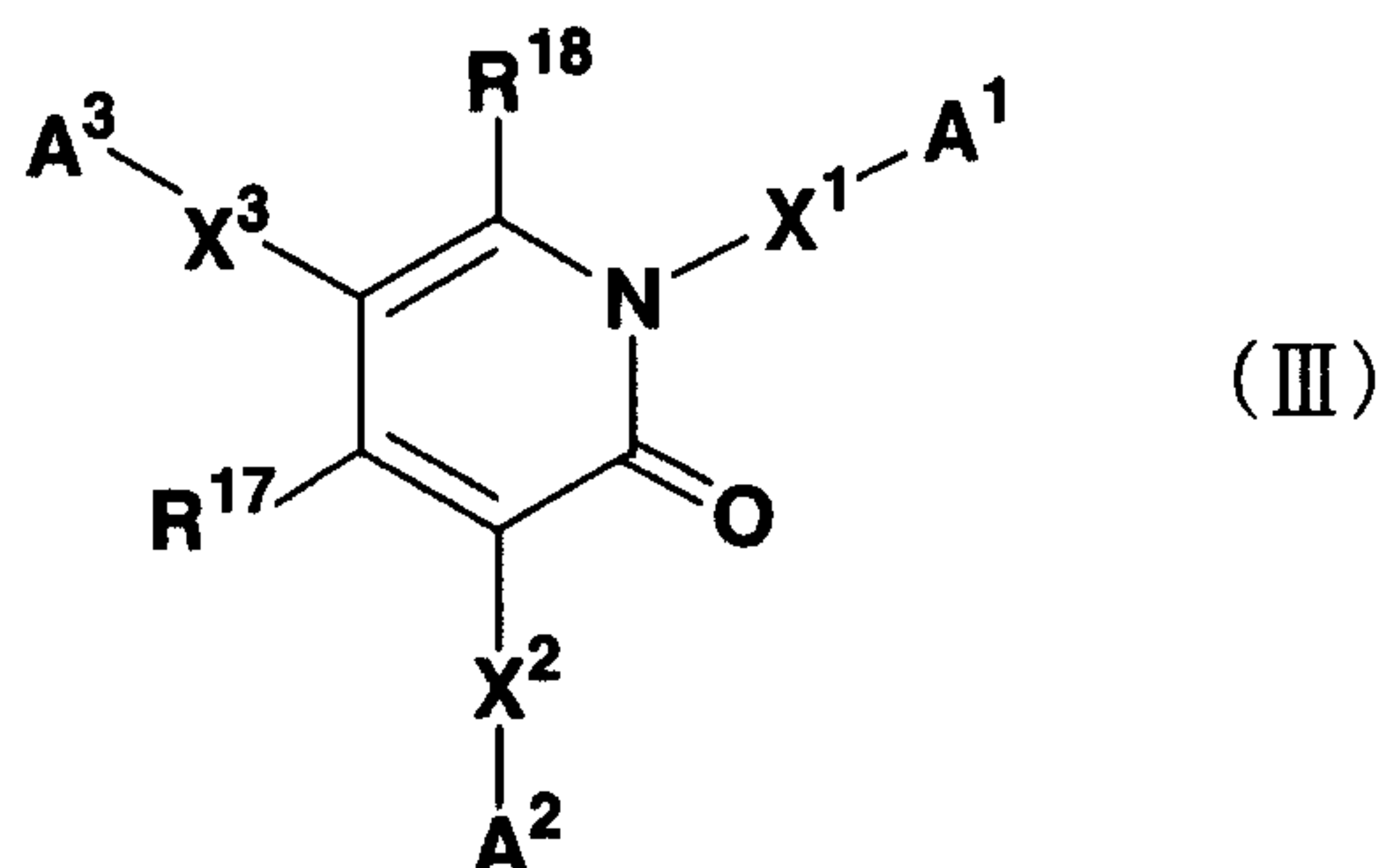


(wherein Q , R^1 , R^2 , R^3 , R^4 and R^5 have the same meanings as defined above), a salt thereof or hydrates thereof is not specifically limited. Among them, the preferable mode includes the compound, a salt thereof or hydrates thereof, wherein R^1 (namely, 1-position of a pyridone ring) is a group represented by the formula $-\text{X}-\text{A}$ (X and A have the same meanings as defined above), two of the residual R^2 , R^3 , R^4 and R^5 are a group represented by the formula $-\text{X}-\text{A}$ (X and A have the same meanings as defined above), and the other two are hydrogen atom, a halogen atom or a C_{1-6} alkyl group; namely, the compound represented by the formula:

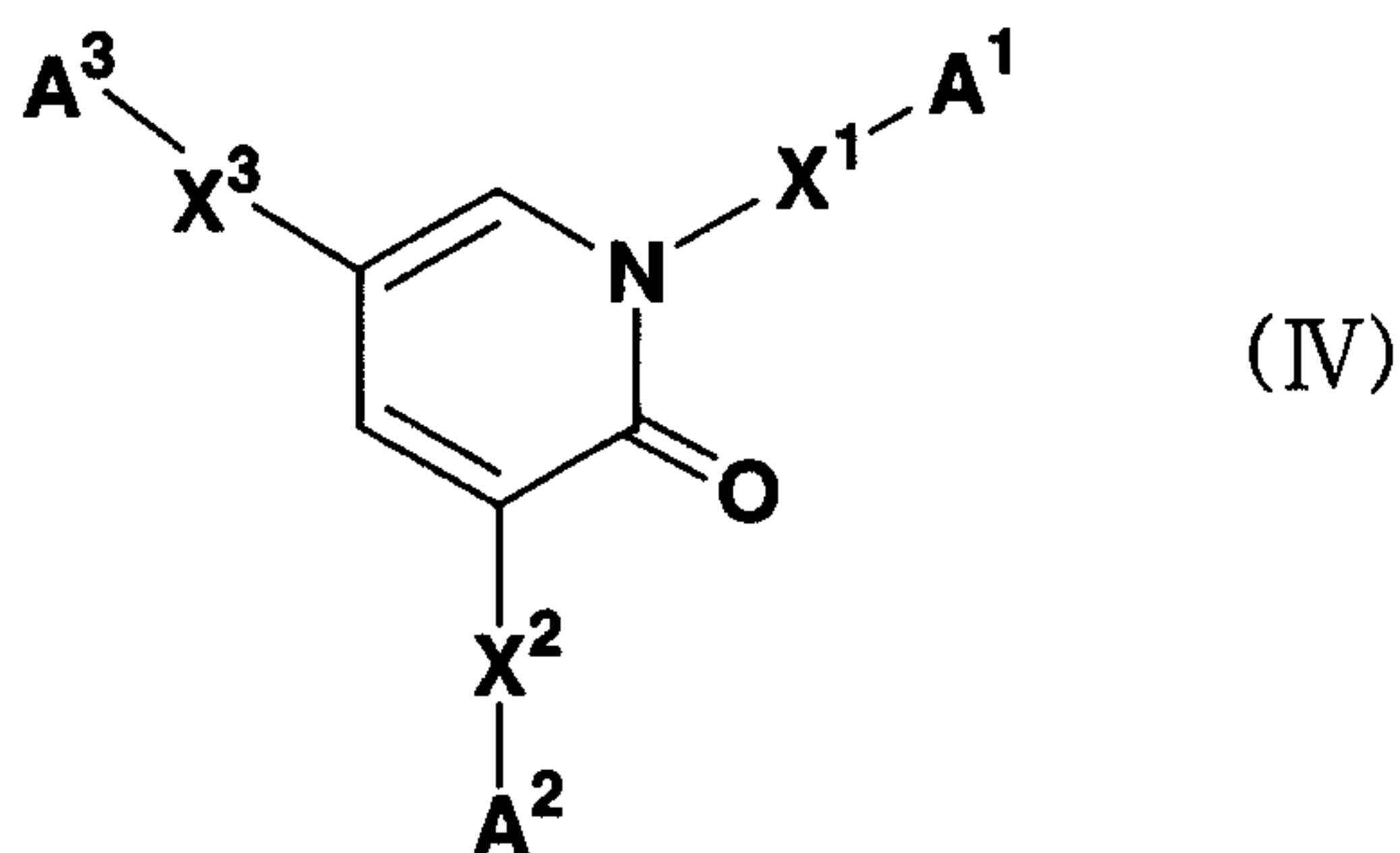


(wherein Q , X^1 , X^2 , X^3 , A^1 , A^2 , A^3 , R^{17} and R^{18} have the same meanings

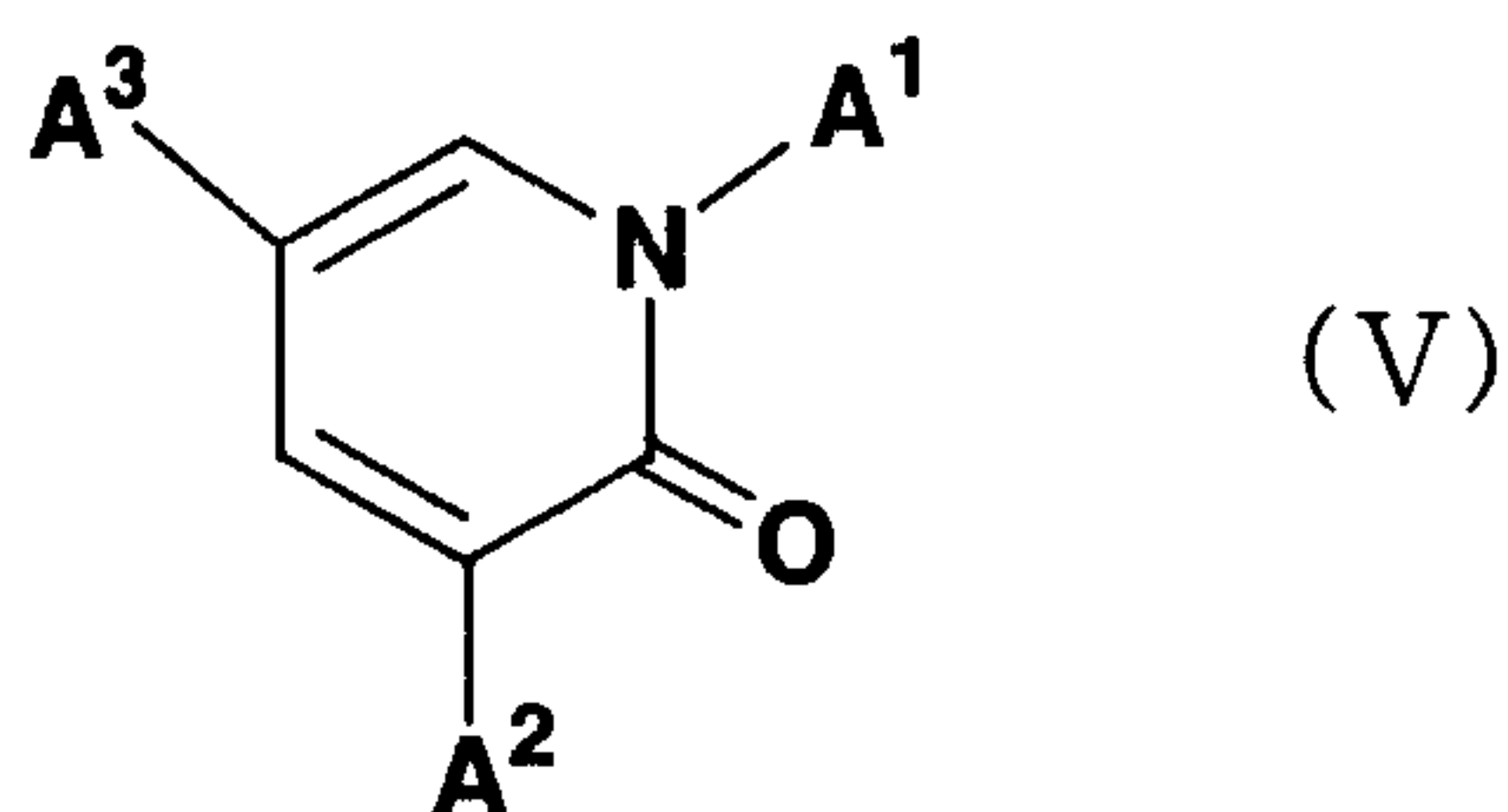
as defined above), a salt thereof or hydrates thereof. The more preferable mode includes the compound, a salt thereof or hydrates thereof, wherein Q is oxygen in the above formula (II); namely, the pyridone compound represented by the formula:



(wherein X^1 , X^2 , X^3 , A^1 , A^2 , A^3 , R^{17} and R^{18} have the same meanings as defined above), a salt thereof or hydrates thereof. The further preferable mode includes the compound, a salt thereof or hydrates thereof, wherein R^{17} and R^{18} are hydrogen atoms in the above formula (III); namely, 1,3,5-substituted pyridone compound represented by the formula:



(wherein X^1 , X^2 , X^3 , A^1 , A^2 and A^3 have the same meanings as defined above), a salt thereof or hydrates thereof. The most preferable mode includes the compound, a salt thereof or hydrates thereof, wherein X^1 , X^2 and X^3 are single bonds in the above formula (IV); namely, 1,3,5-substituted pyridone compound represented by the formula:



(wherein A^1 , A^2 and A^3 have the same meanings as defined above), a salt thereof or hydrates thereof. The preferable groups in A^1 , A^2 and A^3 are as in the above exemplification.

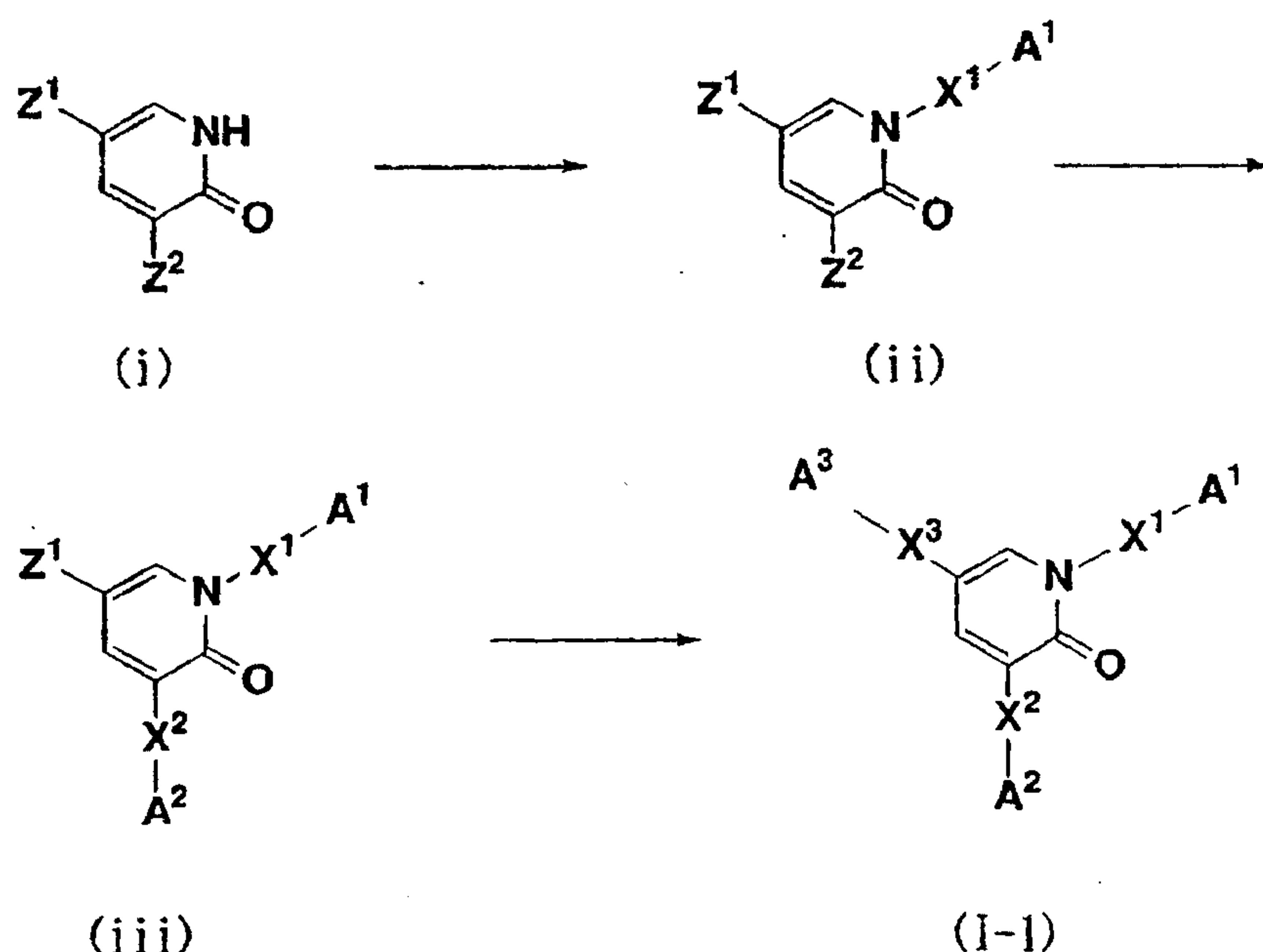
There is no particular limitation for "a salt" in the specification of the present application so far as it forms a salt with the compound of the present invention and is a pharmacologically acceptable one. Preferably, salt with a hydrogen halide (such as hydrofluoride, hydrochloride, hydrobromide or hydroiodide), salt with an inorganic acid (such as sulfate, nitrate, perchlorate, phosphate, carbonate or bicarbonate), salt with an organic carboxylic acid (such as acetate, trifluoroacetate, oxalate, maleate, tartrate, fumarate or citrate), salt with an organic sulfonic acid (such as methanesulfonate, trifluoromethanesulfonate, ethanesulfonate, benzenesulfonate, toluenesulfonate or camphor-sulfonate), salt with an amino acid (such as aspartate or glutamate), salt with a quaternary amine, salt with an alkaline metal (such as sodium salt or potassium salt) and salt with an alkaline earth metal (such as magnesium salt or calcium salt). More preferred examples of the "pharmacologically acceptable salt" are hydrochloride, oxalate etc.

Representative manufacturing methods for the compounds

65702-519

represented by the above formula (I) and (II) according to the present invention will be illustrated as hereunder.

Production process 1



Wherein A^1 , A^2 and A^3 may be the same as or different from each other and each indicates optionally substituted C_{3-8} cycloalkyl group, the C_{3-8} cycloalkenyl group, 5- to 14-membered non-aromatic heterocyclic group, C_{6-14} aromatic hydrocarbocyclic group or 5- to 14-membered aromatic heterocyclic group; Z^1 and Z^2 are the same as or different from each other and each represents halogen atoms; and X^1 , X^2 and X^3 have the same meanings as defined above. In the present production process, the most preferable A^1 , A^2 and A^3 are optionally substituted C_{6-14} aromatic hydrocarbocyclic group or 5- to 14-membered aromatic heterocyclic group. The above-mentioned production process 1 is a process of producing the compound (I-1) which is related to the present invention, by

introducing A^1 , A^2 and A^3 in the pyridone compound which has the substituents Z^1 and Z^2 . Namely, the compound (I-1) which is related to the present invention can be produced by the process that the pyridone compound (i) which has the substituents Z^1 and Z^2 and an aryl boronic acid derivative are provided to a coupling reaction using a copper compound to obtain the compound (ii), and then A^2 and A^3 are introduced in the compound (ii) by carrying out the coupling reaction with an organometallic reagent using a transition metal catalyst or an organoboron compound, preferably carrying out the coupling reaction with an aryl tin derivative, an aryl zinc derivative or an aryl boronic acid derivative, using a palladium catalyst. The preferable aryl boronic acid derivative which is used for the reaction of producing the compound (ii) differs depending on a starting raw material, a solvent used and the like, and is not specifically limited unless the reaction is not disturbed, but the aryl boronic acid derivative which has a group corresponding to A^1 introduced as an aryl group, such as preferably a phenyl boronic acid derivative which may be optionally substituted, a heterocyclic boronic acid derivative which may be optionally substituted, or the like, can be used. Preferable result can be also obtained by the present reaction in the presence of a base, and at this time, the base used differs depending on a starting raw material, a solvent used and the like. When the base is used in the coupling reaction of the present reaction, it is not specifically limited, and

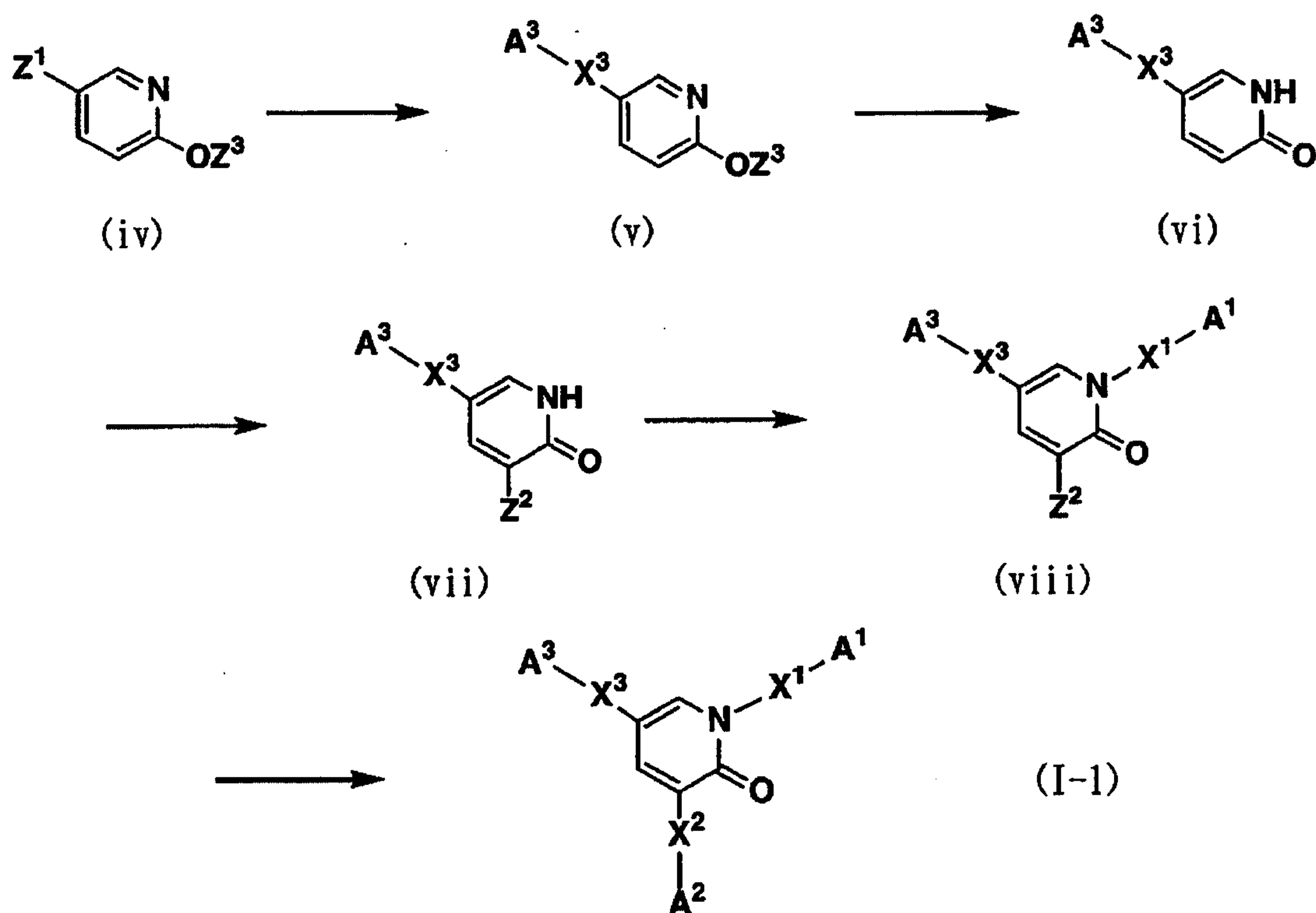
preferably triethylamine, pyridine, tetramethylethylenediamine and the like. Preferable examples of the copper compound used include copper acetate, di- μ -hydroxo-bis[(N,N,N',N'-tetramethylethylenediamine)copper (II)] chloride, and the like. The more preferable result can be obtained by carrying out the reaction of producing the compound (ii) from (i) in the presence of a solvent. The solvent used differs usually depending on a starting raw material, a reagent and the like, and is not specifically limited so long as it is inert to the reaction and dissolves the raw material in a certain amount. Preferably, dichloromethane, tetrahydrofuran, ethyl acetate and the like may be proposed. Further, the present reaction is preferably carried out under atmosphere of oxygen or in air flow, and good results (the reduction of the reaction time and the improvement of yield etc.) can be obtained thereby. The aryl tin compound, the aryl zinc compound or the aryl boronic acid derivative which is used for the reaction of producing the compound (I-1) by introducing A² and A³ in the compound (ii) differs depending on a starting raw material, a solvent used and the like, and is not specifically limited unless the reaction is not disturbed, but a phenyl tin compound which may be optionally substituted, a heterocyclic tin compound which may be optionally substituted, a phenyl zinc compound which may be optionally substituted, a heterocyclic zinc compound which may be optionally substituted, a phenyl boronic acid derivative, a heterocyclic boronic acid

65702-519

derivative which may be optionally substituted, an aryl tin compound, an aryl zinc compound or an aryl boronic acid derivative which has a group corresponding to A² or A³ introduced as an aryl group, can be preferably used. Preferable result can be also obtained by the present reaction in the presence of a base, and at this time, the base used differs depending on a starting raw material, a solvent used and the like. Further, it is not specifically limited, unless the reaction is not disturbed, and preferably cesium carbonate, sodium carbonate, potassium carbonate, and the like. The palladium catalyst used is not specifically limited in usual, and known palladium catalysts such as tetrakis(triphenylphosphine) palladium and the like are preferably mentioned. The reaction of producing the compound (I-1) by introducing A² and A³ in the compound (ii) is preferably carried out in the presence of a solvent from the viewpoints of operation property and stirring property, and the solvent used is not specifically limited in usual, but dimethylformamide, toluene, xylene, benzene and the like are preferably mentioned. The reaction temperature is not specifically limited, and usually room temperature, or under refluxing by heating, and preferably 50 to 160°C. In addition to them, the compound (I-1) related to the present invention can be also produced by the process that the pyridone compound (iii) after introduction of A¹ and A² is introduced to an organoboron compound or an organometallic reagent, preferably a boronic acid derivative, a tin compound or a zinc compound,

and the derivative is provided to a coupling reaction with a halogenated aryl derivative using a transition metal catalyst, preferably a palladium catalyst.

Production process 2



Wherein X^1 , X^2 , X^3 , A^1 , A^2 , A^3 , Z^1 and Z^2 indicate the same meanings as defined above; and Z^3 indicates a protecting group of hydroxy group of an alcohol (for example, a C_{1-6} alkyl group, a benzyl group and the like). In the present production process, the most preferable A^1 , A^2 and A^3 are optionally substituted C_{6-14} aromatic hydrocarbocyclic group or 5- to 14-membered aromatic heterocyclic group. The compound (I-1) according to the present invention can be also produced by introducing A^1 , A^2 and A^3 to the pyridine compound (iv) having substituents Z^1 and $-OZ^3$. The reaction of producing the compound (V) by

introducing A³ to the compound (IV) can be carried out by providing to the coupling reaction with an organometallic reagent or an organoboron compound using a transition metal catalyst, preferably by providing the compound (IV) to the coupling reaction with an aryl tin derivative, an aryl zinc derivative, or an aryl boronic acid derivative in the presence of a base, using a palladium catalyst. The aryl tin derivative, the aryl zinc derivative or the aryl boronic acid derivative used for the present reaction differs depending on a starting raw material, a solvent used and the like, and is not specifically limited unless the reaction is not disturbed, but a phenyl tin derivative which may be optionally substituted, a heterocyclic tin derivative which may be optionally substituted, a phenyl zinc derivative which may be optionally substituted, a heterocyclic zinc derivative which may be optionally substituted, a phenyl boronic acid derivative, a heterocyclic boronic acid derivative which may be optionally substituted, an aryl tin derivative, an aryl zinc derivative or an aryl boronic acid derivative which has a group corresponding to A³ introduced as an aryl group, can be preferably used. The base used differs depending on a starting raw material, a solvent used and the like and is not specifically limited unless the reaction is not disturbed, but preferably cesium carbonate, sodium carbonate, potassium carbonate, and the like. The palladium catalyst used is not specifically limited in usual, and known palladium complex such as

tetrakis(triphenylphosphine) palladium and the like are preferably mentioned. Further, the present reaction is preferably carried out in the presence of a solvent from the viewpoints of operation property and stirring property. The solvent used differs depending on a starting material, a solvent used and the like, and those which dissolve the starting material to a certain degree are not specifically limited unless the reaction is not disturbed, but dimethylformamide, toluene, xylene, benzene and the like are preferably mentioned. The reaction temperature is not specifically limited, and usually room temperature, or under refluxing by heating, and preferably 50 to 160°C. The reaction of producing the pyridone compound (vi) by de-protecting of Z^3 can be carried out by some known processes, and for example, a conventional process described in T.W.Greene and P.G.M.Wuts "Protecting groups in organic synthesis 2nd Edition (1991)" is mentioned as the representative process. The reaction of producing the pyridone compound (vii) by introducing the substituent Z^2 to the compound (vi) can be usually carried out by a known halogenation method. The halogenating agent differs depending on a starting raw material, a solvent used and the like and is not specifically limited unless the reaction is not disturbed, but a bromination agent such as acetic acid-bromine, N-bromosuccinimide or the like, an iodination agent such as iodine, N-iodosuccinimide or the like, and the like are preferably used. The compound (viii) can be produced by providing the compound (vii) and an aryl

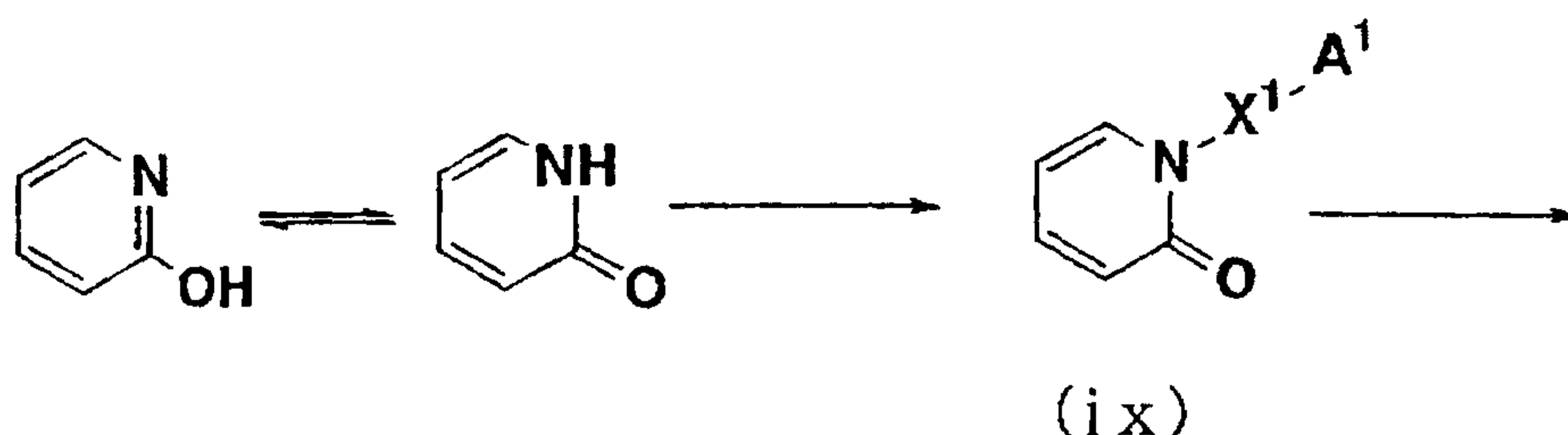
boronic acid derivative to the coupling reaction using a copper compound and by introducing A¹. The aryl boronic acid derivative used is not specifically limited in usual, and an aryl boronic acid derivative which may be optionally substituted, a heterocyclic boronic acid derivative which may be optionally substituted, and an aryl boronic acid derivative which has a group corresponding to A¹ introduced as an aryl group, can be used. Preferable result can be also obtained by the present reaction in the presence of a base, and at this time, the base used differs depending on a starting raw material, a solvent used and the like. Further, the base is not specifically limited, and preferably triethylamine, pyridine, tetramethylethylenediamine and the like. Preferable examples of the copper compound used include copper acetate, di- μ -hydroxo-bis[(N,N,N',N'-tetramethylethylenediamine)copper (II)] chloride, and the like. Further, the present reaction is preferably carried out in the presence of a solvent. The solvent used differs usually depending on a starting raw material, a reagent and the like, and is not specifically limited so long as it is inert to the reaction and dissolves the starting materials in a certain amount, but is preferably dichloromethane, tetrahydrofuran, ethyl acetate and the like. Further, the present reaction is preferably carried out under atmosphere of oxygen or in air flow, and good results (the reduction of the reaction time and the improvement of yield etc.) can be obtained thereby. The final step of producing the

compound (I-1) related to the present invention can be carried out by providing the compound (viii) to the coupling reaction with an organometallic reagent or an organoboron compound using a transition metal catalyst, preferably by providing to the coupling reaction with an aryl tin derivative, an aryl zinc derivative or an aryl boronic acid derivative using a palladium catalyst, and by introducing A^2 to the compound (viii). The aryl tin derivative, the aryl zinc derivative or the aryl boronic acid derivative which is used is not specifically limited usually, and a phenyl tin derivative which may be optionally substituted, a heterocyclic tin derivative which may be optionally substituted, a phenyl zinc derivative which may be optionally substituted, a heterocyclic zinc derivative which may be optionally substituted, a phenyl boronic acid derivative, a heterocyclic boronic acid derivative which may be optionally substituted, an aryl tin derivative, an aryl zinc derivative or an aryl boronic acid derivative which has a group corresponding to A^2 introduced as an aryl group, can be preferably used. The sequential reaction of producing (I-1) from (viii) which was mentioned in the production process 2 can also obtain a preferable result in the presence of a base, and at this time, the base used differs depending on a starting raw material, a solvent used and the like. Further, it is not specifically limited, unless the reaction is not disturbed, and preferably cesium carbonate, sodium carbonate, potassium carbonate, and the like. The palladium catalyst used is not

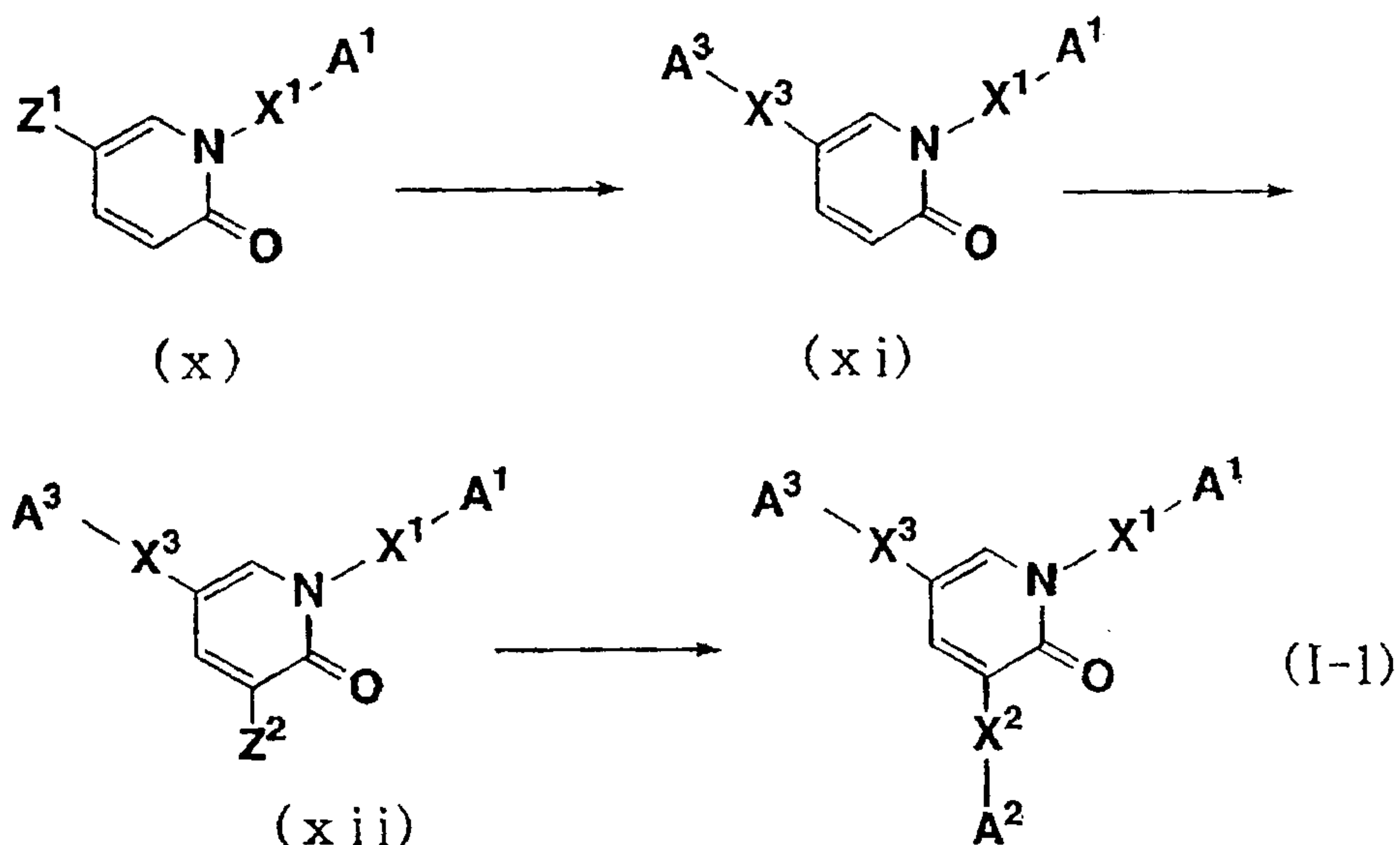
65702-519

specifically limited in usual, and known palladium catalysts such as tetrakis(triphenylphosphine) palladium and the like are preferably mentioned. Further, a more preferable result can be obtained by carrying out the present reaction in the presence of a solvent, and the solvent used is not specifically limited in usual, and the solvent used differs depending on a starting raw material, a reagent and the like, and the solvent which does not disturb the reaction and dissolves the starting raw material to a certain degree is not specifically limited, but is preferably dimethylformamide, toluene, xylene, benzene and the like. The reaction temperature is not specifically limited, and usually room temperature, or under refluxing by heating, and preferably 50 to 160°C. In addition to them, the compound (I-1) related to the present invention can be also produced by the process that the pyridone compound (viii) after introduction of A¹ is introduced to an organoboron compound or an organometallic reagent, preferably a boronic acid derivative, a tin compound or a zinc compound, and the derivative is provided to a coupling reaction with a halogenated aryl derivative using a transition metal catalyst, preferably a palladium catalyst.

Production process 3



65702-519



Wherein X¹, X², X³, A¹, A², A³, Z¹ and Z² have the same meanings as defined above, and each of the most preferable group of A¹, A² and A³ in the present production process is the C₆₋₁₄ aromatic hydrocarbocyclic group or the 5 to 14 membered aromatic heterocyclic group which may optionally have substituents, respectively. The compound (I-1) according to the present invention can be also produced by introducing A¹, A² and A³ to 2-hydroxypyridine. The reaction of producing the compound (ix) can be conducted by providing an aryl boronic acid derivative to the coupling reaction using a copper compound, the Ullmann reaction with a halogenated aryl derivative, or a substitution reaction for the halogenated aryl derivative and by introducing A¹ to 2-hydroxypyridine. The aryl boronic acid derivative used in the coupling reaction differs usually depending on a starting raw material, a reagent and the like, and is not specifically limited unless the reaction is not disturbed. The aryl boronic acid derivative having a group

corresponding to A¹ introduced as an aryl group such as a phenyl boronic acid derivative which may be optionally substituted, a heterocyclic boronic acid derivative which may be optionally substituted, and the like can be preferably used. Preferable result can be also obtained by the present reaction in the presence of a base, and at this time, the base used differs depending on a starting raw material, a solvent used and the like. Further, the base is not specifically limited unless the reaction is not disturbed, but is preferably triethylamine, pyridine, tetramethylethylenediamine and the like. Preferable examples of the copper compound used include copper acetate, di- μ -hydroxo-bis[(N,N,N',N'-tetramethylethylenediamine) copper (II)] chloride, and the like. Further, the present reaction is preferably carried out in the presence of a solvent. The solvent used differs usually depending on a starting raw material, a reagent and the like, and the solvent which does not disturb the reaction and dissolves the starting raw material to a certain degree is not specifically limited, but is preferably dichloromethane, tetrahydrofuran, ethyl acetate and the like. Further, the present reaction is preferably carried out under atmosphere of oxygen or in air flow, and good results (the reduction of the reaction time and the improvement of yield etc.) can be obtained thereby. The Ullmann reaction is carried out at 60°C to under refluxing by heating, preferably 100 to 200°C in the presence of a base such as potassium carbonate, sodium carbonate or

sodium acetate, using copper or a copper compound such as copper iodide, copper chloride, copper bromide or the like, which is not specifically limited usually. The solvent used differs depending on a starting raw material, a reagent and the like, and the solvent which does not disturb the reaction and dissolves the starting raw material to a certain degree is not specifically limited, but is preferably dimethylformamide, toluene, xylene, tetralin, dichlorobenzene, nitrobenzene and the like. The substitution reaction with the halogenated aryl derivative is not specifically limited, but carried out under ice-cooling to under refluxing by heating, preferably at room temperature to 60°C in a solvent such as tetrahydrofuran or dimethylformamide or the like, using a base such as potassium carbonate, sodium hydride, potassium hydride, sodium butoxide, or potassium butoxide or the like. The reaction of producing the compound (x) by introducing the substituent Z¹ to the compound (ix) can be usually carried out by known halogenation method. The halogenating agent used differs depending on a starting raw material, a solvent used and the like, and is not specifically limited, unless the reaction is not disturbed, but a bromination agent such as acetic acid-bromine, N-bromosuccinimide or the like, an iodination agent such as iodine, N-iodosuccinimide or the like, and the like are preferably used. The reaction of producing the compound (xi) by introducing A³ to the compound (x) can be usually carried out by providing the compound (x) to the coupling reaction with an organometallic

reagent or an organoboron compound using a transition metal catalyst, preferably by providing it to the coupling reaction with an aryl tin derivative, an aryl zinc derivative, or an aryl boronic acid derivative in the presence of a base, using a palladium catalyst. The aryl tin derivative, the aryl zinc derivative or the aryl boronic acid derivative which is used for the present reaction is not specifically limited usually, but an aryl tin derivative, an aryl zinc derivative or an aryl boronic acid derivative having a group corresponding to A³ introduced as an aryl group such as a phenyl tin derivative which may be optionally substituted, a heterocyclic tin derivative which may be optionally substituted, a phenyl zinc derivative which may be optionally substituted, a heterocyclic zinc derivative which may be optionally substituted, a phenyl boronic acid derivative, a heterocyclic boronic acid derivative which may be optionally substituted, can be preferably used. The base used differs depending on a starting raw material, a solvent used and the like and is not specifically limited unless the reaction is not disturbed, but preferably cesium carbonate, sodium carbonate, potassium carbonate, and the like. The palladium catalyst used is not specifically limited in usual, and known palladium catalysts such as tetrakis(triphenylphosphine) palladium and the like are preferably mentioned. Further, the present reaction is preferably carried out in the presence of a solvent from the viewpoints of operation property and stirring property. The

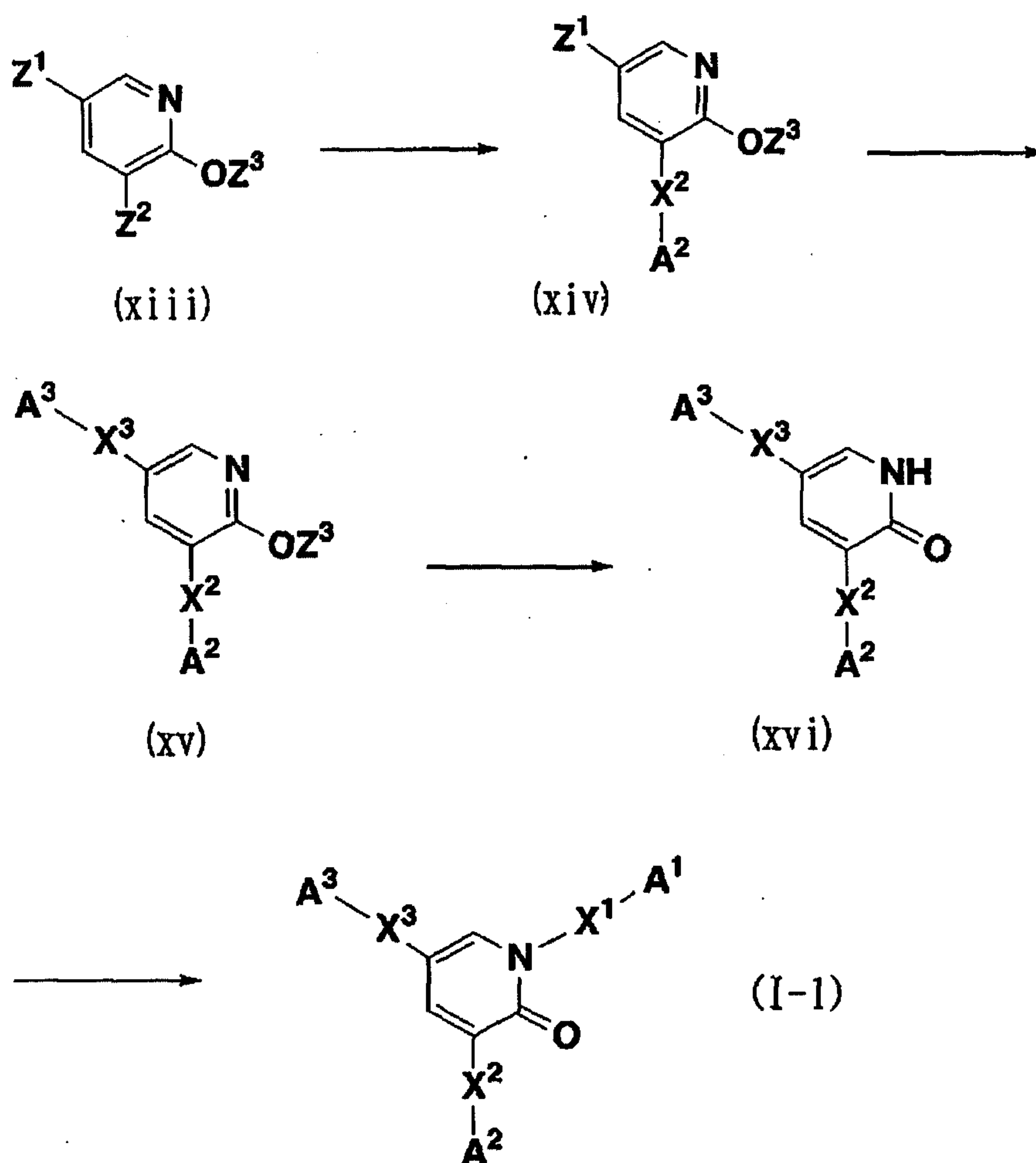
solvent used differs depending on a starting material, a solvent used and the like, and the solvent which does not disturb the reaction and dissolves the starting material to a certain degree is not specifically limited, but is preferably dimethylformamide, toluene, xylene, benzene and the like. The reaction temperature is not specifically limited, and usually room temperature, or under refluxing by heating, and preferably 50 to 160°C. The reaction of producing the compound (xii) by introducing the substituent Z^2 to the compound (xi) can be usually carried out by known halogenation method. The halogenating agent used differs depending on a starting raw material, a solvent used and the like, and is not specifically limited, unless the reaction is not disturbed, but a bromination agent such as acetic acid-bromine, N-bromosuccinimide or the like, an iodination agent such as iodine, N-iodosuccinimide or the like, and the like are preferably used. The final step of producing the compound (I-1) related to the present invention can be carried out by providing the compound (xii) to the coupling reaction with an organometallic reagent or an organoboron compound using a transition metal catalyst, preferably by providing it to the coupling reaction with an aryl tin derivative, an aryl zinc derivative or an aryl boronic acid derivative using a palladium catalyst, and by introducing A^2 to the compound (xii). The aryl tin derivative, the aryl zinc derivative or the aryl boronic acid derivative which is used differs depending on a starting raw material, a solvent used

65702-519

and the like, and is not specifically limited unless the reaction is not disturbed. The aryl tin derivative, aryl zinc derivative or aryl boronic acid derivative having a group corresponding to A² introduced as an aryl group, such as a phenyl tin derivative which may be optionally substituted, a heterocyclic tin derivative which may be optionally substituted, a phenyl zinc derivative which may be optionally substituted, a heterocyclic zinc derivative which may be optionally substituted, a phenyl boronic acid derivative, a heterocyclic boronic acid derivative which may be optionally substituted, can be used. At this time, the base used differs depending on a starting raw material, a solvent used and the like, and is not specifically limited unless the reaction is not disturbed, but is preferably cesium carbonate, sodium carbonate, potassium carbonate, and the like. The palladium catalyst used differs depending on a starting raw material, a solvent used and the like, and is not specifically limited unless the reaction is not disturbed, but known palladium catalysts such as tetrakis(triphenylphosphine) palladium and the like are mentioned. Further, a more preferable result can be obtained by carrying out the present reaction in the presence of a solvent, and the solvent used is not specifically limited in usual, but is preferably dimethylformamide, toluene, xylene, benzene and the like. The reaction temperature is not specifically limited, and usually room temperature, or under refluxing by heating, and preferably 50 to 160°C. In addition to them, the compound

(I-1) related to the present invention can be also produced by the process that the compound (xii) is introduced to an organoboron compound or an organometallic reagent, preferably a boronic acid derivative, a tin compound or a zinc compound or the like, and the derivative is provided to a coupling reaction with a halogenated aryl derivative using a transition metal catalyst, preferably a palladium catalyst.

