carbonyl group at position 3, examples described in Non-Patent Documents 1 and 2 have been known. However, the pyrazino[2,3-d]isoxazole of the present invention cannot be synthesized by such synthetic methods.

Prior Art Documents

Patent Documents

[0004]

Patent Document 1: International Publication WO01/60834

Patent Document 2: International Publication WO09/41473

Non Patent Documents

[0005]

Non Patent Document 1: Journal of Organic Chemistry, 1972, Vol. 37, #15, pp. 2498-2502

Non Patent Document 2: Journal of Organic Chemistry, 1988, Vol. 53, #9, pp. 2052-2055

Summary ~~of Invention~~

Object to be Solved ~~by the Invention~~

[0006]

It is an object of the present ~~invention~~embodiments disclosed herein to provide a production intermediate of T-705 and a method for producing the same, which provides high safety and ease in handling, and to further provide a method for safely and easily producing T-705 and the like.

Means for Solving the Object

[0007]

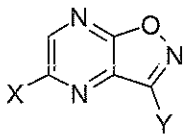
Thus, the present ~~invention~~disclosure provides the following [1] to [15].

[1] In one aspect, there is ~~A~~a pyrazino[2,3-d]isoxazole derivative represented by the following formula (I):

[0008]

[Chem.1]

formula (I)



[0009]

wherein X represents a halogen atom, a hydroxyl group or a sulfamoyloxy group, and Y represents –C(=O)R or –CN; wherein R represents a hydrogen atom, an alkoxy group, an aryloxy group, an alkyl group, an aryl group or an amino group; wherein the sulfamoyloxy group, alkoxy group, aryloxy group, alkyl group, aryl group and amino group may be optionally substituted.

[2] The pyrazino[2,3-d]isoxazole derivative according to [1], wherein Y represents –C(=O)R where R represents an alkoxy group or an amino group, and the alkoxy group and amino group may be optionally substituted.

[0010]

[3] The pyrazino[2,3-d]isoxazole derivative according to [1] or [2], wherein X represents a hydroxyl group, a chlorine atom or a fluorine atom.

[4] The pyrazino[2,3-d]isoxazole derivative according to [1], wherein X represents a fluorine atom or a chlorine atom, and Y represents –C(=O)R where R represents an optionally substituted alkoxy group.

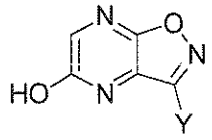
[5] The pyrazino[2,3-d]isoxazole derivative according to [1], wherein X represents a fluorine atom or a chlorine atom, and Y represents –C(=O)R where R represents a methoxy group, an ethoxy group, an n-propoxy group, an isopropoxy group, or an n-butoxy group.

[6] In another aspect, there is ~~A~~a method for producing a pyrazino[2,3-d]isoxazole derivative represented by the following formula (I-1):

[0011]

[Chem.3]

formula (I-1)



[0012]

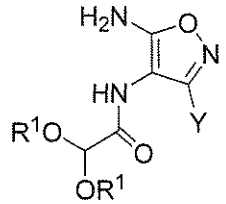
wherein Y has the same meanings as those described below,

which comprises treating with an acid an isoxazole derivative represented by the following formula (II):

[0013]

[Chem.2]

formula (II)



[0014]

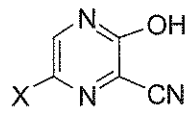
wherein Y represents –C(=O)R or –CN; where R represents a hydrogen atom, an alkoxy group, an aryloxy group, an alkyl group, an aryl group or an amino group; and R^1 represents a hydrogen atom or an alkyl group; wherein the alkoxy group, aryloxy group, alkyl group, aryl group and amino group may be optionally substituted.

[7] In another aspect, there is ~~A~~a method for producing a pyrazinecarbonitrile derivative represented by the following formula (III):

[0015]

[Chem.5]

formula (III)



[0016]

wherein X has the same meanings as those described below,

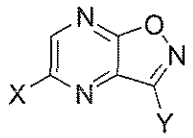
which comprises treating with a base a pyrazino[2,3-d]isoxazole derivative represented

by the following formula (I):

[0017]

[Chem.4]

formula (I)



[0018]

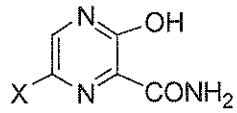
wherein X represents a halogen atom, a hydroxyl group or a sulfamoyloxy group, and Y represents –C(=O)R or –CN; where R represents a hydrogen atom, an alkoxy group an aryloxy group, an alkyl group, an aryl group or an amino group; wherein the sulfamoyloxy group, alkoxy group, aryloxy group, alkyl group, aryl group and amino group may be optionally substituted.