Production process 4



Wherein X^1 , X^2 , X^3 , A^1 , A^2 , A^3 , Z^1 , Z^2 and Z^3 have the same meanings as defined above, and each of the most preferable group of A^1 , A^2 and A^3 in the present production process is the C_6 .

¹⁴ aromatic hydrocarbocyclic group or the 5 to 14 membered aromatic heterocyclic group which may optionally have substituents, respectively. The compound (I-1) related to the present invention can be also produced by introducing A¹, A² and A³ to the compound (xiii) having the substituents Z¹, Z² and -OZ³. The reaction of producing the compound (xiv) by introducing A² to the compound (xiii) can be conducted by providing the compound (xiii) to the coupling reaction with an organometallic reagent or an organoboron compound using a transition metal catalyst, preferably by providing it to the coupling reaction with an aryl tin derivative, an aryl zinc derivative, or an aryl boronic acid derivative in the presence of a base, using a palladium catalyst. The aryl tin compound, aryl zinc compound or aryl boronic acid derivative used in the present reaction differs usually depending on a starting raw material, a reagent and the like, and is not specifically limited unless the reaction is not disturbed. The aryl tin compound, aryl zinc compound or aryl boronic acid derivative having a group corresponding to A² introduced as an aryl group, such as a phenyl tin derivative which may be optionally substituted, a heterocyclic tin derivative which may be optionally substituted, a phenyl zinc derivative which may be optionally substituted, a heterocyclic zinc derivative which may be optionally substituted, a phenyl boronic acid derivative, a heterocyclic boronic acid derivative which may be optionally substituted and the like can be used. The base used differs

depending on a starting raw material, a solvent used and the like and is not specifically limited unless the reaction is not disturbed, but is cesium carbonate, sodium carbonate, potassium carbonate, and the like. The palladium catalyst used differs depending on a starting raw material, a solvent used and the like and is not specifically limited unless the reaction is not disturbed, but known palladium catalysts such as tetrakis(triphenylphosphine) palladium and the like are mentioned. Further, the present reaction is preferably carried out in the presence of a solvent from the viewpoints of operation property and stirring property. The solvent used differs depending on a starting material, a solvent used and the like, and the solvent which does not disturb the reaction and dissolves the starting material to a certain degree is not specifically limited, but is preferably dimethylformamide, toluene, xylene, benzene and the like. The reaction temperature is not specifically limited, and usually room temperature, or under refluxing by heating, and preferably 50 to 160°C. The reaction of producing the compound (xv) by introducing the substituent A³ to the compound (xiv) can be carried out by providing the compound (xiv) to the coupling reaction with an organometallic reagent or an organoboron compound using a transition metal catalyst, preferably by providing it to the coupling reaction with an aryl tin compound, aryl zinc compound, or aryl boronic acid derivative in the presence of a base, using a palladium catalyst. The aryl tin

compound, aryl zinc compound or aryl boronic acid derivative used in the present reaction differs usually depending on a starting raw material, a reagent and the like, and is not specifically limited unless the reaction is not disturbed. The aryl tin compound, aryl zinc compound or aryl boronic acid derivative having a group corresponding to A³ introduced as an aryl group, such as a phenyl tin derivative which may be optionally substituted, a heterocyclic tin derivative which may be optionally substituted, a phenyl zinc derivative which may be optionally substituted, a heterocyclic zinc derivative which may be optionally substituted, a phenyl boronic acid derivative, a heterocyclic boronic acid derivative which may be optionally substituted and the like can be preferably used. The base used differs depending on a starting raw material, a solvent used and the like and is not specifically limited unless the reaction is not disturbed, but is preferably cesium carbonate, sodium carbonate, potassium carbonate, and the like. The palladium catalyst used is not specifically limited usually, but known palladium catalysts such as tetrakis(triphenylphosphine) palladium and the like are preferably mentioned. Further, the present reaction is preferably carried out in the presence of a solvent from the viewpoints of operation property and stirring property. The solvent used differs depending on a starting material, a solvent used and the like, and the solvent which does not disturb the reaction and dissolves the starting material to a certain degree is not specifically limited, but

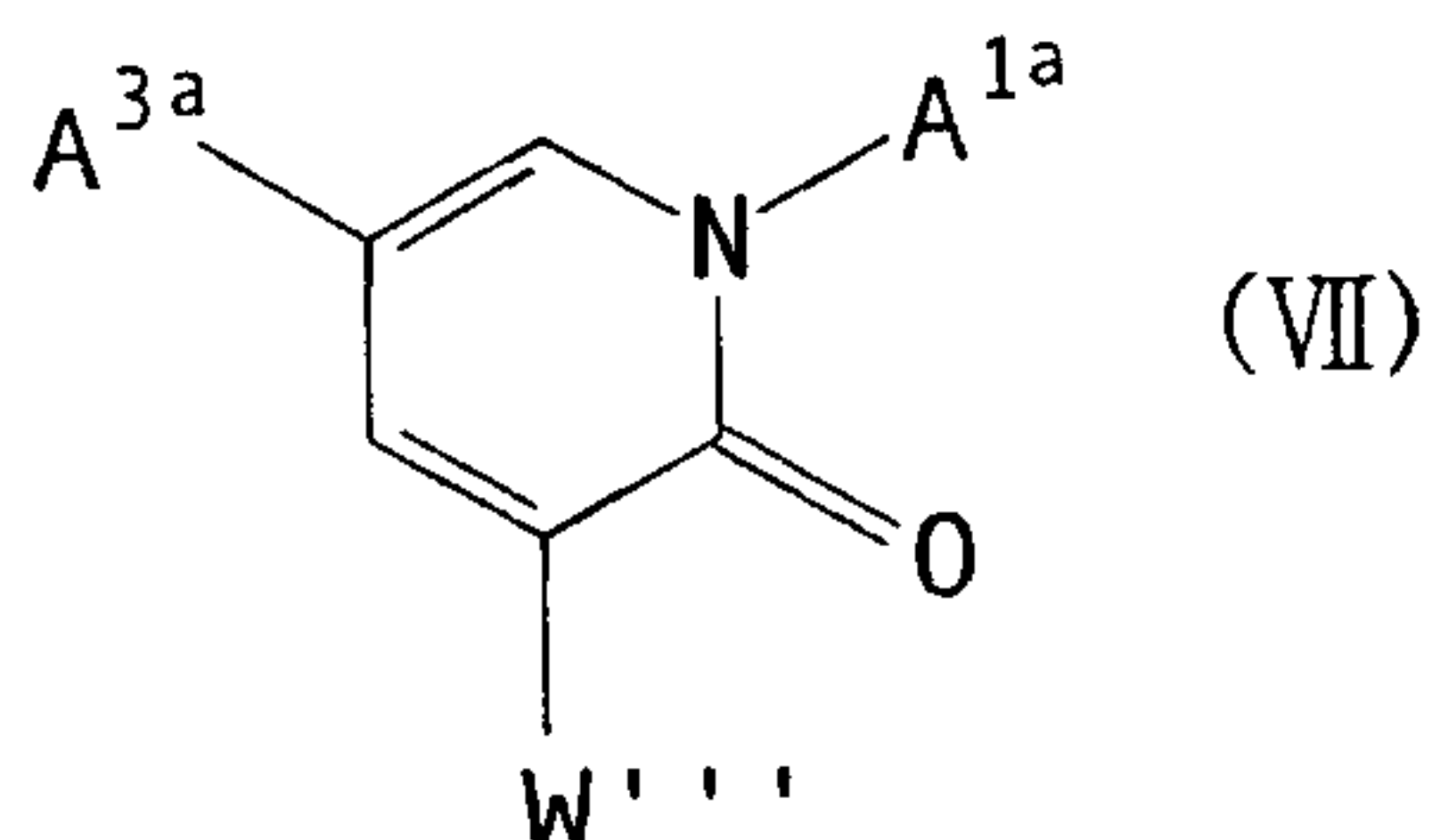
is preferably dimethylformamide, toluene, xylene, benzene and the like. The reaction temperature is not specifically limited, and usually room temperature, or under refluxing by heating, and preferably 50 to 160°C. The reaction of producing the pyridone compound (xvi) by de-protecting the removal of Z³ can be carried out by some known processes, and for example, a conventional process described in T.W.Greene and P.G.M.Wuts "Protecting groups in organic synthesis 2nd Edition (1991)" is mentioned as the representative process. The final step of producing the compound (I-1) related to the present invention can be conducted by providing the compound (xvi) and an aryl boronic acid derivative to the coupling reaction using a copper compound, the Ullmann reaction with a halogenated aryl derivative, or a substitution reaction for the halogenated aryl derivative and by introducing A¹. The aryl boronic acid derivative used differs depending on a starting raw material, a solvent used and the like, and is not specifically limited unless the reaction is not disturbed. The aryl boronic acid derivative having a group corresponding to A¹ introduced as an aryl group, such as a phenyl boronic acid derivative which may be optionally substituted, a heterocyclic boronic acid derivative which may be optionally substituted and the like can be used. Preferable result can be also obtained by the present reaction in the presence of a base, and at this time, the base used differs depending on a starting raw material, a solvent used and the like. Further, the base is not specifically

limited unless the reaction is not disturbed, but is preferably triethylamine, pyridine, tetramethylethylenediamine and the like. Preferable examples of the copper compound used include copper acetate, di- μ -hydroxo-bis[(N,N,N',N'-tetramethylethylenediamine) copper (II)] chloride, and the like. Further, the present reaction is preferably carried out in the presence of a solvent. The solvent used differs usually depending on a starting raw material, a reagent and the like, and the solvent which does not disturb the reaction and dissolves the starting raw material to a certain degree is not specifically limited, but is preferably dichloromethane, tetrahydrofuran, ethyl acetate and the like. Further, the present reaction is preferably carried out under atmosphere of oxygen or in air flow, and good results (the reduction of the reaction time and the improvement of yield etc.) can be obtained thereby. The Ullmann reaction is carried out at 60°C to under refluxing by heating, preferably 100 to 200°C in the presence of a base such as potassium carbonate, sodium carbonate or sodium acetate, using copper or a copper compound such as copper iodide, copper chloride, copper bromide or the like, which is not specifically limited usually. The solvent used differs depending on a starting raw material, a reagent and the like, and the solvent which does not disturb the reaction and dissolves the starting raw material to a certain degree is not specifically limited, but is preferably dimethylformamide, toluene, xylene, tetralin, dichlorobenzene, nitrobenzene and

65702-519

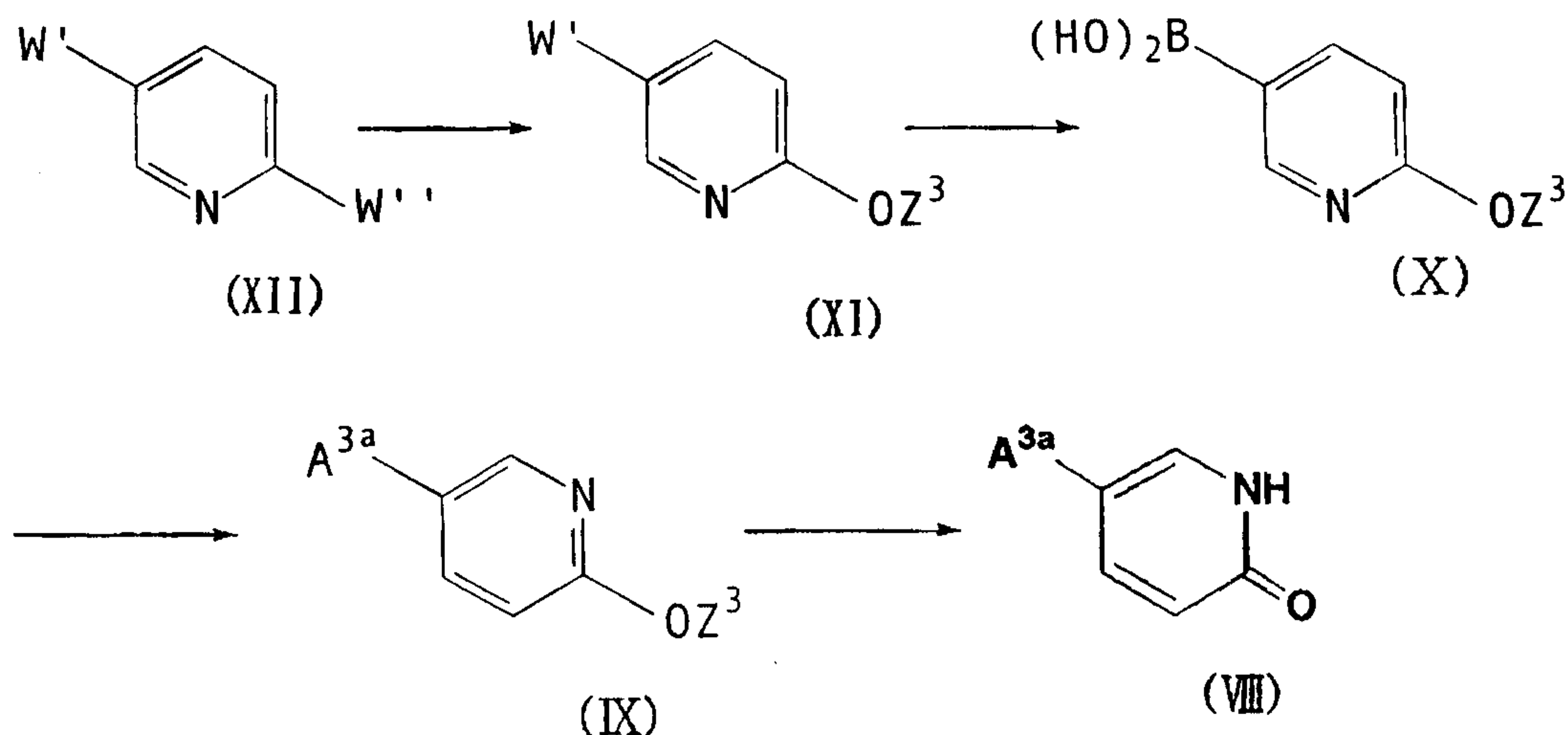
the like. The substitution reaction with the halogenated aryl derivative is not specifically limited, but carried out under ice-cooling to under refluxing by heating, preferably at room temperature to 60°C in a solvent such as tetrahydrofuran or dimethylformamide or the like, using a base such as potassium carbonate, sodium hydride, potassium hydride, sodium butoxide, or potassium butoxide or the like.

In the above production process, the production intermediate represented by the formula:

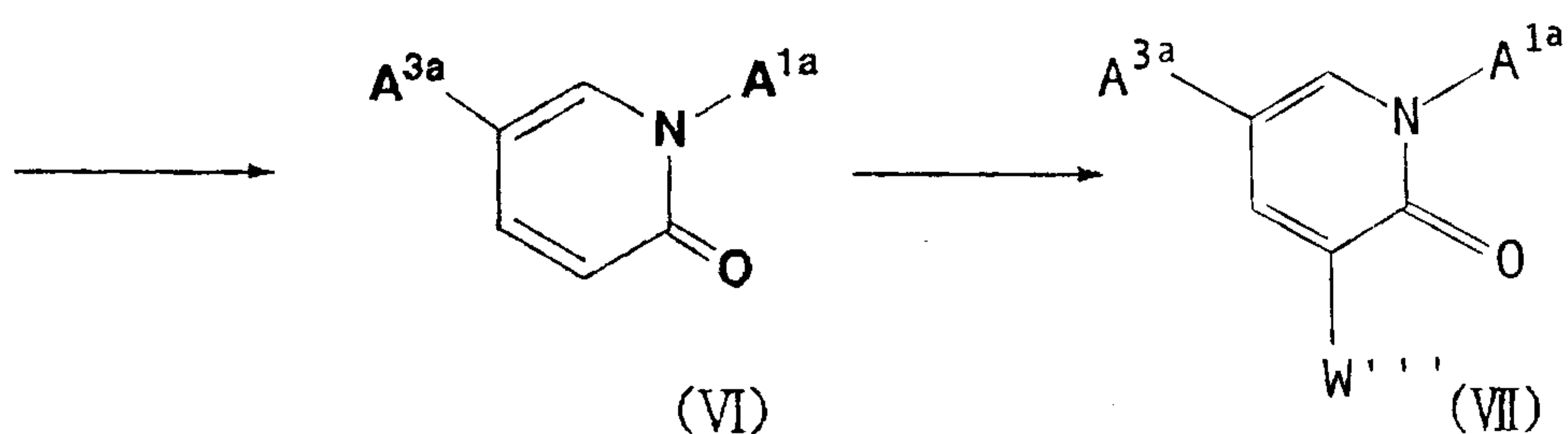


(wherein A^{1a}, A^{3a} and W' have the same meanings as defined above) can be also produced by the following method (Production process 5).

Production process 5



65702-519



W' , W'' and W''' in the above formula indicate the same or different halogen atom, and the most preferable atom is bromine atom.

The compound (XII) can be easily produced according to known methods or corresponding methods, and further, can be easily obtained as a commercially available substance. The step of producing the compound (XI) from the compound (XII) is a step of reacting the compound (XII) with the base represented by the formula Z^3OM (M indicates an alkali metal atom). The base differs depending on a starting raw material, a solvent used and the like, and is not specifically limited unless the reaction is not disturbed, but is preferably sodium alkoxide, and preferably sodium methoxide, sodium ethoxide and the like in particular. In this case, it is preferable to carry out the reaction in an alcohol corresponding to the alkoxide used, and for example, it is preferable to carry out in methanol in case of using sodium methoxide and ethanol in case of using sodium ethoxide, etc.

The step of producing the compound (X) from the compound (XI) is a step of reacting the compound (XI) with trimethoxyborane in the presence of a base. The base used differs depending on a starting raw material, a solvent used

and the like, and is not specifically limited unless the reaction is not disturbed, but is preferably n-butyllithium and the like. The solvent used differs depending on a starting raw material, a solvent used and the like, and the solvent which does not disturb the reaction and dissolves the starting material to a certain degree is not specifically limited, but is preferably ethers such as tetrahydrofuran, and the like. When n-butyllithium is used as a base, the reaction can be terminated by an acid such as hydrochloric acid, or the like according to a conventional method.

The step of producing the compound (IX) from the compound (X) is a step of carrying out the coupling reaction of the compound (X) with a halogenoaryl or a halogenoheteroaryl which corresponds to the substituent A^{3a} introduced, in the presence of a base and a palladium catalyst and producing the compound (IX). The palladium catalyst used is not specifically limited, but palladium acetate/triphenylphosphine catalyst and the like can be mentioned as the preferable example. The base used differs depending on a starting raw material, a solvent used and the like, and is not specifically limited unless the reaction is not disturbed, but is preferably cesium carbonate, sodium carbonate, potassium carbonate, and the like. Further, the present step is preferably carried out in the presence of a solvent from the viewpoints of operation property and stirring property. The solvent used differs depending on a starting raw material, a solvent used and the like, and the solvent which

does not disturb the reaction and dissolves the starting material to a certain degree is not specifically limited, but is preferably 1,2-dimethoxyethane, dimethylformamide, toluene, xylene, benzene and the like. The reaction temperature is not specifically limited, and usually room temperature, or under refluxing by heating, and preferably 50 to 160°C.

The step of producing the compound (VIII) from the compound (IX) is a step of submitting to the reaction of protecting the removal of Z³ of the compound (IX). The present step can be carried out by some known processes, and for example, a method of refluxing the compound (IX) by heating in the presence of an acid (preferably, hydrochloric acid and the like) is mentioned. Additionally, for example, a conventional process described in T.W.Greene and P.G.M.Wuts "Protecting groups in organic synthesis 2nd Edition (1991)" is mentioned as the representative process.

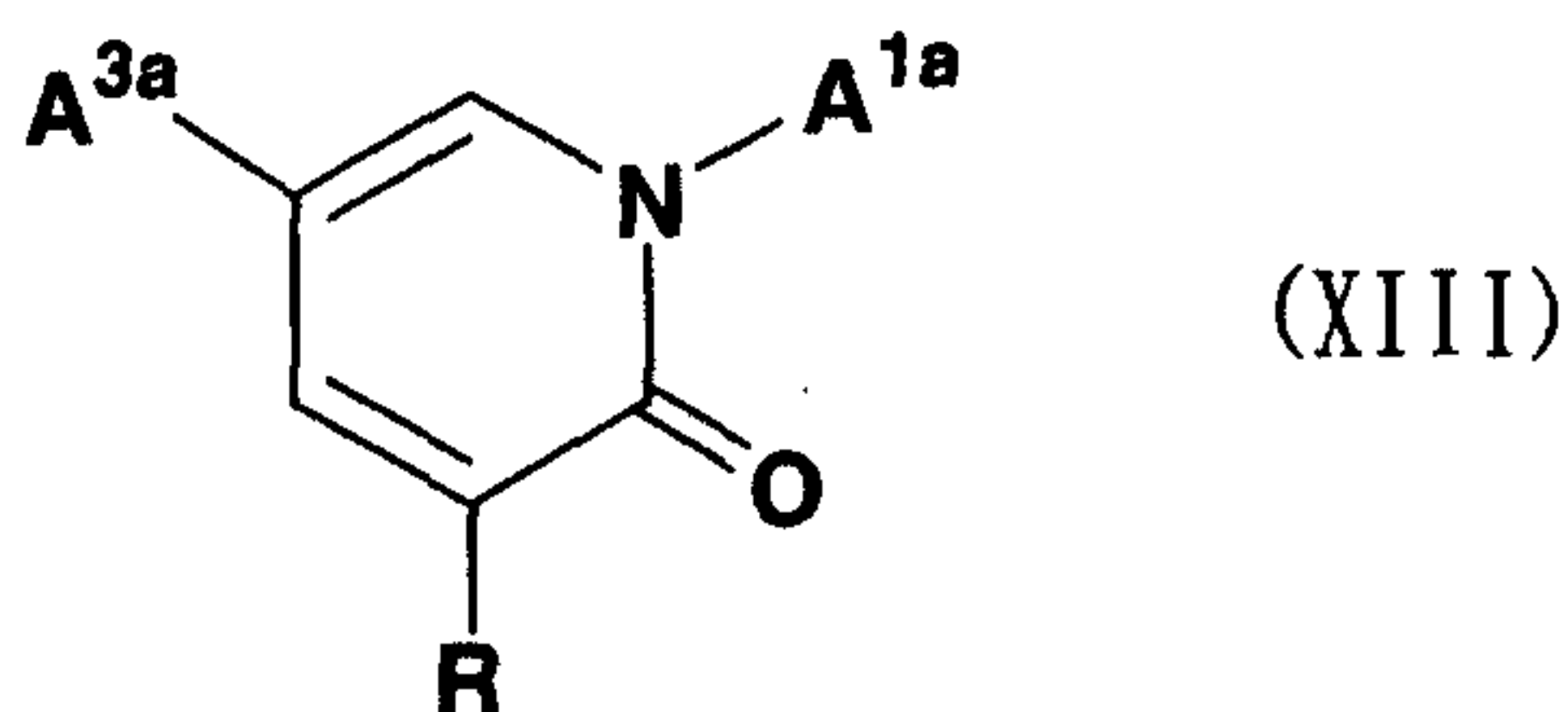
The step of producing the compound (VI) from the compound (VIII) is a step of submitting the compound (VIII) and the aryl boronic acid derivative represented by the formula A^{1a}B(OH)₂ to the coupling reaction using a copper compound and introducing A^{1a}. The aryl boronic acid derivative used is not specifically limited usually. The aryl boronic acid derivative which has a group corresponding to A^{1a} introduced as an aryl group, such as a phenyl boronic acid derivative which may be optionally substituted, a heterocyclic boronic acid derivative which may be optionally substituted and the like can be used. Preferable

result can be also obtained by the present reaction in the presence of a base, and at this time, the base used differs depending on a starting raw material, a solvent used and the like. Further, the base is not specifically limited unless the reaction is not disturbed, but is preferably triethylamine, pyridine, tetramethylethylenediamine and the like. Preferable examples of the copper compound used include copper acetate, di- μ -hydroxobis[(N,N,N',N'-tetramethylethylenediamine)copper (II)] chloride, and the like. Further, the present reaction is preferably carried out in the presence of a solvent. The solvent used differs usually depending on a starting raw material, a reagent and the like, and the solvent which does not disturb the reaction and dissolves the starting raw material to a certain degree is not specifically limited, but is preferably N,N-dimethylformamide, dichloromethane, tetrahydrofuran, ethyl acetate and the like. Further, the present reaction is preferably carried out under atmosphere of oxygen or in air flow, and good results (the reduction of the reaction time and the improvement of yield etc.) can be obtained thereby.

The step of producing the compound (VII) from the compound (VI) is a step of submitting the compound (VI) to the halogenation reaction. The halogenation reaction can be usually carried out by known halogenation methods. The halogenating agent used differs depending on a starting raw material, a solvent used and the like, and is not specifically

limited unless the reaction is not disturbed, but is preferably a bromination agent such as acetic acid-bromine, N-bromosuccinimide or the like, an iodination agent such as iodine, N-iodosuccinimide or the like, and the like.

According to the above production process 5, the production intermediates (VI) and (VII) can be produced in high yield. Further, when the production intermediates the production intermediates of the compounds related to the present invention are produced according to the production processes, the contamination of a copper compound to the final product can be easily prevented, and the compounds of the present invention satisfying the point of safety (toxicity and the like) can be provided. Accordingly, the production processes are extremely excellent production processes from the viewpoints of yield and safety, experimentally and industrially. The novel compound represented by the formula:

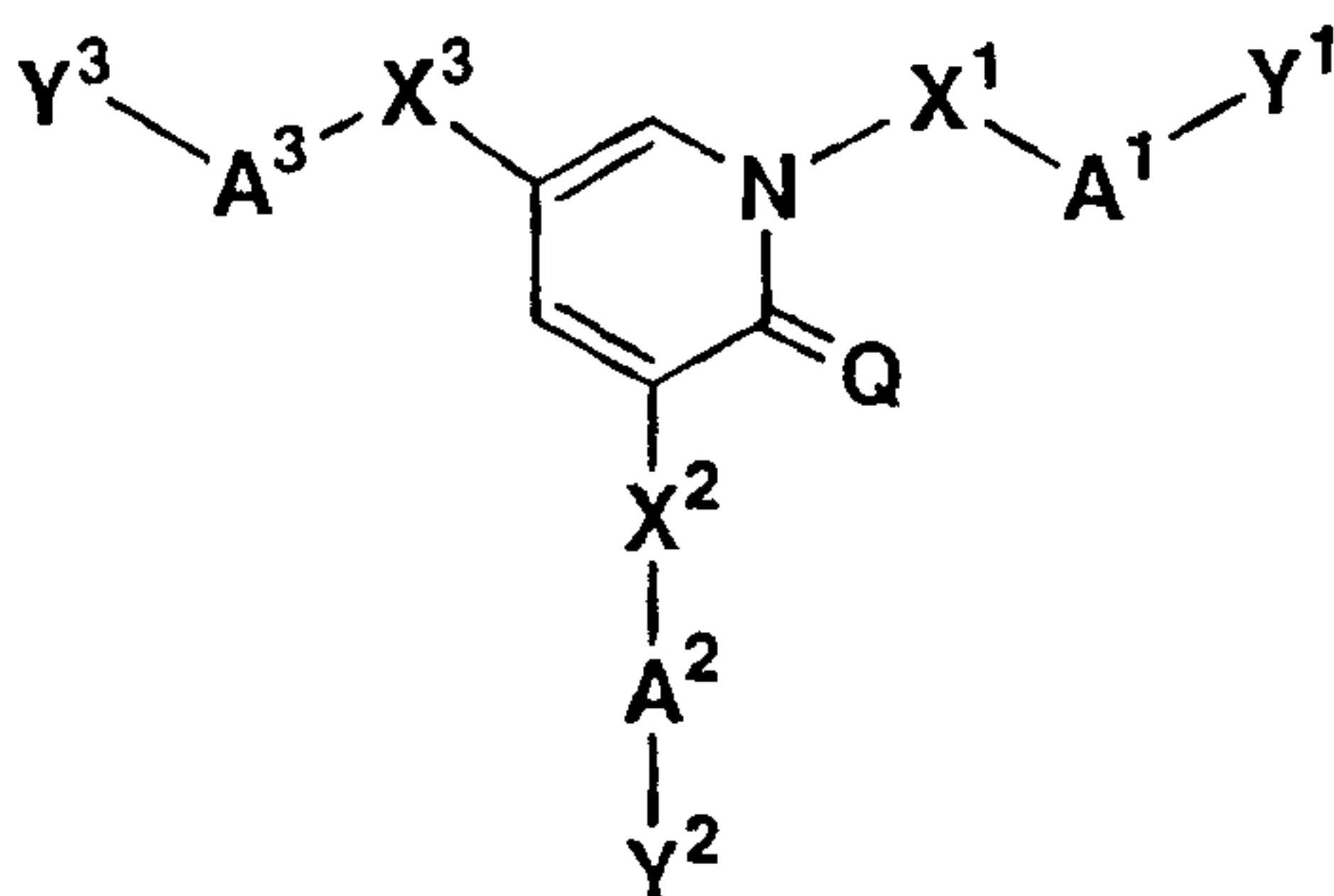


(wherein A^{1a} and A^{3a} are the same as or different from each other and each indicates a C₆₋₁₄ aromatic hydrocarbocyclic group or 5 to 14 membered aromatic heterocyclic group which may optionally have a substituent, respectively; and R indicates hydrogen atom or a halogen atom) or a salt thereof is useful as the production intermediate in the production of the compound (I) according

.65702-519

to the present invention or a salt thereof. In the formula (XIII), the preferable examples in A^{1a} and A^{3a} may be the same as or different from each other, and each includes phenyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, thienyl group, thiazolyl group, furyl group, naphthyl group, quinolyl group, iso-quinolyl group, indolyl group, benzimidazolyl group, benzothiazolyl group, benzoxazolyl group, imidazopyridyl group, carbazolyl group etc., which may optionally have substituents, respectively. The more preferable examples may be the same as or different from each other, and each includes a phenyl group, pyridyl group, pyrimidinyl group, thienyl group, furyl group etc., which may optionally have substituents, respectively. Further, the preferable examples in R in particular are hydrogen atom or bromine atom.

The substituents on A^1 , A^2 and A^3 in the compound represented by the formula:



(wherein Q, X^1 , X^2 , X^3 , A^1 , A^2 and A^3 have the same meanings as defined above; Y^1 , Y^2 and Y^3 indicates the same or different substituents; and each of the most preferable group in A^1 , A^2 and A^3 is a C_{6-14} aromatic hydrocarbocyclic group or 5 to 14

membered aromatic heterocyclic group which may optionally have substituents, respectively) can be converted by various reactions. For example, the representative processes are as below. That is, various reactions are known for changing to a functional group from a nitro group when (1) Y^1 , Y^2 and/or Y^3 are/is nitro group(s) and, although there is no particular limitation for the method and for the resulting substance, a method of changing to an amine derivative by a reduction reaction may be exemplified. Although there is usually no particular limitation for the reduction condition, preferred conditions are a method where iron, zinc or tin is used under acidic conditions, a hydrogenation method where palladium, rhodium, ruthenium, platinum or a complex thereof is used as a catalyst. When the amine derivative produced by the said reduction reaction is used, it is possible to further change to an amide compound, a carbamate compound, a sulfonamide compound, a halogen compound, a substituted amine compound etc., easily. (2) When Y^1 , Y^2 and/or Y^3 are/is alkoxy group(s), an example for changing to a functional group from an alkoxy group is a method to change to an alcohol derivative by means of deprotection. The alcohol derivative which is prepared by the said method may be easily changed to an ester compound by a dehydrating condensation with carboxylic acid derivative or by a reaction with an acid chloride or may be easily changed to an ether compound by a *Mitsunobu* reaction or by a condensation reaction with a halogen compound. (3) When Y^1 , Y^2 and/or Y^3

65702-519

are/is aldehyde group(s), various reactions are known for changing to a functional group from an aldehyde group and, although there is no particular limitation for the method therefor and the resulting substance by the change, an example is a method of changing to a carboxylic acid derivative by an oxidation reaction. The carboxylic acid derivative prepared by the said method may be easily changed further to an ester compound, a ketone compound, etc. In addition, starting from the said aldehyde derivative, it is possible to easily manufacture an alcohol derivative by a reduction reaction, an amine derivative by a reductive amination reaction, a secondary alcohol compound by an addition reaction with an organic metal reagent and various alkyl derivatives by a Wittig reaction. (4) When Y^1 , Y^2 and/or Y^3 are/is halogen atom(s), an example for changing to a functional group from a halogen atom as a substituent is a method of changing to a nitrile derivative by a substitution reaction. Besides the above, it is also possible to easily change to various kinds of compounds via, for example, an organolithium compound, an organomagnesium compound, an organotin compound or an organoboronic acid derivative etc.

The above-mentioned methods is the method for the manufacture of the compound (I) of the present invention. The starting compound in the above-mentioned methods may form a salt or a hydrate and there is no particular limitation for such salt and hydrate so far as they do not inhibit the reaction. When the compound (I) of the present invention is obtained in a free

substance, it may be changed to a state of a salt by conventional methods. Further, various isomers (for example, a geometrical isomer, an enantiomer based on an asymmetric carbon, a rotamer, a stereoisomer, a tautomer, and the like) which are obtained for the compound (I) related to the present invention are purified by using usual separation procedures, for example, such as recrystallization, a diastereomer salt method, an enzymolysis method, various chromatographies (for example, thin layer chromatography, column chromatography, gas chromatography, and the like), and can be separated.

The compound of the present invention represented by the above formula (I), a salt thereof or hydrates thereof may be made into pharmaceutical preparations such as tablets, diluted powder, fine granules, granules, coated tablets, capsules, syrup, troche, inhalation preparation, suppositories, injections, ointments, eye ointments, eye drops, nasal preparations, ear drops, cataplasma or lotions by means of conventional methods. In the manufacture of the pharmaceutical preparations, it is possible to use commonly used fillers, binders, disintegrating agent, lubricants, coloring agents, corrigents and, if necessary, stabilizers, emulsifiers, absorption promoters, surfactant, pH adjusting agents, antiseptics, antioxidants, etc. and, after compounding with the ingredients commonly used as materials for the pharmaceutical preparations, it is made into pharmaceutical preparations by a common method. Examples of the components

therefor are 1) animal and plant oil such as soybean oil, beef tallow or synthetic glyceride; 2) hydrocarbon such as liquid paraffin, squalane or solid paraffin; 3) ester oil such as octyldodecyl myristate or isopropyl myristate; 4) higher alcohol such as cetostearyl alcohol or behenyl alcohol; 5) silicone resin; 6) silicone oil; 7) surfactant such as polyoxyethylene fatty acid ester, sorbitan fatty acid ester, glycerol fatty acid ester, polyoxyethylene sorbitan fatty acid ester, polyoxyethylene hydrogenated castor oil or polyoxyethylene-polyoxypropylene block copolymer; 8) water-soluble high-molecular substance such as hydroxyethyl cellulose, polyacrylic acid, carboxyvinyl polymer, polyethylene glycol, polyvinylpyrrolidone or methylcellulose; 9) lower alcohol such as ethanol or isopropanol; 10) polyhydric alcohol such as glycerol, propylene glycol, dipropylene glycol or sorbitol; 11) saccharide such as glucose or sucrose; 12) inorganic powder such as silicic acid anhydride, aluminum magnesium silicate or aluminum silicate; 13) pure water and the like. Applicable examples of (1) a filler are lactose, corn starch, pure sugar, glucose, mannitol, sorbitol, crystalline cellulose, silicon dioxide etc.; those of (2) a binder are polyvinyl alcohol, polyvinyl ether, methyl cellulose, ethyl cellulose, gum arabic, tragacanth, gelatin, shellac, hydroxypropyl methyl cellulose, hydroxypropyl cellulose, polyvinylpyrrolidone, polypropylene glycol-polyoxyethylene block copolymer, meglumine, calcium citrate, dextrin, pectin

etc.; those of (3) a disintegrating agent are starch, agar, gelatin powder, crystalline cellulose, calcium carbonate, sodium bicarbonate, calcium citrate, dextrin, pectin, carboxymethyl cellulose calcium etc.; those of (4) a lubricant are magnesium stearate, talc, polyethylene glycol, silica, hydrogenated plant oil etc.; those of (5) a coloring agent are those which are allowed to add to pharmaceuticals; those of (6) a corrigent are cocoa powder, menthol, aromatic powder, peppermint oil, borneol and cinnamon powder; and those of (7) an antioxidant are those which are permitted to be added to pharmaceuticals, such as ascorbic acid, α -tocopherol and the like, are respectively used.

(1) In the manufacture of preparations for oral use, the compound of the present invention or a pharmacologically acceptable salt is mixed with a filler and, if necessary, further with a binder, a disintegrating agent, a lubricant, a coloring agent, a corrigent, etc. and the mixture is made into diluted powder, fine particles, granules, tablets, coated tablets, capsules, etc. by a common method. (2) In case of tablets and coated tablets, there is of course no problem that such tablets and granules are sugar-coated, gelatin-coated, or appropriately coated upon necessity. (3) In case of the manufacture of liquid preparations such as syrup, injection preparations and eye drops, a pH adjusting agent, a solubilizer, an isotonizing agent, etc. and, if necessary, a solubilizing aid, a stabilizer, buffer, suspending agent, antioxidant etc.

are added, and then made into pharmaceutical preparations by a common method. It can be made as a freeze drying product, and a injections can be dosed in vena, subcutis, and muscle. Preferable examples in a suspending agent include methyl cellulose, polysorbate 80, hydroxyethyl cellulose, gum arabic, tragacanth powder, sodium carboxymethyl cellulose, polyoxyethylene sorbitan monolaurate, and the like; preferable examples in a resolving aid include polyoxyethylene hardened castor oil, polysorbate 80, nicotinic acid amide, polyoxyethylene sorbitan monolaurate, and the like; preferable examples in a stabilizer include sodium sulfite, meta sodium sulfite, ether, and the like; preferable examples in a preservative include methyl p-oxybenzoate, ethyl p-oxybenzoate, sorbic acid, phenol, cresol, chlorocresol and the like. Further, (4) in case of external use, there is no particular limitation for a method of manufacturing a pharmaceutical preparation, but a common method is used for the manufacture. Thus, with regard to a base material used, various materials which are commonly used for pharmaceuticals, quasi drugs, cosmetics, etc. may be used. Specific examples of the base material used are animal/plant oil, mineral oil, ester oil, waxes, higher alcohols, fatty acids, silicone oil, surfactant, phospholipids, alcohols, polyhydric alcohols, water-soluble high-molecular substances, clay minerals and pure water and, if necessary, it is possible to add pH adjusting agent, antioxidant, chelating agent, antiseptic antifungal, coloring

agent, perfume, etc. If necessary, it is further possible to compound other components such as a component having a differentiation-inducing action, blood flow promoter, bactericide, anti-inflammatory agent, cell activator, vitamins, amino acid, moisturizer and keratin solubilizing agent.

Dose of the pharmaceutical agent according to the present invention varies depending upon degree of symptom, age, sex, body weight, dosage form, type of salt, sensitivity to the pharmaceuticals, specific type of the disease, etc. and, in the case of adults, the daily dose is usually about 30 μ g to 10 g, preferably, 100 μ g to 5 g or, more preferably, 100 μ g to 100 mg in the case of oral administration while, in the case of administration by injection, it is usually about 30 μ g to 1 g, preferably 100 μ g to 500 mg or, more preferably, 100 μ g to 30 mg. That is administered once daily or in several portions a day.

In accordance with the present invention, it is possible to provide a novel compound (I) which show an excellent inhibiting action to AMPA receptor and/or kainate receptor and are useful as pharmaceutical agents. Further, a useful production process for producing the compound or its salt and a production intermediate could be provided. According to this process, the compound relating to the present invention can be obtained in high yield, and the highly safe compound can be obtained. The compound (I) of the present invention suppress the neurotoxicity of excitatory neurotransmitters and is able

65702-519

to achieve an excellent neuroprotecting action as a pharmaceutical agent. Accordingly, the compounds of the present invention may be used as therapeutic, preventive and improving agents for various nervous diseases and may be used, for example, as therapeutic and preventive agents for acute neurodegenerative diseases (such as cerebrovascular disorders at acute stage, subarachnoid hemorrhag, head injury, spinal cord injury, neuropathy caused by hypoxia or hypoglycemia etc.), chronic neurodegenerative diseases (such as Alzheimer's disease, Parkinson's disease, Huntington's chorea, amyotrophic lateral sclerosis or spinocerebellar degeneration), epilepsy, hepatic encephalopathy, peripheral neuropathy, Parkinson's syndrome, spasticity, pain, neuralgia, schizophrenia, anxiety, drug abuse, nausea, vomiting, urinary disturbance, visual disturbance due to glaucoma, auditory disturbance due to antibiotics, food poisoning, infectious cerebrospinal meningitis (such as HIV cerebrospinal meningitis), cerebrovascular dementia, or dementia or nervous symptoms due to meningitis. Further, the compound of the present invention may be used as an agent for treating or preventing demyelinating disorder (such as encephalitis, acute disseminated encephalomyelitis, multiple sclerosis, acute demyelinating polyneuropathy, Guillain Barre syndrome, chronic inflammatory demyelinating polyneuropathy, Marchifava-Bignami disease, central pontine myelinolysis, neuromyelitis optica, Devic syndrome, Balo disease, HIV-

65702-519(S)

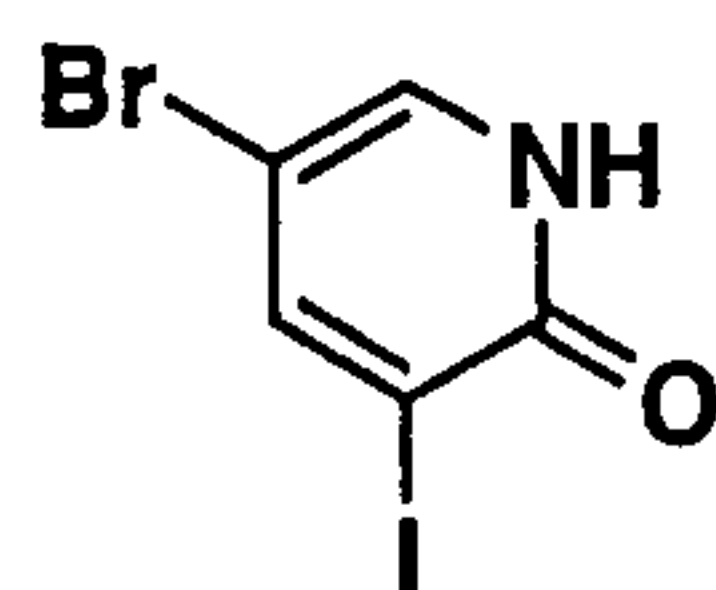
myelopathy, HTLV-myelopathy, progressive multifocal leucoencephalopathy and a secondary demyelinating disorder (such as CNS lupus erythematoses, polyarteritis nodosa, Sjogren syndrome, sarcoidosis and isolated cerebral vasculitis)).

Examples

The following Reference Examples, Examples and Test Examples are exemplary, and not intended to limit the present invention. One skilled in the art may make various variations of Reference Examples, Examples and Test Examples to fully utilize the invention. These variations shall be included in claims of the invention.

Referential Example 1

5-Bromo-3-iodo-1,2-dihydropyridin-2-one



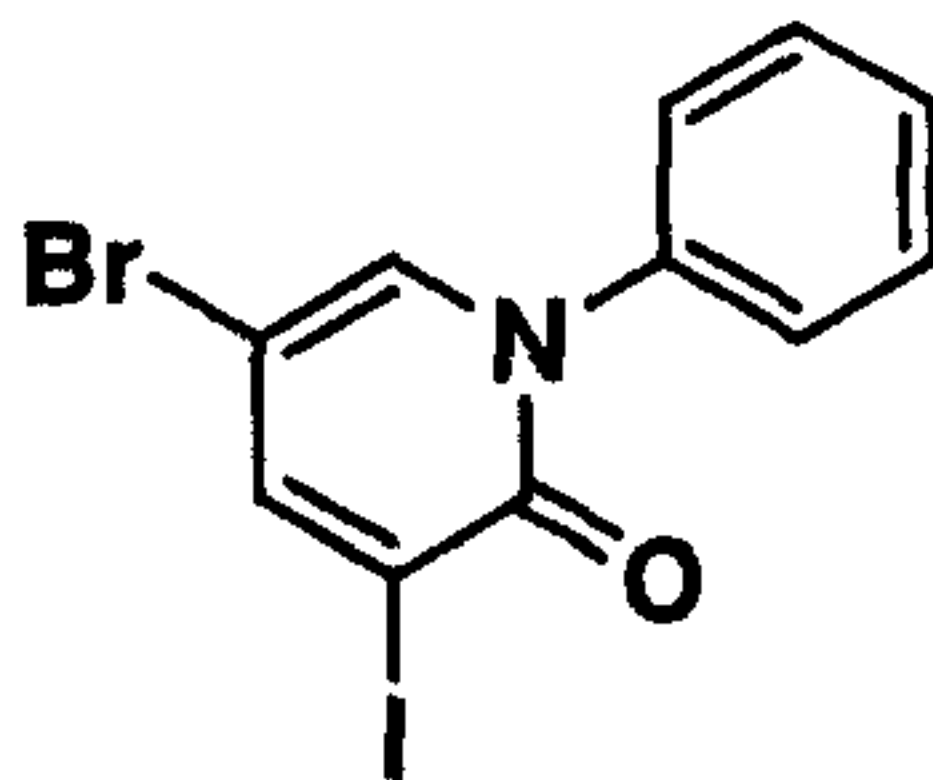
2-Amino-5-bromopyridine (CAS No. 1072-97-5) (300 g) was dissolved in a mixed solvent consisting of 1000 ml of acetic acid and 200 ml of water, 30 ml of concentrated sulfuric acid were gradually dropped thereinto under stirring. Then, 79.1 g of periodic acid hydrate and 176 g of iodine were added thereto, followed by stirring at 80°C for 4 hours. To the reaction mixture were added periodic acid hydrate (40g) and iodine (22g), followed by further stirring at 80°C for 2 hours. After cooling to room temperature, the reaction mixture was poured onto ice

(3000ml) and neutralized to pH 7.0 with 5N aqueous sodium hydroxide. The resulting crystals were collected by filtration, dissolved in a mixed solvent of ethyl acetate/diethyl ether, successively washed with aqueous sodium thiosulfate, water, 1N aqueous sodium hydroxide and brine, and dried over anhydrous magnesium sulfate. Then, the solvent was evaporated, to give 392g of 2-amino-5-bromo-3-iodopyridine (yield: 76%). 2-Amino-5-bromo-3-iodopyridine (100 g) was gradually added to 300 ml of concentrated sulfuric acid under ice-cooling. After the reaction mixture was stirred at room temperature for 2 hours, it was ice-cooled again. 35 g of sodium nitrite were gradually added thereto, followed by stirring at room temperature for 3 days and nights. The reaction solution was poured onto ice (3000 ml) and neutralized to pH 4.0 with sodium hydroxide. The resulting crystals were collected by filtration, washed with water and warm air-dried at 60°C for one day and night, to give 102 g (quantitative) of the title compound.

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.60 (d, 1H), 8.14 (d, 1H).

Referential Example 2.

5-Bromo-1-phenyl-3-iodo-1,2-dihydropyridin-2-one



5-Bromo-3-iodo-1,2-dihydropyridin-2-one (10.0 g)

obtained in Referential Example 1, 10.0 g of phenylboronic acid

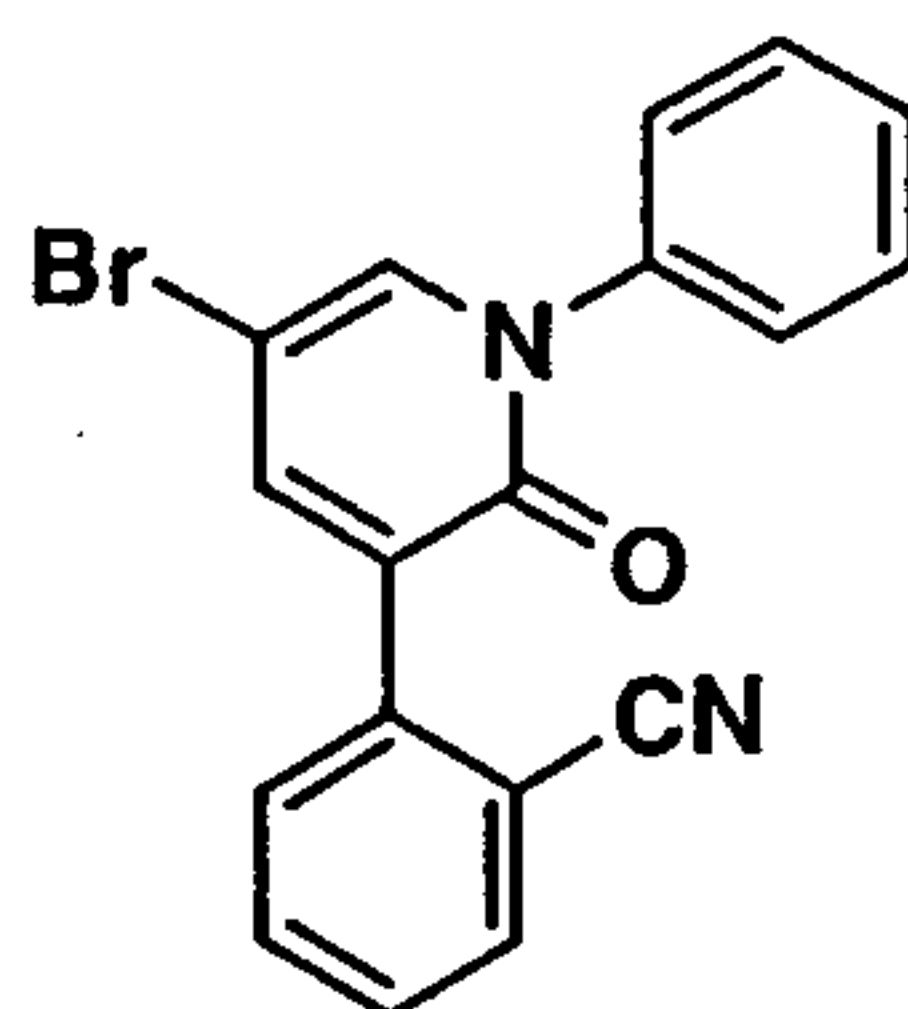
65702-519

and 8.1 g of copper acetate were suspended in 500 ml of dichloromethane. 15 ml of triethylamine were added thereto, followed by stirring at room temperature for 5 days and nights. To the reaction solution were added 200 ml of water and 50 ml of aqueous ammonia, followed by stirring vigorously. Then the insoluble matters were filtered off through Celite*, the filtrate was extracted with dichloromethane, the extract was dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was recrystallized from ethyl acetate/hexane, to give 6.54 g (yield: 52%) of the title compound.

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.34-7.38 (m, 2H), 7.44-7.52 (m, 3H), 7.53 (d, 1H), 8.10 (d, 1H).

Referential Example 3.

5-Bromo-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one



5-Bromo-1-phenyl-3-iodo-1,2-dihydropyridin-2-one

(11.69 g) obtained in Referential Example 2, 8.0 g of 2-(2-cyanophenyl)-1,3,2-dioxaborinate and 16.0 g of cesium carbonate were suspended in 150 ml of dimethylformamide. 3.0 g of tetrakis(triphenylphosphine) palladium were added thereto, followed by stirring at 80°C in nitrogen atmosphere for 2 hours. The reaction solution was poured into water, the mixture was

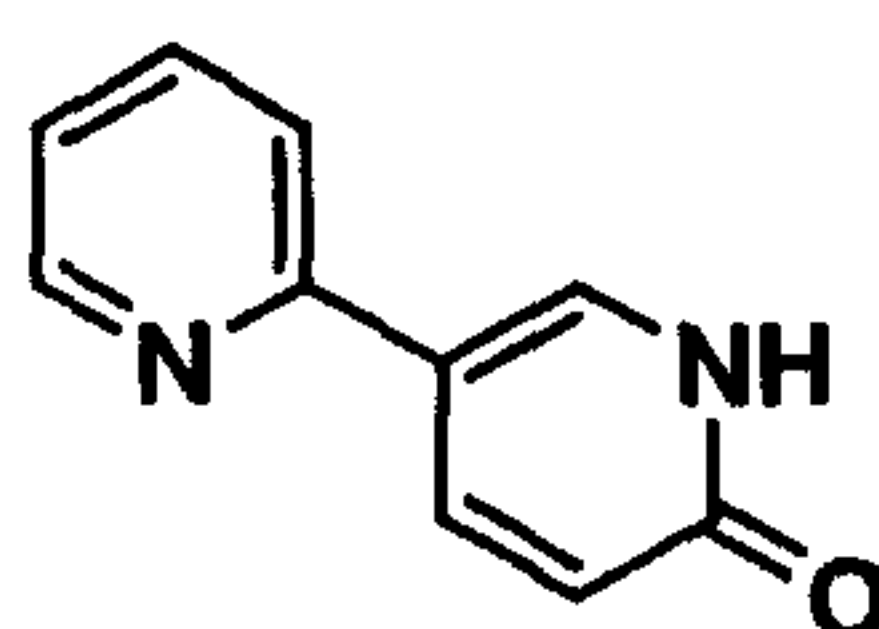
*Trade-mark

extracted with ethyl acetate, the extract was successively washed with water and brine and dried over anhydrous magnesium sulfate. Then, the solvent was evaporated, and the residue was purified by a silica gel column chromatography (hexane/ethyl acetate system), followed by recrystallizing from ethyl acetate/hexane, to give 5.67 g (yield: 52%) of the title compound.

$^1\text{H-NMR}$ (400 MHz, CDCl_3); δ (ppm) 7.42-7.54 (m, 6H), 7.61-7.65 (m, 4H), 7.66 (d, 1H), 7.74-7.77 (m, 1H).

Referential Example 4.

5-(2-Pyridyl)-1,2-dihydropyridin-2-one

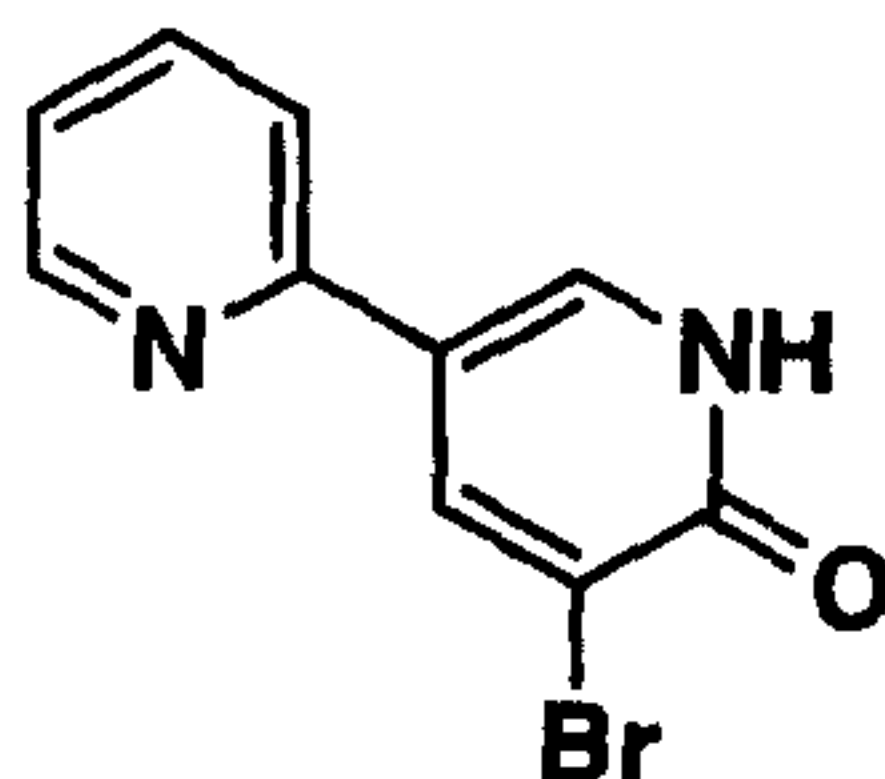


2,5-Diboromopyridine [CAS No. 624-28-2] (400 g) was added to 3500 ml of a 28% methanolic solution of sodium methoxide, the mixture was stirred at 60°C for 3 hours and allowed to cool, the reaction solution was poured into 3 liters of water, the mixture was extracted with 9000 ml of diethyl ether, the extract was washed with a saturated saline solution for three times and dried over anhydrous magnesium sulfate and the solvent was evaporated *in vacuo*. The residue was dissolved in 2 liters of dimethylformamide, 900 g of tri-N-butyl-(2-pyridyl) tin [CAS No. 59020-10-9] and 20 g of tetrakis(triphenylphosphine) palladium and mixture was stirred at 120°C in a nitrogen atmosphere for 3 hours. The reaction solution was allowed to

cool and poured into 3 liters of water, the mixture was extracted with 10 liters of diethyl ether, the extract was successively washed with a saturated sodium bicarbonate solution and a saturated saline solution and the solvent was evaporated in vacuo. A 48% aqueous solution (800 ml) of hydrogen bromide was added to the residue and the mixture was stirred at 110°C for 3 hours. After allowing to cool, the reaction solution was washed with 3 liters of diethyl ether, poured into 2 liters of ice, adjusted to pH 11.0 with a 5N sodium hydroxide solution and washed with 3 liters of diethyl ether again. The aqueous layer was adjusted to pH 7.0 and extracted with dichloromethane. The crude crystals prepared by evaporating the solvent in vacuo were washed with a mixed solvent consisting of diethyl ether and hexane to give 201.5 g (yield: 69%) of the title compound. ¹H-NMR (400MHz, CDCl₃); δ(ppm) 6.72 (d, 1H), 7.20 (ddd, 1H), 7.50-7.54 (m, 1H), 7.73 (dt, 1H), 8.12-8.15 (m, 1H), 8.19 (dd, 1H), 8.60-8.64 (m, 1H).

Referential Example 5.

3-Bromo-5-(2-pyridyl)-1,2-dihydropyridin-2-one



5-(2-Pyridyl)-1,2-dihydropyridin-2-one (201.5 g)

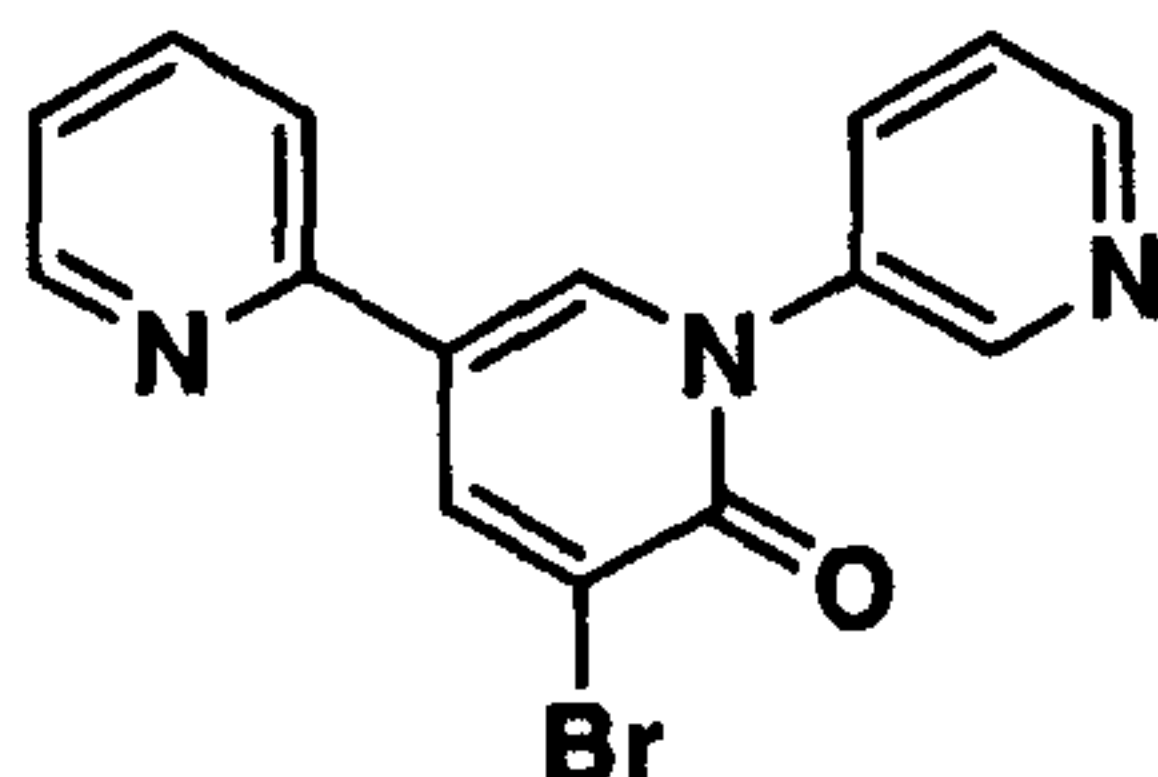
obtained in Referential Example 4 was dissolved in 1300 ml of dimethylformamide, 208.3 g of N-bromosuccimide were added thereto and the mixture was stirred at room temperature for 2

hours. The reaction mixture was poured into 4 liters of ice water and the precipitate was filtered and dried with warm air at 50°C for two days and nights to give 230 g (yield: 79%) of the title compound.

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.21-7.26 (m, 1H), 7.52 (d, 1H), 7.75 (dt, 1H), 8.21 (d, 1H), 8.61-8.64 (m, 1H), 8.67 (d, 1H).

Referential Example 6.

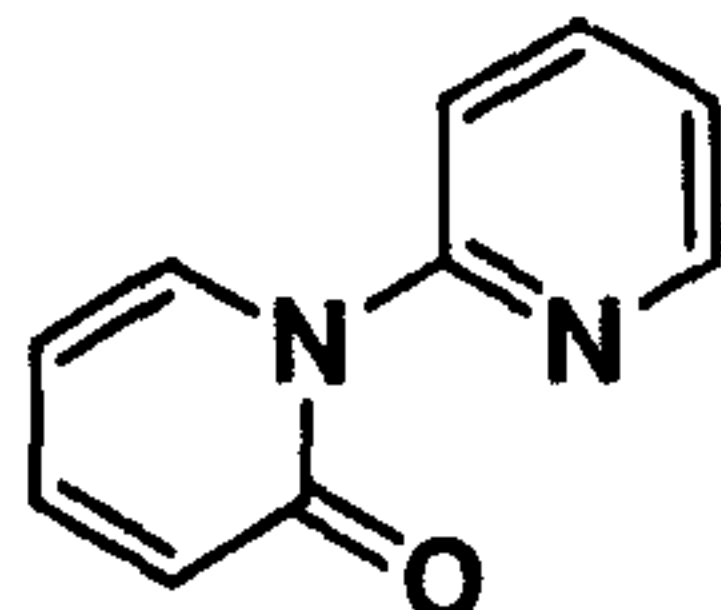
3-Bromo-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one



Dichloromethane (300 ml) was added to 18.75 g of 3-bromo-5-(2-pyridyl)-1,2-dihydropyridin-2-one obtained in Referential Example 5 and 18.36 of 3-pyridineboronic acid, then 3.47 g of di-μ-hydroxo-bis[(N,N,N',N'-tetramethylethylenediamine) copper (II)] chloride were added and the mixture was stirred in an oxygen atmosphere for 4 days and nights. The reaction solution was purified by an NH silica gel short column (eluted by ethyl acetate), the solvent was evaporated in vacuo and the resulting crude crystals were washed with diethyl ether to give 24.26 g (yield: 99%) of the title compound.

¹H-NMR (400MHz, CDCl₃); δ (ppm) 7.23-7.26 (m, 1H), 7.47-7.51 (m, 1H), 7.52-7.56 (m, 1H), 7.77 (dt, 1H), 7.87-7.91 (m, 1H), 8.19 (d, 1H), 8.53 (d, 1H), 8.59-8.62 (m, 1H), 8.71-8.75 (m, 2H).

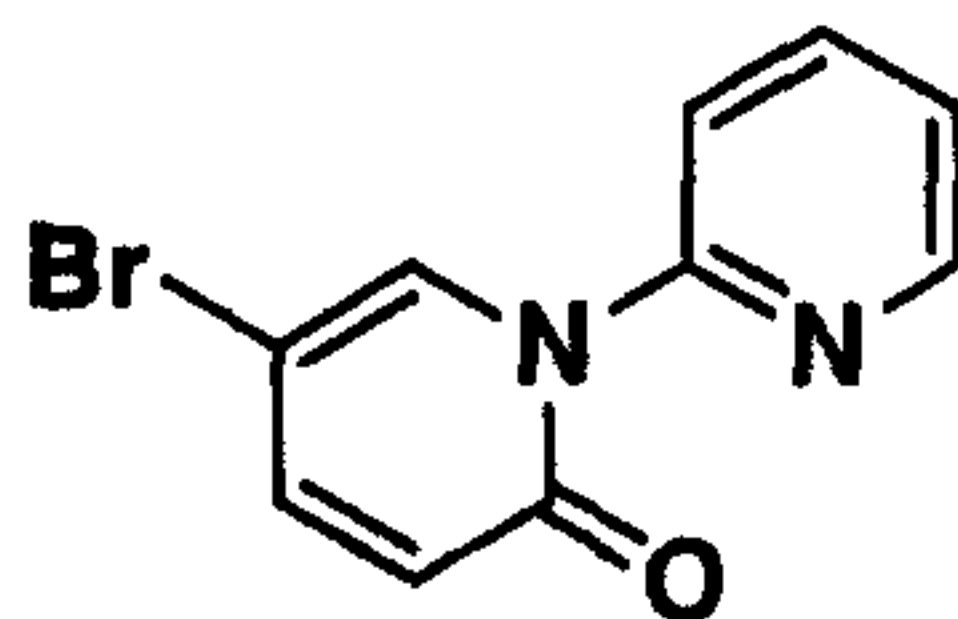
Referential Example 7.

1-(2-Pyridyl)-1,2-dihydropyridin-2-one

25ml of a dimethylformamide solution containing 4.00g of 2(1H)-pyridone and 8.00g of 2-bromopyridine was incorporated with 3.80g of potassium carbonate and 0.51g of cuprous iodide, followed by stirring at 120°C for 2 hours. After the mixture was returned to room temperature, water was added thereto. The mixture was extracted with ethyl acetate, and the ethyl acetate layer was washed with water and brine, and then dried over magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (ethyl acetate/hexane=1:1), to give 1.58g of the title compound as a pale yellow wax.

$^1\text{H-NMR}$ (400MHz, CDCl_3); δ (ppm) 6.31 (dt, 1H), 6.67 (d, 1H), 7.33 (ddd, 1H), 7.40 (ddd, 1H), 7.82-7.90 (m, 2H), 7.96 (dd, 1H), 8.57 (dd, 1H).

Referential Example 8.

1-(2-Pyridyl)-5-bromo-1,2-dihydropyridin-2-one

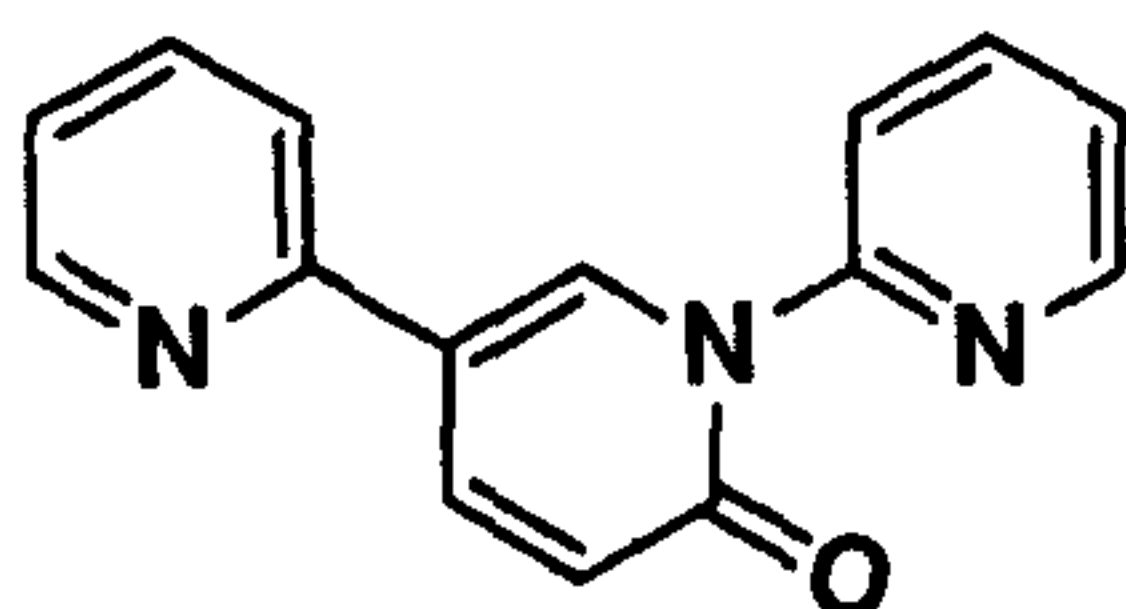
Under ice-cooling, 15ml of a dimethylformamide solution containing 1.50g of 1-(2-pyridyl)-1,2-dihydropyridin-2-one

was incorporated with 1.60g of N-bromosuccinic acid imide. The mixture was stirred at room temperature for 2 hours, and then diluted with water and extracted with ethyl acetate. The organic layer was washed with water and brine, and then dried over magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (ethyl acetate/hexane=1:3), to give 1.13g of the title compound as a pale brown powder.

$^1\text{H-NMR}$ (400MHz, CDCl_3); δ (ppm) 6.57(d, 1H), 7.34(ddd, 1H), 7.42(dd, 1H), 7.85(dt, 1H), 7.97(dd, 1H), 8.10(d, 1H), 8.57(dd, 1H).

Referential Example 9.

1-(2-Pyridyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one



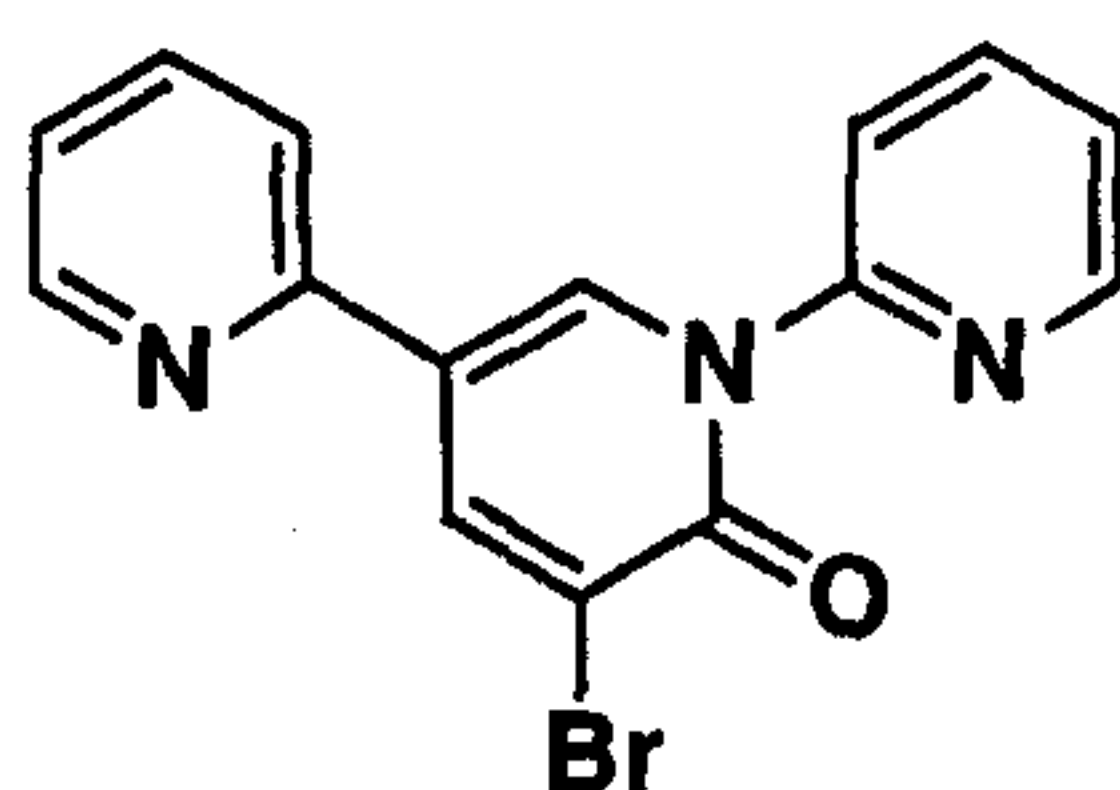
2.5ml of a dimethylformamide solution containing 0.10g of 1-(2-Pyridyl)-5-bromo-1,2-dihydropyridin-2-one and 0.30g of 2-tributyl stannyl pyridine was incorporated with 0.05g of dichlorobistriphenylphosphine palladium, followed by stirring at 130°C for 2 hours. The mixture was returned to room temperature, followed by diluting with water and extracting with ethyl acetate. The organic layer was washed with water and brine, and then dried over magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (ethyl acetate), to give 0.076g of the title

compound as a pale yellow powder.

$^1\text{H-NMR}$ (400MHz, CDCl_3); δ (ppm) 6.77(d, 1H), 7.22(dd, 1H), 7.36(dd, 1H), 7.61(d, 1H), 7.76(dt, 1H), 7.87(dt, 1H), 7.97(d, 1H), 8.12(dd, 1H), 8.60-8.65(m, 2H), 8.67(d, 1H).

Referential Example 10.

1-(2-Pyridyl)-5-(2-pyridyl)-3-bromo-1,2-dihydropyridin-2-one

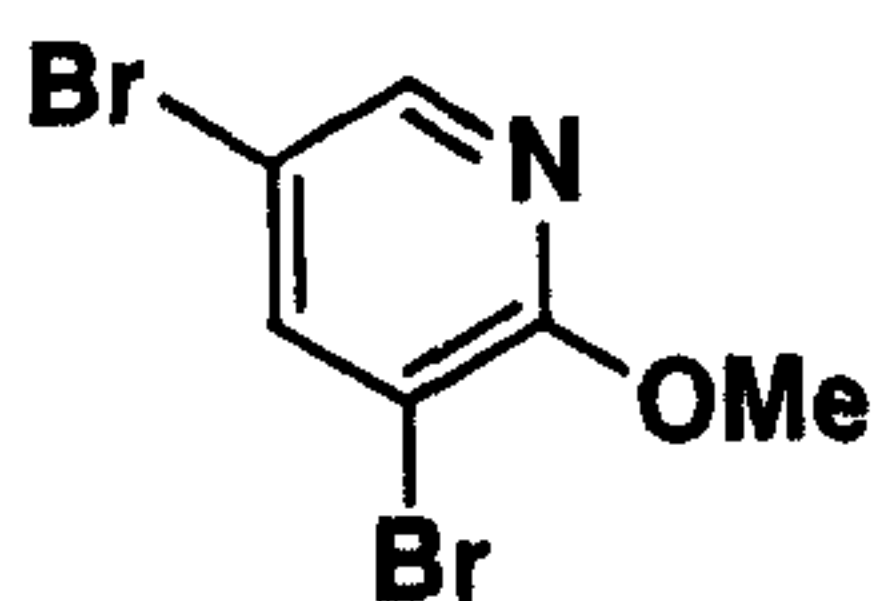


2ml of a dimethylformamide solution containing 0.07g of 1-(2-pyridyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one was incorporated with 0.07g of N-bromosuccinic acid imide, under stirring and ice-cooling. After stirring the mixture at room temperature for 2 hours, it was diluted with water and extracted with ethyl acetate. The organic layer was washed with water and brine, and then dried over magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (ethyl acetate/hexane=3:1), to give 0.05g of the title compound as a pale brown powder.

$^1\text{H-NMR}$ (400MHz, $\text{DMSO}-d_6$); δ (ppm) 7.33(ddd, 1H), 7.58(ddd, 1H), 7.83-7.88(m, 2H), 7.97(dd, 1H), 8.07(dt, 1H), 8.59-8.62(m, 1H), 8.65-8.80(m, 1H), 8.72(d, 1H), 8.81(d, 1H).

Referential Example 11.

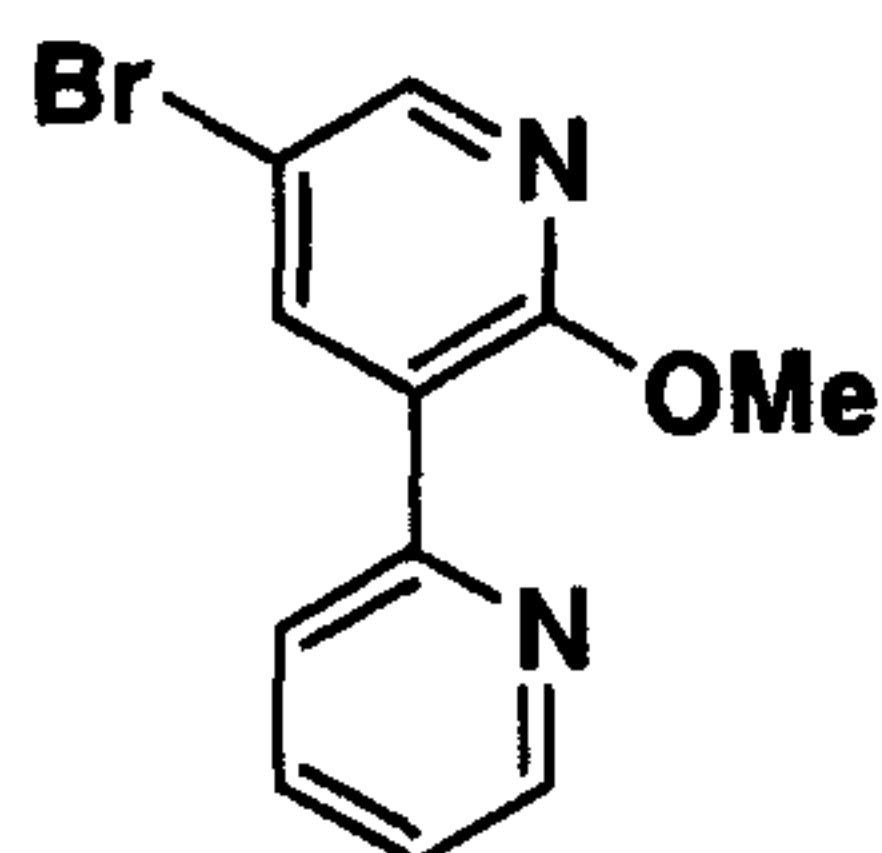
3,5-Dibromo-2-methoxypyridine



80ml of a 28% sodium methoxide solution was incorporated with 30.0g of 2,3,5-tribromopyridine under ice-cooling, followed by stirring at 50°C for 2 hours. The reaction solution was diluted with water and extracted with diethyl ether. The organic layer was washed with brine, and then dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (ethyl acetate/hexane=1:20), to give 18.5g of the title compound. ¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.99(s, 3H), 7.93(d, 1H), 8.14(d, 1H).

Referential Example 12.

3-(2-Pyridyl)-5-bromo-2-methoxypyridine



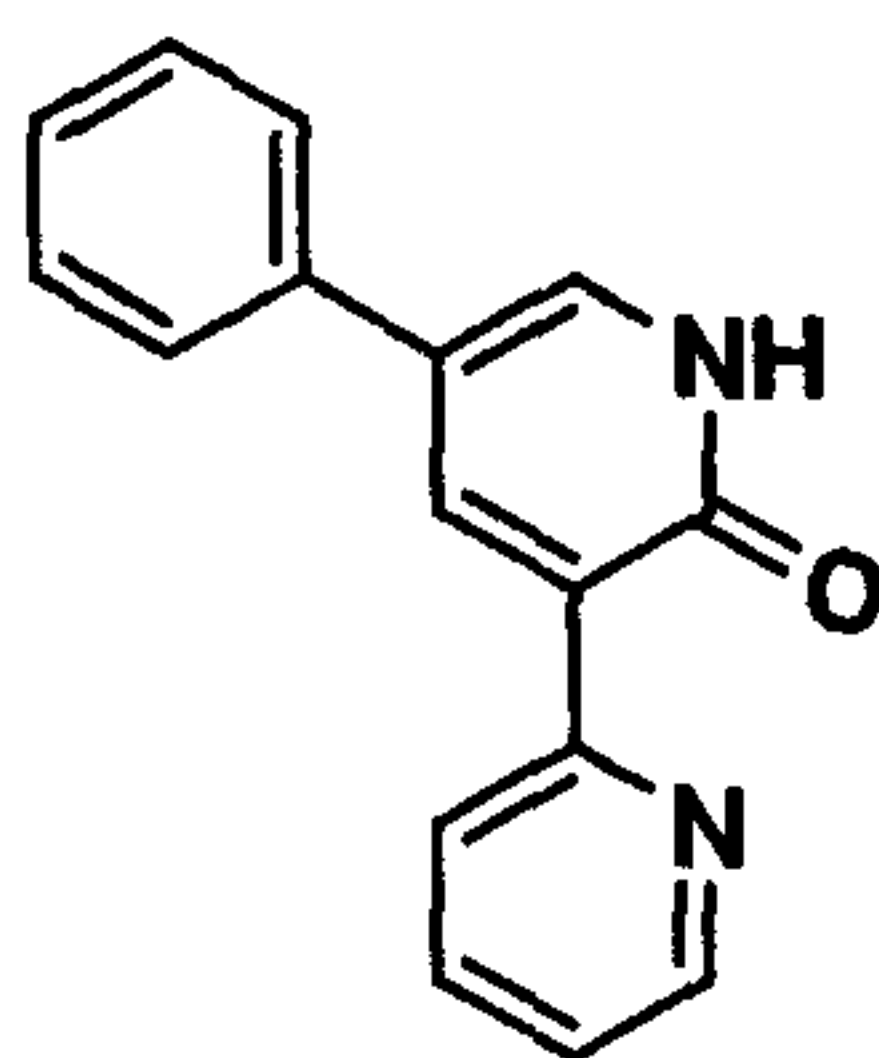
100ml of a dimethylformamide solution containing 6.3g of 3,5-dibromo-2-methoxypyridine and 8.1g of 2-tributyl stannyl pyridine was incorporated with 1.0g of tetrakis(triphenylphosphine) palladium, followed by stirring at 120°C for 2 hours in nitrogen atmosphere. After the mixture was returned to room temperature, the solvent was evaporated, and the residue was extracted with ethyl acetate. The organic

layer was washed with water and brine, and then dried over magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (ethyl acetate/hexane=1:3), to give 2.8g of the title compound as a pale yellow powder.

$^1\text{H-NMR}$ (400MHz, CDCl_3); δ (ppm) 4.02(s, 3H), 7.31(dd, 1H), 7.80(dt, 1H), 8.02(ddd, 1H), 8.25(d, 1H), 8.40(d, 1H), 8.71-8.74(m, 1H).

Referential Example 13.

3-(2-Pyridyl)-5-phenyl-2-(1H)-pyridone



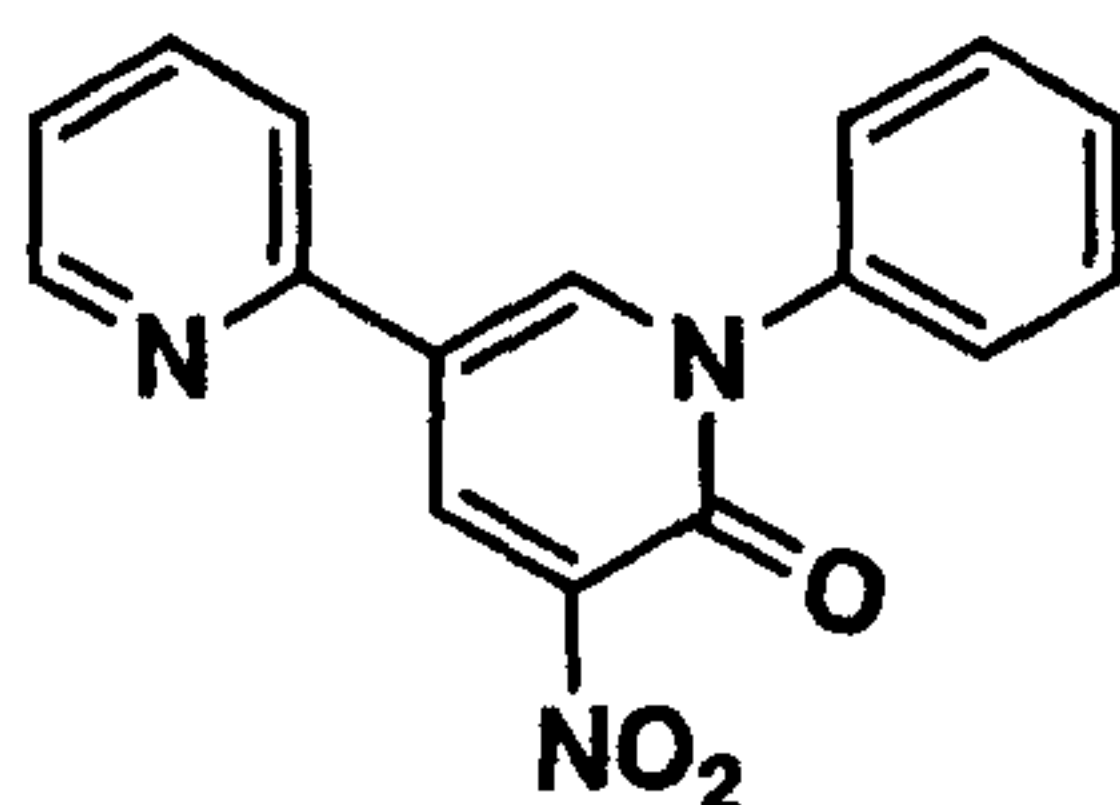
A mixture of 1.0g of 3-(2-pyridyl)-5-bromo-2-methoxypyridine, 0.9g of phenylboronic acid, 0.3g of dichlorobistriphenylphosphine palladium and 2ml of triethylamine was stirred at 120°C for 1.5 hours in 30ml of xylene in nitrogen atmosphere. The mixture was returned to room temperature, diluted with ethyl acetate, washed with water and brine, and dried over magnesium sulfate. The solvent was evaporated, and the residue was incorporated with 47% hydrobromic acid and heated at 70°C for 1 hour. The reaction solution was ice-cooled, diluted with water, and neutralized with potassium carbonate. The resulting precipitates were collected by filtration, washed with water and ether, and then

air-dried, to give 0.5g of the title compound as a pale yellow powder.

$^1\text{H-NMR}$ (400MHz, DMSO-d_6); δ (ppm) 7.30-7.37 (m, 2H), 7.43 (dd, 2H), 7.62 (d, 2H), 7.82-7.90 (m, 1H), 7.87 (d, 1H), 8.64-8.69 (m, 2H), 8.57 (d, 1H), 12.30 (brs, 1H).

Referential Example 14.

1-Phenyl-3-nitro-5-(2-pyridyl)-1,2-dihydropyridin-2-one



(14a) 3-Nitro-1-phenyl-1,2-dihydropyridin-2-one

5g of 2-hydroxy-3-nitropyridine, 7.14g of phenylboronic acid, 2.6g of copper (II) acetate, 9.9ml of triethylamine and 5.8ml of pyridine were added to 100ml of tetrahydrofuran, followed by stirring overnight. The reaction mixture was poured into aqueous ammonia, and extracted with ethyl acetate. The organic layer was washed with water, dried, and concentrated. The residue was suspended into ether, and collected by filtration, to give 4.71g of the title compound.

$^1\text{H-NMR}$ (400MHz, CDCl_3); δ (ppm) 6.39 (dd, 1H), 7.36-7.40 (m, 2H), 7.49-7.54 (m, 3H), 7.73 (dd, 1H), 8.38 (dd, 1H).

(14b) 5-Bromo-3-nitro-1-phenyl-1,2-dihydropyridin-2-one

10ml of a dimethylformamide solution containing 1g of 3-nitro-1-phenyl-1,2-dihydropyridin-2-one was incorporated with 988mg of N-bromosuccinimide, followed by stirring at room

temperature overnight. Further, it was stirred at 50°C for 3 hours. The reaction mixture was poured into ice-water, and the resulting precipitates were collected by filtration, to give 1.27g of the title compound.

¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.36-7.39 (m, 2H) , 7.50-7.57 (m, 3H) , 7.88 (d, 1H) , 8.42 (d, 1H) .

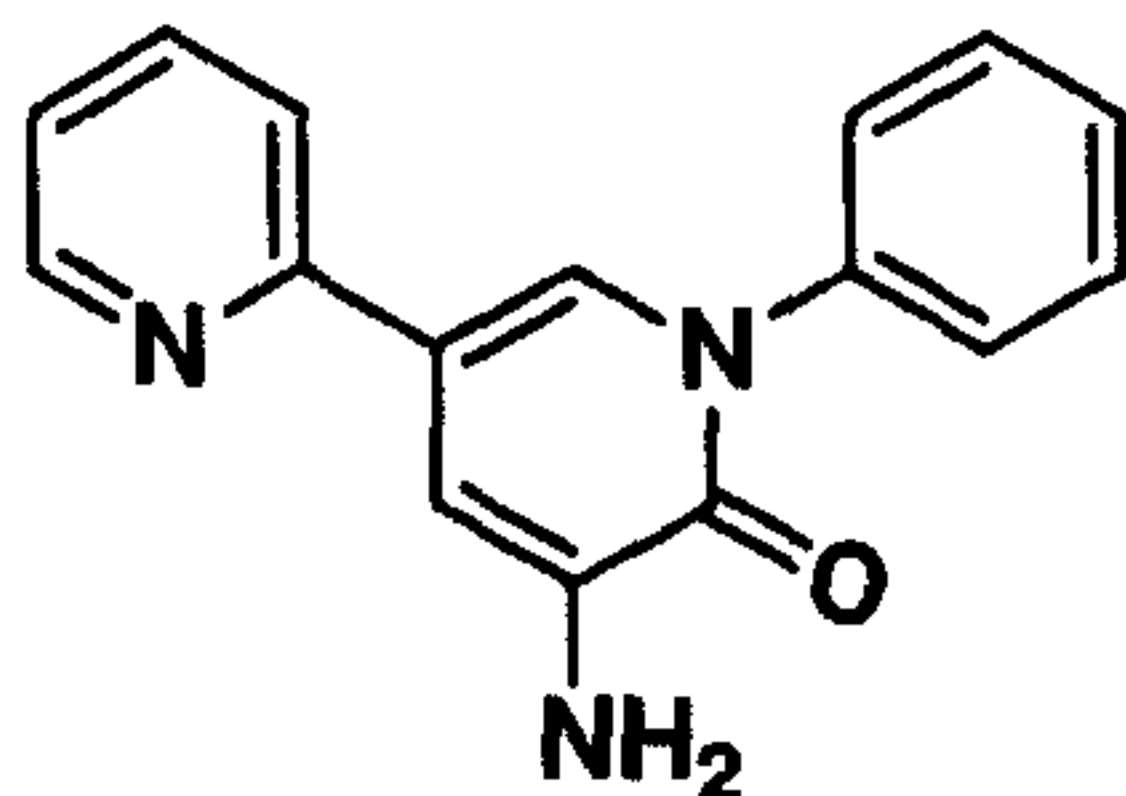
(14c) 3-Nitro-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

1.27g of 5-bromo-3-nitro-1-phenyl-1,2-dihydropyridin-2-one, 2.38g of 2-tri-n-butyl stannyl pyridine and 248mg of tetrakis(triphenylphosphine) palladium were added to 20ml of xylene, followed by stirring at 120°C overnight in nitrogen atmosphere. The reaction mixture was purified by silica gel chromatography (ethyl acetate/hexane system), to give 638mg of the title compound.

¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.28 (ddd, 1H) , 7.45-7.63 (m, 6H) , 7.80 (dt, 1H) , 8.61 (ddd, 1H) , 8.63 (d, 1H) , 9.03 (d, 1H) .

Referential Example 15.

3-Amino-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one



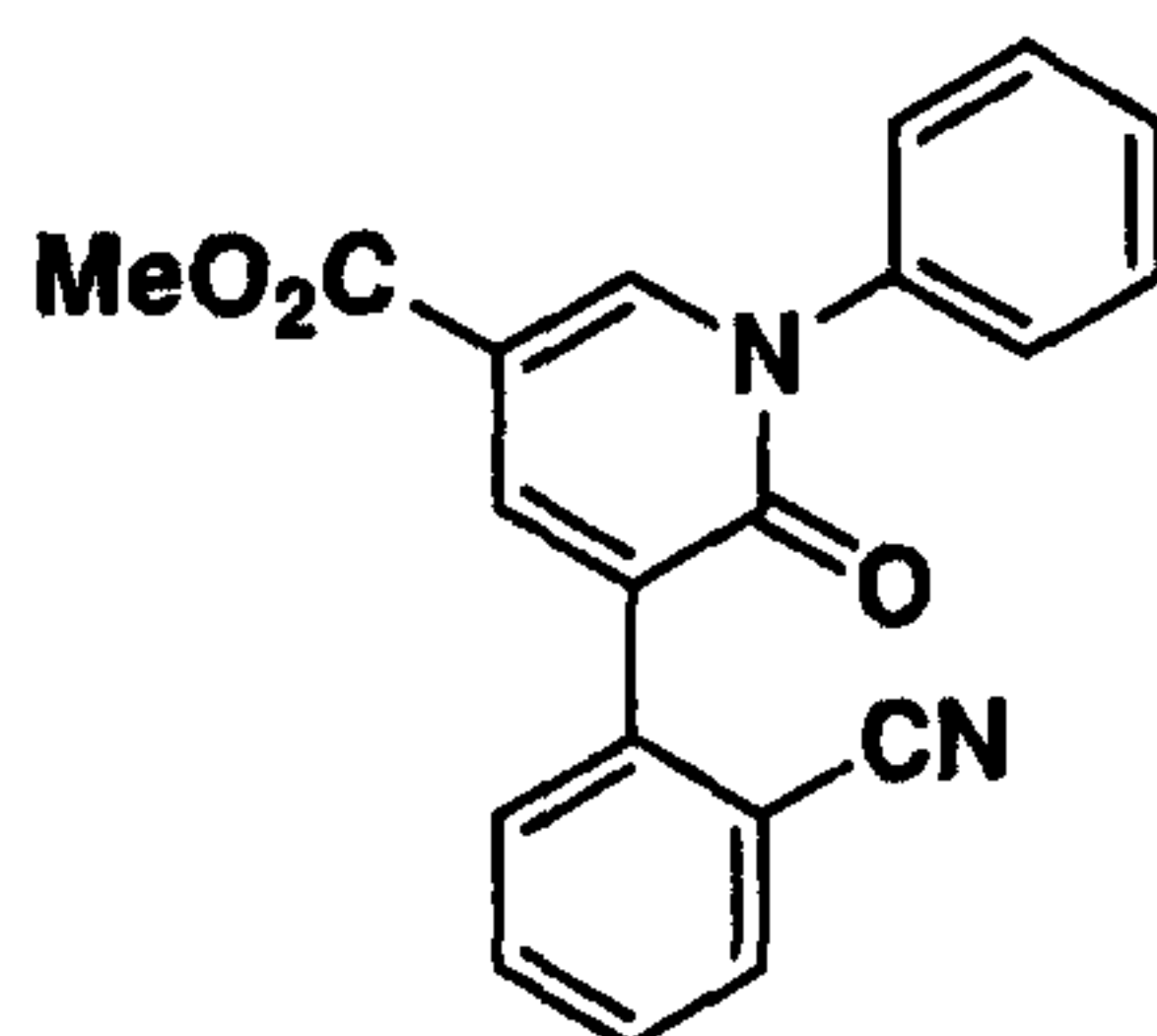
100mg of 10% palladium-carbon was added to 20ml of an ethanol solution containing 546mg of 3-nitro-1-phenyl-5-(pyridin-2-yl)-1,2-dihydropyridin-2-one, followed by stirring overnight in hydrogen atmosphere. The reaction

mixture was filtered through silica gel and concentrated, to give 411mg of the title compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 4.36-4.42 (m, 1H), 7.18 (dd, 1H), 7.28 (d, 1H), 7.44-7.54 (m, 6H), 7.61 (d, 1H), 7.70 (dt, 1H), 8.57-8.60 (m, 1H).