[8] In another aspect, there is ~~A~~a method for producing a compound represented by the following formula (IV):

[0019]

[Chem.8]

formula (IV)



[0020]

wherein X has the same meanings as those described below,

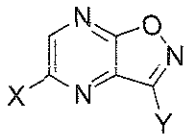
which comprises

a step of treating with a base a pyrazino[2,3-d]isoxazole derivative represented by the following formula (I):

[0021]

[Chem.6]

formula (I)



[0022]

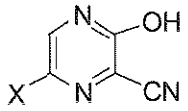
wherein X represents a halogen atom, a hydroxyl group or a sulfamoyloxy group, and Y represents –C(=O)R or –CN; where R represents a hydrogen atom, an alkoxy group an aryloxy group, an alkyl group, an aryl group or an amino group; wherein the sulfamoyloxy group, alkoxy group, aryloxy group, alkyl group, aryl group and amino group may be optionally substituted,

so as to produce a compound represented by the following formula (III):

[0023]

[Chem.7]

formula (III)



[0024]

wherein X has the same meanings as describe above, and

a step of adding water to the compound represented by the formula (III).

[9] The production method according to [7] or [8], wherein X represents a fluorine atom and Y represents –C(=O)R where R represents an optionally substituted alkoxy group.

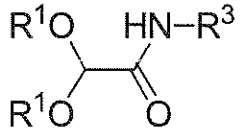
[10] The production method according to [7] or [8], wherein X represents a fluorine atom and Y represents –C(=O)R where R represents a methoxy group, an ethoxy group, an n-propoxy group, an isopropoxy group, or an n-butoxy group.

[11] In another aspect, there is ~~A~~a compound represented by the following formula (C-2):

[0025]

[Chem.9]

formula (C-2)



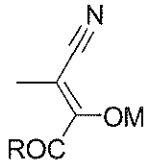
[0026]

wherein R^1 represents an alkyl group, R^3 represents $-CH_2CN$, the following formula (C-2a):

[0027]

[Chem.10]

formula (C-2a)



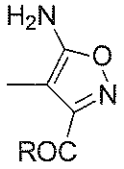
[0028]

or the following formula (C-2b)

[0029]

[Chem.11]

formula (C-2b)



[0030]

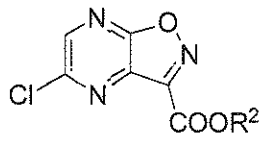
wherein R represents an alkoxy group, M represents H, Li, K or Na; where the alkoxy and alkyl group may be optionally substituted.

[12] In another aspect, there is ~~A~~a method for producing a pyrazino[2,3-d]isoxazole derivative represented by the following formula (J-4):

[0031]

[Chem.13]

formula (J-4)



[0032]

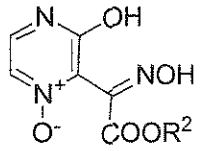
wherein R^2 has the same meanings as those described below,

which comprises allowing a compound represented by the following formula (J-3):

[0033]

[Chem.12]

formula (J-3)



[0034]

wherein R^2 represents an alkyl group or an aryl group; wherein the alkyl group and aryl group may be optionally substituted,

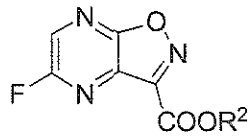
to react with a chlorinating agent.

[13] In another aspect, there is ~~A~~a method for producing a pyrazino[2,3-d]isoxazole derivative represented by the following formula (J-5):

[0035]

[Chem.15]

formula (J-5)



[0036]

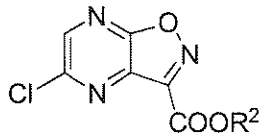
wherein R^2 represents an alkyl group or an aryl group; wherein the alkyl group and aryl group may be optionally substituted,

which comprises allowing a pyrazino[2,3-d]isoxazole derivative represented by the following formula (J-4):

[0037]

[Chem.14]

formula (J-4)



wherein R^2 represents an alkyl group or an aryl group; wherein the alkyl group and aryl group may be optionally substituted,

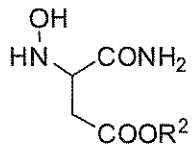
to react with a fluorinating agent in the presence of 2,4-dinitrochlorobenzene or 2,4-dinitrofluorobenzene.

[14] In another aspect, there is ~~A~~a compound represented by the following formula (J-1):

[0038]

[Chem.16]

formula (J-1)



[0039]

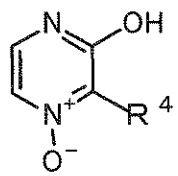
wherein R^2 represents an alkyl group or an aryl group; wherein the alkyl group and aryl group may be optionally substituted.

[15] In another aspect, there is ~~A~~a compound represented by the following formula (J-2a):

[0040]

[Chem.17]

formula (J-2a)



[0041]

wherein R^4 represents $-CH_2COOR^2$, or the following formula (J-2b):