Referential Example 16.

3-(2-Cyanophenyl)-5-(methoxycarbonyl)-1-phenyl-1,2-dihydropyridin-2-one



6g of methyl 5-bromo-6-hydroxynicotinate synthesized by a known method from 6-hydroxynicotinic acid, and 6.3g of phenylboronic acid were dissolved in 200ml of tetrahydrofuran. To the mixture were added 939mg of copper acetate and 1ml of pyridine, followed by stirring at room temperature for 3 nights. Aqueous ammonia was added to the reaction solution, and the solution was extracted with chloroform. The organic layer was washed with brine, and then dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue obtained as a solid was washed with diethyl ether, to give 7.35g of 3-bromo-5-(methoxycarbonyl)-1-phenyl-1,2-dihydropyridin-2-one as white crystals. 5g of the product was dissolved in 100ml of dimethylformamide, followed by adding 4.6g of 2-(2-cyanophenyl)-1,3,2-dioxaborinate, 7.9g of cesium carbonate

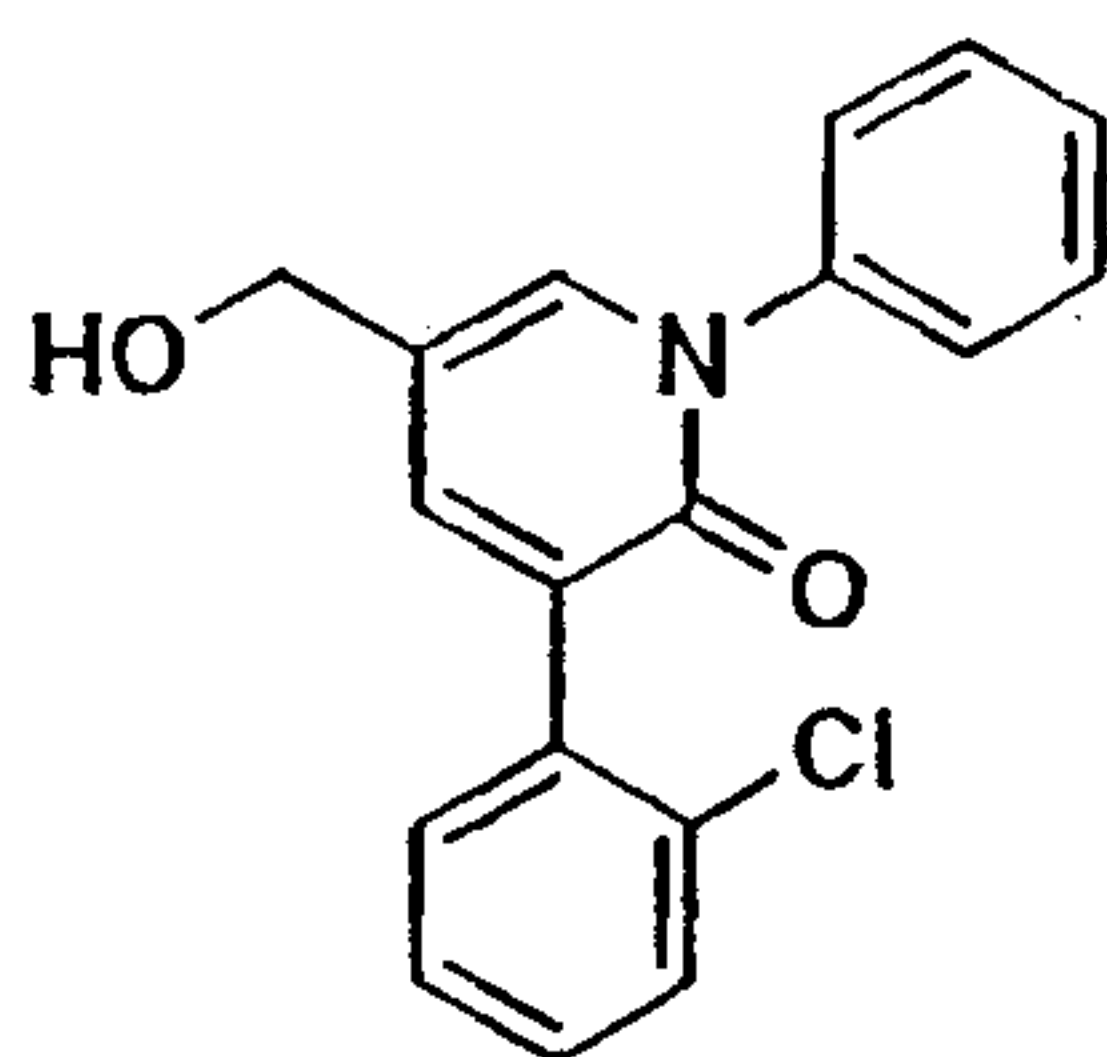
65702-519

and 375mg of tetrakis(triphenylphosphine) palladium, and stirring at 140°C for 1 hour in nitrogen atmosphere. After cooling to room temperature, the reaction mixture was poured into water, and extracted with ethyl acetate. Then, the extract was successively washed with water and brine, and dried over anhydrous magnesium sulfate. Then, the solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 3.23g of the title compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.89 (s, 3H), 7.42-7.55 (m, 6H), 7.61-7.66 (m, 2H), 7.75 (dd, 1H), 8.14 (d, 1H), 8.35 (d, 1H).

Referential Example 17.

3-(2-Chlorophenyl)-5-hydroxymethyl-1-phenyl-1,2-dihydropyridin-2-one



36mg of 3-(2-chlorophenyl)-5-methoxycarbonyl-1-phenyl-1,2-dihydropyridin-2-one synthesized by the method of Referential Example 3 from 3-bromo-5-methoxycarbonyl-1-phenyl-1,2-dihydropyridin-2-one and 2-chloroboronic acid, was dissolved in 20ml of toluene. After cooling to -78°C, 0.1ml diisopropyl aluminum hydride (1.5M tetrahydrofuran solution) was added dropwise thereinto. While heating from -78°C to room temperature, the mixture was stirred overnight. Then, 1N

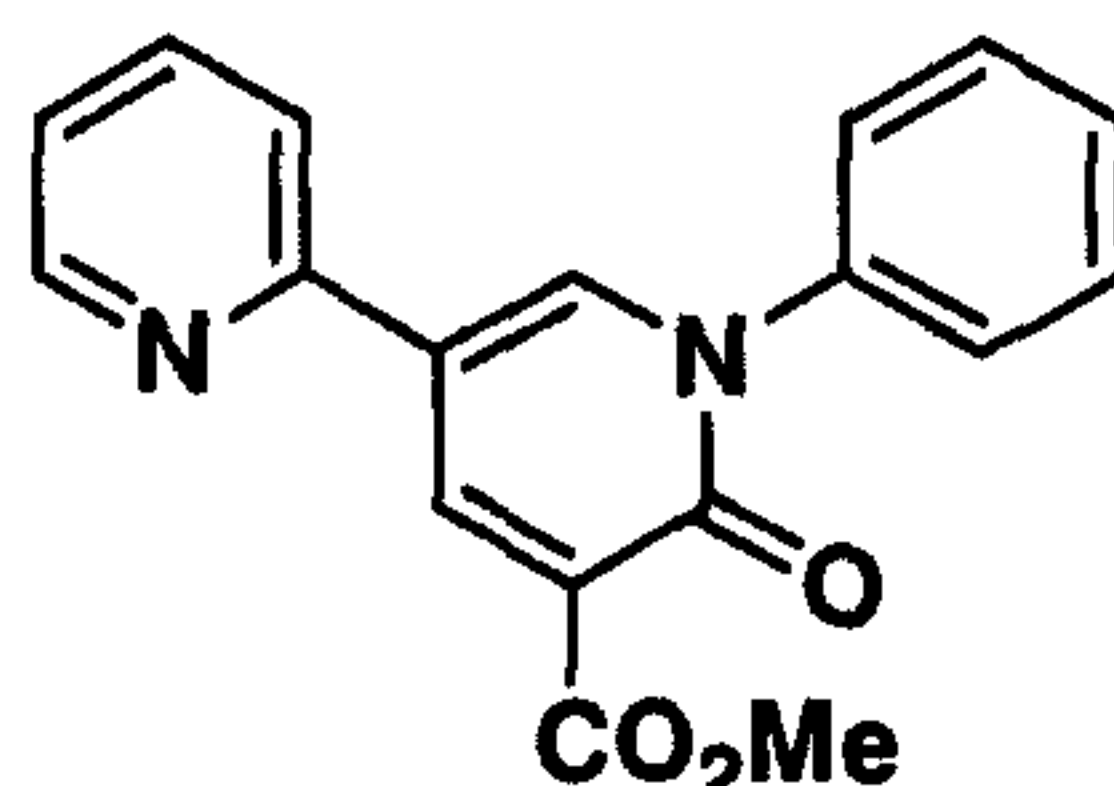
hydrochloric acid was added thereto, followed by stirring. The mixture was neutralized with an aqueous solution of sodium hydrogen carbonate, and then extracted with ethyl acetate. Then, the extract was successively washed with water and brine, and dried over anhydrous magnesium sulfate. Then, the solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 12mg of the title compound.

$^1\text{H-NMR}$ (400MHz, CDCl_3); δ (ppm) 4.48 (s, 2H), 7.25-7.29 (m, 3H), 7.37-7.51 (m, 8H).

ESI-Mass; 312 $[\text{M}^+ + \text{H}]$

Referential Example 18.

3-Methoxycarbonyl-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one



4.5g of methyl 5-bromo-2-hydroxynicotinate synthesized by a known method from 2-hydroxynicotinic acid, and 4.7g of phenylboronic acid were dissolved in 200ml of tetrahydrofuran. To the mixture were added 705mg of copper acetate and 1ml of pyridine, followed by stirring at room temperature for 3 nights in a flow of air. Aqueous ammonia was added to the reaction solution, and the solution was extracted with chloroform. The organic layer was washed with brine, and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue

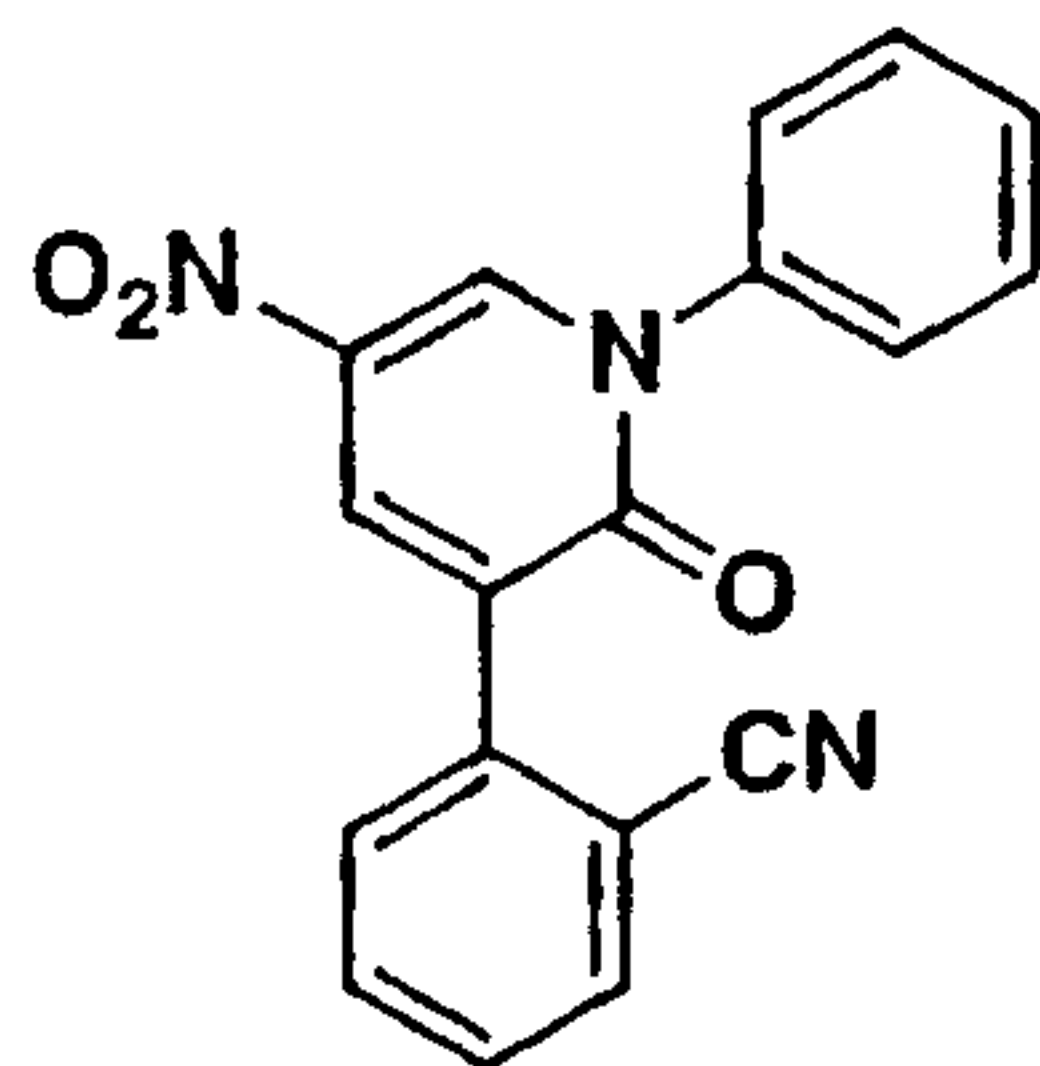
65702-519

obtained as a solid was washed with diethyl ether, to obtain 3.59g of 5-bromo-3-methoxycarbonyl-1-phenyl-1,2-dihydropyridin-2-one as white crystals. 3.2g of the product was dissolved in 100ml of dimethylformamide, to which 7.7g of tri-N-butyl-(2-pyridyl)tin [CAS No.59020-10-9] and 240mg of tetrakis(triphenylphosphine) palladium were added, followed by stirring at 110°C for 3 hours in nitrogen atmosphere. After cooling to room temperature, the reaction solution was poured into water, extracted with ethyl acetate. Then, the extract was successively washed with water and brine, dried over anhydrous magnesium sulfate, and then filtered through NH silica gel and silica gel. Then, the filtrate was evaporated, and the resulting precipitates were washed with ether and hexane, and dried, to give 1.59g of the title compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.95 (s, 3H), 7.22 (ddd, 1H), 7.42-7.54 (m, 5H), 7.62 (dt, 1H), 7.76 (td, 1H), 8.52 (d, 1H), 8.58 (ddd, 1H), 8.85 (d, 1H).

Referential Example 19.

3-(2-Cyanophenyl)-5-nitro-1-phenyl-1,2-dihydropyridin-2-one



(19a) 5-Nitro-1-phenyl-1,2-dihydropyridin-2-one

5.93g of the title compound was obtained in accordance with the method used for Referential Example (14a), from 5g

65702-519

of 2-hydroxy-5-nitropyridine.

¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 6.67(d, 1H), 7.39-7.43(m, 2H), 7.53-7.59(m, 3H), 8.18(dd, 1H), 8.68(dd, 1H).

(19b) 3-Bromo-5-nitro-1-phenyl-1,2-dihydropyridin-2-one

4.72g of the title compound was obtained in accordance with the method used for Referential Example (14b), from 5.93g of 5-nitro-1-phenyl-1,2-dihydropyridin-2-one.

¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.38-7.42(m, 2H), 7.54-7.58(m, 3H), 8.59-8.61(m, 1H), 8.66-8.68(m, 1H).

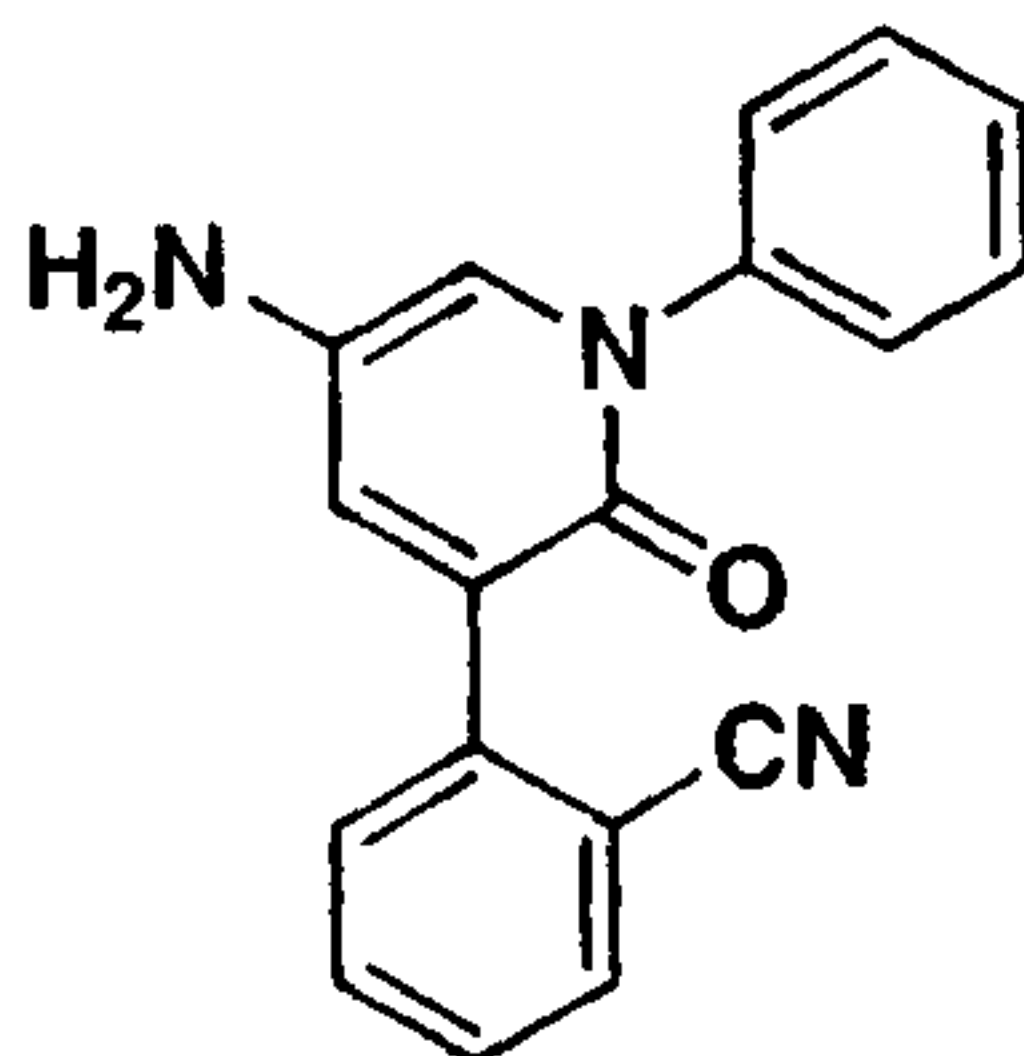
(19c) 5-Nitro-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one

758mg of the title compound was obtained in accordance with the method used for Referential Example 3, from 3g of 3-bromo-5-nitro-1-phenyl-1,2-dihydropyridin-2-one.

¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.47-7.63(m, 7H), 7.68(dt, 1H), 7.80(ddd, 1H), 8.38(d, 1H), 8.78(d, 1H).

Referential Example 20.

5-Amino-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one



414mg of the title compound was obtained in accordance with the method used for Referential Example 15, from 708mg of 5-nitro-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one.

^1H -NMR (400MHz, CDCl_3) ; δ (ppm) 6.99(d, 1H), 7.39-7.49(m, 7H), 7.60(dt, 1H), 7.73(d, 1H), 7.75(d, 1H).

Example 1.

3-(2-Cyanophenyl)-5-(2-nitrophenyl)-1-phenyl-1,2-dihydropyridin-2-one

5-Bromo-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one (100 mg), 60 mg of 2-nitrophenylboronic acid and 130 mg of cesium carbonate were suspended in 10 ml of dimethylformamide, then 20 mg of tetrakis(triphenylphosphine) palladium were added and the mixture was stirred at 120°C in a nitrogen atmosphere for 4 hours. After allowing to cool, the reaction solution was poured into water, the mixture was extracted with ethyl acetate, the extract was dried over anhydrous magnesium sulfate, the solvent was evaporated in vacuo and the residue was purified by a silica gel column chromatography (hexane-ethyl acetate system) to give 35 mg of the title compound.

^1H -NMR (400 MHz, CDCl_3) ; δ (ppm) 7.40-7.80 (m, 14H), 7.97 (dd, 1H).

Example 2.

5-(2-Aminophenyl)-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one

3-(2-Cyanophenyl)-5-(2-nitrophenyl)-1-phenyl-1,2-dihydropyridin-2-one (32 mg) was dissolved in 15 ml of ethyl acetate, 5 mg of 10% palladium-carbon (water-containing substance) were added and the mixture was stirred at room temperature in a hydrogen atmosphere for 15 minutes. The

catalyst was filtered off and the solvent was evaporated in vacuo to give 20 mg of the title compound.

¹H-NMR (400 MHz, CDCl₃); δ(ppm) 3.95 (bs, 2H), 6.76 (dd, 1H), 6.80 (dt, 1H), 7.14 (dd, 1H), 7.17 (dt, 1H), 7.41-7.55 (m, 6H), 7.59 (d, 1H), 7.62 (dt, 1H), 7.74-7.82 (m, 2H), 7.88 (d, 1H).

Example 3.

3-(2-Cyanophenyl)-5-(2-methylsulfonylaminophenyl)-1-phenyl-1,2-dihydropyridin-2-one

5-(2-Aminophenyl)-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one (16 mg) was dissolved in 10 ml of dimethylformamide, then 0.05 ml of triethylamine and 3 drops of methanesulfonyl chloride were added and the mixture was stirred at room temperature for one hour. Ethyl acetate was added to the reaction solution, the mixture was washed with water and a saturated saline solution, the solvent was evaporated in vacuo and the residue was purified by a silica gel column chromatography (hexane-ethyl acetate system) to give 5 mg of the title compound.

¹H-NMR (400 MHz, CDCl₃); δ(ppm) 2.19 (s, 3H), 6.88-6.95 (m, 1H), 7.08-7.15 (m, 1H), 7.38-7.55 (m, 8H), 7.61 (dt, 1H), 7.69-7.76 (m, 3H), 7.91 (d, 1H), 7.92-7.97 (m, 1H).

Example 4.

3-(2-Chloro-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

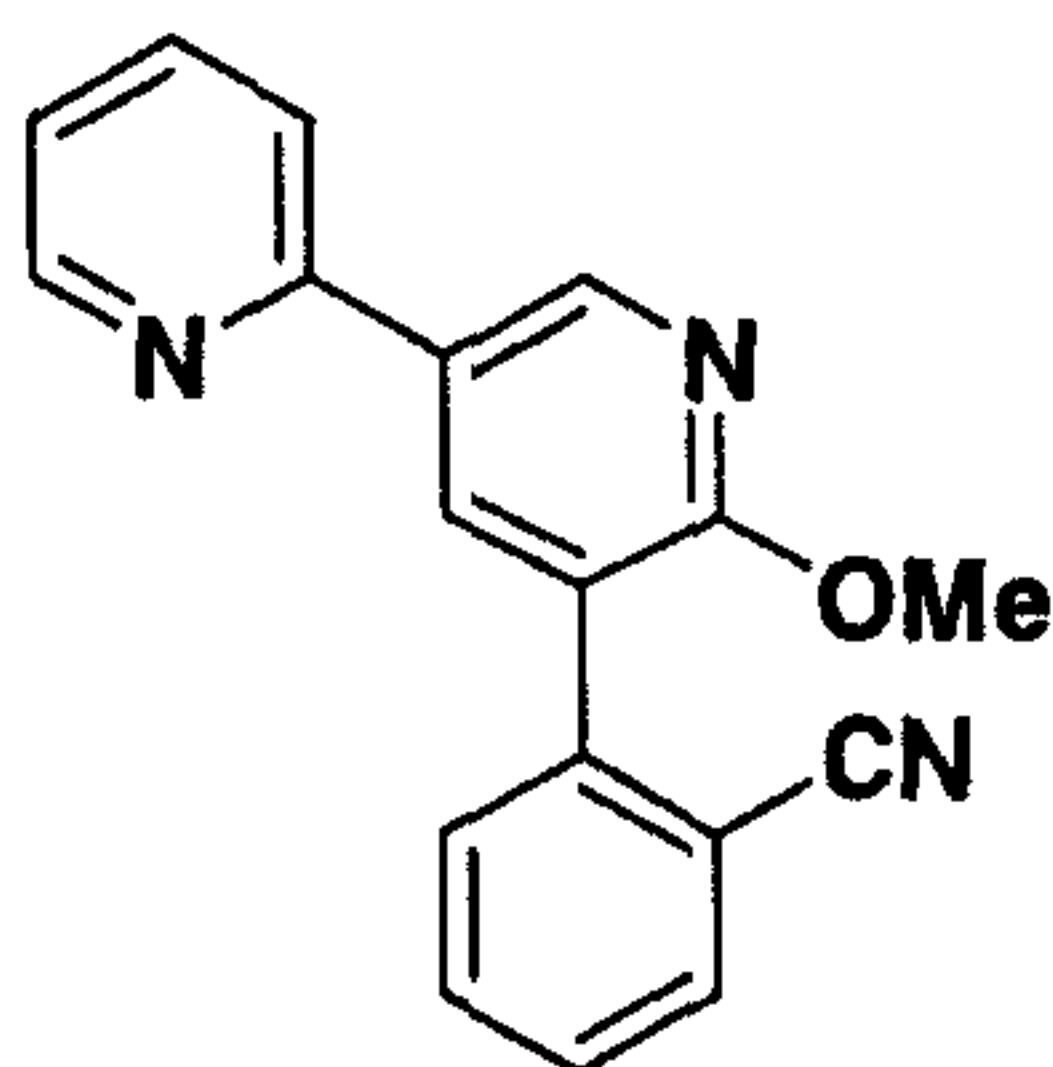
3-Iodo-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one (200 mg) synthesized by the same method as mentioned in

Referential Example 6, 130 mg of 2-chloro-3-pyridyl boronic acid and 250 mg of cesium carbonate were suspended in 10 ml of dimethylformamide, 40 mg of tetrakis(triphenyl)phosphine palladium were added and the mixture was stirred at 100°C in a nitrogen atmosphere for 3 hours. After allowing to cool, the reaction solution was poured into water, the mixture was extracted with ethyl acetate, the extract was dried over anhydrous magnesium sulfate, the solvent was evaporated in vacuo and the residue was purified by a silica gel column chromatography (hexane-ethyl acetate system) to give 143 mg of the title compound.

¹H-NMR (400 MHz, CDCl₃); δ(ppm) 7.20-7.24 (m, 1H), 7.31 (dd, 1H), 7.44-7.59 (m, 6H), 7.75 (dt, 1H), 7.91 (dd, 1H), 8.25 (d, 1H), 8.33 (d, 1H), 8.41 (dd, 1H), 8.59-9.62 (m, 1H).

Example 5.

3-(2-Cyanophenyl)-5-(2-pyridyl)-2-methoxypyridine



Tetrakis(triphenyl)phosphine palladium (0.15 g) was added to a mixed solution of 0.50 g of 5-(2-pyridyl)-3-bromo-2-methoxypyridine, 0.42 g of 2-(2-cyanophenyl)-1,3,2-dioxaborinate, 0.82 g of cesium carbonate and 20 ml of dimethylformamide and the mixture was stirred at 140°C in a nitrogen atmosphere for 5 hours. After cooling to room

temperature, ethyl acetate was added thereto, the mixture was washed with water and a saturated saline solution and dried over magnesium sulfate. The solvent was concentrated *in vacuo* and the residue was purified by a silica gel column chromatography (ethyl acetate:hexane = 1:3) to give 0.36 of the title compound as pale yellow powder.

¹H-NMR (CDCl₃, 400MHz); δ (ppm) 4.03 (3H, s), 7.24-7.28 (1H, m), 7.46-7.51 (1H, ddd), 7.57 (1H, dd), 7.65-7.69 (1H, ddd), 7.72-7.82 (3H, m), 8.31 (1H, d), 8.66-8.69 (1H, m), 8.83 (1H, d).

Example 6.

3-(2-Cyanophenyl)-5-(2-pyridyl)-2(1H)-pyridone

Chlorotrimethylsilane (0.1 ml) was added to a suspension of 0.20 g of 3-(2-cyanophenyl)-5-(2-pyridyl)-2-methoxypyridine and 0.12 g of sodium iodide in 10 ml of acetonitrile and the mixture was stirred at room temperature for 3 hours. A saturated sodium bicarbonate solution was added to the mixture followed by extracting with ethyl acetate. The ethyl acetate layer was washed with water and a saturated saline solution and dried over magnesium sulfate. The solvent was concentrated *in vacuo* and the residue was purified by a silica gel column chromatography (ethyl acetate:hexane = 1:1) to give 0.11 g of the title compound in pale yellow powder.

¹H-NMR (DMSO-d₆, 400 MHz); δ (ppm) 7.26-7.30 (1H, ddd), 7.55-7.60 (1H, ddd), 7.66 (1H, dd), 7.74-7.79 (1H, ddd), 7.80-7.86 (1H, ddd), 7.89-7.94 (2H, m), 8.28 (1H, d), 8.37 (1H, d), 8.56-8.59 (1H, m).

65702-519

Example 7.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one (also known as 2-(2-oxo-1-phenyl-5-pyridin-2-yl-1,2-dihydropyridin-3-yl) benzonitrile).

A suspension of 0.11 g of 3-(2-cyanophenyl)-5-(2-pyridyl)-2(1H)-pyridone, 0.12 g of phenyl boronic acid 0.1 g of copper acetate and 0.3 ml of triethylamine in 10 ml of methylene chloride was stirred at room temperature for overnight. To this were added 5 ml of concentrated aqueous ammonia, 10 ml of water and 40 ml of ethyl acetate and the organic layer was separated, washed with water and a saturated saline solution and dried over magnesium sulfate. The solvent was concentrated *in vacuo* and the residue was purified by a silica gel column chromatography (ethyl acetate:hexane = 1:2) to give 0.06 g of the title product as pale yellow powder.

¹H-NMR (DMSO-d₆, 400MHz); δ(ppm) 7.29-7.33 (1H, m), 7.48-7.63 (6H, m), 7.71-7.75 (1H, dd), 7.76-7.88 (2H, m), 7.92-7.95 (1H, m), 8.01 (1H, d), 8.48 (1H, d), 8.54 (1H, d), 8.58-8.61 (1H, m).

Example 8.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-nitrophenyl)-1,2-dihydropyridin-2-one

The title compound was obtained in the same manner as in Example 7.

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.24-7.28 (m, 1H), 7.49 (dt, 1H), 7.63-7.81 (m, 6H), 7.95-7.98 (m, 1H), 8.31-8.37 (m, 3H), 8.45 (t, 1H), 8.60-8.63 (m, 1H).

Example 9.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-aminophenyl)-1,2-dihydropyridin-2-one

Iron powder (180 mg) and 342 mg of ammonium chloride were added to a solution of 317 mg of 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-nitrophenyl)-1,2-dihydropyridin-2-one in a mixture of 10 ml of 2-propanol and 5 ml of water followed by refluxing for 4 hours. The reaction mixture was concentrated, partitioned in ethyl acetate-water, the organic layer was washed with water, dried and concentrated and the residue was purified by a silica gel column chromatography (ethyl acetate/hexane system) to give 235 mg of the title compound as a pale yellow solid.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.84 (s, 2H), 6.75 (dd, 1H), 6.82-6.87 (m, 2H), 7.20 (dd, 1H), 7.26-7.30 (m, 1H), 7.45 (td, 1H), 7.59-7.65 (m, 2H), 7.72-7.80 (m, 3H), 8.29 (s, 2H), 8.56-8.61 (m, 1H)

Example 10.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-methylsulfonylaminophenyl)-1,2-dihydropyridin-2-one

Triethylamine (0.2 ml) was added to a solution of 31 mg of 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-aminophenyl)-1,2-dihydropyridin-2-one in 2 ml of tetrahydrofuran, 0.1 ml of methanesulfonic acid chloride was dropped thereinto with ice cooling and the mixture was stirred for 10 minutes. To this were added 2 ml of 2N sodium hydroxide, the mixture was stirred

65702-519

at room temperature for 5 minutes and partitioned to ethyl acetate-water, the organic layer was washed with water, dried and concentrated and the residue was purified by a silica gel column chromatography (ethyl acetate-hexane system) to give 38 mg of the title compound as a pale yellow amorphous substance.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.93 (s, 3H), 4.00-4.09 (m, 1H), 7.22-7.31 (m, 3H), 7.36 (t, 1H), 7.43 (t, 1H), 7.46 (dd, 1H), 7.61 (dt, 1H), 7.65 (td, 1H), 7.73-7.78 (m, 3H), 8.27 (d, 1H), 8.31 (d, 1H), 8.59-8.61 (m, 1H).

Example 11.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-methylaminophenyl)-1,2-dihydropyridin-2-one

Paraformaldehyde (41 mg) and 119 mg of triacetoxysodium borohydride were added to a solution of 50 mg of 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-aminophenyl)-1,2-dihydropyridin-2-one in 3 ml of acetic acid followed by stirring at room temperature for one night. To this was added an aqueous solution of sodium bicarbonate, the mixture was extracted with ethyl acetate, the organic layer was washed with water, dried and concentrated and the residue was purified by a silica gel column chromatography (ethyl acetate/hexane system) to give 11 mg of the title compound as a pale yellow solid.

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 2.00 (s, 3H), 7.11-7.14 (m, 1H), 7.21 (ddd, 1H), 7.35 (t, 1H), 7.44-7.49 (m, 2H), 7.59 (d, 1H), 7.66 (td, 1H), 7.70-7.77 (m, 4H), 8.25 (d, 1H), 8.51 (s, 1H), 8.58-8.61 (m, 1H).

Example 12.

65702-519

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-dimethylaminophenyl)-1,2-dihydropyridin-2-one

Paraformaldehyde (41 mg) and 119 mg of triacetoxy sodium borohydride were added to a solution of 50 mg of 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-aminophenyl)-1,2-dihydropyridin-2-one in 3 ml of acetic acid followed by stirring at room temperature for 6 hours. To this were further added 41 mg of paraformaldehyde and 119 mg of triacetoxy sodium borohydride, the mixture was stirred for one night, an aqueous solution of sodium bicarbonate was added thereto, the mixture was extracted with ethyl acetate, the organic layer was washed with water, dried and concentrated and the residue was purified by a silica gel column chromatography (ethyl acetate/hexane system) to give 38 mg of the title compound as a pale yellow amorphous substance.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.99 (s, 6H), 6.77-6.80 (m, 3H), 7.18-7.21 (m, 1H), 7.32-7.37 (m, 1H), 7.44 (t, 1H), 7.59-7.64 (m, 2H), 7.71-7.83 (m, 3H), 8.32 (s, 2H), 8.58-8.60 (m, 1H).

Example 13.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-[3-(5-methoxymethyl-2-oxazolidinon-3-yl)-phenyl]-1,2-dihydropyridin-2-one

Glycidyl methyl ether (0.01 ml) and 22 mg of magnesium periodate were added to a solution of 38 mg of 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-aminophenyl)-1,2-dihydropyridin-2-one in 6 ml of acetonitrile followed by stirring at room temperature. After 2 hours, 0.01 ml of

65702-519

glycidyl methyl ether and 22 mg of magnesium periodate were further added thereto and the mixture was stirred at room temperature for 1 hours and then stirred at 50°C for 1 hour more. The reaction mixture was partitioned to ethyl acetate-water, the organic layer was washed with water, dried and concentrated, the residue was dissolved in 6 ml of tetrahydrofuran, 32 mg of carbonyldiimidazole were added thereto and the mixture was heated to reflux for 2 hours. This was partitioned to ethyl acetate-water, the organic layer was washed with water, dried and concentrated and the residue was purified by a preparative thin layer chromatography (ethyl acetate/hexane system) to give 21 mg of the title compound as a pale yellow solid.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.43 (s, 3H), 3.64 (dd, 2H), 3.97 (dd, 1H), 4.09 (t, 1H), 4.77 (ddd, 1H), 7.22 (ddd, 1H), 7.29 (ddd, 1H), 7.46 (td, 1H), 7.53 (t, 1H), 7.59-7.79 (m, 7H), 8.30 (d, 1H), 8.31 (d, 1H), 8.58-8.61 (m, 1H).

Example 14.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-methoxycarbonylphenyl)-1,2-dihydropyridin-2-one

The title compound was obtained in the same manner as in Example 7.

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 3.94 (s, 3H), 7.23 (ddd, 1H), 7.47 (td, 1H), 7.59-7.68 (m, 4H), 7.73-7.80 (m, 3H), 7.88-7.91 (m, 2H), 8.31 (d, 1H), 8.32 (d, 1H), 8.59-8.61 (m, 1H).

Example 15.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-

methylaminocarbonylphenyl)-1,2-dihydropyridin-2-one

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-methoxycarbonylphenyl)-1,2-dihydropyridin-2-one (10 mg) was added to 6 ml of a 40% methanolic solution of methylamine followed by stirring at room temperature for one night. The reaction solution was concentrated *in vacuo* to give 10 mg of the title compound as a pale yellow solid.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.00 (d, 3H), 6.51 (brs, 1H), 7.23 (ddd, 1H), 7.47 (td, 1H), 7.58-7.68 (m, 4H), 7.73-7.80 (m, 3H), 7.88-7.91 (m, 2H), 8.31 (d, 1H), 8.32 (d, 1H), 8.59-8.61 (m, 1H).

Example 16.

3-(2-Cyano-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

(Route 1)

3-(2-Chloro-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one (281 mg) was dissolved in 20 ml of dimethylformamide, 170 mg of copper cyanide were added and the mixture was stirred at 130°C for 10 hours. The reaction solution was cooled to room temperature, aqueous ammonia and ethyl acetate were added, the organic layer was partitioned, washed with water and dried over anhydrous sodium sulfate, the drying agent was filtered off, the filtrate was concentrated *in vacuo* and the residue was purified by a silica gel column chromatography (hexane-ethyl acetate system) to give 120 mg of the title compound as a colorless amorphous substance.

(Route 2)

3-Bromo-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one (2.9 g) synthesized by the same method as mentioned in Referential Example 6 was dissolved in 200 ml of xylene, 5 ml of bis(tributyl tin) and 400 mg of tetrakis(triphenylphosphine) palladium were added and the mixture was stirred at 140°C for 2 hours. 3-Bromo-2-cyanopyridine (3.2 g) and 100 mg of tetrakis(triphenylphosphine) palladium were added thereto and the mixture was stirred at 140°C for 2 hours.

Tetrakis(triphenylphosphine) palladium (1.0 g) and 800 mg of copper iodide were divided into four and added every 1 hour, then 2 g of 3-bromo-2-cyanopyridine were added thereto and the mixture was stirred at 140°C for one night. The reaction solution was cooled to room temperature, water and ethyl acetate were added thereto, the organic layer was partitioned, washed with water and dried over anhydrous sodium sulfate, the drying agent was filtered off, the filtrate was concentrated in vacuo and the residue was purified by a silica gel column chromatography (hexane-ethyl acetate system) to give 1.8 g of the title compound as a colorless amorphous substance.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.24 (ddd, 1H), 7.47-5.57 (m, 6H), 7.63 (d, 1H), 7.68 (td, 1H), 8.22 (dd, 1H), 8.37 (dd, 1H), 8.43 (d, 1H), 8.59-8.61 (m, 1H), 8.69 (dd, 1H).

ESI-Mass; 351 [M⁺ + H]

Example 17.

3-(2-Chlorophenyl)-5-(2-pyridyl)-1-(4-methoxyphenyl)-1,2-dihydropyridin-2-one

The title compound was obtained in the same manner as in Example 4.

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 3.84 (s, 3H), 6.98-7.03 (m, 2H), 7.19 (ddd, 1H), 7.28-7.33 (m, 2H), 7.40-7.46 (m, 2H), 7.46-7.51 (m, 2H), 7.53-7.57 (m, 1H), 7.72 (ddd, 1H), 8.12 (d, 1H), 8.29 (d, 1H), 8.57-8.61 (m, 1H).

Example 18.

3-(2-Chlorophenyl)-5-(2-pyridyl)-1-(4-hydroxyphenyl)-1,2-dihydropyridin-2-one

3-(2-Chlorophenyl)-5-(2-pyridyl)-1-(4-methoxyphenyl)-1,2-dihydropyridin-2-one (440 mg) was dissolved in 5 ml of 48% hydrobromic acid and heated to reflux for 1 hours. After the reaction solution was allowed to cool at room temperature, it was diluted with a saturated aqueous solution of sodium bicarbonate and extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate. The drying agent was filtered off and the filtrate was concentrated in vacuo and purified by a silica gel column chromatography (hexane-ethyl acetate system) to give 292 mg of the title compound.

¹H-NMR (400MHz, CDCl₃); δ (ppm) 6.67-6.73 (m, 2H), 7.12-7.18 (m, 2H), 7.19-7.24 (m, 1H), 7.30-7.38 (m, 2H), 7.47-7.53 (m, 2H), 7.56 (d, 1H), 7.70 (s, 1H), 7.73 (ddd, 1H), 8.18 (d, 1H), 8.26 (d, 1H), 8.57-8.62 (m, 1H).

Example 19.

3-(2-Chlorophenyl)-5-(2-pyridyl)-1-(4-

dimethylaminoethoxyphenyl)-1,2-dihydropyridin-2-one

3-(2-Chlorophenyl)-5-(2-pyridyl)-1-(4-hydroxyphenyl)-1,2-dihydropyridin-2-one (82 mg) and 57 mg of N,N-dimethylaminoethyl chloride were dissolved in 2 ml of dimethylformamide, 55 mg of potassium carbonate were added thereto at 60°C and the mixture was stirred for one night. The reaction solution was diluted with water and extracted with ethyl acetate. The organic layer was washed with a saturated saline solution and dried over anhydrous magnesium sulfate. The drying agent was filtered off and the filtrate was concentrated in vacuo and purified by an NH silica gel column chromatography (hexane-ethyl acetate system) to give 27 mg of the title compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.55 (s, 6H), 2.76 (t, 2H), 4.11 (t, 2H), 6.99-7.05 (m, 2H), 7.19 (ddd, 1H), 7.26-7.34 (m, 2H), 7.39-7.45 (m, 2H), 7.45-7.51 (m, 2H), 7.55 (d, 1H), 7.72 (ddd, 1H), 8.12 (d, 1H), 8.28 (d, 1H), 8.57-8.61 (m, 1H).

Example 20.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-formylphenyl)-1,2-dihydropyridin-2-one

The title compound was obtained in the same manner as in Example 7.

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.24 (ddd, 1H), 7.84 (ddd, 1H), 7.63 (d, 1H), 7.66 (ddd, 1H), 7.72 (dd, 1H), 7.75-7.82 (m, 3H), 7.84-7.88 (m, 1H), 8.00 (ddd, 1H), 8.05-8.08 (m, 1H), 8.32 (d, 1H), 8.35 (d, 1H), 8.59-8.62 (m, 1H), 10.08 (s, 1H).

65702-519

Example 21.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-hydroxymethylphenyl)-
1,2-dihydropyridin-2-one

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-formylphenyl)-1,2-dihydropyridin-2-one (585 mg) was dissolved in 20 ml of methanol, 260 mg of sodium borohydride were added with ice cooling and the mixture was stirred at room temperature for one night. The reaction solution was diluted with ethyl acetate, washed with a saturated saline solution and dried over anhydrous magnesium sulfate. The drying agent was filtered off and the filtrate was concentrated *in vacuo* and purified by an NH silica gel column chromatography (ethyl acetate). The resulting crude crystals were recrystallized from ethyl acetate-diethyl ether to give 320 mg of the title compound.

¹H-NMR (400 MHz, DMSO-d₆); δ(ppm) 4.60 (d, 2H), 5.37 (t, 1H), 7.29-7.33 (m, 1H), 7.42-7.47 (m, 2H), 7.48-7.55 (m, 2H), 7.59 (ddd, 1H), 7.73 (dd, 1H), 7.78 (dd, 1H), 7.83 (ddd, 1H), 7.94 (dd, 1H), 8.01 (d, 1H), 8.48 (d, 1H), 8.52 (d, 1H), 8.57-8.61 (m, 1H).

Example 22.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-cyanomethylphenyl)-
1,2-dihydropyridin-2-one

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-hydroxyphenyl)-1,2-dihydropyridin-2-one (53 mg) was dissolved in 2 ml of tetrahydrofuran, then 60 µl of triethylamine and 20 µl of methanesulfonyl chloride were added thereto with ice cooling

and the mixture was stirred at room temperature for 3 hours. The reaction solution was diluted with an aqueous solution of sodium bicarbonate and extracted with ethyl acetate and the extract was dried over anhydrous magnesium sulfate. The drying agent was filtered off, the filtrate was concentrated *in vacuo*, the resulting residue was dissolved in 1 ml of dimethyl sulfoxide, 3 mg of sodium cyanide were added and the mixture was stirred at room temperature for 1 hour. The reaction solution was diluted with ethyl acetate, washed with an aqueous solution of sodium bicarbonate and a saturated saline solution and dried over anhydrous magnesium sulfate. The drying agent was filtered off, the filtrate was concentrated *in vacuo* and the resulting crude crystals were recrystallized from ethyl acetate-diethyl ether-hexane to give 12 mg of the title compound.

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 3.85 (s, 2H), 7.21-7.26 (m, 1H), 7.41-7.81 (m, 10H), 8.29-8.32 (m, 2H), 8.59-8.62 (m, 1H).

The following compounds were prepared by the same manner as in the above Example 22.

Example 23.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-acetylaminoethylphenyl)-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 2.04 (s, 3H) 4.47-4.52 (m, 2H), 7.22 (ddd, 1H), 7.37-7.53 (m, 5H), 7.61 (d, 1H), 7.65 (ddd, 1H), 7.72-7.81 (m, 3H), 8.28 (d, 1H), 8.31 (d, 1H), 8.59-8.62 (m, 1H).

Example 24.

65702-519

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-methylsulfonylaminomethylphenyl)-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 2.91 (s, 3H), 4.36 (d, 2H), 5.00-5.06 (m, 1H), 7.22 (ddd, 1H), 7.43-7.49 (m, 3H), 7.50-7.55 (m, 2H), 7.61 (ddd, 1H), 7.64 (ddd, 1H), 7.73-7.79 (m, 3H), 8.28-8.31 (m, 2H), 8.60 (ddd, 1H).

Example 25.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-acetoxymethylphenyl)-1,2-dihydropyridin-2-one

To 56 mg of 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-hydroxymethylphenyl)-1,2-dihydropyridin-2-one were added 1 ml of acetic anhydride and 1 ml of pyridine and the mixture was stirred at room temperature for one night. The reaction solution was concentrated *in vacuo* and purified by an NH silica gel chromatography (hexane-ethyl acetate system) to give 30 mg of the title compound.

¹H-NMR (400MHz, CDCl₃); δ (ppm) 2.13 (s, 3H), 5.18 (s, 2H), 7.23 (ddd, 1H), 7.44-7.56 (m, 5H), 7.60-7.67 (m, 2H), 7.73-7.81 (m, 3H), 8.30-8.33 (m, 2H), 8.59-8.62 (m, 1H).

Example 26.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(4-methylthiophenyl)-1,2-dihydropyridin-2-one

The title compound was obtained in the same manner as in Example 7.

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 2.53 (s, 3H), 7.21-7.24 (m, 1H), 7.36-8.79 (m, 10H), 8.28-8.32 (m, 2H), 8.59-8.61 (m, 1H).

Example 27.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(4-methylsulfonylphenyl)-1,2-dihydropyridin-2-one

A 70% m-chloroperbenzoic acid (500 mg) was added little by little during 2 hours to a solution of 50 mg of 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-methylthiophenyl)-1,2-dihydropyridin-2-one in 4 ml of methylene chloride followed by stirring with ice cooling. A saturated aqueous solution of sodium bicarbonate was added thereto, the mixture was partitioned to ethyl acetate-water, the organic layer was washed with water, dried and concentrated and the residue was purified by a silica gel column chromatography (ethyl acetate/hexane system) to give 5 mg of the title compound as a yellow solid.

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 3.11 (s, 3H), 7.24-7.28 (m, 1H), 7.50 (dt, 1H), 7.61-7.82 (m, 7H), 8.20 (d, 2H), 8.30-8.33 (m, 2H), 8.60-8.63 (m, 1H).

Example 28.

3-(2-Cyanophenyl)-5-(2-formylthiophen-3-yl)-1-phenyl-1,2-dihydropyridin-2-one

The title compound was prepared according to Example 1.

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.29 (d, 1H), 7.42-7.57 (m, 6H), 7.65 (dt, 1H), 7.71 (d, 1H), 7.77-7.82 (m, 3H), 7.85 (d, 1H), 10.10 (s, 1H).

Example 29.

3-(2-Cyanophenyl)-5-(2-diethylaminomethylthiophen-3-yl)-1-

phenyl-1,2-dihydropyridin-2-one

A solution of 20 mg of 3-(2-cyanophenyl)-5-(2-formylthiophen-3-yl)-1-phenyl-1,2-dihydropyridin-2-one, 0.1 ml of a 2M solution of diethylamine in tetrahydrofuran and 0.1 ml acetic acid in 2 ml of tetrahydrofuran was stirred at room temperature for 15 minutes, 20 mg of sodium triacetoxyborohydride were added and the mixture was stirred for 3 hours more. A 2N aqueous solution of sodium hydroxide was added thereto, the mixture was extracted with ethyl acetate and the organic layer was washed with water and a saturated saline solution and dried over magnesium sulfate. The solvent was concentrated *in vacuo* and the residue was purified by an NH silica gel column chromatography to give 15 mg of the title compound as white powder.

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 1.38 (t, 6H), 2.99-3.20 (m, 4H), 4.57 (d, 2H), 7.07 (d, 1H), 7.40-7.58 (m, 8H), 7.60-7.67 (m, 2H), 7.77 (d, 1H), 7.87 (d, 1H).

Example 30.

3-(2-Cyanophenyl)-5-(2-hydroxymethylthiophen-3-yl)-1-phenyl-1,2-dihydropyridin-2-one

Sodium triacetoxyborohydride (10 mg) was added to a solution of 10 mg of 3-(2-cyanophenyl)-5-(2-formylthiophen-3-yl)-1-phenyl-1,2-dihydropyridin-2-one in 2 ml of tetrahydrofuran and the mixture was stirred for 1 hour. A 10% aqueous solution of sodium carbonate was added thereto, the mixture was extracted with ethyl acetate and the organic layer

was washed with water and a saturated saline solution and dried over magnesium sulfate. The solvent was concentrated *in vacuo* and the residue was purified by an NH silica gel column chromatography to give 8 mg of the title compound as white powder.

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 4.86 (s, 2H), 7.11 (d, 1H), 7.33 (d, 1H), 7.42-7.54 (m, 6H), 7.60-7.65 (m, 1H), 7.75 (d, 1H), 7.76-7.79 (m, 1H), 7.81-7.84 (m, 1H), 7.91 (d, 1H).

MS (ESI): 385 (MH⁺)

Example 31.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-benzyl-1,2-dihydropyridin-2-one

3-(2-Cyanophenyl)-5-(2-pyridyl)-2(1H)-pyridone (46 mg), 36 mg of benzyl alcohol and 88 mg of triphenylphosphine were dissolved in 2 ml of tetrahydrofuran, 147 mg of a 40% solution of diethylazo dicarboxylate in toluene were added with ice cooling and the mixture was stirred at room temperature for 1 hour. The reaction solution was concentrated *in vacuo* and purified by a silica gel chromatography (hexane-ethyl acetate system) to give 12 mg of the title compound.

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 5.33 (s, 2H), 7.18 (ddd, 1H), 7.31-7.40 (m, 3H), 7.42-7.48 (m, 3H), 7.53 (dd, 1H), 7.64 (ddd, 1H), 7.68-7.79 (m, 3H), 8.18 (d, 1H), 8.30 (d, 1H), 8.56-8.60 (m, 1H).

Example 32.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

3-Bromo-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one (5.39 g) was dissolved in 200 ml of dimethylformamide, then 6.42 g of cesium carbonate, 3.69 g of 2-(2'-cyanophenyl)-1,3,2-dioxaboronane and 949 mg of tetrakis(triphenylphosphine) palladium were added thereto and the mixture was stirred at 120°C for 1 hour. The reaction solution was cooled to room temperature, water and ethyl acetate were added thereto, the organic layer was partitioned, washed with water and dried over anhydrous magnesium sulfate, the drying agent was filtered off, the filtrate was concentrated *in vacuo* and the residue was purified by a silica gel column chromatography (hexane-ethyl acetate system) to give 4.8 g of the title compound as a colorless amorphous substance.

¹H-NMR (400MHz, CDCl₃); δ (ppm) 7.22-7.26 (m, 1H), 7.46-7.52 (m, 2H), 7.62 (dt, 1H), 7.66 (td, 1H), 7.74-7.81 (m, 3H), 7.97 (ddd, 1H), 8.32 (s, 2H), 8.61 (ddd, 1H), 8.72 (dd, 1H), 8.80-8.81 (m, 1H).

ESI-Mass; 351 [M⁺ + H]

The following compounds were synthesized by the same method as mentioned in Example 1.

Example 33.

3-(2-Pyridyl)-5-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, DMSO-d₆); δ (ppm) 7.35-7.40 (1H, m), 7.49-7.64 (5H, m), 7.77-7.81 (2H, m), 7.86 (1H, dt), 7.96 (1H, d), 8.22 (1H, d), 8.51 (1H, d), 8.66-8.71 (2H, m).

Example 34.

3-(2-Cyanophenyl)-5-(3-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.38 (dd, 1H), 7.45-7.58 (m, 6H), 7.65 (ddd, 1H), 7.72 (d, 1H), 7.77-7.86 (m, 3H), 7.94 (d, 1H), 8.60 (dd, 1H), 8.79 (d, 1H).

Example 35.

3-(2-Cyanophenyl)-5-(4-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.44 (dd, 2H), 7.46-7.58 (m, 6H), 7.66 (ddd, 1H), 7.81 (dd, 2H), 7.84 (d, 1H), 8.01 (d, 1H), 8.66 (dd, 2H).

Example 36.

3-(2-Cyanophenyl)-5-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 7.26-7.59 (m, 7H), 7.62-7.72 (m, 3H), 7.76-7.80 (m, 2H), 7.82-7.84 (m, 1H), 7.86-7.88 (m, 2H).

ESI-Mass; 374 [M⁺+H]

Example 37.

3,5-Diphenyl-1-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, DMSO-d₆); δ (ppm) 7.36-7.40 (3H, m), 7.41-7.47 (4H, m), 7.52-7.56 (2H, m), 7.74-7.78 (2H, m), 7.84-7.90 (2H, m), 7.98-8.01 (1H, m), 8.11 (1H, d), 8.61-8.63 (1H, m).

Example 38.

3-Phenyl-5-(2-cyanophenyl)-1-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, DMSO-d₆); δ (ppm) 7.34-7.40 (2H, m), 7.40-7.50 (3H, m), 7.53 (2H, dd), 7.67 (1H, dt), 7.75-7.81 (2H, m), 7.83 (1H, d), 7.88 (1H, dt), 8.02 (1H, d), 8.15 (1H, d), 8.59-8.62 (1H, m).

Example 39.

3-(2-Cyanophenyl)-5-phenyl-1-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, DMSO-d₆); δ (ppm) 7.33-7.40 (2H, m), 7.41-7.50 (3H, m), 7.54-7.59 (2H, m), 7.65 (1H, dt), 7.75 (1H, dd), 7.80 (1H, dd), 7.88 (1H, dt), 7.96 (1H, d), 8.03 (1H, d), 8.23 (1H, d), 8.60-8.64 (1H, m).

Example 40.

3-(2-Cyanophenyl)-5-(2-cyanophenyl)-1-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, DMSO-d₆); δ (ppm) 7.36-7.40 (1H, m), 7.45-7.51 (2H, m), 7.61-7.66 (1H, m), 7.66-7.71 (2H, m), 7.75-7.80 (3H, m), 7.86-7.91 (2H, m), 8.05-8.09 (1H, m), 8.34 (1H, d), 8.59-8.62 (1H, m).

Example 41.

3-(2-Cyanophenyl)-1,5-diphenyl-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.32-7.37 (m, 1H), 7.41-7.56 (m, 10H), 7.63 (td, 1H), 7.69 (d, 1H), 7.77-7.82 (m, 2H), 7.98 (d, 1H).

ESI-Mass; 349 [M⁺ + H]

Example 42.

3-(2-Cyanophenyl)-5-(2-methoxyphenyl)-1-phenyl-1,2-

dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 3.88 (s, 3H), 6.95-7.04 (m, 3H), 7.29-7.54 (m, 7H), 7.58-7.64 (m, 1H), 7.71 (d, 1H), 7.74-7.79 (m, 2H), 7.95 (d, 1H).

Example 43.

3-(2-Cyanophenyl)-5-(3,4-dimethoxyphenyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 3.91 (s, 3H), 3.94 (s, 3H), 6.92 (d, 1H), 7.00-7.02 (m, 1H), 7.04 (dd, 1H), 7.40-7.59 (m, 6H), 7.60-7.68 (m, 2H), 7.76-7.79 (m, 1H), 7.82-7.86 (m, 1H), 7.97 (d, 1H).

Example 44.

3-(2-Cyanophenyl)-5-(thiophen-3-yl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.24 (dd, 1H), 7.35 (dd, 1H), 7.41 (dd, 1H), 7.43-7.56 (m, 6H), 7.63 (dt, 1H), 7.70 (d, 1H), 7.76-7.81 (m, 2H), 7.96 (d, 1H).

Example 45.

3-(2-Cyanophenyl)-5-(2-fluorophenyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.16 (ddd, 1H), 7.23 (dt, 1H), 7.29-7.36 (m, 1H), 7.42-7.54 (m, 6H), 7.60-7.67 (m, 2H), 7.74-7.81 (m, 3H), 7.92 (dd, 1H).

Example 46.

3-(2-Cyanophenyl)-5-(thiophen-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

65702-519

$^1\text{H-NMR}$ (400 MHz, CDCl_3); δ (ppm) 7.07 (dd, 1H), 7.17 (dd, 1H), 7.25-7.28 (m, 1H), 7.43-7.56 (m, 6H), 7.64 (dt, 1H), 7.72 (d, 1H), 7.74-7.80 (m, 2H), 7.93 (d, 1H).

Example 47.

3-(2-Cyanophenyl)-5-phenyl-1-(3-pyridyl)-1,2-dihydropyridin-2-one

$^1\text{H-NMR}$ (400 MHz, DMSO-d_6); δ (ppm) 7.32-7.39 (1H, m), 7.41-7.47 (2H, m), 7.52-7.65 (2H, m), 7.73-7.80 (4H, m), 7.94 (1H, d), 8.06-8.11 (1H, m), 8.20 (1H, d), 8.25 (1H, d), 8.68 (1H, dd), 8.83 (1H, d).

Example 48.

3-(2-Cyanophenyl)-5-(3-furyl)-1-(phenyl)-1,2-dihydropyridin-2-one

$^1\text{H-NMR}$ (400 MHz, CDCl_3); δ (ppm) 6.55 (dd, 1H), 7.42-7.56 (m, 7H), 7.58 (d, 1H), 7.60-7.67 (m, 2H), 7.74-7.79 (m, 2H), 7.82 (d, 1H).

Example 49.

3-(2-Cyanophenyl)-5-(2-furyl)-1-phenyl-1,2-dihydropyridin-2-one

$^1\text{H-NMR}$ (400 MHz, CDCl_3); δ (ppm) 7.12-7.24 (m, 2H), 7.42-7.55 (m, 6H), 7.58-7.65 (m, 3H), 7.66 (d, 1H), 7.74-7.77 (m, 2H).

Example 50.

3-(2-Cyanophenyl)-5-(2,4-dimethoxypyrimidin-5-yl)-1-phenyl-1,2-dihydropyridin-2-one

$^1\text{H-NMR}$ (400 MHz, CDCl_3); δ (ppm) 4.03 (s, 3H), 4.07 (s, 3H), 7.42-7.57 (m, 5H), 7.60-7.70 (m, 3H), 7.75-7.80 (m, 2H), 7.86

65702-519

(d, 1H), 8.29 (s, 1H).

Example 51.

3-(2-Cyanophenyl)-5-(3-methoxypyridin-5-yl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 3.92 (s, 3H), 7.30-7.34 (m, 1H), 7.44-7.58 (m, 6H), 7.65 (ddd, 1H), 7.72 (d, 1H), 7.77-7.84 (m, 2H), 7.95 (d, 1H), 8.28-8.33 (m, 1H), 8.36-8.40 (m, 1H).

Example 52.

3-(2-Cyanophenyl)-5-(2-methoxyphenyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 3.89 (s, 3H), 7.00 (d, 1H), 7.03-7.08 (ddd, 1H), 7.35-7.40 (m, 2H), 7.46-7.51 (ddd, 1H), 7.63-7.72 (m, 2H), 7.72 (d, 1H), 7.77-7.80 (dd, 1H), 7.82-7.88 (m, 1H), 7.95 (d, 1H), 8.47-8.52 (d, 1H), 8.75-8.80 (m, 1H), 8.96 (brs, 1H).

Example 53.

3-(2-Cyanophenyl)-5-[2-methoxy-5-(2-cyanophenyl)phenyl]-1-(3-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 3.97 (s, 3H), 7.12 (d, 1H), 7.41-7.50 (m, 2H), 7.54-7.62 (m, 3H), 7.62-7.68 (ddd, 2H), 7.70-7.80 (m, 5H), 8.03 (d, 1H), 8.32-8.38 (m, 1H), 8.71-8.76 (m, 1H), 8.93 (brs, 1H).

Example 54.

3-(2-Cyanophenyl)-5-(3-methyl-2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 2.56 (s, 3H), 7.42-7.70 (m, 10H), 7.71-7.78 (m, 2H), 7.89-7.93 (m, 1H), 8.46-8.54 (m, 1H).

The following compounds were synthesized by the method which is the same as or according to the method mentioned in Example 4.

Example 55.

3-(2-Methoxyphenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (DMSO-d₆, 400 MHz); δ (ppm) 3.76 (3H, s), 7.00 (1H, dt), 7.09 (1H, d), 7.25-7.40 (3H, m), 7.46-7.60 (4H, m), 7.76-7.84 (2H, m), 7.94 (1H, d), 8.23 (1H, d), 8.38 (1H, d), 8.55-8.58 (1H, m).

Example 56.

3-(2-Methoxyphenyl)-5-(2-pyridyl)-1-(4-fluorophenyl)-1,2-dihydropyridin-2-one

¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 3.82 (3H, s), 6.97-7.05 (2H, m), 7.16-7.23 (2H, m), 7.24-7.32 (1H, m), 7.36 (1H, dt), 7.44 (1H, dd), 7.50-7.66 (2H, m), 7.74-7.90 (1H, m), 8.02-8.08 (1H, m), 8.18-8.45 (2H, m), 8.58-8.64 (1H, m).

Example 57.

3-(2-Chlorophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (CDCl₃, 400MHz); δ (ppm) 6.76-6.81 (2H, m), 6.86-6.91 (1H, m), 7.17-7.22 (2H, m), 7.26-7.75 (5H, m), 7.61 (1H, d), 7.78-7.86 (1H, m), 8.11 (1H, d), 8.41 (1H, brs), 8.60-8.64 (1H, m).

Example 58.

3-(2-Methoxycarbonylphenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

65702-519

^1H -NMR (DMSO- d_6 , 400 MHz); δ (ppm) 3.65 (3H, s), 7.28-7.32 (1H, m), 7.47-7.71 (8H, m), 7.78-7.86 (2H, m), 8.01-8.20 (1H, m), 8.33 (1H, d), 8.42 (1H, d), 8.58-8.60 (1H, m).

Example 59.

3-(2-Methylaminocarbonylphenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

^1H -NMR (DMSO- d_6 , 400 MHz); δ (ppm) 2.65 (3H, d), 7.26-7.31 (1H, m), 7.40-7.45 (1H, m), 7.46-7.53 (5H, m), 7.53-7.59 (2H, m), 7.80-7.86 (1H, m), 7.96 (1H, d), 8.06-8.12 (1H, m), 8.22 (1H, d), 8.37 (1H, d), 8.57-8.60 (1H, m).

Example 60.

3-(2-Tolyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

^1H -NMR (DMSO- d_6 , 400 MHz); δ (ppm) 2.24 (3H, s), 7.22-7.34 (4H, m), 7.47-7.60 (6H, m), 7.78-7.84 (1H, m), 7.99 (1H, d), 8.21-8.24 (1H, m), 8.44-8.47 (1H, m), 8.55-8.59 (1H, m).

Example 61.

3-Phenyl-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

^1H -NMR (DMSO- d_6 , 400 MHz); δ (ppm) 7.28-7.32 (1H, m), 7.35-7.40 (1H, m), 7.41-7.47 (2H, m), 7.49-7.54 (2H, m), 7.56-7.60 (3H, m), 7.76-7.86 (3H, m), 8.02 (1H, dd), 8.42 (1H, d), 8.44 (1H, d), 8.58-8.61 (1H, m).

Example 62.

3-(2-Pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

^1H -NMR (DMSO- d_6 , 400 MHz); δ (ppm) 7.29-7.40 (2H, m), 7.50-7.63 (5H, m), 7.80-7.88 (2H, m), 7.99 (1H, d), 8.50 (1H, d), 8.54

65702-519

(1H, d), 8.62-8.66 (1H, m), 8.70-8.74 (1H, m), 9.31 (1H, d).

Example 63.

3-(3-Cyanophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 7.24 (ddd, 1H), 7.46-7.66 (m, 8H), 7.78 (td, 1H), 8.10 (dt, 1H), 8.16 (t, 1H), 8.25 (d, 1H), 8.31 (d, 1H), 8.61-8.63 (m, 1H).

Example 64.

3-(4-Cyanophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 7.22-7.26 (m, 1H), 7.47-7.60 (m, 6H), 7.70-7.78 (m, 3H), 7.95-7.98 (m, 2H), 8.26 (d, 1H), 8.33 (d, 1H), 8.61-8.63 (m, 1H).

Example 65.

3-(3-Chlorophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 7.21-7.36 (m, 3H), 7.47-7.76 (m, 5H), 7.58-7.60 (m, 1H), 7.71-7.75 (m, 2H), 7.84-7.87 (m, 1H), 8.23-8.26 (m, 2H), 8.60-8.63 (m, 1H).

ESI-Mass; 359 [M⁺ + H]

Example 66.

3-(4-Chlorophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 7.22 (ddd, 1H), 7.37-7.41 (m, 2H), 7.44-7.60 (m, 5H), 7.72-7.80 (m, 3H), 8.12-8.16 (m, 1H), 8.21-8.25 (m, 2H), 8.62 (ddd, 1H).

ESI-Mass; 359 [M⁺ + H]

Example 67.

3-(3-Pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 7.22-7.52 (m, 1H), 7.33-7.37 (m, 1H), 7.45-7.57 (m, 5H), 7.59-7.61 (m, 1H), 7.56 (td, 1H), 8.24-8.27 (m, 2H), 8.30 (d, 1H), 8.59 (dd, 1H), 8.61-8.63 (m, 1H), 8.95-8.96 (m, 1H).

ESI-Mass; 326 [M⁺ + H]

Example 68.

3-(2-Aminocarbonyl-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 5.46 (brs, 1H), 7.19 (ddd, 1H), 7.39-7.53 (m, 6H), 7.55-7.58 (m, 1H), 7.58 (brs, 1H), 7.71 (ddd, 1H), 7.82 (dd, 1H), 8.08 (d, 1H), 8.21 (d, 1H), 8.57 (dd, 1H), 8.59 (ddd, 1H).

Example 69.

3-(3-Methoxyphenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 3.84 (s, 3H), 6.92 (ddd, 1H), 7.20 (ddd, 1H), 7.31-7.38 (m, 2H), 7.42-7.55 (m, 6H), 7.57-7.59 (m, 1H), 7.73 (td, 1H), 8.23 (d, 1H), 8.24 (d, 1H), 8.60 (ddd, 1H).

ESI-Mass; 355 [M⁺ + H]

Example 70.

3-(4-Methoxyphenyl)-5-(2-pyridyl)-1-phenyl-1,2-

dihydropyridin-2-one

¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 3.85 (s, 3H), 6.94-6.98 (m, 2H), 7.20 (ddd, 1H), 7.42-7.55 (m, 5H), 7.57-7.60 (m, 1H), 7.73 (td, 1H), 7.77-7.81 (m, 2H), 8.18-8.20 (m, 2H), 8.59-8.20 (m, 1H).

ESI-Mass; 355 [M⁺ + H]

Example 71.

3-(2-Fluorophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 7.13-7.22 (m, 3H), 7.31-7.59 (m, 7H), 7.66 (td, 1H), 7.74 (td, 1H), 8.22 (dd, 1H), 8.29 (d, 1H), 8.58-8.60 (m, 1H).

Example 72.

3-(3-Fluorophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 7.03-7.08 (m, 1H), 7.21 (ddd, 1H), 7.35-7.63 (m, 9H), 7.74 (td, 1H), 8.23 (d, 1H), 8.27 (d, 1H), 8.59-8.62 (m, 1H).

Example 73.

3-(4-Fluorophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 7.08-7.14 (m, 2H), 7.21 (ddd, 1H), 7.44-7.60 (m, 6H), 7.74 (td, 1H), 7.78-7.83 (m, 2H), 8.21 (d, 1H), 8.22 (d, 1H), 8.60-8.62 (m, 1H).

Example 74.

3-(2-Chlorophenyl)-5-(2-pyridyl)-1-(3-methoxyphenyl)-1,2-dihydropyridin-2-one

65702-519

¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 3.84 (s, 3H), 6.96-7.01 (m, 1H), 7.04-7.11 (m, 2H), 7.17-7.23 (m, 1H), 7.26-7.34 (m, 2H), 7.40 (dd, 1H), 7.46-7.53 (m, 2H), 7.54-7.58 (m, 1H), 7.73 (ddd, 1H), 8.14 (d, 1H), 8.29 (d, 1H), 8.57-8.62 (m, 1H).

Example 75.

3-(2,4-Dimethoxyphenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 3.93 (s, 6H), 6.93 (d, 1H), 7.19-7.23 (m, 1H), 7.33 (dd, 1H), 7.41-7.57 (m, 6H), 7.58-7.60 (m, 1H), 7.74 (td, 1H), 8.19 (d, 1H), 8.22 (d, 1H), 8.60-8.62 (m, 1H).

ESI-Mass; 385 [M⁺ + H]

Example 76.

3-(2-Fluoro-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 7.20-7.28 (m, 2H), 7.44-7.56 (m, 5H), 7.56-7.60 (m, 1H), 7.75 (td, 1H), 8.19-8.21 (m, 1H), 8.26 (ddd, 1H), 8.30 (d, 1H), 8.34 (t, 1H), 8.59-8.61 (m, 1H)

ESI-Mass; 344 [M⁺ + H]

Example 77.

3-(2-Methoxy-5-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 3.98 (s, 3H), 6.80 (d, 1H), 7.22 (ddd, 1H), 7.44-7.59 (m, 6H), 7.72-7.77 (m, 1H), 8.15 (dd, 1H), 8.21 (s, 2H), 8.50-8.52 (m, 1H), 8.59-8.62 (m, 1H).

ESI-Mass; 356 [M⁺ + H]

65702-519

Example 78.

3-(3-Cyano-2-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (DMSO-d₆, 400MHz): δ (ppm) 7.30-7.34 (ddd, 1H), 7.49-7.57 (m, 1H), 7.57-7.62 (m, 4H), 7.62-7.66 (dd, 1H), 7.82-7.87 (ddd, 1H), 8.02 (d, 1H), 8.39-8.43 (dd, 1H), 8.59-8.62 (m, 1H), 8.63 (d, 1H), 8.65 (d, 1H), 8.94-8.96 (dd, 1H).

Example 79.

3-(3-Cyano-2-pyridyl)-5-phenyl-1-(3-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (DMSO-d₆, 400MHz): δ (ppm) 7.33-7.38 (m, 1H), 7.44 (d, 1H), 7.46 (d, 1H), 7.64 (d, 1H), 7.65 (d, 1H), 7.72-7.76 (m, 2H), 8.07-8.11 (m, 1H), 8.30 (d, 1H), 8.34 (d, 1H), 8.42 (dd, 1H), 8.68-8.71 (m, 1H), 8.82-8.84 (m, 1H), 8.86-8.93 (m, 1H).

Example 80.

3-(2-Fluoro-3-pyridyl)-5-(2-pyridyl)-1-(3-methoxyphenyl)-1,2-dihydropyridin-2-one

¹H-NMR (CDCl₃, 400MHz); δ (ppm) 3.85 (s, 3H), 6.99-7.10 (m, 3H), 7.20-7.31 (m, 2H), 7.40-7.47 (m, 1H), 7.58 (d, 1H), 7.76 (ddd, 1H), 8.18-8.23 (m, 1H), 8.23-8.32 (m, 2H), 8.32-8.37 (m, 1H), 8.58-8.64 (m, 1H).

Example 81.

3-(2-Methoxy-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 3.98 (s, 3H), 6.96 (dd, 1H), 7.18-7.22 (m, 1H), 7.44-7.59 (m, 6H), 7.74 (dt, 1H), 7.90 (dd, 1H),

8.17 (dd, 1H), 8.25-8.28 (m, 2H), 8.58-8.61 (m, 1H).

Example 82.

3-(2-Fluoro-3-pyridyl)-5-(2-pyridyl)-1-(4-fluorophenyl)-
1,2-dihydropyridin-2-one

¹H-NMR (CDCl₃, 400MHz); δ (ppm) 7.18-7.30 (m, 4H), 7.46-7.52 (m, 2H), 7.58 (d, 1H), 7.76 (ddd, 1H), 8.20-8.27 (m, 2H), 8.29 (d, 1H), 8.31-8.35 (m, 1H), 8.59-8.64 (m, 1H).

Example 83.

3-(2-Fluoro-3-pyridyl)-5-(2-pyridyl)-1-(pyrimidin-5-yl)-
1,2-dihydropyridin-2-one

¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 7.25-7.32 (m, 2H), 7.61 (d, 1H), 7.79 (ddd, 1H), 8.16-8.22 (m, 1H), 8.24-8.27 (m, 1H), 8.29 (d, 1H), 8.34-8.37 (m, 1H), 8.61-8.64 (m, 1H), 9.01 (s, 2H), 9.32 (s, 1H).

Example 84.

3-(2-Fluoro-3-pyridyl)-5-(2-pyridyl)-1-(4-methylthiophenyl)-1,2-dihydropyridin-2-one

¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 2.53 (s, 3H), 7.20-7.28 (m, 2H), 7.36-7.43 (m, 4H), 7.57 (d, 1H), 7.75 (td, 1H), 8.19-8.27 (m, 2H), 8.28 (d, 1H), 8.33 (t, 1H), 8.59-8.61 (m, 1H).

ESI-Mass; 390 [M⁺ + H]

Example 85.

3-(2-Pyridon-5-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 6.67 (d, 1H), 7.21-7.26 (m, 1H), 7.45-7.59 (m, 6H), 7.75 (td, 1H), 7.96 (dd, 1H), 8.14 (d, 1H), 8.26 (d, 1H), 8.32 (m, 1H), 8.62 (m, 1H).

65702-519

ESI-Mass; 342 [M⁺ + H]

Example 86.

3-(2-Fluoro-3-pyridyl)-5-(2-pyridyl)-1-(2-methoxy-5-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 4.00 (s, 3H), 6.88 (dd, 1H), 7.22-7.29 (m, 2H), 7.44-7.79 (m, 5H), 8.20-8.24 (m, 1H), 8.27-8.29 (m, 1H), 8.33-8.36 (m, 1H), 8.61 (ddd, 1H).

Example 87.

3-(2-Fluoro-3-pyridyl)-5-phenyl-1-(3-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (DMSO-d₆, 400MHz): δ (ppm) 7.31-7.37 (m, 1H), 7.41-7.48 (m, 2H), 7.52-7.66 (m, 2H), 7.71-7.76 (m, 2H), 8.06-8.10 (m, 1H), 8.16-8.28 (m, 4H), 8.66-8.70 (m, 1H), 8.80-8.82 (m, 1H).

Example 88.

3-(2-Fluoro-3-pyridyl)-5-(2-pyridyl)-1-(3-fluorophenyl)-1,2-dihydropyridin-2-one

¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 7.17-7.33 (m, 5H), 7.48-7.55 (m, 1H), 7.56-7.61 (m, 1H), 7.76 (ddd, 1H), 8.20-8.27 (m, 2H), 8.29 (d, 1H), 8.32-8.35 (m, 1H), 8.59-8.63 (m, 1H).

Example 89.

3-(2-Dimethylamino-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (CDCl₃, 400MHz): δ (ppm) 1.70 (s, 6H), 7.19 (ddd, 1H), 7.41-7.60 (m, 7H), 7.71 (td, 1H), 7.82 (d, 1H), 8.08 (d, 1H), 8.21 (d, 1H), 8.57 (dd, 1H), 8.58-8.60 (m, 1H).

ESI-Mass; 369 [M⁺ + H]

The following compounds were synthesized by the same method as mentioned in Example 7.

Example 90.

3,5-Diphenyl-1-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 7.33-7.40 (3H, m), 7.41-7.47 (4H, m), 7.54 (2H, dd), 7.76 (2H, dd), 7.86-7.90 (2H, m), 7.99 (1H, ddd), 8.11 (1H, d), 8.61-8.64 (1H, m).

Example 91.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(4-fluorophenyl)-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.18-7.25 (m, 3H), 7.44-7.55 (m, 3H), 7.59-7.67 (m, 2H), 7.72-7.81 (m, 3H), 8.27-8.33 (m, 2H), 8.58-8.63 (m, 1H).

Example 92.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-fluorophenyl)-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.15-7.25 (m, 2H), 7.28-7.36 (m, 2H), 7.44-7.54 (m, 2H), 7.58-7.68 (m, 2H), 7.72-7.82 (m, 3H), 8.28-8.33 (m, 2H), 8.57-8.63 (m, 1H).

Example 93.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(4-cyanophenyl)-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.23-7.26 (m, 1H), 7.49 (dt, 1H), 7.61-7.86 (m, 9H), 7.28-8.30 (m, 2H), 8.60-8.62 (m, 1H).

Example 94.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-cyanophenyl)-1,2-

dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.23-7.26 (m, 1H), 7.49 (dt, 1H), 7.61-7.89 (m, 9H), 8.30 (s, 2H), 8.60-8.62 (m, 1H).

Example 95.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(4-methoxyphenyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 3.86 (s, 3H), 7.02 (d, 2H), 7.21 (ddd, 1H), 7.42-7.80 (m, 8H), 8.29 (d, 1H), 8.31 (d, 1H), 8.58-8.60 (m, 1H).

Example 96.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-methoxyphenyl)-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 3.85 (s, 3H), 6.95-7.03 (m, 1H), 7.06-7.10 (m, 2H), 7.20-7.22 (m, 1H), 7.41-7.81 (m, 7H), 8.31 (s, 2H), 8.59-8.61 (m, 1H).

Example 97.

3-Phenyl-5-(2-pyridyl)-1-(3-fluorophenyl)-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.15-7.24 (m, 2H), 7.26-7.33 (m, 2H), 7.34-7.40 (m, 1H), 7.40-7.53 (m, 3H), 7.57-7.62 (m, 1H), 7.72-7.82 (m, 3H), 8.20-8.23 (m, 2H), 8.59-8.63 (m, 1H).

Example 98.

3-Phenyl-5-(2-pyridyl)-1-(4-fluorophenyl)-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.18-7.24 (m, 3H), 7.34-7.39 (m, 1H), 7.40-7.45 (m, 2H), 7.46-7.52 (m, 2H), 7.57-7.61 (m,

1H), 7.72-7.77 (m, 1H), 7.77-7.82 (m, 2H), 8.19-8.23 (m, 2H), 8.59-8.62 (m, 1H).

Example 99.

3-(2-Chlorophenyl)-5-(2-pyridyl)-1-(4-fluorophenyl)-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.16-7.24 (m, 3H), 7.29-7.35 (m, 2H), 7.45-7.54 (m, 4H), 7.56 (d, 1H), 7.70-7.76 (m, 1H), 8.12 (d, 1H), 8.28 (d, 1H), 8.58-8.62 (m, 1H).

Example 100.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(4-formylphenyl)-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.22-7.27 (m, 1H), 7.48 (ddd, 1H), 7.60-7.69 (m, 2H), 7.72-7.82 (m, 5H), 8.03-8.09 (m, 2H), 8.29 (d, 1H), 8.33 (d, 1H), 8.58-8.62 (m, 1H), 10.10 (s, 1H).

Example 101.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-formylphenyl)-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.20-7.25 (m, 1H), 7.44-7.52 (m, 2H), 7.61-7.70 (m, 3H), 7.73-7.83 (m, 4H), 8.06 (dd, 1H), 8.31 (d, 1H), 8.36 (d, 1H), 8.57-8.60 (m, 1H), 10.05 (s, 1H).

Example 102.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-chlorophenyl)-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.21-7.25 (m, 1H), 7.43-7.50 (m, 4H), 7.55-7.58 (m, 1H), 7.59-7.68 (m, 2H), 7.73-7.81 (m, 3H), 8.27-8.31 (m, 2H), 8.58-8.62 (m, 1H).

65702-519

Example 103.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-tolyl)-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 2.43 (s, 3H), 7.20-7.23 (m, 1H), 7.26-7.35 (m, 3H), 7.39-7.48 (m, 2H), 7.60-7.66 (m, 2H), 7.72-7.81 (m, 3H), 8.31 (s, 2H), 8.58-8.61 (m, 1H).

Example 104.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-trifluoromethylphenyl)-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.22-7.25 (m, 1H), 7.47 (t, 1H), 7.61-7.82 (m, 9H), 8.31 (s, 2H), 8.59-8.62 (m, 1H).

Example 105.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(thiophen-3-yl)-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.22-7.25 (m, 1H), 7.37-7.49 (m, 3H), 7.59-7.67 (m, 3H), 7.74-7.80 (m, 3H), 8.27 (d, 1H), 8.40 (d, 1H), 8.60-8.62 (m, 1H).

Example 106.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-furyl)-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 6.83-6.86 (m, 1H), 7.19-7.26 (m, 1H), 7.48 (ddd, 1H), 7.52 (dd, 1H), 7.60-7.69 (m, 2H), 7.73-7.82 (m, 3H), 8.21 (d, 1H), 8.27-8.30 (m, 1H), 8.47 (d, 1H), 8.61-8.65 (m, 1H).

Example 107.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(4-tolyl)-1,2-

dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 2.41 (s, 3H), 7.18-7.22 (m, 1H), 7.30-7.46 (m, 5H), 7.59-7.65 (m, 2H), 7.71-7.80 (m, 3H), 8.29 (d, 1H), 8.31 (d, 1H), 8.58-8.60 (m, 1H).

Example 108.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(4-trifluoromethylphenyl)-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.22-7.25 (m, 1H), 7.48 (td, 1H), 7.61-7.82 (m, 9H), 8.30 (d, 1H), 8.32 (d, 1H), 8.59-8.61 (m, 1H).

Example 109.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-methoxypyridyn-5-yl)-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 4.00 (s, 3H), 6.88 (d, 1H), 7.23 (ddd, 1H), 7.47 (td, 1H), 7.59-7.62 (m, 1H), 7.65 (td, 1H), 7.73-7.82 (m, 4H), 8.28-8.31 (m, 3H), 8.60 (ddd, 1H).

ESI-Mass; 381 [M⁺ + H]

Example 110.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-cyanophenyl)-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.26-7.35 (m, 2H), 7.52-7.58 (m, 2H), 7.64-7.71 (m, 2H), 7.72-7.85 (m, 5H), 8.51 (d, 1H), 8.68-8.72 (m, 1H), 8.77 (d, 1H).

Example 111.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(pyrimidin-5-yl)-1,2-dihydropyridin-2-one

65702-519

^1H -NMR (400 MHz, CDCl_3); δ (ppm) 7.24-7.32 (m, 1H), 7.48-7.54 (m, 1H), 7.61-7.72 (m, 2H), 7.73-7.85 (m, 3H), 8.31 (d, 1H), 8.33 (d, 1H), 8.60-8.65 (m, 1H), 9.04 (s, 2H), 9.32 (s, 1H).

Example 112.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-[2-(pyrrolidin-1-yl)-pyridin-5-yl]-1,2-dihydropyridin-2-one

^1H -NMR (400 MHz, CDCl_3); δ (ppm) 2.01-2.07 (m, 4H), 3.49-3.52 (m, 4H), 6.44 (dd, 1H), 7.21 (ddd, 1H), 7.45 (td, 1H), 7.58-7.67 (m, 3H), 7.72 (dd, 1H), 7.76-7.88 (m, 2H), 8.23 (dd, 1H), 8.28 (dd, 2H), 8.59 (ddd, 1H).

ESI-Mass; 420 [M^+ + H]

Example 113.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-[2-(4-benzylpiperazin-1-yl)-pyridin-5-yl]-1,2-dihydropyridin-2-one

^1H -NMR (400 MHz, CDCl_3); δ (ppm) 2.57 (t, 4H), 3.57 (s, 2H), 3.63 (t, 4H), 6.70 (d, 1H), 7.21 (ddd, 1H), 7.25-7.38 (m, 5H), 7.45 (td, 1H), 7.58 (d, 1H), 7.63 (td, 1H), 7.68 (dd, 1H), 7.73 (dd, 1H), 7.75-7.79 (m, 2H), 8.26-8.29 (m, 3H), 8.58-8.60 (m, 1H).

Example 114.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-benzyloxyethoxypyridin-5-yl)-1,2-dihydropyridin-2-one

^1H -NMR (400 MHz, CDCl_3); δ (ppm) 3.84-3.87 (m, 2H), 4.55-4.58 (m, 2H), 4.64 (s, 2H), 6.93 (d, 1H), 7.23 (ddd, 1H), 7.25-7.40 (m, 5H), 7.47 (td, 1H), 7.60 (d, 1H), 7.65 (td, 1H), 7.74-7.82 (m, 4H), 8.27 (d, 1H), 8.28 (d, 1H), 8.30 (d, 1H), 8.59-8.61 (m, 1H).

ESI-Mass; 501 [M^+ + H]

Example 115.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-benzyloxymethylpyridin-5-yl)-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 4.64 (s, 2H), 4.66 (s, 2H), 7.23-7.26 (m, 1H), 7.26-7.38 (m, 5H), 7.48 (td, 1H), 7.61 (d, 1H), 7.68 (td, 1H), 7.74-7.81 (m, 3H), 7.95-7.98 (m, 1H), 8.29 (d, 1H), 8.32 (d, 1H), 8.61 (d, 1H), 8.69 (d, 1H), 8.72 (d, 1H).

ESI-Mass; 471 [M⁺ + H]

Example 116.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-ethylthiopyridin-5-yl)-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 1.41 (t, 3H), 3.23 (q, 2H), 7.23 (ddd, 1H), 7.29 (dd, 1H), 7.47 (td, 1H), 7.60 (dt, 1H), 7.65 (td, 1H), 7.72 (dd, 1H), 7.74-7.80 (m, 3H), 8.28 (d, 1H), 8.30 (d, 1H), 8.57 (dd, 1H), 8.60 (ddd, 1H).

Example 117.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(4-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.23-7.26 (m, 1H), 7.49 (td, 1H), 7.55-7.57 (m, 2H), 7.61 (d, 1H), 7.67 (td, 1H), 7.73-7.81 (m, 3H), 8.29 (d, 1H), 8.30 (d, 1H), 8.61 (ddd, 1H), 8.82 (d, 2H).

ESI-Mass; 351 [M⁺ + H]

Example 118.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-methoxypyridin-5-yl)-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 3.91 (s, 3H), 7.22-7.27 (m, 1H),

7.46-7.51 (m, 2H), 7.60-7.64 (m, 1H), 7.66 (ddd, 1H), 7.74-7.82 (m, 3H), 8.30 (d, 1H), 8.32 (d, 1H), 8.38 (d, 1H), 8.43 (d, 1H), 8.60-8.63 (m, 1H).

Example 119.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-hydroxyethoxypyridin-5-yl)-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 3.04 (brs, 1H), 3.97-4.03 (m, 2H), 4.51-4.54 (m, 2H), 6.93 (d, 1H), 7.23 (dd, 1H), 7.47 (td, 1H), 7.61 (dd, 1H), 7.65 (td, 1H), 7.74-7.80 (m, 3H), 7.84 (dd, 1H), 8.27-8.30 (m, 3H), 8.61 (ddd, 1H).

ESI-Mass; 411 [M⁺ + H]

Example 120.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-chloropyridin-5-yl)-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.23-7.28 (m, 1H), 7.47-7.52 (m, 2H), 7.61 (d, 1H), 7.67 (t, 1H), 7.72-7.81 (m, 3H), 7.95 (dd, 1H), 8.28 (d, 1H), 8.30 (d, 1H), 8.59 (d, 1H), 8.61 (dt, 1H).

ESI-Mass; 385 [M⁺ + H]

Example 121.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-[2-(4-methylpiperazin-1-yl)-pyridin-5-yl]-1,2-dihydropyridin-2-one

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 2.37 (s, 3H), 2.54 (t, 4H), 3.66 (t, 4H), 6.73 (d, 1H), 7.21 (ddd, 1H), 7.46 (td, 1H), 7.59 (d, 1H), 7.64 (td, 1H), 7.70 (dd, 1H), 7.72-7.79 (m, 3H), 8.27-8.29 (m, 3H), 8.58-8.60 (m, 1H).

ESI-Mass; 449 [M⁺ + H]

Example 122.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-tert-butyl
dimethylsilyloxymethylpyridin-5-yl)-1,2-
dihydropyridin-2-one

$^1\text{H-NMR}$ (400 MHz, CDCl_3); δ (ppm) 0.13 (s, 6H), 0.95 (s, 9H); 4.85 (s, 2H), 7.24 (dd, 1H), 7.45-7.81 (m, 7H), 7.88 (s, 1H), 8.29 (d, 1H), 8.32 (d, 1H), 8.61 (dd, 1H), 8.68 (d, 1H).

Example 123.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-fluoropyridin-5-yl)-
1,2-dihydropyridin-2-one

$^1\text{H-NMR}$ (400 MHz, CDCl_3); δ (ppm) 7.11 (dd, 1H), 7.25 (ddd, 1H), 7.42-7.84 (m, 6H), 8.08 (ddd, 1H), 8.30 (t, 2H), 8.41 (dd, 1H), 8.61 (ddd, 1H).

ESI-Mass; 369 [M^+ + H]

Example 124.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-ethylpyridine-5-yl)-
1,2-dihydropyridin-2-one

$^1\text{H-NMR}$ (400 MHz, CDCl_3); δ (ppm) 1.36 (t, 3H), 2.91 (q, 2H), 7.23 (m, 1H), 7.33 (d, 1H), 7.47 (td, 1H), 7.60 (d, 1H), 7.65 (td, 1H), 7.73-7.80 (m, 3H), 7.86 (dd, 1H), 8.30 (d, 1H), 8.31 (d, 1H), 8.60 (d, 1H), 8.68 (d, 1H).

ESI-Mass; 379 [M^+ + H]

Example 125.

3-Phenyl-5-(2-pyridyl)-1-(2-cyanophenyl)-1,2-
dihydropyridin-2-one

$^1\text{H-NMR}$ ($\text{DMSO}-d_6$, 400 MHz); δ (ppm) 7.24-7.54 (6H, m), 7.62-

7.81 (4H, m), 7.93 (1H, dt), 8.11 (1H, d), 8.57 (1H, d), 8.69-8.72 (1H, m), 8.89-8.94 (1H, m).

Example 126.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-methoxyphenyl)-1,2-dihydropyridin-2-one

¹H-NMR (DMSO-d₆, 400MHz); δ (ppm) 3.80 (3H, s), 7.12 (1H, t), 7.24-7.33 (2H, m), 7.44 (1H, dd), 7.49 (1H, dt), 7.59 (1H, dt), 7.71 (1H, d), 7.75-7.86 (2H, m), 7.90-8.00 (2H, m), 8.42 (1H, d), 8.47 (1H, d), 8.56-8.60 (1H, m).

The following compounds were synthesized by the same method as mentioned in Example 32.

Example 127.

3-Phenyl-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 7.23 (ddd, 1H), 7.36-7.50 (m, 4H), 7.60 (td, 1H), 7.75 (dd, 1H), 7.76-7.80 (m, 2H), 7.94 (ddd, 1H), 8.22 (d, 1H), 8.24 (d, 1H), 8.62 (ddd, 1H), 8.71 (dd, 1H), 8.75-8.79 (m, 1H).

ESI-Mass; 326 [M⁺ + H]

Example 128.

3-(2-Chlorophenyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 7.23 (ddd, 1H), 7.31-7.36 (m, 2H), 7.41-7.51 (m, 3H), 7.56-7.59 (m, 1H), 7.75 (td, 1H), 7.95 (ddd, 1H), 8.15 (d, 1H), 8.30 (d, 1H), 8.60-8.62 (m, 1H), 8.69 (dd, 1H), 8.80 (d, 1H).

ESI-Mass; 360 [M⁺ + H]

Example 129.

3-(2-Methoxyphenyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 3.84 (s, 3H), 6.98-7.05 (m, 2H), 7.21 (ddd, 1H), 7.37 (td, 1H), 7.41-7.49 (m, 2H), 7.56 (d, 1H), 7.74 (td, 1H), 7.94-7.97 (m, 1H), 8.13 (d, 1H), 8.25 (d, 1H), 8.58-8.60 (m, 1H), 8.67 (dd, 1H), 8.79 (d, 1H).

ESI-Mass; 356 [M⁺ + H]

Example 130.

3-(2-Formylthiophen-3-yl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 7.24-7.28 (m, 1H), 7.46-7.52 (m, 2H), 7.57 (d, 1H), 7.50-7.79 (m, 2H), 7.92-7.96 (m, 1H), 8.24 (d, 1H), 8.30 (d, 1H), 8.61-8.63 (m, 1H), 8.74 (dd, 1H), 8.79 (d, 1H), 9.99 (d, 1H).

Example 131.

3-(2,4-Dichlorophenyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 7.22-7.25 (m, 1H), 7.32 (dd, 1H), 7.41-7.61 (m, 4H), 7.74-7.79 (m, 1H), 7.93-7.96 (m, 1H), 8.15 (d, 1H), 8.29 (d, 1H), 8.59-8.63 (m, 1H), 8.69-8.72 (m, 1H), 8.79 (d, 1H).

ESI-Mass; 394 [M⁺ + H]

Example 132.

3-(2-Trifluoromethylphenyl)-5-(2-pyridyl)-1-(3-pyridyl)-

1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 7.22 (ddd, 1H), 7.44-7.56 (m, 4H), 7.59-7.63 (m, 2H), 7.72-7.78 (m, 1H), 7.94 (ddd, 1H), 8.04 (d, 1H), 8.30 (d, 1H), 8.59-8.61 (m, 1H), 8.69 (dd, 1H), 8.78-8.79 (m, 1H).

ESI-Mass; 394 [M⁺ + H]

Example 133.

3-(Thiophen-3-yl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 7.24 (ddd, 1H), 7.39 (dd, 1H), 7.50 (dd, 1H), 7.60-7.63 (m, 1H), 7.65 (dd, 1H), 7.77 (td, 1H), 7.93 (ddd, 1H), 8.15 (d, 1H), 8.32 (dd, 1H), 8.44 (d, 1H), 8.62-8.64 (m, 1H), 8.72-8.73 (m, 1H), 8.77 (d, 1H).

ESI-Mass; 332 [M⁺ + H]

Example 134.

3-(1-tert-Butoxycarbonylpyrrol-2-yl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 1.47 (s, 9H), 6.25 (t, 1H), 6.36-6.34 (m, 1H), 7.21 (dd, 1H), 7.37 (dd, 1H), 7.43-7.48 (m, 1H), 7.57 (d, 1H), 7.72-7.77 (m, 1H), 7.88-7.92 (m, 1H), 8.06 (d, 1H), 8.22 (d, 1H), 8.59-8.61 (m, 1H), 8.68 (dd, 1H), 8.76 (d, 1H).

ESI-Mass; 415 [M⁺ + H]

Example 135.

3-(2,6-Dimethylphenyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 2.23 (s, 6H), 7.11-7.27 (m, 3H), 7.45-7.55 (m, 3H), 7.65-8.02 (m, 2H), 8.20-8.33 (m, 1H), 8.59-

65702-519

8.61 (m, 1H), 8.68-8.81 (m, 3H).

ESI-Mass; 354 [M⁺ + H]

Example 136.

3-(3-Acetylaminophenyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 2.08 (s, 3H), 7.21-7.26 (m, 1H), 7.34 (d, 1H), 7.44-7.49 (m, 2H), 7.58-7.61 (m, 2H), 7.75 (td, 1H), 7.82 (brs, 1H), 7.84-7.88 (m, 1H), 7.89-7.92 (m, 1H), 8.20-8.23 (m, 2H), 8.59-8.61 (m, 1H), 8.69-8.71 (m, 1H), 8.77-8.78 (m, 1H).

ESI-Mass; 383 [M⁺ + H]

Example 137.

3-(2-Cyanothiophen-3-yl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 7.23-7.26 (m, 1H), 7.50 (dd, 1H), 7.61-7.74 (m, 3H), 7.79 (td, 1H), 7.91-7.94 (m, 1H), 8.36 (d, 1H), 8.57 (d, 1H), 8.60-8.61 (m, 1H), 8.74 (dd, 1H), 8.79 (d, 1H).

ESI-Mass; 357 [M⁺ + H]

Example 138.

3-(2-Cyano-6-methoxyphenyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 3.82 (s, 3H), 7.18-7.27 (m, 2H), 7.35-7.38 (dd, 1H), 7.43-7.50 (m, 2H), 7.60 (d, 1H), 7.74-7.80 (m, 1H), 7.98-8.02 (m, 1H), 8.16 (d, 1H), 8.35 (d, 1H), 8.59-8.62 (m, 1H), 8.67-8.72 (m, 1H), 8.83 (d, 1H).

Example 139.

3-(2-Fluoro-3-pyridyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-

dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 7.21-7.29 (m, 2H), 7.45-7.52 (m, 1H), 7.59 (d, 1H), 7.78 (dt, 1H), 7.91-7.95 (m, 1H), 8.19-8.25 (m, 2H), 8.30 (d, 1H), 8.35 (t, 1H), 8.60-8.63 (m, 1H), 8.70-8.73 (m, 1H), 8.79 (d, 1H).

The following compound was synthesized by the same method as mentioned in Example 15.

Example 140.

3-(2-Aminocarbonylphenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (DMSO-d₆, 400MHz); δ (ppm) 7.17 (1H, brs), 7.26-7.31 (1H, m), 7.40-7.64 (10H, m), 7.82 (1H, dt), 7.96 (1H, d), 8.21 (1H, d), 8.36 (1H, d), 8.56-8.59 (1H, m).

The following compounds were synthesized by the same method as mentioned in Example 18.

Example 141.

3-(2-Hydroxyphenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (DMSO-d₆, 400MHz); δ (ppm) 6.87-6.93 (2H, m), 7.22 (1H, dt), 7.30 (1H, ddd), 7.38 (1H, dd), 7.48-7.60 (5H, m), 7.82 (1H, dt), 7.99 (1H, d), 8.41 (1H, d), 8.45 (1H, d), 8.57-8.60 (1H, m), 9.43 (1H, s).

Example 142.

3-(2-Hydroxyphenyl)-5-(2-pyridyl)-1-(4-fluorophenyl)-1,2-dihydropyridin-2-one

¹H-NMR (DMSO-d₆, 400MHz); δ (ppm) 6.86-6.93 (2H, m), 7.22 (1H, dt),

7.30 (1H, ddd), 7.36-7.44 (3H, m), 7.62-7.68 (2H, m), 7.83 (1H, dt),
7.98 (1H, d), 8.40 (1H, d), 8.45 (1H, d), 8.57-8.60 (1H, m),
9.40 (1H, s).

Example 143.

3-(2-Chlorophenyl)-5-(2-pyridyl)-1-(3-hydroxyphenyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 6.71-6.76 (m, 1H), 6.85-6.91 (m, 2H), 7.19-7.34 (m, 4H), 7.41-7.50 (m, 2H), 7.56 (d, 1H), 7.74 (ddd, 1H), 8.17 (d, 1H), 8.23 (d, 1H), 8.58-8.62 (m, 1H).

The following compounds were synthesized by the same method as mentioned in Example 19.

Example 144.

3-(2-Chlorophenyl)-5-(2-pyridyl)-1-(3-dimethylaminoethoxyphenyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 2.89 (s, 6H), 3.41 (t, 2H), 4.54 (t, 2H), 6.99-7.04 (m, 1H), 7.13 (dd, 1H), 7.14-7.18 (m, 1H), 7.21 (ddd, 1H), 7.30-7.35 (m, 2H), 7.43-7.51 (m, 3H), 7.58 (d, 1H), 7.74 (ddd, 1H), 8.15 (d, 1H), 8.28 (d, 1H), 8.59-8.62 (m, 1H).

Example 145.

3-(2-Chlorophenyl)-5-(2-pyridyl)-1-(4-dimethylaminopropoxyphenyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 1.98 (tt, 2H), 2.26 (s, 6H), 2.46 (t, 2H), 4.06 (t, 2H), 6.97-7.03 (m, 2H), 7.19 (ddd, 1H), 7.28-7.33 (m, 2H), 7.39-7.44 (m, 2H), 7.46-7.51 (m, 2H), 7.53-7.58 (m, 1H), 7.72 (ddd, 1H), 8.12 (d, 1H), 8.28 (d, 1H), 8.58-8.61 (m, 1H).

Example 146.

3-(2-Chlorophenyl)-5-(2-pyridyl)-1-(3-dimethylaminopropoxyphenyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 1.96 (tt, 2H), 2.25 (s, 6H), 2.44 (t, 2H), 4.05 (t, 2H), 6.95-7.01 (m, 1H), 7.04-7.11 (m, 2H), 7.17-7.24 (m, 1H), 7.28-7.35 (m, 2H), 7.36-7.43 (m, 1H), 7.45-7.53 (m, 2H), 7.56 (d, 1H), 7.73 (ddd, 1H), 8.14 (d, 1H), 8.29 (d, 1H), 8.58-8.63 (m, 1H).

The following compounds were synthesized by the same method as mentioned in Example 21.

Example 147.

3-(2-Hydroxymethylphenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (DMSO-d₆; 400MHz); δ (ppm) 4.46 (2H, d), 5.04 (1H, t), 7.24-7.60 (10H, m), 7.78-7.84 (1H, m), 7.96-8.00 (1H, m), 8.25 (1H, d), 8.45 (1H, d), 8.55-8.59 (1H, m).

Example 148.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(4-hydroxymethylphenyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 1.81 (t, 1H), 4.78 (d, 2H), 7.19-7.24 (m, 1H), 7.46 (ddd, 1H), 7.51-7.55 (m, 4H), 7.59-7.66 (m, 2H), 7.72-7.80 (m, 3H), 8.28-8.32 (m, 2H), 8.58-8.61 (m, 1H).

Example 149.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-hydroxymethylphenyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 3.35 (dd, 1H), 4.52 (dd, 1H),

4.62 (dd, 1H), 7.21-7.24 (m, 1H), 7.35 (dd, 1H), 7.46-7.57 (m, 3H), 7.60-7.69 (m, 3H), 7.72-7.81 (m, 3H), 8.26 (d, 1H), 8.36 (d, 1H), 8.58-8.62 (m, 1H).

The following compounds were synthesized by the same method as mentioned in Example 22.

Example 150.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(4-cyanomethylphenyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 3.84 (s, 2H), 7.23 (ddd, 1H), 7.47 (ddd, 1H), 7.49-7.54 (m, 2H), 7.55-7.63 (m, 3H), 7.65 (ddd, 1H), 7.73-7.81 (m, 3H), 8.28-8.32 (m, 2H), 8.58-8.62 (m, 1H).

Example 151.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-cyanomethylphenyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 3.81 (d, 1H), 3.91 (d, 1H), 7.24 (ddd, 1H), 7.39-7.44 (m, 1H), 7.46-7.58 (m, 3H), 7.62 (d, 1H), 7.64-7.71 (m, 3H), 7.73-7.81 (m, 2H), 8.22 (d, 1H), 8.34 (d, 1H), 8.59-8.63 (m, 1H).

The following compounds were synthesized by the same method as mentioned in Example 27.

Example 152.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-ethylsulfonylpyridin-5-yl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 1.36 (t, 3H), 3.47 (q, 2H), 7.26-7.29 (m, 1H), 7.51 (td, 1H), 7.63 (d, 1H), 7.68 (td, 1H), 7.71-7.82 (m, 3H), 8.23-8.29 (m, 2H), 8.31-8.33 (m, 2H), 8.61-

8.63 (m, 1H), 8.97-8.98 (m, 1H).

ESI-Mass; 443 [M⁺ + H]

Example 153.

3-(2-Fluoro-3-pyridyl)-5-(2-pyridyl)-1-(4-methylsulfonylphenyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 3.11 (s, 3H), 7.24-7.30 (m, 2H), 7.60 (d, 1H), 7.75-7.80 (m, 3H), 8.12 (t, 1H), 8.14 (t, 1H), 8.17-8.24 (m, 2H), 8.30 (d, 1H), 8.35 (t, 1H), 8.61-8.63 (m, 1H).

ESI-Mass; 422 [M⁺ + H]

The following compounds were synthesized by the same manner as mentioned in Example 29.

Example 154.

3-(2-Dimethylaminomethylphenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one dihydrochloride

¹H-NMR (DMSO-d₆, 400MHz); δ (ppm) 2.06 (6H, s), 3.37 (2H, s), 7.25-7.39 (4H, m), 7.44-7.61 (6H, m), 7.81 (1H, dt), 7.96 (1H, d), 8.24 (1H, d), 8.43 (1H, d), 8.55-8.58 (1H, m).

Example 155.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-dimethylaminomethylphenyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 2.16 (s, 6H), 3.30 (d, 1H), 3.46 (d, 1H), 7.18-7.23 (m, 1H), 7.34-7.38 (m, 1H), 7.40-7.49 (m, 3H), 7.55-7.66 (m, 3H), 7.70-7.79 (m, 3H), 8.21 (d, 1H), 8.37 (d, 1H), 8.58-8.61 (m, 1H).

Example 156.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(4-

dimethylaminomethylphenyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 2.28 (s, 6H), 3.49 (s, 2H), 7.22 (ddd, 1H), 7.43-7.49 (m, 5H), 7.59-7.66 (m, 2H), 7.72-7.81 (m, 3H), 8.30 (d, 1H), 8.33 (d, 1H), 8.58-8.61 (m, 1H).

Example 157.

3-(2-Cyanophenyl)-5-(6-diethylaminomethyl-2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 1.49 (6H, t), 3.10-3.33 (4H, m), 4.36 (2H, brs), 7.46-7.60 (7H, m), 7.63-7.68 (2H, m), 7.79-7.89 (3H, m), 8.28 (1H, d), 8.39 (1H, d).

The following compound was synthesized by the same method as mentioned in Example 31.

Example 158.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-phenethyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 3.18 (t, 2H), 4.33 (t, 2H), 7.19 (ddd, 1H), 7.22-7.34 (m, 3H), 7.39 (d, 1H), 7.43-7.50 (m, 3H), 7.62-7.74 (m, 4H), 7.96 (d, 1H), 8.18 (d, 1H), 8.56-8.60 (m, 1H).

Example 159.

3-(2-Cyanophenyl)-1-(2-pyridyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

A mixture of 0.05g of 1-(2-pyridyl)-5-(2-pyridyl)-3-bromo-1,2-dihydropyridin-2-one, 0.04g of 2-(2-cyanophenyl)-1,3,2-dioxaborinate, 0.02g of tetrakis(triphenylphosphine) palladium and 0.1g of cesium carbonate was stirred at 120°C in a nitrogen atmosphere for 2 hours in dimethylformamide. The

mixture was diluted with water, and extracted with ethyl acetate. The organic layer was washed with water and then saturated saline water, and dried by magnesium sulfate anhydride. The solvent was concentrated under a vacuum, and the residue was refined by silica gel chromatography (ethyl acetate/hexane=3:1), to obtain 0.04g of the white, powdery subject compound.

¹H-NMR (400MHz, DMSO-d₆); δ(ppm) 7.33(dd, 1H), 7.56-7.64(m, 2H), 7.75(d, 1H), 7.78-7.83(m, 1H), 7.84-7.90(m, 2H), 7.95(d, 1H), 8.00(d, 1H), 8.07(dt, 1H), 8.50(d, 1H), 8.61(d, 1H), 8.70(d, 1H), 8.83(d, 1H).

Example 160.

1-(2-Cyanophenyl)-3-(2-pyridyl)-5-phenyl-1,2-dihydropyridin-2-one

5ml of a dimethylformamide solution containing 0.26g of 3-(2-pyridyl)-5-phenyl-2(1H)-pyridone was incorporated with 0.04g of sodium hydride. After 15 minutes, the solution was further incorporated with 0.15g of 2-fluorobenzonitrile and 0.10g of cuprous iodide, and vigorously stirred at 100°C for 2 hours. The solution was cooled to room temperature, diluted with water, and extracted with ethyl acetate. The organic layer was washed with water and then saturated saline water, and dried by magnesium sulfate anhydride. The solvent was distilled off under a vacuum. The residue was refined by silica gel chromatography (ethyl acetate/hexane=1:2), to obtain 0.03g of the light yellow, powdery subject compound.

¹H-NMR (400MHz, DMSO-d₆) ; δ(ppm) 7.34-7.42 (m, 2H), 7.45-7.50 (m, 2H), 7.70-7.78 (m, 3H), 7.84-7.90 (m, 2H), 7.96 (dt, 1H), 8.11 (d, 1H), 8.31 (d, 1H), 8.47 (dd, 1H), 8.71-8.74 (m, 1H), 8.88 (d, 1H).

Example 161.

1-Phenyl-3-(1-phenylacetylen-2-yl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

100mg of 3-bromo-1-phenyl-5-(pyridin-2-yl)-1,2-dihydropyridin-2-one, 55mg of phenylacetylene, 1mg of copper (I) iodide and 4mg of dichlorobis(triphenylphosphine) palladium were added to a mixed solvent of 1.5ml of triethylamine and 1ml of dimethylformamide, and stirred at 50°C in a nitrogen atmosphere for a night. The reaction mixture was distributed into the ethyl acetate and water layers. The organic layer was washed with water, dried and concentrated, and the residue was refined by silica gel chromatography (ethyl acetate/hexane-based solvent), to obtain 7mg of the subject compound.

¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.22 (dd, 1H), 7.33-7.35 (m, 3H), 7.46-7.60 (m, 8H), 7.75 (dt, 1H), 8.26 (d, 1H), 8.34 (d, 1H), 8.60 (ddd, 1H).

Example 162.

5-(5-Acetoxypyridin-2-yl)-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one

(162a) 3-(2-Cyanophenyl)-1-phenyl-5-(tri-n-butyl stannyl)-1,2-dihydropyridin-2-one

5.50g of 5-bromo-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one, 45.5g of bistributyl tin and 907mg of tetrakis(triphenylphosphine) palladium were added to 60ml of xylene, and the mixture was stirred at 120°C in a nitrogen atmosphere for 40 minutes. The reaction mixture was refined by silica gel chromatography (ethyl acetate/hexane-based solvent), to obtain 3.42g of the subject compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 0.90(t, 9H), 1.07-1.11(m, 6H), 1.30-1.39(m, 6H), 1.52-1.60(m, 6H), 7.29(d, 1H), 7.39-7.47(m, 5H), 7.49-7.52(m, 2H), 7.60(d, 1H), 7.71-7.75(m, 2H).

(162b) 5-(5-acetoxypyridin-2-yl)-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one

3.42g of 3-(2-cyanophenyl)-1-phenyl-5-(tri-n-butylstannyl)-1,2-dihydropyridin-2-one, 1.57g of 5-acetoxy-2-chloropyridine and 352mg of tetrakis(triphenylphosphine) palladium were added to 40ml of xylene, and the mixture was stirred at 120°C in a nitrogen atmosphere for 8.5 hours. The reaction mixture was refined by silica gel chromatography (ethyl acetate/hexane-based solvent), to obtain 953mg of the subject compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.36(s, 3H), 7.44-7.56(m, 6H), 7.62-7.68(m, 3H), 7.77-7.80(m, 2H), 8.27(d, 1H), 8.28(d, 1H), 8.40(dd, 1H).

Example 163.

3-(2-Cyanophenyl)-5-(5-hydroxypyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

953mg of 5-(5-acetoxypyridin-2-yl)-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one and 192mg of potassium carbonate were added to 50ml of methanol, and the mixture was stirred at room temperature for 30 minutes. The mixture was further incorporated with 50ml of methanol, and stirred at 40°C for 15 minutes. The reaction mixture was diluted with ethyl acetate, and filtered by silica gel. The filtrate was concentrated under a vacuum and washed with a ether/methanol-based solvent, to obtain 786mg of the subject compound.

¹H-NMR (400MHz, DMSO-d₆); δ(ppm) 7.19(dd, 1H), 7.49-7.52(m, 1H), 7.55-7.61(m, 5H), 7.71(dd, 1H), 7.78(dt, 1H), 7.82(d, 1H), 7.93(dd, 1H), 8.14(d, 1H), 8.34(d, 1H), 8.37(d, 1H).

Example 164.

3-(2-Cyanophenyl)-1-phenyl-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one

63mg of 2-tributyl tin pyrimidine, prepared in accordance with Tetrahedron 50(1), 275, (1994), 50mg of 5-bromo-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one and 5mg tetrakis(triphenylphosphine) palladium were added to 2ml of xylene, and the mixture was stirred at 120°C in a nitrogen atmosphere for a night. The reaction mixture was refined by silica gel chromatography (ethyl acetate/hexane-based solvent), to obtain 10mg of the subject compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.15(t, 1H), 7.44-7.54(m, 6H), 7.64(dt, 1H), 7.72-7.78(m, 2H), 8.70(s, 1H), 8.71(s, 1H),

8.72(d, 1H), 8.76(d, 1H).

Example 165.

3-(2-Hydroxypyridin-6-yl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

20mg of 3-(2-methoxypyridin-6-yl)-1-phenyl-5-(pyridin-2-yl)-1,2-dihydropyridin-2-one is added to 3ml of 5N hydrochloric acid. The mixture was heated under reflux for 3 hours, to which 0.5ml of concentrated hydrochloric acid was added, and further stirred for 1 hour. The reaction mixture was concentrated under a vacuum and washed with ether, to quantitatively obtain the subject compound.

¹H-NMR (400MHz, DMSO-d₆); δ(ppm) 6.44(d, 1H), 7.08(brs, 1H), 7.47(dd, 1H), 7.52-7.62(m, 6H), 8.02-8.06(m, 1H), 8.18(d, 1H), 8.62(d, 1H), 8.68(dd, 1H), 8.82(dd, 1H).

Example 166.

1-(2-Aminobenzothiazol-6-yl)-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

150mg of 1-(3-aminophenyl)-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one and 63mg of ammonium thiocyanate were added to 2ml of acetic acid. The mixture was stirred at room temperature for 1 hour, to which 0.022ml of bromine was added, and further stirred for 1 hour. The reaction mixture was distributed into the ethyl acetate and water layers, and neutralized with 20% aqueous solution of potassium carbonate. The organic layer was washed with water, dried and concentrated, and the residue was refined by silica gel

chromatography (ethyl acetate/hexane-based solvent), to obtain 58mg of the subject compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 5.37 (brs, 1H), 6.76 (d, 1H), 7.20-7.24 (m, 1H), 7.41-7.80 (m, 8H), 8.28-9.40 (m, 2H), 8.59-8.61 (m, 1H).

Example 167.

1,3-Diphenyl-4-methyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

The subject compound was obtained, at a yield of 27%, in accordance with the method for Referential Examples 4, 5 and 6 and Example 32 from 2,5-dibromo-4-methylpyridine.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.10 (s, 3H), 7.27 (ddd, 1H), 7.30-7.51 (m, 12H), 7.76 (ddd, 1H), 8.66-8.70 (m, 1H).

Example 168.

1-Phenyl-3-[N-(N'-phenylureylenyl)]-5-(2-pyridyl)-1,2-dihydropyridin-2-one

50mg of 3-amino-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one and 25mg of phenyl isocyanate were dissolved in 1ml of tetrahydrofuran, and the solution was stirred at room temperature for 2 hours and at 60°C for 2 hours. The reaction solution was left to cool to room temperature, to which diethyl ether was added. The resultant crystal was separated by filtration, to obtain 30mg of the subject compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.03-7.14 (m, 3H), 7.17-7.33 (m, 4H), 7.38-7.44 (m, 2H), 7.45-7.50 (m, 2H), 7.59 (br s, 1H), 7.68-7.76 (m, 2H), 8.02 (d, 1H), 8.54-8.57 (m, 1H), 8.58 (br s, 1H),

9.00 (d, 1H) .

Example 169.

3-Benzoylamino-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

30mg of 3-amino-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one was dissolved in 1ml of methylene chloride and 1ml of pyridine, to which 19mg of benzoyl chloride was added with cooling with ice, and the mixture was stirred at room temperature for a night. The reaction mixture was concentrated, diluted with ethyl acetate, and washed with a saturated aqueous solution of sodium bicarbonate. The organic layer was dried by magnesium sulfate, and refined by NH silica gel chromatography (ethyl acetate). The solvent was concentrated, and the resultant crude crystal was washed with ethyl acetate/hexane, to obtain 35mg of the subject compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.23 (ddd, 1H), 7.47-7.60 (m, 8H), 7.70-7.80 (m, 2H), 7.95-8.00 (m, 2H), 8.12 (d, 1H), 8.57-8.61 (m, 1H), 9.28 (d, 1H), 9.35 (br s, 1H) .

Example 170.

3-Benzylamino-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

40mg of 3-amino-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one and 10mg of sodium hydride were added to 1ml of toluene, to which 30mg of benzyl chloride was added dropwise at 70°C. The mixture was stirred for 30 minutes, and heated for 1 hour under reflux. The reaction mixture was left

to cool to room temperature, diluted with ethyl acetate, and washed with a water and a saturated saline water. The organic layer was dried by magnesium sulfate, and refined by NH silica gel chromatography (ethyl acetate/hexane-based solvent), to obtain 13mg of the subject compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 4.48(d, 2H), 5.60(br t, 1H), 6.86(d, 1H), 7.15(ddd, 1H), 7.26-7.32(m, 1H), 7.34-7.40(m, 2H), 7.40-7.56(m, 9H), 7.66(ddd, 1H), 8.55-8.58(m, 1H).

Example 171.

3-(2-Cyanophenyl)-1-cyclopentyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

2.00g of 3-bromo-5-(2-pyridyl)-1,2-dihydropyridin-2-one as the stock material was N-alkylated by the normal method with 5.94g of bromocyclopentane and 5.50g of potassium carbonate, to obtain 506mg of 3-bromo-1-cyclopentyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one, 150mg of which was treated in accordance with the method for Example 32, to obtain 120mg of the subject compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.73-2.02(m, 6H), 2.23-2.35(m, 2H), 5.37(quintet, 1H), 7.20(ddd, 1H), 7.45(ddd, 1H), 7.57(d, 1H), 7.64(ddd, 1H), 7.70-7.79(m, 3H), 8.11(d, 1H), 8.36(d, 1H), 8.59-8.63(m, 1H).

Example 172.

1-{3-[1-(Benzyloxycarbonyl)piperidin-4-yl-oxy]phenyl}-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

0.99g of 3-bromo-1-(3-hydroxyphenyl)-5-(2-pyridyl)-

1,2-dihydropyridin-2-one was obtained in accordance with the method for Example 18 from 1.02g of 3-bromo-1-(3-methoxyphenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one, synthesized in accordance with the method for Referential Example 6. It was dissolved 30ml of tetrahydrofuran and 10ml of N,N-dimethylformamide, to which 1.52g of triphenyl phosphine and 1.36g of N-benzyloxycarbonyl-4-piperidinol were added, and further 2.52g of a 40% toluene solution of diethylazodicarboxylate was added dropwise with cooling with ice, and the mixture was stirred at room temperature for a night. The reaction solution was concentrated under a vacuum and refined by silica gel chromatography (ethyl acetate/hexane-based solvent) to obtain 0.98g of 1-{3-[N-(benzyloxycarbonyl)piperidin-4-yl-oxy]phenyl}-3-bromo-5-(2-pyridyl)-1,2-dihydropyridin-2-one, from which 0.85g of the subject compound was obtained in accordance with the method for Example 32.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.73-1.87 (m, 2H), 1.88-2.02 (m, 2H), 3.43-3.52 (m, 2H), 3.70-3.80 (m, 2H), 4.50-4.58 (m, 1H), 5.14 (s, 2H), 6.98-7.02 (m, 1H), 7.06-7.11 (m, 2H), 7.22 (dd, 1H), 7.30-7.38 (m, 5H), 7.40-7.49 (m, 2H), 7.60 (ddd, 1H), 7.64 (ddd, 1H), 7.72-7.80 (m, 3H), 8.29 (d, 1H), 8.31 (d, 1H), 8.58-8.61 (m, 1H).
Example 173.

3-(2-Cyanophenyl)-5-(2-pyridyl 1-oxide)-1-phenyl-1,2-dihydropyridin-2-one

1.00g of 3-(2-cyanophenyl)-5-(2-pyridyl)-1-phenyl-

1,2-dihydropyridin-2-one was dissolved in 30ml of chloroform, to which 0.99g of 60% m-chloroperbenzoic acid was added, and the mixture was stirred at room temperature for 2 hours. Another 1.00g of 60% m-chloroperbenzoic acid was added to the mixture, and the mixture was stirred for 3 hours. The reaction solution was incorporated with 50ml of an aqueous solution of 1N sodium hydroxide, and extracted with ethyl acetate. The organic layer was washed with saturated saline water, dried by magnesium sulfate anhydride, and the solvent was distilled off under a vacuum. The residue was recrystallized from ethyl acetate/diethyl ether, to obtain 0.46g of the subject compound. ¹H-NMR(400MHz, CDCl₃); δ(ppm) 7.21-7.27(m, 1H), 7.36(dt, 1H), 7.43-7.48(m, 2H), 7.50-7.54(m, 4H), 7.61(dd, 1H), 7.63(dt, 1H), 7.78(dd, 1H), 7.81-7.85(m, 1H), 8.10(d, 1H), 8.21(dd, 1H), 8.83(d, 1H).

Example 174.

3-Phenylamino-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

53mg of 3-bromo-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one and 23mg of aniline were dissolved in 10ml of toluene, to which 2mg of palladium acetate, 7mg of 1,1'-bis(diphenylphosphino)ferrocene and 23mg of sodium tert-butoxide were added, and the mixture was stirred at 110°C for a night. The reaction solution was cooled to room temperature, filtered by silica gel and washed with ether, and the filtrate was distilled under a vacuum to remove the solvent. The residue

was refined by silica gel chromatography (NH silica) (hexane/ethyl acetate-based solvent), to obtain 47mg of the subject compound.

$^1\text{H-NMR}$ (400MHz, CDCl_3); δ (ppm) 7.06(tt, 1H), 7.15-7.19(m, 2H), 7.29-7.31(m, 2H), 7.38(tt, 2H), 7.43-7.56(m, 5H), 7.67(d, 1H), 7.69(td, 1H), 7.75(d, 1H), 8.58(ddd, 1H).

ESI-Mass; 340 $[\text{M}^+ + \text{H}]$

Example 175.

3-Phenoxy-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

100mg of 3-bromo-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one and 58mg of phenol were dissolved in 10ml of dimethylformamide, to which 84mg of potassium carbonate and 6mg of copper iodide were added, and the mixture was stirred at 150°C for 5 hours. The reaction solution was cooled to room temperature, to which ammonia water was added, and extracted with ethyl acetate. The organic layer was washed with saturated saline water and dried by magnesium sulfate anhydride, and the solvent was distilled off under a vacuum. The residue was refined by silica gel chromatography (hexane/ethyl acetate-based solvent), to obtain 66mg of the subject compound.

$^1\text{H-NMR}$ (400MHz, CDCl_3); δ (ppm) 7.13-7.19(m, 3H), 7.26-7.27(m, 2H), 7.36-7.54(m, 7H), 7.60-7.61(m, 1H), 7.66-7.71(m, 1H), 8.03-8.04(m, 1H), 8.54-8.57(m, 1H).

ESI-Mass; 341 $[\text{M}^+ + \text{H}]$

Example 176.

3-(1-Adamantylamino)-5-(2-pyridyl)-1-phenyl-1,2-

dihydropyridin-2-one

27mg of 3-bromo-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one and 130mg of 1-adamantylamine were dissolved in 10ml of dimethylformamide. To the mixture was added 20mg of sodium hydride, followed by stirring at 130°C in nitrogen atmosphere. After the reaction solution was cooled to room temperature, a saturated aqueous solution of ammonium chloride and water were added thereto, followed by extracting with ethyl acetate. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 3mg of the title compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.19-2.29 (m, 16H), 7.06-7.33 (m, 3H), 7.34-7.61 (m, 5H), 7.66-7.69 (m, 1H), 8.08-8.11 (m, 2H).

ESI-Mass; 398 [M⁺+H]

Example 177.

3-[4-(2-Cyanophenyl)piperadin-1-yl]-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

29mg of 3-bromo-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one was dissolved in 200mg of 1-(2-cyanophenyl)piperazine, followed by heating at 130°C for 72 hours. After the reaction solution was cooled to room temperature, water was added thereto, followed by extracting with ethyl acetate. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. The solvent was

evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 8mg of the title compound.

$^1\text{H-NMR}$ (400MHz, CDCl_3); δ (ppm) 3.20-3.22 (m, 4H), 3.50-3.56 (m, 4H), 7.00-7.13 (m, 3H), 7.32-7.61 (m, 10H), 7.79-7.84 (m, 2H).

ESI-Mass; 434 $[\text{M}^+ + \text{H}]$

Example 178.

3-(1-Adamantyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

40mg of 3-bromo-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one was dissolved in 10ml of tetrahydrofuran. To the mixture were added 5mg of [1,1-bis(diphenylphosphino)ferrocene]dichloropalladium (II) and 1.2mg of copper (I) iodide. While stirring the mixture at room temperature in nitrogen atmosphere overnight, 0.4ml of 1-adamantyl zinc bromide (0.5M tetrahydrofuran solution) was added dropwise thereinto. After stirring in nitrogen atmosphere overnight, an aqueous ammonia was added thereto, followed by extracting with ethyl acetate. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 12mg of the title compound.

$^1\text{H-NMR}$ (400MHz, CDCl_3); δ (ppm) 1.44-2.19 (m, 15H), 7.13 (ddd, 1H), 7.31-7.55 (m, 6H), 7.66 (td, 1H), 7.93 (d, 1H), 8.05 (d, 1H), 8.55-8.58 (m, 1H).

65702-519

ESI-Mass; 383 [M⁺+H]

Example 179.

3-(1,1-Dichlorohexyl-1-hydroxymethyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

13mg of 3-methoxycarbonyl-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one was dissolved in 20ml of tetrahydrofuran, followed by the dropwise addition of 0.05ml of cyclohexyl magnesiumchloride (2.0M diethyl ether solution) in nitrogen atmosphere, under ice-cooling and stirring. After the mixture was stirred for 3hr while heating to room temperature, a saturated aqueous solution of ammonium chloride was added thereto, followed by extracting with ethyl acetate. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 8mg of the title compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 0.89-1.84 (m, 20H), 2.72-2.90 (m, 2H), 7.06-7.12 (m, 1H), 7.25-7.49 (m, 8H), 7.59-7.68 (m, 1H), 8.50-8.54 (m, 1H).

ESI-Mass; 443 [M⁺+H]

Example 180.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(1-benzyl-1,2,5,6-tetrahydropyridin-3-yl)-1,2-dihydropyridin-2-one

718mg of 3-bromo-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one was dissolved in 40ml of acetonitrile. 383mg of benzyl bromide was added thereto, followed by stirring

65702-519

at 70°C overnight. Further, 383mg of benzyl bromide was added thereto, followed by stirring at 70°C for 2 nights. After cooling to room temperature, the mixture was evaporated. The residue was dissolved in 30ml of methanol, followed by cooling to 0°C under stirring. 265mg of sodium borohydride was added thereto, followed by stirring overnight under heating from 0°C to room temperature. Water was added thereto, the solvent was evaporated, and then the residue was extracted with ethyl acetate. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 550mg of 3-bromo-5-(2-pyridyl)-1-(1-benzyl-1,2,5,6-tetrahydropyridin-3-yl)-1,2-dihydropyridin-2-one. 270mg of the product was dissolved in 20ml of dimethylformamide. 179mg of 2-(2-cyanophenyl)-1,3,2-dioxaborinate, 313mg of cesium carbonate and 15mg of tetrakis(triphenylphosphine) palladium were added thereto, followed by stirring at 120°C for 1 hour. After cooling to room temperature, water was added thereto, followed by extracting with ethyl acetate. The organic layer was washed with brine and dried over magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 174mg of the title compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.38-2.42(m, 2H), 2.70(t, 2H), 3.43(d, 2H), 3.68(s, 2H), 6.05(t, 1H), 7.21(dd, 1H), 7.22-7.26(m, 1H),

7.30 (t, 2H), 7.36 (d, 2H), 7.44 (t, 1H), 7.54 (d, 1H), 7.63 (t, 1H), 7.70-7.77 (m, 3H), 8.19 (d, 1H), 8.23 (d, 1H), 8.60 (dd, 1H).

Example 181.

3-(2-Cyanophenyl)-5-phenylaminocarbonyl-1-phenyl-1,2-dihydropyridin-2-one

41mg of carboxylate obtained by hydrolyzing the ester group of 3-(2-cyanophenyl)-5-(methoxycarbonyl)-1-phenyl-1,2-dihydropyridin-2-one was dissolved in 5ml of dichloromethane. Under ice-cooling, a solution of 25mg of oxalyl chloride in dichloromethane was added dropwise thereinto and a catalytic amount of dimethylformamide was added thereto, followed by stirring at room temperature in nitrogen atmosphere for 1 hour. The reaction solution was evaporated, and the residue was dissolved in dichloromethane. The solution was added dropwise into a solution of 13mg of aniline and 0.03ml of triethylamine in dichloromethane under ice-cooling. After heating to room temperature, it was stirred in nitrogen atmosphere for 3 hours. Under ice-cooling, the mixture was poured into a saturated aqueous solution of sodium hydrogen carbonate, followed by extracting with ethyl acetate. The organic layer was washed with brine, and then dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 11mg of the title compound as white crystals.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.15 (tt, 1H), 7.33-7.39 (m, 2H),

7.55-7.42 (m, 6H), 7.56-7.60 (m, 2H), 7.65 (td, 1H), 7.73-7.79 (m, 2H), 7.85 (brs, 1H), 8.06 (d, 1H), 8.25 (d, 1H).

Example 182.

3-(2-Cyanophenyl)-5-(1-phenylbenzimidazol-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

24mg of carboxylate obtained by hydrolyzing the ester group of 3-(2-cyanophenyl)-5-(methoxycarbonyl)-1-phenyl-1,2-dihydropyridin-2-one was dissolved in 20ml of dichloromethane. Under ice-cooling, a solution of 16mg of oxalyl chloride in dichloromethane was added dropwise thereinto. A catalytic amount of dimethylformamide was added thereto, followed by stirring at room temperature in nitrogen atmosphere for 1 hour. The reaction solution was evaporated, and the residue was dissolved in dichloromethane. The solution was added dropwise into a solution of 21mg of N-phenyl-1,2-phenylenediamine in dichloromethane, under ice-cooling. The mixture was heated to room temperature, followed by stirring in nitrogen atmosphere overnight. Dichloromethane was evaporated, 10ml of acetic acid was added, and the mixture was stirred at 100°C for 5 hours. After cooling to room temperature, acetic acid was evaporated. Under ice-cooling, the residue was poured into a saturated aqueous solution of sodium hydrogen carbonate, followed by extracting with ethyl acetate. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate

65702-519

system), to give 18mg of the title compound as white crystals.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.19-7.30(m, 4H), 7.33-7.37(m, 1H), 7.39-7.43(m, 4H), 7.44-7.45(m, 1H), 7.46-7.47(m, 1H), 7.55-7.61(m, 3H), 7.61-7.66(m, 2H), 7.68(d, 1H), 7.71(dd, 1H), 7.81-7.84(m, 1H), 7.87(d, 1H).

ESI-Mass; 465 [M⁺+H]

Example 183.

3-(2-Chlorophenyl)-5-(benzothiazol-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

19mg of carboxylate obtained by hydrolyzing the ester group of 3-(2-chlorophenyl)-5-(methoxycarbonyl)-1-phenyl-1,2-dihydropyridin-2-one (synthesized from 3-bromo-5-(methoxycarbonyl)-1-phenyl-1,2-dihydropyridin-2-one and 2-chlorophenylboronic acid in accordance with the method for Referential Example 3) was dissolved in 20ml of dichloromethane. Under ice-cooling, a solution of 11mg of oxalyl chloride in dichloromethane was added dropwise thereto and a catalytic amount of dimethylformamide was added thereto, followed by stirring at room temperature in nitrogen atmosphere for 1 hour. The reaction solution was evaporated, and the residue was dissolved in dichloromethane. The solution was added dropwise into a solution of 22mg of 2-aminobenzothiol in dichloromethane under ice-cooling. After heating to room temperature, dichloromethane was evaporated. To the residue was added 1ml of polyphosphoric acid, followed by stirring at 180°C overnight. After cooling to room temperature, the reaction mixture was

65702-519

neutralized with 1N aqueous solution of sodium hydroxide and saturated aqueous solution of sodium hydrogen carbonate under ice-cooling and extracted with ethyl acetate. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 4mg of the title compound as white crystals.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.32-7.35(m, 2H), 7.37-7.41(m, 1H), 7.46-7.51(m, 4H), 7.51-7.55(m, 4H), 7.87-7.89(m, 1H), 8.00(d, 1H), 8.14(d, 1H), 8.42(d, 1H).

ESI-Mass; 415 [M⁺+H]

Example 184.

3-(2-Chlorophenyl)-5-(benzoxazol-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

19mg of carboxylate obtained by hydrolyzing the ester group of 3-(2-chlorophenyl)-5-(methoxycarbonyl)-1-phenyl-1,2-dihydropyridin-2-one (synthesized from 3-bromo-5-(methoxycarbonyl)-1-phenyl-1,2-dihydropyridin-2-one and 2-chlorophenylboronic acid in accordance with the method of Referential Example 3) was dissolved in 20ml of dichloromethane. Under ice-cooling, a solution of 11mg of oxalyl chloride in dichloromethane was added dropwise thereto and a catalytic amount of dimethylformamide was added thereto, followed by stirring at room temperature in nitrogen atmosphere for 1 hour. The reaction solution was evaporated, and the residue was dissolved in dichloromethane. The solution was added dropwise

into a solution of 19mg of 2-aminophenol in dichloromethane under ice-cooling. After heating to room temperature, dichloromethane was evaporated. To the residue was added 1ml of polyphosphoric acid, followed by stirring at 180°C overnight. After cooling to room temperature, the reaction mixture was neutralized with 1N aqueous solution of sodium hydroxide and saturated aqueous solution of sodium hydrogen carbonate under ice-cooling. The mixture was extracted with ethyl acetate, and the resulting organic layer was washed with brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 3mg of the title compound as white crystals.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.31-7.38 (m, 4H), 7.45-7.57 (m, 8H), 7.69-7.71 (m, 1H), 8.29 (d, 1H), 8.49 (d, 1H).

ESI-Mass; 399 [M⁺+H]

Example 185.

3-(2-Chlorophenyl)-5-phenoxyethyl-1-phenyl-1,2-dihydropyridin-2-one

24mg of 3-(2-Chlorophenyl)-5-hydroxyethyl-1-phenyl-1,2-dihydropyridin-2-one was dissolved in 10ml of tetrahydrofuran. 9.4mg of phenol, 33mg of triphenylphosphine polymer (3mmol/g resin) and 17mg of 1,1'-azobis(N,N-dimethylformamide) were added thereto, followed by stirring at 60°C overnight. Further, 50mg of triphenylphosphine polymer (3mmol/g resin) and 30mg of 1,1'-azobis(N,N-

65702-519

dimethylformamide) were added, followed by stirring at 60°C overnight. After cooling to room temperature, ethyl acetate was added thereto and the triphenylphosphine polymer was removed by filtration through CeliteTM. The filtrate was washed with water and 1N aqueous solution of sodium hydroxide. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 12mg of the title compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 4.87(s, 2H), 6.97(dd, 2H), 7.01(dd, 1H), 7.26-7.34(m, 4H), 7.40-7.51(m, 7H), 7.54-7.56(m, 1H), 7.60(d, 1H).

ESI-Mass; 388 [M⁺+H]

Example 186.

3-(2-Cyanophenyl)-5-(1-methyl-1,2,3,6-tetrahydropyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

99mg of 3-bromo-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one was dissolved in 10ml of acetonitrile. 2ml of methyl benzenesulfonate was added thereto, followed by stirring at 100°C for 2 nights. After cooling to room temperature, the solvent was evaporated. The residue was dissolved in 10ml of methanol, followed by cooled to 0°C under stirring. Sodium borohydride was added 5 times at intervals of 5 hours, 1g for each time, followed by further stirring at 0°C overnight. Then the solvent was evaporated and a saturated aqueous solution of ammonium chloride was added to the residue,

followed by extracting with ethyl acetate. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 107mg of 3-bromo-5-(1-methyl-1,2,3,6-tetrahydropyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one. The product was dissolved in 10ml of dimethylformamide. 81mg of 2-(2-cyanophenyl)-1,3,2-dioxaborinate, 142mg of cesium carbonate and 7mg of tetrakis(triphenylphosphine) palladium were added thereto, followed by stirring at 140°C for 2 hours. After cooling to room temperature, water was added thereto, followed by extracting with ethyl acetate. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 41mg of the title compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.26(s, 3H), 2.30-2.50(m, 1H), 2.90-2.98(m, 1H), 3.15(dd, 1H), 3.31-3.40(m, 1H), 3.85(t, 1H), 5.72-5.78(m, 1H), 5.79-5.85(m, 1H), 7.40(d, 1H), 7.40-7.57(m, 5H), 7.60(td, 1H), 7.64-7.70(m, 1H), 7.72-7.73(m, 1H), 7.74-7.75(m, 1H), 7.76(d, 1H).

Example 187.

3-(2-Pyridylethenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

23mg of 3-bromo-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one was dissolved in 20ml of acetonitrile.

65702-519

To the mixture were added 0.2mg of palladium acetate, 4.3mg of tri-*o*-tolylphosphine and 0.04ml of triethylamine, followed by stirring at 110°C in nitrogen atmosphere overnight. To the mixture was added 9.2mg of 2-vinylpyridine, followed by stirring at 110°C in nitrogen atmosphere for 5 hours. After cooling to room temperature, the reaction mixture was poured into water, followed by extracting with ethyl acetate. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 2mg of the title compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.12-7.16 (m, 1H), 7.18-7.23 (m, 1H), 7.36 (d, 1H), 7.44-7.51 (m, 3H), 7.51-7.55 (m, 2H), 7.57-7.60 (m, 1H), 7.64 (dt, 1H), 7.70-7.79 (m, 1H), 7.78-7.82 (m, 1H), 8.03-8.07 (m, 1H), 8.24 (d, 1H), 8.28 (d, 1H), 8.57-8.63 (m, 2H).

ESI-Mass; 352 [M⁺+H]

Example 188.

3-(4-Chlorophenylthio)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

25mg of 3-bromo-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one was dissolved in 20ml of dimethylformamide. To the mixture were added 17mg of 4-chlorothiophenol, 3mg of sodium hydroxide and 2mg of copper iodide, followed by stirring at 150°C in nitrogen atmosphere overnight. After cooling to room temperature, the reaction mixture was poured into water. An

aqueous ammonia was added thereto, followed by extracting with ethyl acetate. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 8mg of the title compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.17(ddd, 1H), 7.30(d, 1H), 7.39-7.56(m, 9H), 7.61(d, 1H), 7.67(td, 1H), 8.08(d, 1H), 8.52-8.54(m, 1H).

ESI-Mass; 391 [M⁺+H]

Example 189.

3-(2-Chlorophenyl)-5-cyclohexyl-1-phenyl-1,2-dihydropyridin-2-one

30mg of 5-bromo-3-(2-chlorophenyl)-1-phenyl-1,2-dihydropyridin-2-one synthesized from 5-bromo-1-phenyl-3-iodo-1,2-dihydropyridin-2-one and 2-chlorophenyl boronic acid in accordance with the method of Referential Example 3 was dissolved in 20ml of tetrahydrofuran, followed by adding 1mg of [1,3-bis(diphenylphosphino)propane] nickel (II) chloride. Under stirring in nitrogen atmosphere, 0.1ml of cyclohexyl magnesium chloride (2.0M ether solution) was added dropwise thereinto. After stirring at room temperature in nitrogen atmosphere overnight, the mixture was heated under reflux for 1 hour. After cooling to room temperature, a saturated aqueous solution of ammonium chloride was added thereto, followed by extracting with ethyl acetate. The organic layer was washed

65702-519

with brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (chloroform/methanol system), to give 6mg of the title compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.15-1.47 (m, 5H), 1.53-1.93 (m, 5H), 2.33-2.37 (m, 1H), 6.99-7.34 (m, 3H), 7.36-7.60 (m, 8H).
ESI-Mass; 364 [M⁺+H]

Example 190.

3-(1H-Benzimidazol-2-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

25mg of carboxylate obtained by de-protecting the ester group of 3-methoxycarbonyl-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one in a convention manner was dissolved in 20ml of dichloromethane. Under ice-cooling, a solution of 16mg of oxalyl chloride in dichloromethane was added dropwise thereinto and a catalytic amount of dimethylformamide was added thereto, followed by stirring at room temperature in nitrogen atmosphere for 1 hour. The reaction solution was evaporated, and to the residue was added dichloromethane. The solution was added dropwise into a solution of 17mg of o-phenylenediamine in dichloromethane under ice-cooling. After heating to room temperature, the mixture was stirred in nitrogen atmosphere overnight. Dichloromethane was evaporated, followed by adding methanol and heating under reflux for 5 hours. After cooling to room temperature, the reaction mixture was poured into an ice-cooled saturated aqueous solution of sodium hydrogen

65702-519

carbonate, followed by extracting with ethyl acetate. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was refined by silica gel chromatography (hexane/ethyl acetate system), to give 1.3mg of the title compound as white crystals.

$^1\text{H-NMR}$ (400MHz, CDCl_3); δ (ppm) 7.10-7.94 (m, 13H), 8.57 (d, 1H), 8.58-8.62 (m, 1H), 9.43 (d, 1H).

ESI-Mass; 365 $[\text{M}^+ + \text{H}]$

Example 191.

3-(2-Pyridon-1-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

40mg of 3-bromo-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one and 23mg of 2-hydroxypyridine were dissolved in 10ml of dimethylformamide. 34mg of potassium carbonate and 3mg of copper iodide were added thereto, followed by stirring at 140°C overnight. After cooling the reaction mixture to room temperature, an aqueous ammonia was added thereto, followed by extracting with ethyl acetate. The organic layer was washed with brine and dried over magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (NH silica) (chloroform/methanol system), to give 10mg of the title compound.

$^1\text{H-NMR}$ (400MHz, CDCl_3); δ (ppm) 6.24 (td, 1H), 6.69 (dd, 1H), 7.22 (dd, 1H), 7.37-7.42 (m, 2H), 7.45-7.57 (m, 6H), 7.73 (td, 1H), 8.33 (d, 1H), 8.36 (d, 1H), 8.58-8.60 (m, 1H).

Example 192.

3-Cyclohexyl-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

34mg of 3-bromo-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one was dissolved in 10ml of tetrahydrofuran, followed by adding 1mg of [1,3-bis(diphenylphosphino)propane] nickel (II) chloride. Under stirring in nitrogen atmosphere, 0.1ml of cyclohexyl magnesium chloride (2.0M ether solution) was added dropwise thereinto. The mixture was stirred at room temperature in nitrogen atmosphere for 1 hour, followed by heating under reflux for 72 hours. After cooling to room temperature, water was added thereto, followed by extracting with ethyl acetate. The organic layer was washed with brine, and then dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (chloroform/methanol system), to give 5mg of the title compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.22-1.52 (m, 5H), 1.73-1.80 (m, 1H), 1.81-1.89 (m, 2H), 1.97- 2.04 (m, 2H), 2.90-2.99 (m, 1H), 7.18 (ddd, 1H), 7.53-7.55 (m, 6H), 7.71 (td, 1H), 7.78 (dd, 1H), 8.04 (d, 1H), 8.59 (ddd, 1H).

Example 193.

3-[2-(5-Methyl-1,2,4-oxadiazol-3-yl)phenyl]-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

53mg of 3-(2-cyanophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one was dissolved in 10ml of ethanol

containing 20% of water. 19mg of hydroxylamine hydrochloride and 17mg of sodium acetate were added thereto, followed by heating under reflux for 24 hours. Further, 19mg of hydroxylamine hydrochloride and 17mg of sodium acetate were added thereto, followed by heating under reflux for 36 hours. After cooling to room temperature, the mixture was evaporated, and the resulting crystals were washed with water, dried, and 50mg of amidoxime compound was collected by filtration. 20mg of the product was dissolved in 4ml of toluene. 16mg of acetic anhydride was added thereto, followed by heating under reflux for 96 hours. After cooling to room temperature, the mixture was neutralized with potassium carbonate under ice-cooling. After extracting with ethyl acetate, the extract was successively washed with water and brine, and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 4mg of the title compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.56(s, 3H), 7.18(ddd, 1H), 7.38-7.59(m, 8H), 7.72(ddd, 1H), 7.71(ddd, 1H), 8.08(ddd, 1H), 8.11(d, 1H), 8.27(d, 1H), 8.58(ddd, 1H).

ESI-Mass; 410 [M⁺+H]

The following compounds were synthesized by the methods similar to, or in accordance with, the method for Example 1. Example 194.

3-(2-Cyanophenyl)-5-(1-methylpyrazol-4-yl)-1-phenyl-1,2-

65702-519

dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 4.01(s, 3H), 7.46-7.56(m, 8H), 7.62-7.68(m, 3H), 7.78-7.81(m, 2H).

Example 195.

3-(2-Cyanophenyl)-5-(6-methylpyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.56(s, 3H), 7.07(d, 1H), 7.40-7.66(m, 9H), 7.76-7.80(m, 2H), 8.28(d, 1H), 8.30(d, 1H).

Example 196.

3-(2-Cyanophenyl)-5-(5-methylpyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.36(s, 3H), 7.42-7.56(m, 8H), 7.63(dt, 1H), 7.76-7.80(m, 2H), 8.26(d, 1H), 8.28(d, 1H), 8.41-8.42(m, 1H).

Example 197.

3-(2-Cyanophenyl)-5-(4-methylpyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.36(s, 3H), 7.43-7.57(m, 8H), 7.63(dt, 1H), 7.77-7.80(m, 2H), 8.27(d, 1H), 8.28(d, 1H), 8.41-8.42(m, 1H).

Example 198.

3-(2-Cyanophenyl)-5-(3-hydroxypyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.20(dd, 1H), 7.31(dd, 1H), 7.51-7.60(m, 6H), 7.68(dd, 1H), 7.75(dt, 1H), 7.83(dd, 1H), 8.11(dd, 1H), 8.51(d, 1H), 8.55(d, 1H).

65702-519

Example 199.

3-(2-Cyanophenyl)-1-phenyl-5-(2-pyrazinyl)-1,2-
dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.46-7.57(m, 6H), 7.66(dt, 1H),
 7.75-7.81(m, 2H), 8.33(d, 1H), 8.35(d, 1H), 8.50(d, 1H),
 8.55(dd, 1H), 8.93(d, 1H).

Example 200.

3-(2-Cyanophenyl)-5-(2-methoxypyridin-5-yl)-1-phenyl-1,2-
dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.69(s, 3H), 6.67(d, 1H),
 7.18(d, 1H), 7.44-7.66(m, 8H), 7.78-7.81(m, 2H), 8.27(d, 1H),
 8.34(d, 1H).

Example 201.

3-(2-Cyanophenyl)-1-phenyl-5-(2-thiazolyl)-1,2-
dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.31(d, 1H), 7.45-7.56(m, 6H),
 7.65(dt, 1H), 7.72(dd, 1H), 7.77-7.80(m, 2H), 8.18(d, 1H),
 8.25(d, 1H).

Example 202.

3-(2-Cyanophenyl)-1-phenyl-5-(4-pyrimidinyl)-1,2-
dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.46-7.59(m, 7H), 7.66(dt, 1H),
 7.76-7.81(m, 2H), 8.31(d, 1H), 8.56(d, 1H), 8.74(d, 1H),
 9.16(d, 1H).

Example 203.

3-(2-Cyanophenyl)-1-phenyl-5-(5-pyrimidinyl)-1,2-

65702-519

dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.47-7.58(m, 6H), 7.66(dt, 1H), 7.75(d, 1H), 7.78-7.81(m, 2H), 7.92(d, 1H), 8.92(s, 2H), 9.22(s, 1H).

Example 204.

3-(2-Cyanophenyl)-1-phenyl-5-(3-pyridazinyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.46-7.56(m, 7H), 7.66(dt, 1H), 7.77-7.83(m, 3H), 8.32(d, 1H), 8.54(d, 1H), 9.15(dd, 1H).

Example 205.

3-(2-Cyanophenyl)-1-phenyl-5-(4-pyridazinyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.48-7.61(m, 7H), 7.67(dt, 1H), 7.79-7.83(m, 2H), 7.92(d, 1H), 8.00(d, 1H), 9.23(dd, 1H), 9.40(dd, 1H).

Example 206.

3-(2-Cyanophenyl)-5-(6-methoxypyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.96(s, 3H), 6.67(dd, 1H), 7.18(dd, 1H), 7.44-7.66(m, 8H), 7.77-7.81(m, 2H), 8.27(d, 1H), 8.33(d, 1H).

Example 207.

3-(2-Cyanophenyl)-1-phenyl-5-(thiazol-4-yl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.46-7.57(m, 6H), 7.66(ddd, 1H), 7.72-7.81(m, 3H), 7.87(d, 1H), 7.97(s, 1H), 8.76(s, 1H).

Example 208.

3-(2-Cyanophenyl)-5-(3-oxo-1-cyclohexen-1-yl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.12-2.19 (m, 2H), 2.46-2.50 (m, 2H), 2.65-2.69 (m, 2H), 6.36 (s, 1H), 7.45-7.57 (m, 6H), 7.62-7.70 (m, 2H), 7.76-7.79 (m, 2H), 7.88 (d, 1H).

Example 209.

3-(2-Cyanophenyl)-5-(5,6-dihydro-1,4-dioxin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 4.12-4.14 (m, 2H), 4.21-4.23 (m, 2H), 7.42-7.78 (m, 12H).

Example 210.

3-(2-Cyanophenyl)-5-(1-naphthyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.41-7.67 (m, 9H), 7.55-7.83 (m, 2H), 7.88-7.94 (m, 2H), 8.02 (ddd, 1H), 8.11 (d, 1H), 8.70 (d, 1H), 8.83 (d, 1H).

ESI-Mass; 400 [M⁺+H]

Example 211.

3-(2-Cyanophenyl)-5-(2-naphthyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.44-7.58 (m, 4H), 7.61-7.70 (m, 3H), 7.78-7.82 (m, 2H), 7.83-7.90 (m, 2H), 7.92 (d, 1H), 7.95-7.96 (m, 1H), 8.00 (ddd, 1H), 8.12 (d, 1H), 8.72 (dd, 1H), 8.83 (d, 1H).

ESI-Mass; 400 [M⁺+H]

65702-519

Example 212.

3-(2-Cyanophenyl)-5-(8-quinolinyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.43-7.50 (m, 3H), 7.60-7.69 (m, 2H), 7.75-7.79 (m, 1H), 7.81-7.87 (m, 2H), 8.03-8.10 (m, 2H), 8.18 (d, 1H), 8.23 (dd, 1H), 8.68-8.72 (m, 2H), 8.87 (d, 1H), 8.98 (dd, 1H).

ESI-Mass; 401 [M⁺+H]

Example 213.

3-(2-Cyanophenyl)-5-(3-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, DMSO-d₆); δ(ppm) 7.45-7.51 (m, 1H), 7.59 (ddd, 1H), 7.64 (dd, 1H), 7.75-7.82 (m, 2H), 7.94 (d, 1H), 8.10 (ddd, 1H), 8.15-8.20 (m, 1H), 8.28 (d, 1H), 8.39-8.41 (m, 1H), 8.53-8.56 (m, 1H), 8.69 (dd, 1H), 8.84 (d, 1H), 8.98-8.90 (m, 1H).

ESI-Mass; 351 [M⁺+H]

Example 214.

5-[(1-Benzenesulfonyl)indol-2-yl]-3-(2-cyanophenyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 6.70 (d, 1H), 7.23-7.43 (m, 4H), 7.45-7.56 (m, 5H), 7.65 (d, 1H), 7.68 (td, 2H), 7.78 (td, 2H), 7.83 (d, 1H), 8.02 (ddd, 1H), 8.30 (dd, 1H), 8.72 (dd, 1H), 8.79 (d, 1H).

ESI-Mass; 529 [M⁺+H]

The following compounds were synthesized by the methods similar to, or in accordance with, the method for Example 2.

65702-519

Example 215.

1-(4-Aminophenyl)-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.86(brs, 2H), 6.76(td, 2H), 7.20(ddd, 1H), 7.28(td, 2H), 7.44(dt, 1H), 7.60(td, 1H), 7.64(dd, 1H), 7.71-7.80(m, 3H), 8.28(d, 1H), 8.29(d, 1H), 8.60(ddd, 1H).

Example 216.

5-(3-Aminopyridin-2-yl)-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 4.05(br s, 2H), 7.07-7.08(m, 2H), 7.42-7.47(m, 2H), 7.51-7.53(m, 4H), 7.62(ddd, 1H), 7.75-7.78(m, 1H), 7.79-7.82(m, 1H), 7.99(dd, 1H), 8.06(dd, 1H), 8.15(dd, 1H).

Example 217.

5-(5-Aminopyridin-2-yl)-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.77(brs, 2H), 7.04(dd, 1H), 7.39-7.52(m, 7H), 7.60-7.64(m, 1H), 7.76-7.80(m, 2H), 8.08(dd, 1H), 8.13(d, 1H), 8.22(d, 1H).

Example 218.

1-(3-Aminophenyl)-3-(2-cyanophenyl)-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.85(brs, 2H), 6.76(ddd, 1H), 6.84(t, 1H), 6.86(ddd, 1H), 7.14(t, 1H), 7.27-7.31(m, 1H), 7.45(dt, 1H), 7.63(dt, 1H), 7.71-7.78(m, 2H), 8.69-8.71(m, 3H),

65702-519

8.75 (d, 1H) .

Example 219.

3-(2-Aminophenyl)-1-phenyl-5-(2-pyridyl)-1,2-
dihydropyridin-2-one

¹H-NMR (400MHz, DMSO-d₆); δ(ppm) 7.23-7.37 (m, 3H), 7.40-7.47 (m, 1H), 7.47-7.56 (m, 2H), 7.56-7.66 (m, 5H), 7.88 (ddd, 1H), 8.08 (d, 1H), 8.46 (d, 1H), 8.58 (d, 1H), 8.59-8.64 (m, 1H) .

Example 220.

3-(3-Aminophenyl)-1-phenyl-5-(2-pyridyl)-1,2-
dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.70 (br s, 2H), 6.68-6.72 (m, 1H), 7.13-7.26 (m, 3H), 7.42-7.56 (m, 5H), 7.56-7.60 (m, 1H), 7.64-7.76 (m, 2H), 8.22 (s, 2H), 8.58-8.61 (m, 1H) .

Example 221.

3-(4-Aminophenyl)-1-phenyl-5-(2-pyridyl)-1,2-
dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.77 (br s, 2H), 6.70-6.76 (m, 2H), 7.17-7.21 (m, 1H), 7.42-7.60 (m, 6H), 7.64-7.75 (m, 3H), 8.15 (s, 2H), 8.58-8.61 (m, 1H) .

Example 222.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-amino-4-methylphenyl)-1,2-
dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.21 (s, 3H), 3.76 (s, 2H), 6.78-6.83 (m, 2H), 7.17 (d, 1H), 7.20 (ddd, 1H), 7.44 (td, 1H), 7.58 (d, 1H), 7.63 (td, 1H), 7.73 (td, 1H), 7.78 (td, 2H), 8.29 (s, 2H), 8.59 (ddd, 1H) .

65702-519

ESI-Mass; 379 [M⁺+H]

The following compounds were synthesized by the methods similar to, or in accordance with, the method for Example 3. Example 223.

3-Benzenesulfonylamino-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.22(ddd, 1H), 7.31-7.33(m, 2H), 7.44-7.60(m, 7H), 7.76(dt, 1H), 7.92-7.95(m, 2H), 7.97(d, 1H), 8.21(d, 1H), 8.56-8.58(m, 1H).

Example 224.

3-(2-Cyanophenyl)-5-benzenesulfonylamino-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.26-7.27(m, 1H), 7.30-7.33(m, 2H), 7.41-7.65(m, 10H), 7.70-7.73(m, 1H), 7.83-7.86(m, 2H).

Example 225.

3-(2-Cyanophenyl)-5-(3-methylsulfonylaminopyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.40(s, 3H), 7.43-7.48(m, 4H), 7.50-7.54(m, 4H), 7.64-7.66(m, 2H), 7.74(dd, 1H), 7.95(d, 1H), 8.20(d, 1H), 8.77(dd, 1H).

Example 226.

3-(2-Methylsulfonylaminophenyl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.96(s, 3H), 7.25(ddd, 1H), 7.30-7.35(m, 1H), 7.43-7.63(m, 9H), 7.76(ddd, 1H), 8.30(br s, 1H),

65702-519

8.33 (d, 1H), 8.39 (d, 1H), 8.60-8.64 (m, 1H).

Example 227.

3-(4-Methylsulfonylaminophenyl)-1-phenyl-5-(2-pyridyl)-
1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.01 (s, 3H), 6.57 (br s, 1H),
7.20-7.28 (m, 3H), 7.45-7.61 (m, 6H), 7.77 (ddd, 1H), 7.79-
7.85 (m, 2H), 8.22 (d, 1H), 8.24 (d, 1H), 8.60-8.64 (m, 1H).

Example 228.

3-(3-Methylsulfonylaminophenyl)-1-phenyl-5-(2-pyridyl)-
1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.92 (s, 3H), 6.98 (br s, 1H),
7.20-7.32 (m, 2H), 7.36-7.61 (m, 8H), 7.69-7.78 (m, 2H),
8.22 (d, 1H), 8.26 (d, 1H), 8.59-8.63 (m, 1H).

The following compounds were synthesized by the methods similar to, or in accordance with, the method for Example 10.

Example 229.

5-(6-Acetylaminopyridin-2-yl)-3-(2-cyanophenyl)-1-phenyl-
1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.22 (s, 3H), 7.33 (dd, 1H),
7.44-7.80 (m, 10H), 7.85 (d, 1H), 8.08-8.12 (m, 1H), 8.24 (d, 1H),
8.28 (d, 1H).

Example 230.

3-(2-Acetylaminophenyl)-1-phenyl-5-(2-pyridyl)-1,2-
dihydropyridin-2-one

¹H-NMR (400MHz, DMSO-d₆); δ(ppm) 1.96 (s, 3H), 7.19-7.26 (m, 1H),
7.30 (ddd, 1H), 7.34-7.40 (m, 1H), 7.40-7.46 (m, 1H), 7.48-

.65702-519

7.56 (m, 1H), 7.56-7.64 (m, 4H), 7.72 (d, 1H), 7.83 (ddd, 1H),
8.01 (d, 1H), 8.32 (d, 1H), 8.50 (d, 1H), 8.57-8.61 (m, 1H), 9.16 (br
s, 1H).

Example 231.

3-(2-Diacetylaminophenyl)-1-phenyl-5-(2-pyridyl)-1,2-
dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 2.28 (s, 6H), 7.18 (ddd, 1H),
7.23-7.27 (m, 1H), 7.42-7.60 (m, 9H), 7.71 (ddd, 1H), 7.95 (d, 1H),
8.35 (d, 1H), 8.54-8.58 (m, 1H).

Example 232.

3-(3-Acetylaminophenyl)-1-phenyl-5-(2-pyridyl)-1,2-
dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.11 (s, 3H), 7.19-7.23 (m, 1H),
7.34-7.40 (m, 1H), 7.42-7.56 (m, 6H), 7.60 (d, 1H), 7.64-
7.77 (m, 3H), 7.83-7.87 (m, 1H), 8.24 (d, 1H), 8.26 (d, 1H), 8.58-
8.62 (m, 1H).

Example 233.

3-(4-Acetylaminophenyl)-1-phenyl-5-(2-pyridyl)-1,2-
dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.15 (s, 3H), 7.21 (ddd, 1H),
7.34 (br s, 1H), 7.44-7.57 (m, 8H), 7.59 (ddd, 1H), 7.74 (ddd, 1H),
7.80 (d, 1H), 8.21 (s, 2H), 8.59-8.62 (m, 1H).

The following compound was synthesized by the method
similar to, or in accordance with, the method for Example 12.

Example 234.

3-(4-Dimethylaminophenyl)-1-phenyl-5-(2-pyridyl)-1,2-

65702-519

dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.00(s, 6H), 6.75-6.80(m, 2H), 7.19(ddd, 1H), 7.41-7.54(m, 5H), 7.57-7.60(m, 1H), 7.73(ddd, 1H), 7.76-7.81(m, 2H), 8.14-8.17(m, 2H), 8.58-8.61(m, 1H).

The following compound was synthesized by the method similar to, or in accordance with, the method for Example 15.
Example 235.

5-(6-Aminocarbonylpyridin-2-yl)-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.46-7.60(m, 6H), 7.64(dt, 1H), 7.74(dd, 1H), 7.80-7.83(m, 1H), 7.91-7.95(m, 2H), 8.14-8.17(m, 2H), 8.52(d, 1H).

The following compounds were synthesized by the methods similar to, or in accordance with, the method of Example 16, Route 1.

Example 236.

3-(2-Cyanophenyl)-5-(2-cyanopyridin-6-yl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.46-7.57(m, 6H), 7.60(dd, 1H), 7.66(dt, 1H), 7.79-7.83(m, 3H), 7.89(dd, 1H), 8.29(d, 1H), 8.41(d, 1H).

The following compounds were synthesized by methods similar to, or in accordance with, the method of Example 18.
Example 237.

3-(3-Hydroxyphenyl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, DMSO-d₆); δ(ppm) 6.74-6.78(m, 1H), 7.15-7.26(m, 3H), 7.27-7.32(m, 1H), 7.47-7.61(m, 5H), 7.83(ddd, 1H).

65702-519

8.02(d, 1H), 8.41(s, 2H), 8.57-8.62(m, 1H), 9.43(br s, 1H).

Example 238.

3-(4-Hydroxyphenyl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, DMSO-d₆); δ(ppm) 6.79-6.84(m, 2H), 7.28(ddd, 1H), 7.47-7.59(m, 5H), 7.61-7.66(m, 2H), 7.82(ddd, 1H), 8.00(d, 1H), 8.33(d, 1H), 8.35(d, 1H), 8.57-8.61(m, 1H), 9.57(br s, 1H).

The following compounds were synthesized by the same methods as in Example 19.

Example 239.

3-(2-Cyanophenyl)-1-(3-dimethylaminoethoxyphenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.34(s, 6H), 2.74(t, 2H), 4.10(t, 2H), 7.01-7.05(m, 1H), 7.07-7.11(m, 2H), 7.21(ddd, 1H), 7.42(dd, 1H), 7.45(ddd, 1H), 7.59-7.66(m, 2H), 7.72-7.81(m, 3H), 8.30(s, 2H), 8.58-8.61(m, 1H).

Example 240.

3-(2-Cyanophenyl)-1-(3-piperidinoethoxyphenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.39-1.48(m, 2H), 1.56-1.64(m, 4H), 2.46-2.56(m, 4H), 2.78(t, 2H), 4.14(t, 2H), 6.99-7.03(m, 1H), 7.06-7.11(m, 2H), 7.21(ddd, 1H), 7.41(dd, 1H), 7.45(ddd, 1H), 7.59-7.66(m, 2H), 7.72-7.81(m, 3H), 8.30(s, 2H), 8.58-8.61(m, 1H).

Example 241.

3-(2-Cyanophenyl)-1-(3-pyrrolidinoethoxyphenyl)-5-(2-

65702-519

pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.76-1.86(m, 4H), 2.57-2.70(m, 4H), 2.92(t, 2H), 4.16(t, 2H), 7.03(ddd, 1H), 7.06-7.11(m, 2H), 7.21(ddd, 1H), 7.41(dd, 1H), 7.45(ddd, 1H), 7.59-7.66(m, 2H), 7.72-7.81(m, 3H), 8.30(s, 2H), 8.58-8.61(m, 1H).

Example 242.

3-(2-Cyanophenyl)-1-(3-diisopropylaminoethoxyphenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.03(d, 12H), 2.83(t, 2H), 3.04(heptet, 2H), 3.92(t, 2H), 6.97-7.01(m, 1H), 7.04(dd, 1H), 7.07(ddd, 1H), 7.21(ddd, 1H), 7.41(dd, 1H), 7.45(ddd, 1H), 7.59-7.66(m, 2H), 7.72-7.82(m, 3H), 8.29-8.32(m, 2H), 8.58-8.61(m, 1H).

Example 243.

3-(2-Cyanophenyl)-1-(3-dimethylaminopropoxyphenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.96(tt, 2H), 2.24(s, 6H), 2.44(t, 2H), 4.05(t, 2H), 7.00(ddd, 1H), 7.05-7.09(m, 2H), 7.21(ddd, 1H), 7.41(dd, 1H), 7.45(ddd, 1H), 7.59-7.66(m, 2H), 7.72-7.81(m, 3H), 8.30(s, 2H), 8.58-8.61(m, 1H).

Example 244.

3-(2-Cyanophenyl)-1-(3-piperidinopropoxyphenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.37-1.50(m, 2H), 1.53-1.64(m, 4H), 1.97(tt, 2H), 2.30-2.45(m, 4H), 2.47(t, 2H), 4.04(t, 2H), 6.97-7.02(m, 1H), 7.04-7.09(m, 2H), 7.21(ddd, 1H),

65702-519

7.41 (dd, 1H), 7.45 (ddd, 1H), 7.59-7.66 (m, 2H), 7.70-7.82 (m, 3H),
8.31 (s, 2H), 8.58-8.62 (m, 1H).

Example 245.

3-(2-Cyanophenyl)-1-(3-morpholinoethoxyphenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.48-2.65 (m, 4H), 2.81 (t, 2H),
3.68-3.80 (m, 4H), 4.15 (t, 2H), 6.99-7.04 (m, 1H), 7.06-
7.13 (m, 2H), 7.22 (ddd, 1H), 7.42 (dd, 1H), 7.46 (ddd, 1H),
7.61 (dd, 1H), 7.64 (ddd, 1H), 7.74 (ddd, 1H), 7.78 (dd, 2H), 8.28-
8.33 (m, 2H), 8.58-8.62 (m, 1H).

Example 246.

3-(2-Cyanophenyl)-1-(3-diethylaminoethoxyphenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.07 (t, 6H), 2.64 (q, 4H),
2.89 (t, 2H), 4.08 (t, 2H), 7.01 (ddd, 1H), 7.05-7.10 (m, 2H),
7.21 (ddd, 1H), 7.41 (dd, 1H), 7.45 (ddd, 1H), 7.59-7.66 (m, 2H),
7.72-7.81 (m, 3H), 8.31 (s, 2H), 8.58-8.61 (m, 1H).

Example 247.

3-(3-Dimethylaminoethoxyphenyl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.34 (s, 6H), 2.74 (t, 2H),
4.13 (t, 2H), 6.92-6.98 (m, 1H), 7.19-7.24 (m, 1H), 7.33 (dd, 1H),
7.37-7.42 (m, 1H), 7.44-7.56 (m, 6H), 7.57-7.62 (m, 1H),
7.75 (ddd, 1H), 8.25 (s, 2H), 8.59-8.63 (m, 1H).

Example 248.

3-(4-Dimethylaminoethoxyphenyl)-1-phenyl-5-(2-pyridyl)-

65702-519

1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.35(s, 6H), 2.76(t, 2H), 4.12(t, 2H), 6.95-7.00(m, 2H), 7.20(ddd, 1H), 7.43-7.54(m, 5H), 7.59(ddd, 1H), 7.73(ddd, 1H), 7.76-7.81(m, 2H), 8.17-8.20(m, 2H), 8.59-8.62(m, 1H).

Example 249.

3-(2-Cyanophenyl)-1-[3-(4-piperidinobutoxy)phenyl]-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.38-1.46(m, 2H), 1.54-1.61(m, 4H), 1.62-1.71(m, 2H), 1.75-1.83(m, 2H), 2.30-2.43(m, 6H), 4.01(t, 2H), 6.97-7.01(m, 1H), 7.03-7.08(m, 2H), 7.21(ddd, 1H), 7.40(dd, 1H), 7.45(ddd, 1H), 7.59-7.66(m, 2H), 7.72-7.82(m, 3H), 8.30(s, 2H), 8.58-8.61(m, 1H).

The following compounds were synthesized by the methods similar to, or in accordance with, the method for Example 29.

Example 250.

3-(2-Cyanophenyl)-1-(3-pyrrolidinomethylphenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.74-1.84(m, 4H), 2.48-2.58(m, 4H), 3.69(s, 2H), 7.14-7.25(m, 2H), 7.38-7.51(m, 4H), 7.61(d, 1H), 7.63(ddd, 1H), 7.72-7.82(m, 3H), 8.30(d, 1H), 8.32(d, 1H), 8.58-8.62(m, 1H).

Example 251.

1-[3-(4-Acetylpiperazinomethyl)phenyl]-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.07(s, 3H), 2.45(dd, 4H),

65702-519

3.45 (dd, 2H), 3.58 (s, 2H), 3.63 (dd, 2H), 7.22 (ddd, 1H), 7.40-7.54 (m, 5H), 7.60-7.67 (m, 2H), 7.73-7.80 (m, 3H), 8.29 (d, 1H), 8.33 (d, 1H), 8.58-8.62 (m, 1H).

The following compounds were synthesized by the methods similar to, or in accordance with, the method for Example 32.

Example 252.

3-(2-Cyanophenyl)-1-(4-nitrophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.24-7.30 (m, 1H), 7.47-7.52 (m, 1H), 7.61-7.82 (m, 7H), 8.31 (dd, 2H), 8.42 (d, 2H), 8.60-8.63 (m, 1H).

Example 253.

1-Phenyl-3-(2-pyrazinyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.21-7.25 (m, 1H), 7.49-7.59 (m, 5H), 7.72-7.79 (m, 2H), 8.46 (d, 1H), 8.54 (d, 1H), 8.61 (ddd, 1H), 8.65 (dd, 1H), 9.14 (d, 1H), 9.87 (d, 1H).

Example 254.

1-Phenyl-3-(2-pyrimidinyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.20 (ddd, 1H), 7.25 (t, 1H), 7.44-7.54 (m, 5H), 7.66 (d, 1H), 7.75 (dt, 1H), 8.45 (d, 1H), 8.58-8.60 (m, 1H), 8.82 (d, 1H), 8.88 (s, 1H), 8.89 (s, 1H).

Example 255.

1-Phenyl-5-(2-pyridyl)-3-(2-thiazolyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.22-7.26 (m, 1H), 7.48-

65702-519

7.57 (m, 6H), 7.78-7.80 (m, 2H), 8.00 (dd, 1H), 8.52 (dd, 1H),
8.59-8.61 (m, 1H), 9.29 (d, 1H).

Example 256.

1-Phenyl-3-(4-pyrimidinyl)-5-(2-pyridyl)-1,2-
dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.22-7.26 (m, 1H), 7.48-
7.59 (m, 5H), 7.77-7.82 (m, 2H), 8.53 (d, 1H), 8.60-8.62 (m, 1H),
8.73-8.77 (m, 2H), 9.27 (dd, 1H), 9.40 (d, 1H).

Example 257.

1-Phenyl-3-(5-pyrimidinyl)-5-(2-pyridyl)-1,2-
dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.24-7.27 (m, 1H), 7.48-
7.61 (m, 7H), 7.77 (dt, 1H), 8.28 (d, 1H), 8.37 (d, 1H), 8.63 (ddd, 1H),
9.21 (d, 1H), 9.22 (s, 1H).

Example 258.

1-Phenyl-3-(3-pyridazinyl)-5-(2-pyridyl)-1,2-dihydropyridin-
2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.22-7.25 (m, 1H),
7.48-7.58 (m, 6H), 7.78-7.80 (m, 2H),
8.55 (d, 1H), 8.60 (m, 1H), 8.78 (dd, 1H), 9.14 (dd, 1H), 9.34 (d, 1H).

Example 259.

1-Phenyl-3-(4-pyridazinyl)-5-(2-pyridyl)-1,2-dihydropyridin-
2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.24-7.28 (m, 1H), 7.47-
7.62 (m, 6H), 7.78 (dt, 1H), 8.16 (dd, 1H), 8.33 (d, 1H), 8.53 (d, 1H),
8.63-8.65 (m, 1H), 9.23 (dd, 1H), 9.62 (dd, 1H).

Example 260.

65702-519

3-(6-Methoxypyridin-2-yl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 4.07(s, 3H), 6.73(dd, 1H), 7.22(ddd, 1H), 7.46-7.56(m, 5H), 7.62-7.70(m, 2H), 7.78(ddd, 1H), 8.35(dd, 1H), 8.39(d, 1H), 8.66(ddd, 1H), 9.21(d, 1H).

Example 261.

3-(2-Cyanophenyl)-1-(3-pyridyl)-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.18(t, 1H), 7.46-7.52(m, 2H), 7.65(dt, 1H), 7.71(dd, 1H), 7.74-7.80(m, 1H), 7.99(ddd, 1H), 8.72-8.75(m, 5H), 8.82(dd, 1H).

Example 262.

3-(2-Fluoropyridin-3-yl)-1-phenyl-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.16(t, 1H), 7.24-7.27(m, 2H), 7.48-7.57(m, 5H), 8.19-8.23(m, 2H), 8.69-8.76(m, 3H).

Example 263.

3-(2-Fluoropyridin-3-yl)-1-(3-pyridyl)-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.19(t, 1H), 7.26-7.30(m, 1H), 7.47-7.52(m, 1H), 7.94(ddd, 1H), 8.17(ddd, 1H), 8.70-8.80(m, 7H).

Example 264.

3-(2-Cyanopyridin-3-yl)-1-phenyl-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.17(t, 1H), 7.47-7.56(m, 6H),

65702-519

8.14(dd, 1H), 8.70(dd, 1H), 8.72(d, 2H), 8.80(d, 1H), 8.85(d, 1H).

Example 265.

3-(2-Cyanopyridin-3-yl)-1-(3-pyridyl)-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.20(t, 1H), 7.52(ddd, 1H), 7.58(dd, 1H), 7.97(ddd, 1H), 8.11(dd, 1H), 8.71-8.76(m, 4H), 8.78(d, 1H), 8.81(dd, 1H), 8.66(d, 1H).

Example 266.

3-(2-Cyanophenyl)-1-(3-nitrophenyl)-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.20(t, 1H), 7.49(ddd, 1H), 7.65-7.80(m, 5H), 7.98(ddd, 1H), 8.36(ddd, 1H), 8.46(t, 1H), 8.73-8.77(m, 3H).

Example 267.

1-Phenyl-5-(2-pyridyl)-3-(thiazol-4-yl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.24-7.28(m, 1H), 7.48-7.58(m, 5H), 7.64(td, 1H), 7.79(dt, 1H), 8.23(d, 1H), 8.58(d, 1H), 8.64-8.66(m, 2H), 8.85(d, 1H).

Example 268.

3-(3-Oxo-1-cyclohexen-1-yl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.09-2.16(m, 2H), 2.48-2.51(m, 2H), 2.87-2.91(m, 2H), 6.53(t, 1H), 7.22(ddd, 1H), 7.43-7.57(m, 6H), 7.75(dt, 1H), 8.17(d, 1H), 8.25(d, 1H), 8.60(ddd, 1H).

Example 269.

65702-519

3-(5,6-Dihydro-1,4-dioxin-2-yl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 4.18-4.20 (m, 2H), 4.30-4.32 (m, 2H), 7.19 (ddd, 1H), 7.41-7.54 (m, 5H), 7.63 (td, 1H), 7.73 (dt, 1H), 8.02 (s, 1H), 8.10 (d, 1H), 8.28 (d, 1H), 8.58 (ddd, 1H).

Example 270.

3-(2-Nitrophenyl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.22 (ddd, 1H), 7.40-7.61 (m, 9H), 7.68 (ddd, 1H), 7.74 (ddd, 1H), 8.06 (dd, 1H), 8.22-8.25 (m, 2H), 8.60-8.63 (m, 1H).

Example 271.

3-(4-Biphenyl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.20-7.25 (m, 1H), 7.33-7.40 (m, 1H), 7.42-7.57 (m, 6H), 7.60-7.79 (m, 7H), 7.90-7.95 (m, 2H), 8.25 (d, 1H), 8.30 (d, 1H), 8.60-8.64 (m, 1H).

Example 272.

3-(2-Acetylphenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.59 (s, 3H), 7.16-7.21 (m, 1H), 7.40-7.60 (m, 8H), 7.63-7.67 (m, 1H), 7.68-7.75 (m, 1H), 8.16 (d, 1H), 8.22 (d, 1H), 8.57-8.61 (m, 1H).

Example 273.

3-(3-Nitrophenyl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

65702-519

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.24(ddd, 1H), 7.46-7.64(m, 7H), 7.76(ddd, 1H), 8.20-8.26(m, 2H), 8.27(d, 1H), 8.37(d, 1H), 8.61-8.65(m, 1H), 8.69(dd, 1H).

Example 274.

1-Phenyl-3-(4-pyridyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.24(ddd, 1H), 7.46-7.62(m, 6H), 7.73-7.81(m, 3H), 8.28(d, 1H), 8.39(d, 1H), 8.61-8.64(m, 1H), 8.66(dd, 2H).

Example 275.

3-(4-Nitrophenyl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.22-7.26(m, 1H), 7.47-7.58(m, 5H), 7.60(ddd, 1H), 7.76(ddd, 1H), 8.01-8.06(m, 2H), 8.26-8.31(m, 3H), 8.38(d, 1H), 8.61-8.65(m, 1H).

Example 276.

1-(3-Benzoyloxyphenyl)-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 5.10(s, 2H), 7.05-7.14(m, 2H), 7.17(dd, 1H), 7.21(ddd, 1H), 7.30-7.48(m, 7H), 7.60(ddd, 1H), 7.64(ddd, 1H), 7.71-7.81(m, 3H), 8.29-8.32(m, 2H), 8.58-8.61(m, 1H).

Example 277.

1-(3-Acetylphenyl)-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.66(s, 3H), 7.24(ddd, 1H),

7.48 (ddd, 1H), 7.61-7.69 (m, 3H), 7.74-7.81 (m, 4H), 8.07 (ddd, 1H),
8.11 (ddd, 1H), 8.32 (d, 1H), 8.34 (d, 1H), 8.59-8.62 (m, 1H).

Example 278.

3-[4-(tert-Butylaminosulfonyl)phenyl]-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.26 (s, 9H), 4.46 (s, 1H),
7.24 (ddd, 1H), 7.46-7.58 (m, 5H), 7.58-7.61 (m, 1H), 7.76 (ddd, 1H),
7.90-7.99 (m, 4H), 8.26 (d, 1H), 8.33 (d, 1H), 8.61-8.64 (m, 1H).

Example 279.

3-(1-Naphthyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.21 (dd, 1H), 7.42-7.50 (m, 3H),
7.51-7.61 (m, 3H), 7.71 (td, 1H), 7.81-7.85 (m, 1H), 7.87-
7.90 (m, 2H), 7.96-7.99 (m, 1H), 8.20 (d, 1H), 8.37 (d, 1H),
8.60 (d, 1H), 8.67 (d, 1H), 8.84 (d, 1H).

ESI-Mass; 376 [M⁺+H]

Example 280.

3-(1-Naphthyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.19 (ddd, 1H), 7.38-7.59 (m, 9H),
7.71 (td, 2H), 7.84-7.89 (m, 3H), 8.18 (d, 1H), 8.39 (d, 1H),
8.59 (ddd, 1H).

ESI-Mass; 375 [M⁺+H]

Example 281.

3-(8-Quinoliny)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.18-7.23 (m, 1H), 7.38-7.56 (m, 3H), 7.84-7.58 (m, 3H), 7.86-8.01 (m, 3H), 8.19-8.23 (m, 1H), 8.30-8.36 (m, 2H), 8.56-8.62 (m, 1H), 8.66-8.70 (m, 1H), 8.91-8.97 (m, 1H).

ESI-Mass; 377 [M⁺+H]

Example 282.

3-(8-Quinoliny)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.18 (dd, 1H), 7.39-7.54 (m, 4H), 7.55-7.65 (m, 3H), 7.66-7.73 (m, 2H), 7.85 (dd, 1H), 7.98 (dd, 1H), 8.2 (dd, 1H), 8.34 (d, 1H), 8.36 (d, 1H), 8.58 (d, 1H), 8.94 (dd, 1H).

ESI-Mass; 376 [M⁺+H]

Example 283.

3-(2-Naphthyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.23-7.28 (m, 1H), 7.48-7.53 (m, 3H), 7.64 (dt, 1H), 7.78 (td, 1H), 7.85-7.91 (m, 4H), 7.97 (ddd, 1H), 8.25 (d, 1H), 8.35 (s, 1H), 8.38 (d, 1H), 8.64 (ddd, 1H), 8.72 (d, 1H), 8.81 (d, 1H).

ESI-Mass; 376 [M⁺+H]

Example 284.

3-(2-Naphthyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.21 (dd, 1H), 7.44-7.50 (m, 4H), 7.53-7.56 (m, 3H), 7.62 (dd, 1H), 7.72-7.77 (m, 1H), 7.83-7.91 (m, 2H), 7.92 (td, 2H), 8.25 (d, 1H), 8.37 (d, 1H), 8.39 (brs, 1H),

8.61-8.64 (m, 1H) .

Example 285.

3-(2-Pyrrolidinopyridin-5-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.00-2.04 (m, 4H), 3.50 (t, 4H), 7.74-7.78 (m, 9H), 8.03 (d, 1H), 8.06 (d, 1H), 8.21 (d, 1H), 8.57-8.60 (m, 2H) .

ESI-Mass; 396 [M⁺+H]

Example 286.

3-(2-Formylthiophen-3-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.21-7.29 (m, 2H), 7.46-7.57 (m, 6H), 7.73 (d, 1H), 7.75 (td, 1H), 8.22 (d, 1H), 8.31 (d, 1H), 8.60-8.62 (m, 1H), 10.00 (s, 1H) .

ESI-Mass; 359 [M⁺+H]

Example 287.

3-(2-Chloropyridin-5-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.24 (ddd, 1H), 7.37 (d, 1H), 7.44-7.51 (m, 3H), 7.53-7.60 (m, 2H), 7.64-7.70 (m, 1H), 7.76 (td, 1H), 8.24 (d, 1H), 8.26 (t, 1H), 8.31 (d, 1H), 8.62 (ddd, 1H), 8.75 (d, 1H) .

ESI-Mass; 360 [M⁺+H]

Example 288.

3-(2-Fluoropyridin-5-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 6.99(dd, 1H), 7.24(dd, 1H), 7.47-7.57(m, 5H), 7.59(dd, 1H), 7.76(tdd, 1H), 8.25(dd, 1H), 8.30(dd, 1H), 8.37(td, 1H), 8.57-8.58(m, 1H), 8.63(dt, 1H).

Example 289.

3-(2-Ethylthiopyridin-5-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.39(t, 3H), 3.20(q, 2H), 7.20-7.24(m, 2H), 7.44-7.59(m, 6H), 7.75(td, 1H), 8.08(dd, 1H), 8.23(d, 1H), 8.26(d, 1H), 8.61(ddd, 1H), 8.78(d, 1H).

ESI-Mass; 386 [M⁺+H]

Example 290.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-naphthyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.22(ddd, 1H), 7.47(td, 1H), 7.53-7.60(m, 2H), 7.62-7.67(m, 3H), 7.76(td, 1H), 7.81(td, 2H), 7.88-7.94(m, 2H), 7.98(d, 1H), 7.99(s, 1H), 8.34(d, 1H), 8.43(d, 1H), 8.60(ddd, 1H).

ESI-Mass; 400 [M⁺+H]

Example 291.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(1-naphthyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.21(ddd, 1H), 7.45(td, 1H), 7.54-7.65(m, 6H), 7.65-7.83(m, 4H), 7.93-8.02(m, 2H), 8.30(d, 1H), 8.46(d, 1H), 8.57(ddd, 1H).

ESI-Mass; 400 [M⁺+H]

Example 292.

65702-519

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(8-quinolinyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.18(ddd, 1H), 7.43(td, 1H), 7.48(ddd, 1H), 7.61(td, 1H), 7.63(d, 1H), 7.69(dd, 1H), 7.72(td, 1H), 7.78(dd, 1H), 7.86(dd, 1H), 7.92(dd, 1H), 7.98(ddd, 1H), 8.26(dd, 1H), 8.36(d, 1H), 8.43(d, 1H), 8.55-8.57(m, 1H), 8.95(dd, 1H).

Example 293.

3-(1-Benzenesulfonylindol-2-yl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 6.95(d, 1H), 7.21(ddd, 1H), 7.22(ddd, 1H), 7.26-7.33(m, 3H), 7.42(dt, 1H), 7.44-7.49(m, 2H), 7.50-7.56(m, 4H), 7.60(dt, 1H), 7.71-7.77(m, 3H), 8.07(dd, 1H), 8.20(d, 1H), 8.34(d, 1H), 8.60(ddd, 1H).

Example 294.

3-(2-Cyanopyridin-3-yl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.20-7.28(m, 1H), 7.51(dd, 1H), 7.58(dd, 1H), 7.64(d, 1H), 7.79(td, 1H), 7.94-7.97(m, 1H), 8.18(dd, 1H), 8.35(d, 1H), 8.44(d, 1H), 8.60-8.63(m, 1H), 8.72(dd, 1H), 8.74(dd, 1H), 8.81(d, 1H).

ESI-Mass; 352 [M⁺+H]

Example 295.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(pyrrol-3-yl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 6.46-6.50(m, 1H), 6.79(dd, 1H),

65702-519

7.21 (dd, 1H), 7.29-7.32 (m, 1H), 7.45 (t, 1H), 7.60-7.66 (m, 2H),
7.72-7.80 (m, 3H), 8.23 (d, 1H), 8.47 (d, 1H), 8.61 (d, 1H),
8.72 (brs, 1H).

The following compounds were synthesized by the methods similar to, or in accordance with, the method for Example 162.
Example 296.

3-(2-Cyanophenyl)-5-(3-nitropyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 7.43-7.54 (m, 7H), 7.62-7.67 (m, 2H),
7.73-7.76 (m, 2H), 8.03 (d, 1H), 8.24 (dd, 1H), 8.82 (dd, 1H).

Example 297.

3-(2-Cyanophenyl)-5-[2-(2,6-dimethylpyrrol-1-yl)pyridin-6-yl]-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 2.17 (s, 6H), 5.91 (s, 2H),
7.12 (dd, 1H), 7.45-7.56 (m, 6H), 7.61 (dd, 1H), 7.65 (dd, 1H),
7.78-7.80 (m, 2H), 7.88 (t, 1H), 8.35 (d, 1H), 8.40 (d, 1H).

Example 298.

5-(2-Aminopyridin-6-yl)-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 4.44 (brs, 2H), 6.43 (dd, 1H),
6.96 (d, 1H), 7.42-7.54 (m, 7H), 7.63 (dt, 1H), 7.76-7.78 (m, 2H),
8.24 (d, 1H), 8.26 (d, 1H).

Example 299.

3-(2-Cyanophenyl)-5-(5-nitropyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ (ppm) 7.47-7.59 (m, 6H), 7.67 (dt, 1H),

65702-519

7.75-7.82 (m, 3H), 8.35 (d, 1H), 8.52 (dd, 1H), 8.55 (d, 1H),
9.39 (dd, 1H).

Example 300.

5-(6-Bromopyridin-2-yl)-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.39 (dd, 1H), 7.45-7.67 (m, 9H),
7.78-7.80 (m, 2H), 8.23 (d, 1H), 8.34 (d, 1H).

Example 301.

3-(2-Cyanophenyl)-1-phenyl-5-(5-trifluoromethylpyridin-2-yl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.46-7.58 (m, 6H), 7.63-7.68 (m, 1H),
7.72 (d, 1H), 7.78-7.81 (m, 2H), 7.97 (ddd, 1H), 8.33 (d, 1H),
8.44 (d, 1H), 8.83-8.84 (m, 1H).

Example 302.

3-(2-Cyanophenyl)-5-(2-morpholinopyridin-6-yl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.55 (t, 4H), 3.83 (t, 4H),
6.57 (d, 1H), 6.97 (d, 1H), 7.43-7.66 (m, 8H), 7.77-7.80 (m, 2H),
8.18 (d, 1H), 8.31 (d, 1H).

Example 303.

3-(2-Cyanophenyl)-5-(2-methoxycarbonylpyridin-6-yl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.99 (s, 3H), 7.44-7.57 (m, 6H),
7.65 (dt, 1H), 7.78-7.81 (m, 3H), 7.91 (t, 1H), 8.04 (dd, 1H),
8.30 (d, 1H), 8.37 (d, 1H).

The following compound was synthesized by the method

similar to, or in accordance with, the method for Example 164.
Example 304.

5-[4-(tert-Butylaminosulfonyl)phenyl]-3-(2-cyanophenyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.25(s, 9H), 4.72(br s, 1H), 7.47-7.54(m, 2H), 7.60-7.71(m, 4H), 7.73-7.83(m, 2H), 7.93-8.02(m, 4H), 8.73(dd, 1H), 8.79(d, 1H).

The following compound was synthesized by the method similar to, or in accordance with, the method for Example 167.
Example 305.

3-(2-Cyanophenyl)-4-methyl-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.12(s, 3H), 7.28(ddd, 1H), 7.38-7.52(m, 8H), 7.59(s, 1H), 7.66(ddd, 1H), 7.75-7.80(m, 2H), 8.66-8.70(m, 1H).

The following compounds were synthesized by the methods similar to, or in accordance with, the method for Example 168.
Example 306.

1-Phenyl-3-[N-(N'-phenylthioureylenyl)]-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.19-7.24(m, 1H), 7.26-7.36(m, 3H), 7.37-7.54(m, 7H), 7.70(d, 1H), 7.78(ddd, 1H), 7.92(br s, 1H), 8.09(d, 1H), 8.55-8.59(m, 1H), 9.33(br s, 1H), 10.03(d, 1H).

Example 307.

3-(2-Cyanophenyl)-1-phenyl-5-[N-(N'-phenylureylenyl)]-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, DMSO-d₆); δ(ppm) 6.95(dd, 1H), 7.25(dd, 1H), 7.41-7.61(m, 8H), 7.65(d, 1H), 7.71(d, 1H), 7.77(dd, 1H), 7.92(d, 1H), 8.03(d, 1H), 8.56-8.66(m, 1H), 9.02-9.10(m, 1H).

Example 308.

3-{4[N-(N'-butylureylenyl)phenyl]}-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, DMSO-d₆); δ(ppm) 0.90(t, 3H), 1.32(tt, 2H), 1.42(tt, 2H), 3.09(dt, 2H), 6.16(br t, 1H), 7.29(dd, 1H), 7.44(d, 2H), 7.47-7.54(m, 1H), 7.54-7.60(m, 4H), 7.69(d, 2H), 7.82(ddd, 1H), 8.02(d, 1H), 8.35(d, 1H), 8.39(d, 1H), 8.53(br s, 1H), 8.58-8.61(m, 1H).

The following compounds were synthesized by the methods similar to, or in accordance with, the method for Example 169.

Example 309.

3-(2-Cyanophenyl)-1-phenyl-5-(2-pyridincarbonyl)amino-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.42-7.54(m, 7H), 7.63(ddd, 1H), 7.74-7.79(m, 3H), 7.92(ddd, 1H), 8.20(d, 1H), 8.58(d, 1H), 8.59-8.62(m, 1H), 9.80(br s, 1H).

Example 310.

1-Phenyl-3-[2-(1-pyrrolidino)acetylaminol]-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.78-1.86(m, 4H), 2.66-2.74(m, 4H), 3.36(s, 2H), 7.20(ddd, 1H), 7.44-7.56(m, 5H), 7.66(d, 1H), 7.75(ddd, 1H), 8.07(d, 1H), 8.54-8.58(m, 1H), 9.12(d, 1H), 10.15(br s, 1H).

Example 311.

1-Phenyl-3-{3-[1-(4-phenylpiperadino)]propionylamino}-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.66(t, 2H), 2.69-2.76(m, 4H), 2.80(t, 2H), 3.30-3.36(m, 4H), 6.81-6.86(m, 1H), 6.90-6.97(m, 2H), 7.18(ddd, 1H), 7.22-7.29(m, 2H), 7.40-7.53(m, 5H), 7.62-7.67(m, 1H), 7.73(ddd, 1H), 8.03(d, 1H), 8.53-8.57(m, 1H), 9.11(d, 1H), 10.56(br s, 1H).

Example 312.

3-(3-pyrrolidinopropionyl)amino-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.80-1.88(m, 4H), 2.58-2.67(m, 6H), 2.86(t, 2H), 7.17(ddd, 1H), 7.42-7.54(m, 5H), 7.65(d, 1H), 7.73(ddd, 1H), 8.03(d, 1H), 8.53-8.57(m, 1H), 9.11(d, 1H), 10.91(br s, 1H).

The following compounds were synthesized by the methods similar to, or in accordance with, the method for Example 170.

Example 313.

5-Benzylamino-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 4.15(s, 2H), 6.70(d, 1H), 7.30-7.36(m, 1H), 7.36-7.43(m, 8H), 7.43-7.49(m, 3H), 7.59(ddd, 1H), 7.72-7.77(m, 2H).

Example 314.

3-Dibenzylamino-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

65702-519

¹H-NMR (400MHz, CDCl₃); δ(ppm) 4.52 (s, 4H), 7.12 (ddd, 1H), 7.16-7.33 (m, 10H), 7.37-7.54 (m, 7H), 7.63 (ddd, 1H), 7.80 (d, 1H), 8.50-8.54 (m, 1H).

Example 315.

3-(2-Cyanophenyl)-1-(3-hydroxyphenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

52mg of 1-(3-benzyloxyphenyl)-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one and 20mg of 5% palladium-carbon were added to 3ml of methanol, followed by stirring at room temperature in hydrogen atmosphere overnight. After the resulting insoluble matters were filtered off, the filtrate was evaporated. The residue was purified by silica gel chromatography (ethyl acetate/hexane system), to give 26mg the title compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 6.76 (dd, 1H), 6.87-6.92 (m, 1H), 6.93 (dd, 1H), 7.22-7.30 (m, 2H), 7.44 (ddd, 1H), 7.60-7.67 (m, 2H), 7.73-7.80 (m, 3H), 8.25 (d, 1H), 8.32 (d, 1H), 8.33 (br s, 1H), 8.59-8.63 (m, 1H).

The following compounds were synthesized by the methods similar to, or in accordance with, the method for Example 171.

Example 316.

1-Benzyloxymethyl-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 4.76 (s, 2H), 5.63 (s, 2H), 7.22 (ddd, 1H), 7.26-7.42 (m, 5H), 7.47 (ddd, 1H), 7.57 (d, 1H), 7.64-7.80 (m, 4H), 8.23 (d, 1H), 8.34 (d, 1H), 8.60-8.64 (m, 1H).

65702-519

Example 317.

3-(2-Cyanophenyl)-1-cyclopentylmethyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.32-1.42 (m, 2H), 1.55-1.64 (m, 2H), 1.65-1.75 (m, 2H), 1.76-1.86 (m, 2H), 2.53 (ddd, 1H), 4.10 (d, 2H), 7.21 (ddd, 1H), 7.45 (ddd, 1H), 7.58 (d, 1H), 7.64 (ddd, 1H), 7.71-7.79 (m, 3H), 8.16 (d, 1H), 8.28 (d, 1H), 8.59-8.63 (m, 1H).

Example 318.

1-[1-(tert-butoxycarbonyl)piperidin-4-yl]methyl-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.22-1.35 (m, 2H), 1.45 (s, 9H), 1.68-1.78 (m, 2H), 2.14-2.27 (m, 1H), 2.61-2.76 (m, 2H), 3.90-4.25 (m, 4H), 7.22 (ddd, 1H), 7.46 (ddd, 1H), 7.58 (ddd, 1H), 7.65 (ddd, 1H), 7.73 (ddd, 2H), 7.78 (dd, 1H), 8.17 (d, 1H), 8.21 (d, 1H), 8.59-8.63 (m, 1H).

Example 319.

1-(1-Benzylloxycarbonylpiperidin-4-yl)methyl-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.25-1.38 (m, 2H), 1.68-1.81 (m, 2H), 2.17-2.30 (m, 1H), 2.70-2.86 (m, 2H), 3.92-4.08 (m, 2H), 4.15-4.32 (m, 2H), 5.12 (s, 2H), 7.22 (ddd, 1H), 7.28-7.38 (m, 5H), 7.46 (ddd, 1H), 7.57 (d, 1H), 7.65 (ddd, 1H), 7.69-7.79 (m, 3H), 8.17 (d, 1H), 8.20 (d, 1H), 8.59-8.62 (m, 1H).

The following compounds were synthesized by the methods similar to, or in accordance with, the method for Example 174.

DEMANDES OU BREVETS VOLUMINEUX

**LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVETS
COMPREND PLUS D'UN TOME.**

CECI EST LE TOME __1__ DE __2__

NOTE: Pour les tomes additionels, veuillez contacter le Bureau Canadien des Brevets.

JUMBO APPLICATIONS / PATENTS

**THIS SECTION OF THE APPLICATION / PATENT CONTAINS MORE
THAN ONE VOLUME.**

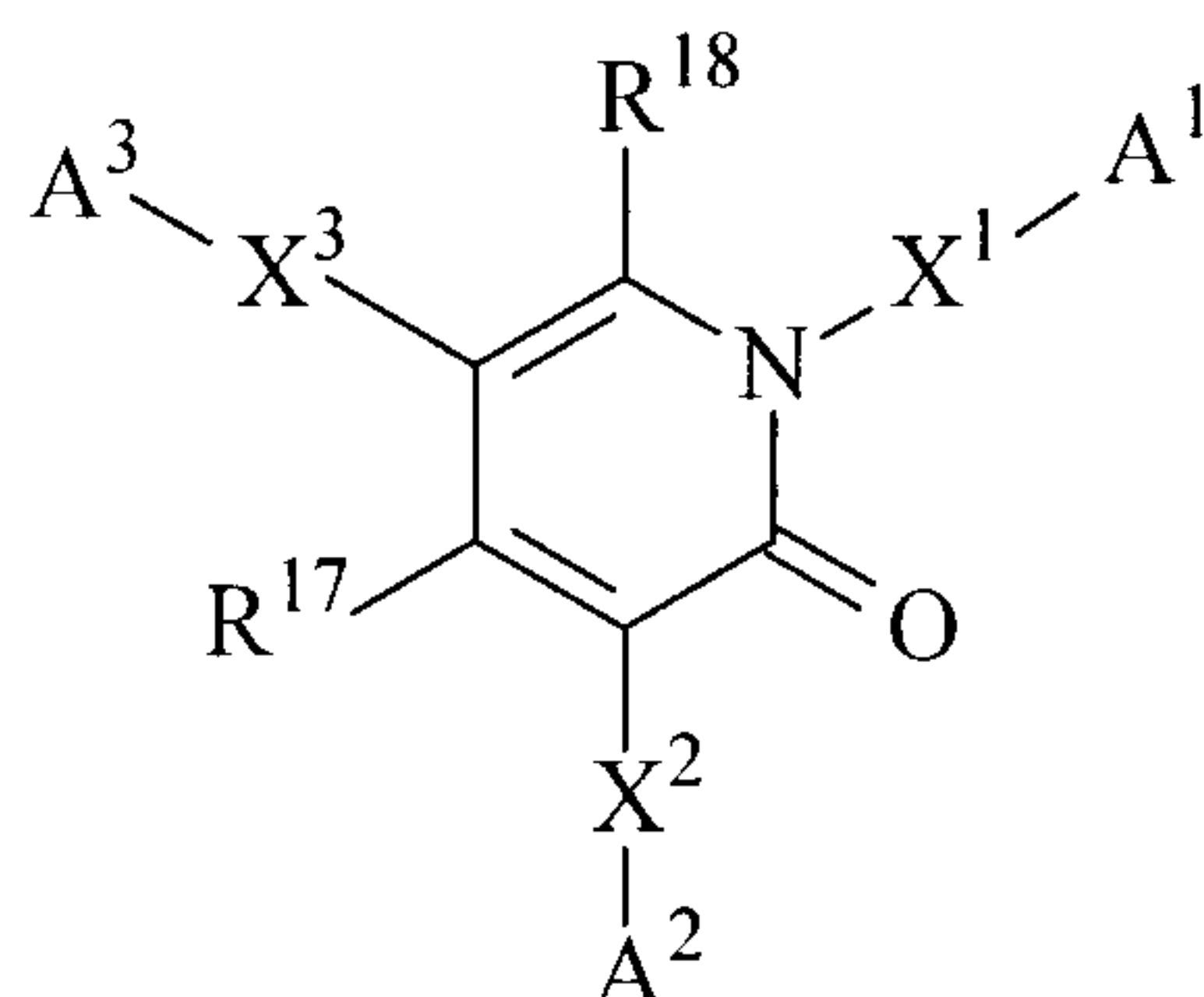
THIS IS VOLUME __1__ OF __2__

NOTE: For additional volumes please contact the Canadian Patent Office.

65702-519(S)

CLAIMS:

1. A compound of formula:



or a salt thereof, or a hydrate of the compound or the salt thereof,

- 5 wherein:

X^1 , X^2 and X^3 each indicates a single bond; A^1 , A^2 and A^3 are the same as or different from each other and each indicates a C_{3-8} cycloalkyl group, a C_{3-8} cycloalkenyl group, a 5- to 14-membered non-aromatic heterocyclic group, a C_{6-14} aromatic hydrocarbocyclic group or a 5- to 14-membered aromatic heterocyclic group which may be substituted respectively; and R^{17} and R^{18} are the same as or different from each other and each indicates hydrogen atom, a halogen atom or a C_{1-6} alkyl group.

2. The compound according to claim 1, or a salt thereof, or a hydrate of the compound or the salt thereof, wherein A^1 , A^2 and A^3 are the same as or different from each other and each represents a C_{3-8} cycloalkyl group, a C_{3-8} cycloalkenyl group, a 5- to 14-membered non-aromatic heterocyclic group, a C_{6-14} aromatic hydrocarbocyclic group or a 5- to 14-membered aromatic heterocyclic group which may be optionally substituted with one or more groups selected from the following substituent group: (1) hydroxy group, (2) a halogen atom, (3) nitrile group, (4) nitro group, (5) a C_{1-6} alkyl group, a C_{2-6} alkenyl group or a C_{2-6} alkynyl group which may be optionally substituted respectively with one or more groups selected from the group

65702-519(S)

consisting of hydroxy group, nitrile group, a halogen atom, a C₁₋₆ alkylamino group, a di-(C₁₋₆ alkyl)amino group, a C₂₋₆ alkenylamino group, a di(C₂₋₆ alkenylamino) group, a C₂₋₆ alkynylamino group, a di(C₂₋₆ alkynylamino) group, an N-C₁₋₆ alkyl-N-C₂₋₆ alkenylamino group, an N-C₁₋₆ alkyl-N-C₂₋₆ alkynylamino group, an N-C₂₋₆ alkenyl-N-C₂₋₆ alkynylamino group, an aralkyloxy group, a TBDMS oxy group, a C₁₋₆ alkylsulfonylamino group, a C₁₋₆ alkylcarbonyloxy group, a C₂₋₆ alkenylcarbonyloxy group, a C₂₋₆ alkynylcarbonyloxy group, an N-C₁₋₆ alkylcarbamoyl group, an N-C₂₋₆ alkenylcarbamoyl group and an N-C₂₋₆ alkynylcarbamoyl group, (6) a C₁₋₆ alkoxy group, a C₂₋₆ alkenyloxy group or a C₂₋₆ alkynyloxy group which may be optionally substituted respectively with one or more groups selected from the group consisting of a C₁₋₆ alkylamino group, an aralkyloxy group and hydroxy group, (7) a C₁₋₆ alkylthio group, a C₂₋₆ alkenylthio group or a C₂₋₆ alkynylthio group which may be optionally substituted respectively with one or more groups selected from the group consisting of hydroxy group, nitrile group, a halogen atom, a C₁₋₆ alkylamino group, an aralkyloxy group, a TBDMS oxy group, a C₁₋₆ alkylsulfonylamino group, a C₁₋₆ alkylcarbonyloxy group and a C₁₋₆ alkylcarbamoyl group, (8) a carbonyl group substituted with a group selected from the group consisting of a C₁₋₆ alkoxy group, amino group, a C₁₋₆ alkylamino group, a di(C₁₋₆ alkyl)amino group, a C₂₋₆ alkenylamino group, a di(C₂₋₆ alkenyl)amino group, a C₂₋₆ alkynylamino group, a di(C₂₋₆ alkynyl)amino group, an N-C₁₋₆ alkyl-N-C₂₋₆ alkenylamino group, an N-C₁₋₆ alkyl-N-C₂₋₆ alkynylamino group and an N-C₂₋₆ alkenyl-N-C₂₋₆ alkynylamino group, (9) amino group which may be optionally substituted with one or two groups selected from the group consisting of a C₁₋₆ alkyl group, a C₂₋₆ alkenyl group, a C₂₋₆ alkynyl group, a C₁₋₆ alkylsulfonyl group, a C₂₋₆ alkenylsulfonyl group, a C₂₋₆ alkynylsulfonyl group, a C₁₋₆ alkylcarbonyl group, a C₂₋₆ alkenylcarbonyl group and a C₂₋₆ alkynylcarbonyl group, (10) a C₁₋₆ alkylsulfonyl group, (11) a C₂₋₆ alkenylsulfonyl group, (12) a C₂₋₆ alkynylsulfonyl group, (13) a C₁₋₆ alkylsulfinyl group, (14) a C₂₋₆ alkenylsulfinyl group, (15) a C₂₋₆ alkynylsulfinyl group, (16) a formyl group, (17) a C₃₋₈ cycloalkyl group or a C₃₋₈ cycloalkenyl group which may be optionally substituted respectively with one or more groups selected from the group consisting of hydroxy

65702-519(S)

group, a halogen atom, nitrile group, a C₁₋₆ alkyl group, a C₁₋₆ alkyloxy group, a C₁₋₆ alkyloxy C₁₋₆ alkyl group and an aralkyl group, (18) a 5- to 14-membered non-aromatic heterocyclic group which may be optionally substituted with one or more groups selected from the group consisting of hydroxy group, a halogen atom, nitrile group, a C₁₋₆ alkyl group, a C₁₋₆ alkyloxy group, a C₁₋₆ alkyloxy C₁₋₆ alkyl group and an aralkyl group, (19) a C₆₋₁₄ aromatic hydrocarbocyclic group which may be optionally substituted with one or more groups selected from the group consisting of hydroxy group, a halogen atom, nitrile group, a C₁₋₆ alkyl group, a C₁₋₆ alkyloxy group, a C₁₋₆ alkyloxy C₁₋₆ alkyl group and an aralkyl group, and (20) a 5- to 14-membered aromatic heterocyclic group which may be optionally substituted with one or more groups selected from the group consisting of hydroxy group, a halogen atom, nitrile group, a C₁₋₆ alkyl group, a C₁₋₆ alkyloxy group, a C₁₋₆ alkyloxy C₁₋₆ alkyl group and an aralkyl group.

3. The compound according to claim 1 or 2, or a salt thereof, or a hydrate of the compound or the salt thereof, wherein R¹⁷ and R¹⁸ are the same as or different from each other and each represent hydrogen atom, fluorine, chlorine, bromine, iodine, methyl group, ethyl group, n-propyl group or iso-propyl group.

4. The compound according to claim 1 or 2, or a salt thereof, or a hydrate of the compound or the salt thereof, wherein R¹⁷ and R¹⁸ represent hydrogen atom.

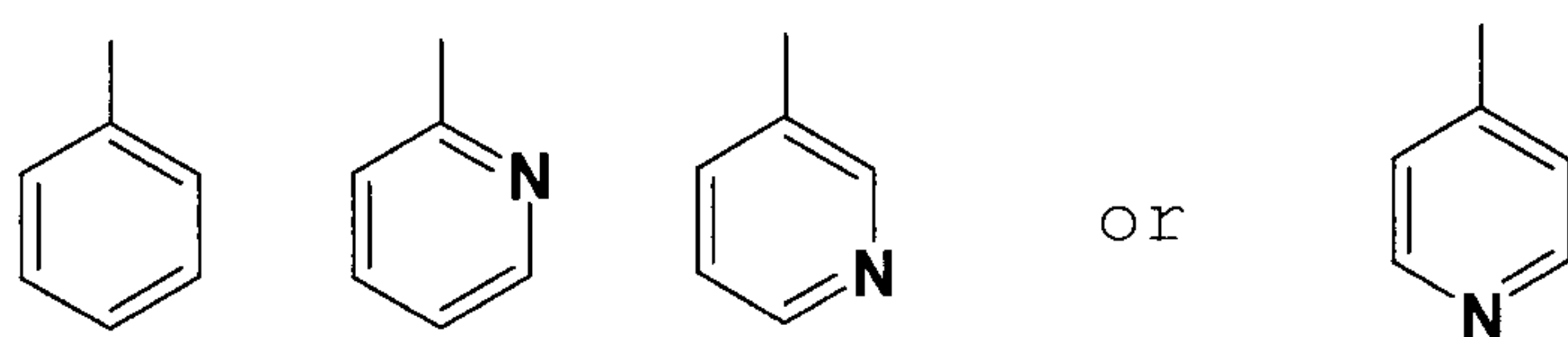
5. The compound according to any one of claims 1 to 4, or a salt thereof, or a hydrate of the compound or the salt thereof, wherein A¹, A² and A³ are the same as or different from each other and each indicates a C₆₋₁₄ aromatic hydrocarbocyclic group or a 5- to 14- membered aromatic heterocyclic group which may be substituted respectively.

6. The compound according to any one of claims 1 to 5, or a salt thereof, or a hydrate of the compound or the salt thereof, wherein A¹, A² and A³ are the same as or different from each other and each represents optionally substituted phenyl group, pyrrolyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, thienyl group, thiazolyl group, furyl group, naphthyl group, quinolyl group,

65702-519(S)

iso-quinolyl group, indolyl group, benzimidazolyl group, benzothiazolyl group, benzoxazolyl group, imidazopyridyl group, carbazolyl group, cyclopentyl group, cyclohexyl group, cyclohexenyl group, dioxinyl group, adamantyl group, pyrrolidinyl group, piperidinyl group, piperazinyl group or morpholinyl group.

- 5 7. The compound according to any one of claims 1 to 5, or a salt thereof, or a hydrate of the compound or the salt thereof, wherein A^1 , A^2 and A^3 are the same as or different from each other and each represents a group represented by the following formula:



- 10 which may be substituted.

8. The compound according to any one of claims 1 to 7, or a salt thereof, or a hydrate of the compound or the salt thereof, wherein the optional substituents of A^1 , A^2 and A^3 are the same as or different from each other and each is hydroxyl group, a halogen atom, amino group, nitrile group or nitro group.

- 15 9. The compound according to any one of claims 1 to 7, or a salt thereof, or a hydrate of the compound or the salt thereof, wherein A^1 , A^2 and A^3 are the same as or different from each other and each is optionally substituted with hydroxyl group, a halogen atom, amino group or nitrile group.

10. The compound according to any one of claims 1 to 9, or a salt thereof,
 20 or a hydrate of the compound or the salt thereof, wherein the bonding site of the optional substituents at A^1 , A^2 and/or A^3 are α -position(s) of the carbon atom bonding to the group X^1 , X^2 and X^3 , respectively.

11. The compound:

65702-519(S)

3-(2-cyanophenyl)-5-(2-methylsulfonylaminophenyl)-1-phenyl-
1,2-dihydropyridin-2-one;

3-(2-chloro-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one;

5 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-nitrophenyl)-1,2-dihydropyridin-2-
one;

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-aminophenyl)-1,2-dihydropyridin-2-
one;

10 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-methylsulfonylaminophenyl)-1,2-
dihydropyridin-2-one;

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-methylaminophenyl)-
1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-dimethylaminophenyl)-
1,2-dihydropyridin-2-one;

15 3-(2-cyanophenyl)-5-(2-pyridyl)-1-[3-(5-methoxymethyl-2-oxazolidinon-
3-yl)-phenyl]-1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-methoxycarbonylphenyl)-
1,2-dihydropyridin-2-one;

20 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-methylaminocarbonylphenyl)-1,2-
dihydropyridin-2-one;

3-(2-cyano-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one;

3-(2-chlorophenyl)-5-(2-pyridyl)-1-(4-hydroxyphenyl)-1,2-dihydropyridin-
2-one;

65702-519(S)

3-(2-chlorophenyl)-5-(2-pyridyl)-1-(4-dimethylaminoethoxyphenyl)-1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-formylphenyl)-1,2-dihydropyridin-2-one;

5 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-hydroxymethylphenyl)-1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-cyanomethylphenyl)-1,2-dihydropyridin-2-one;

10 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-acetylaminoethylphenyl)-1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-methylsulfonylaminoethylphenyl)-1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-acetoxymethylphenyl)-1,2-dihydropyridin-2-one;

15 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-methylthiophenyl)-1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-methylsulfonylphenyl)-1,2-dihydropyridin-2-one;

20 3-(2-cyanophenyl)-5-(2-formylthiophen-3-yl)-1-phenyl-1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-5-(2-diethylaminomethylthiophen-3-yl)-1-phenyl-1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-5-(2-hydroxymethylthiophen-3-yl)-1-phenyl-1,2-dihydropyridin-2-one;

65702-519(S)

3-(2-cyanophenyl)-5-(2-pyridyl)-1-benzyl-1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-5-phenyl-1-(2-pyridyl)-1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-1,5-diphenyl-1,2-dihydropyridin-2-one;

5 3-(2-cyanophenyl)-5-(2-methoxyphenyl)-1-phenyl-1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-5-(3,4-dimethoxyphenyl)-1-phenyl-1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-5-(thiophen-3-yl)-1-phenyl-1,2-dihydropyridin-2-one;

10 3-(2-cyanophenyl)-5-(2-fluorophenyl)-1-phenyl-1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-5-(thiophen-2-yl)-1-phenyl-1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-5-(3-furyl)-1-phenyl-1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-5-(2-furyl)-1-phenyl-1,2-dihydropyridin-2-one;

15 3-(2-chlorophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one;

3-(2-methoxycarbonylphenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one;

3-phenyl-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one;

3-(2-fluorophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one;

20 3-(2-chlorophenyl)-5-(2-pyridyl)-1-(3-methoxyphenyl)-1,2-dihydropyridin-2-one;

3-(2-fluoro-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one;

65702-519(S)

3-(2-methoxy-5-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one;

3-(2-fluoro-3-pyridyl)-5-(2-pyridyl)-1-(3-methoxyphenyl)-
1,2-dihydropyridin-2-one;

5 3-(2-fluoro-3-pyridyl)-5-(2-pyridyl)-1-(3-fluorophenyl)-1,2-dihydropyridin-
2-one;

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-fluorophenyl)-1,2-dihydropyridin-2-
one;

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-fluorophenyl)-1,2-dihydropyridin-2-
one;

10 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-methoxyphenyl)-1,2-dihydropyridin-
2-one;

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-methoxyphenyl)-1,2-dihydropyridin-
2-one;

3-phenyl-5-(2-pyridyl)-1-(3-fluorophenyl)-1,2-dihydropyridin-2-one;

15 3-(2-chlorophenyl)-5-(2-pyridyl)-1-(4-fluorophenyl)-1,2-dihydropyridin-2-
one;

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-formylphenyl)-1,2-dihydropyridin-2-
one;

20 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-formylphenyl)-1,2-dihydropyridin-2-
one;

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-chlorophenyl)-1,2-dihydropyridin-2-
one;

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-tolyl)-1,2-dihydropyridin-2-one;

65702-519(S)

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-trifluoromethylphenyl)-
1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(thiophen-3-yl)-1,2-dihydropyridin-2-
one;

5 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-furyl)-1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-tolyl)-1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-trifluoromethylphenyl)-
1,2-dihydropyridin-2-one;

10 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-methoxypyridin-5-yl)-
1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(pyrimidin-5-yl)-1,2-dihydropyridin-2-
one;

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-benzyloxymethylpyridin-5-yl)-1,2-
dihydropyridin-2-one;

15 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-ethylthiopyridin-5-yl)-
1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-pyridyl)-1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-methoxypyridin-5-yl)-
1,2-dihydropyridin-2-one;

20 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-chloropyridin-5-yl)-
1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-fluoropyridin-5-yl)-
1,2-dihydropyridin-2-one;

65702-519(S)

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-methoxyphenyl)-1,2-dihydropyridin-2-one;

3-phenyl-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one;

3-(2-chlorophenyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one;

5 3-(thiophen-3-yl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one;

3-(2,6-dimethylphenyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one;

3-(2-cyanothiophen-3-yl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one;

10 3-(2-fluoro-3-pyridyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one;

3-(2-chlorophenyl)-5-(2-pyridyl)-1-(3-hydroxyphenyl)-1,2-dihydropyridin-2-one;

3-(2-chlorophenyl)-5-(2-pyridyl)-1-(3-dimethylaminoethoxyphenyl)-1,2-dihydropyridin-2-one;

15 3-(2-chlorophenyl)-5-(2-pyridyl)-1-(3-dimethylaminopropoxyphenyl)-1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-hydroxymethylphenyl)-1,2-dihydropyridin-2-one;

20 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-cyanomethylphenyl)-1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-cyanomethylphenyl)-1,2-dihydropyridin-2-one;

65702-519(S)

3-(2-cyanophenyl)-5-(6-diethylaminomethyl-2-pyridyl)-1-phenyl-
1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-1-phenyl-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one;

5 3-(2-hydroxypyridin-6-yl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-
2-one;

1-(2-aminobenzothiazol-6-yl)-3-(2-cyanophenyl)-5-(2-pyridyl)-
1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(1-benzyl-1,2,5,6-tetrahydropyridin-5-
yl)-1,2-dihydropyridin-2-one;

10 3-[2-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl]-1-phenyl-5-(2-pyridyl)-1,2-
dihydropyridin-2-one;

3-(2-cyanophenyl)-5-(6-methylpyridin-2-yl)-1-phenyl-1,2-dihydropyridin-
2-one;

15 3-(2-cyanophenyl)-5-(5-methylpyridin-2-yl)-1-phenyl-1,2-dihydropyridin-
2-one;

3-(2-cyanophenyl)-5-(3-hydroxypyridin-2-yl)-1-phenyl-
1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-1-phenyl-5-(2-thiazolyl)-1,2-dihydropyridin-2-one;

20 3-(2-cyanophenyl)-5-(6-methoxypyridin-2-yl)-1-phenyl-
1,2-dihydropyridin-2-one;

1-(4-aminophenyl)-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-
one;

1-(3-aminophenyl)-3-(2-cyanophenyl)-5-(2-pyrimidinyl)-
1,2-dihydropyridin-2-one;

65702-519(S)

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-amino-4-methylphenyl)-
1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-1-[3-(dimethylaminoethoxy)phenyl]-5-(2-pyridyl)-1,2-
dihydropyridin-2-one;

5 3-(2-cyanophenyl)-1-[3-(piperidinoethoxy)phenyl]-5-(2-pyridyl)-
1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-1-[3-(pyrrolidinoethoxy)phenyl]-5-(2-pyridyl)-
1,2-dihydropyridin-2-one;

10 3-(2-cyanophenyl)-1-[3-(diisoproylaminoethoxy)phenyl]-5-(2-pyridyl)-
1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-1-[3-(4-piperidinobutoxy)phenyl]-5-(2-pyridyl)-
1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-1-(4-nitrophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-
one;

15 1-phenyl-5-(2-pyridyl)-3-(2-thiazolyl)-1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-1-(3-pyridyl)-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-
one;

3-(2-fluoropyridin-3-yl)-1-phenyl-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-
one;

20 3-(2-cyanopyridin-3-yl)-1-phenyl-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-
one;

3-(2-cyanophenyl)-1-(3-nitrophenyl)-5-(2-pyrimidinyl)-1,2-dihydropyridin-
2-one;

3-(2-nitrophenyl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one;

65702-519(S)

3-(2-formylthiophen-3-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-naphthyl)-1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(1-naphthyl)-1,2-dihydropyridin-2-one;

5 5-(2-aminopyridin-6-yl)-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one;

5-(6-bromopyridin-2-yl)-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one;

10 3-(2-cyanophenyl)-5-(2-morpholinopyridin-6-yl)-1-phenyl-1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-1-(3-hydroxyphenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-1-[3-(4-piperidyloxy)]phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one;

15 1-[3-(N-acetylpiperidin-4-yl-oxy)phenyl]-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-1-{3-[1-(methanesulfonyl)piperidin-4-yl-oxy]phenyl}-5-(2-pyridyl)-1,2-dihydropyridin-2-one;

20 1-[3-(N-methylpiperidin-4-yl-oxy)phenyl]-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one;

3-(6-chloro-1H-benzimidazol-2-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one;

3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-nitro-4-methylphenyl)-1,2-dihydropyridin-2-one;

65702-519(S)

3-(2-cyanothiophen-3-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one;

3-[2-(5-oxazolyl)phenyl]-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one;

5 3-[2-(5-oxazolyl)thiophen-3-yl]-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one; or

3-[(2-ethoxycarbonylvinyl)thiophen-3-yl]-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one;

or a salt thereof or a hydrate of the compound or the salt thereof.

12. The compound: 3-(2-cyanophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one, or a salt thereof, or a hydrate of the compound or the salt thereof.

13. The compound: 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one, or a salt thereof, or a hydrate of the compound or the salt thereof.

15 14. The compound: 3-(2-fluoro-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one, or a salt thereof, or a hydrate of the compound or the salt thereof.

15. The compound: 3-(2-fluoro-3-pyridyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one, or a salt thereof, or a hydrate of the compound or the salt thereof.

16. The compound: 3-(2-cyanophenyl)-1-phenyl-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one, or a salt thereof, or a hydrate of the compound or the salt thereof.

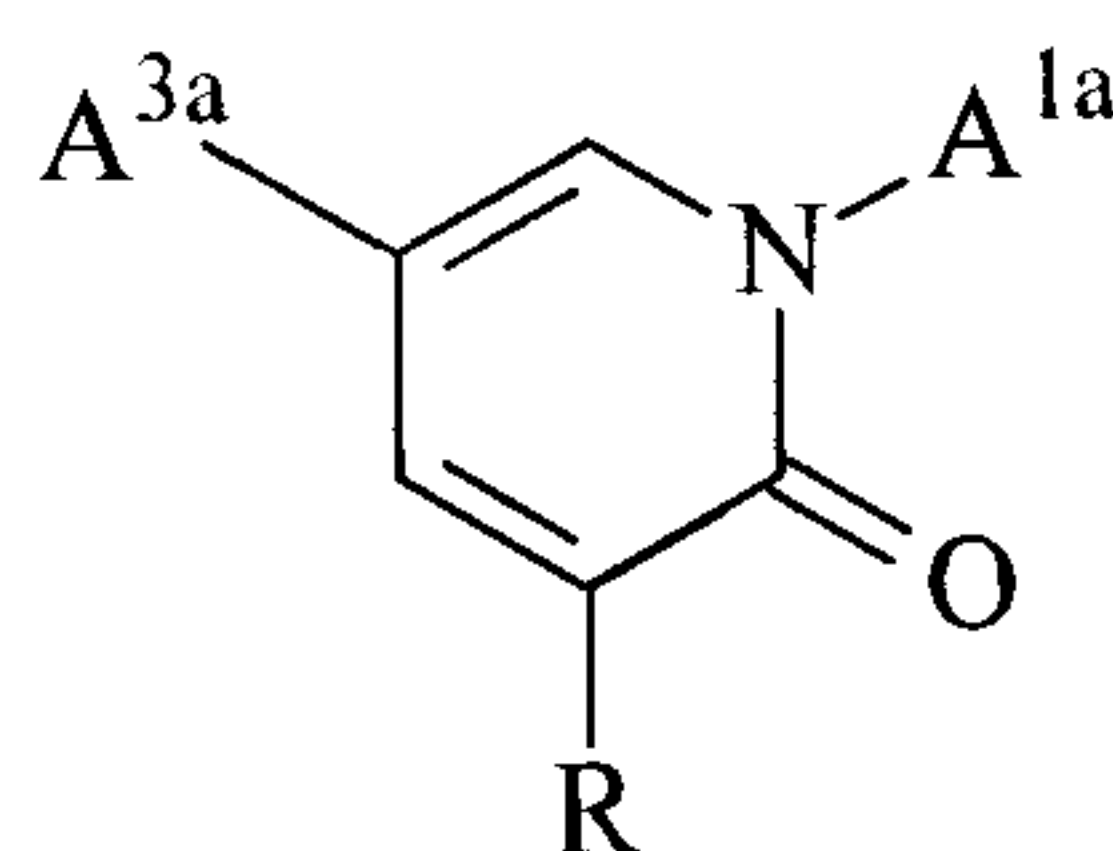
65702-519(S)

17. The compound: 3-(2-cyanophenyl)-1-(3-pyridyl)-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one, or a salt thereof, or a hydrate of the compound or the salt thereof.

18. The compound: 3-(2-fluoropyridin-3-yl)-1-phenyl-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one, or a salt thereof, or a hydrate of the compound or the salt thereof.

19. The compound: 3-(2-cyanopyridin-3-yl)-1-phenyl-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one, or a salt thereof, or a hydrate of the compound or the salt thereof.

10 20. A compound:



or a salt thereof, or a hydrate of the compound or the salt thereof,

wherein A^{1a} and A^{3a} are the same as or different from each other and each indicates optionally substituted C₆₋₁₄ aromatic hydrocarbocyclic group or a 5- to 14-membered aromatic heterocyclic group; and R indicates hydrogen atom or a halogen atom.

21. A compound according to claim 20, or a salt thereof, or a hydrate of the compound or the salt, thereof, wherein A^{1a} and A^{3a} are the same as or different from each other and each represents optionally substituted phenyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, thienyl group, thiazolyl group, furyl group, naphthyl group, quinolyl group, isoquinolyl group, indolyl group, benzimidazolyl group, benzothiazolyl group, benzoxazolyl group, imidazopyridyl group or carbazolyl group.

65702-519(S)

22. A compound according to claim 20, or a salt thereof, or a hydrate of the compound or the salt thereof, wherein A^{1a} and A^{3a} are the same as or different from each other and each represents optionally substituted phenyl group, pyridyl group, pyrimidinyl group, thienyl group or furyl group.
- 5 23. A compound according to any one of claims 20 to 22, or a salt thereof, or a hydrate of the compound or the salt thereof, wherein R is hydrogen atom or bromine.
24. The compound: 3-bromo-1-phenyl-5-pyridin-2-yl-2(1H)-pyridone, or a salt thereof, or a hydrate of the compound or the salt thereof.
- 10 25. A pharmaceutical composition comprising a compound as defined in claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 or 19, or a pharmaceutically acceptable salt thereof, or a hydrate of the compound or the salt thereof, and a pharmaceutically acceptable carrier.
26. The pharmaceutical composition according to claim 25 for use in the
15 treatment or prevention of Parkinson's disease.
27. The pharmaceutical composition according to claim 25 for use in the treatment or prevention of Parkinson's syndrome.
28. The pharmaceutical composition according to claim 25 for use in the treatment or prevention of epilepsy.
- 20 29. The pharmaceutical composition according to claim 25 for use in the treatment or prevention of multiple sclerosis.
30. Use of a compound as defined in claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 or 19, or a pharmaceutically acceptable salt thereof, or a hydrate of the compound or the salt thereof, in the manufacture of a medicament for
25 the treatment or prevention of Parkinson's disease.

65702-519(S)

31. Use of a compound as defined in claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 or 19, or a pharmaceutically acceptable salt thereof, or a hydrate of the compound or the salt thereof, in the manufacture of a medicament for the treatment or prevention of Parkinson's syndrome.

5 32. Use of a compound as defined in claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 or 19, or a pharmaceutically acceptable salt thereof, or a hydrate of the compound or the salt thereof, in the manufacture of a medicament for the treatment or prevention of epilepsy.

10 33. Use of a compound as defined in claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 or 19, or a pharmaceutically acceptable salt thereof, or a hydrate of the compound or the salt thereof, in the manufacture of a medicament for the treatment or prevention of multiple sclerosis.

15 34. Use of a compound as defined in claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 or 19, or a pharmaceutically acceptable salt thereof, or a hydrate of the compound or the salt thereof, for the treatment or prevention of Parkinson's syndrome.

20 35. Use of a compound as defined in claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 or 19, or a pharmaceutically acceptable salt thereof, or a hydrate of the compound or the salt thereof, for the treatment or prevention of Parkinson's disease.

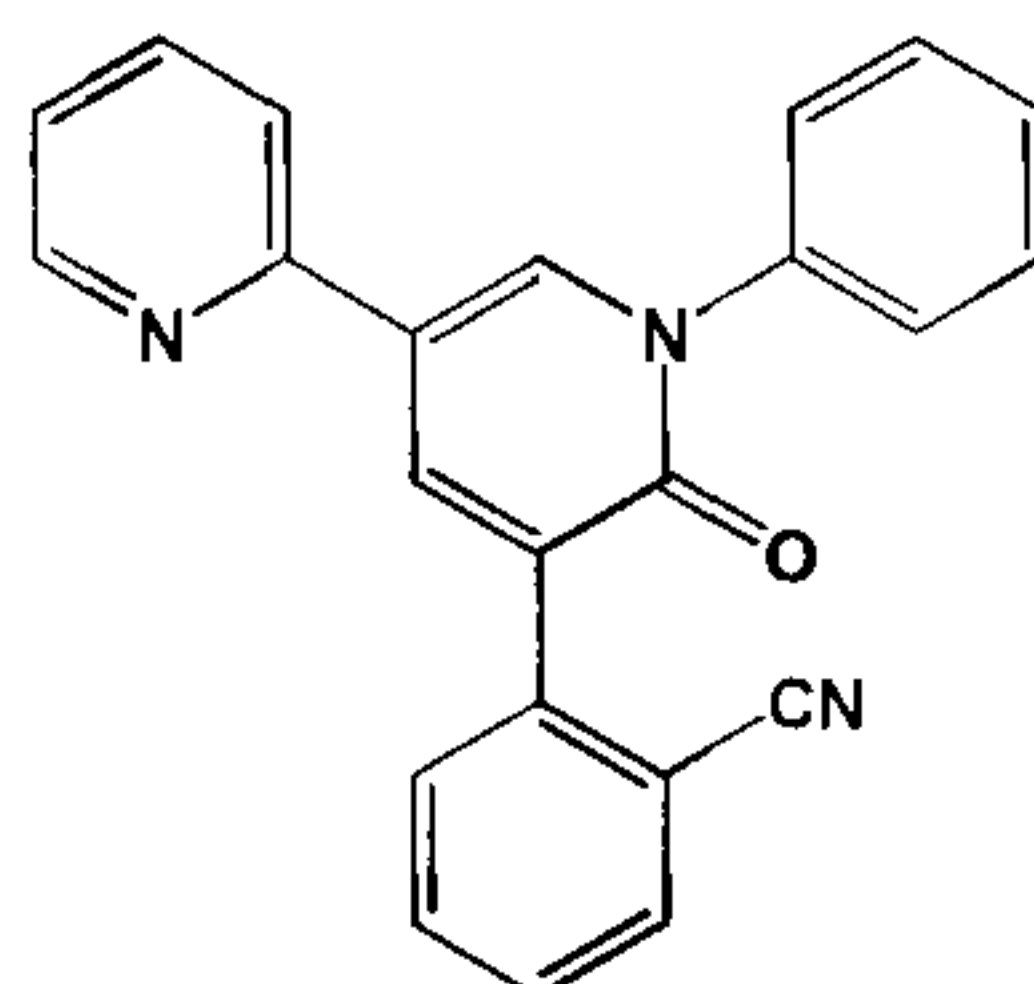
36. Use of a compound as defined in claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 or 19, or a pharmaceutically acceptable salt thereof, or a hydrate of the compound or the salt thereof, for the treatment or prevention of epilepsy.

25 37. Use of a compound as defined in claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 or 19, or a pharmaceutically acceptable salt thereof, or a

65702-519(S)

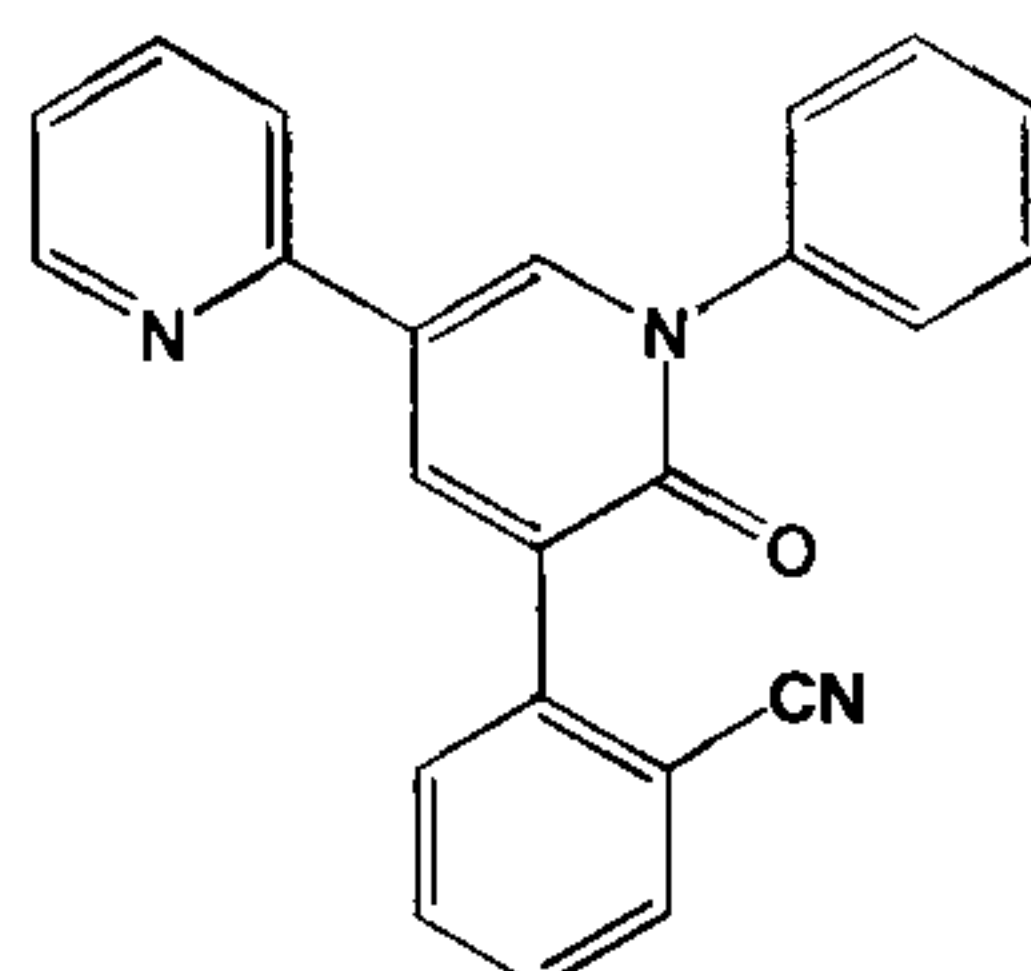
hydrate of the compound or the salt thereof, for the treatment or prevention of multiple sclerosis.

38. A compound of the formula:



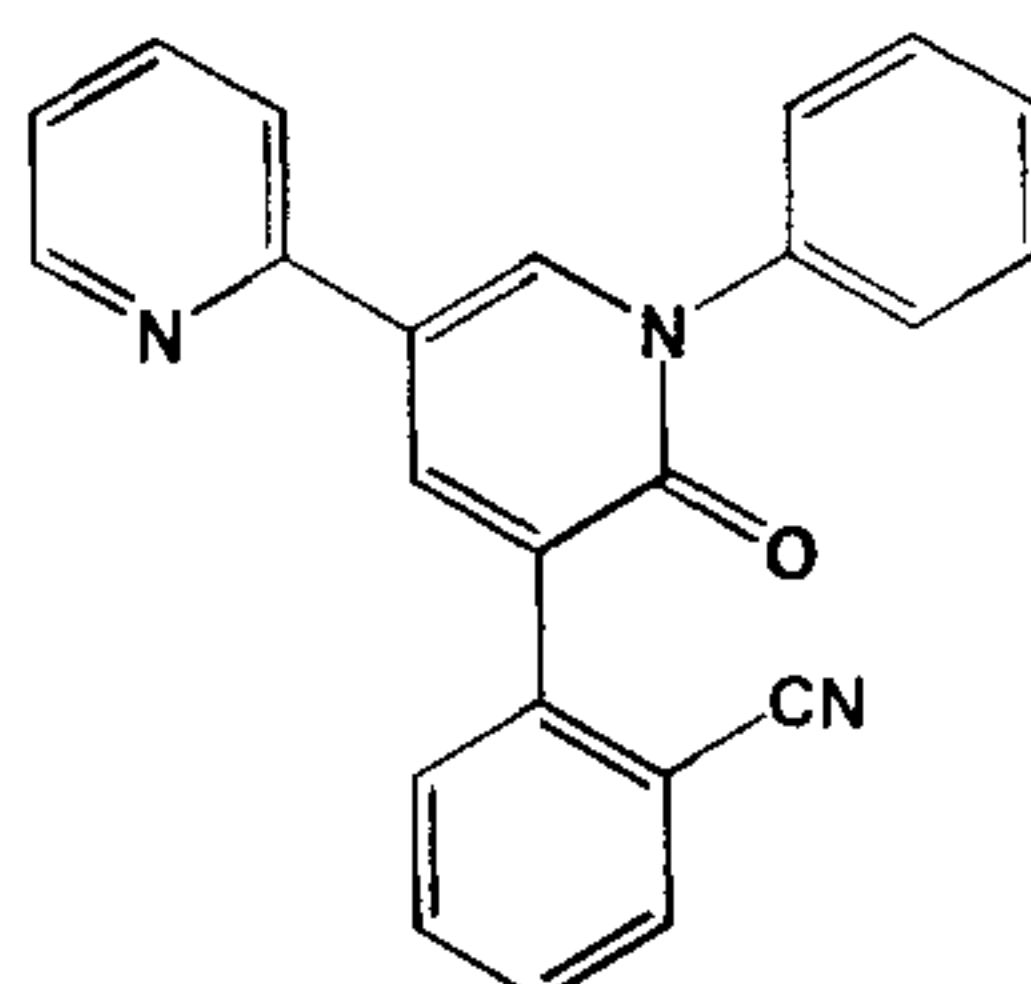
5 which is 3-(2-cyanophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one, or is also known as 2-(2-oxo-1-phenyl-5-pyridin-2-yl-1,2-dihydropyridin-3-yl) benzonitrile, or a hydrate thereof.

39. A hydrate of the compound of the chemical structure of



10 which is 3-(2-cyanophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one, or is also known as 2-(2-oxo-1-phenyl-5-pyridin-2-yl-1,2-dihydropyridin-3-yl) benzonitrile.

40. A pharmaceutically acceptable salt of the compound of the chemical structure of



65702-519(S)

which is 3-(2-cyanophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one, or is also known as 2-(2-oxo-1-phenyl-5-pyridin-2-yl-1,2-dihydropyridin-3-yl) benzonitrile.

41. A pharmaceutical composition comprising the compound as defined in claim 38, 39 or 40, and a pharmaceutically acceptable carrier.

5 42. The pharmaceutical composition according to claim 41 for use as an AMPA receptor antagonist.

43. The pharmaceutical composition according to claim 41 for use in the treatment or prevention of Parkinson's disease.

10 44. The pharmaceutical composition according to claim 41 for use in the treatment or prevention of Parkinson's syndrome.

45. The pharmaceutical composition according to claim 41 for use in the treatment or prevention of epilepsy.

46. The pharmaceutical composition according to claim 41 for use in the treatment or prevention of multiple sclerosis.

15 47. Use of the compound of claim 38, which is 3-(2-cyanophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one, or is also known as 2-(2-oxo-1-phenyl-5-pyridin-2-yl-1,2-dihydropyridin-3-yl) benzonitrile, or a pharmaceutically acceptable salt thereof, or a hydrate of the compound or the salt thereof, for the inhibition of AMPA receptor activity.

20 48. Use of the compound of claim 38, 39 or 40 for the treatment of convulsions.

49. Use of the compound of claim 38, 39 or 40 as a myorelaxation agent.

50. Use of the compound of claim 38, or a pharmaceutical acceptable salt thereof, or a hydrate of the compound or of the salt thereof, as an AMPA receptor
25 antagonist.

65702-519(S)

51. Use of the compound of claim 38, or a pharmaceutical acceptable salt thereof, or a hydrate of the compound or of the salt thereof, for the treatment of convulsions.

52. Use of the compound of claim 38, or a pharmaceutical acceptable salt thereof, or a hydrate of the compound or of the salt thereof, for the treatment of convulsions due to epilepsy.

53. Use of the compound of claim 38, or a pharmaceutical acceptable salt thereof, or a hydrate of the compound or of the salt thereof, for the treatment of epilepsy.

10 54. Use of the compound of claim 38, or a pharmaceutical acceptable salt thereof, or a hydrate of the compound or of the salt thereof, for the manufacture of a medicament.

55. A pharmaceutical composition comprising the compound of claim 38, or a pharmaceutically acceptable salt thereof, or a hydrate of the compound or of the salt thereof, and a pharmaceutically acceptable carrier, for the treatment of epilepsy.

