

DESCRIPTION

PROCESS FOR PRODUCING ALPHA-KETOCARBOXYLIC ACID

5 TECHNICAL FIELD

[0001]

The present application is filed, claiming the priorities based on the Japanese Patent Application Nos. 2010-144589 (filed on June 25, 2010) and 2010-187917 (filed
10 on August 25, 2010), and a whole of the contents of these applications is incorporated herein by reference.

The present invention relates to a process for producing an α -ketocarboxylic acid.

15 BACKGROUND ART

[0002]

Alpha-ketocarboxylic acids are known as useful compounds for an intermediate in the preparation of pharmaceuticals and agrichemicals since α -ketocarboxylic
20 acids can be converted to α -amino acids by reductive amination.

[0003]

As a process for producing an α -ketocarboxylic acid, a process in which phenylglyoxal as an α -ketoaldehyde is
25 oxidized with concentrated sulfuric acid and sodium nitrite

to obtain benzoylformic acid, is disclosed in J. Mol. Catal. A: Chemical, 2005, 235, pp.17-25. In addition, a process in which phenylglyoxal is oxidized with dimethyldioxolan to obtain benzoylformic acid, is disclosed in Org. Biomol. Chem., 2005, 3, pp.2310-2318.

DISCLOSURE OF INVENTION

PROBLEM TO BE SOLVED BY THE INVENTION

[0004]

10 An object of the present invention is to provide a new process for producing an α -ketocarboxylic acid.

MEANS FOR SOLVING THE PROBLEM

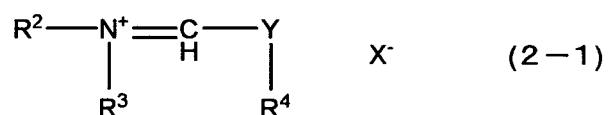
[0005]

15 As a result of the present inventors' intensive studies for solving the above-described problem, the present invention is accomplished.

[0006]

The present invention provides the followings:

20 [1] A process for producing an α -ketocarboxylic acid, comprising a step of oxidizing an α -ketoaldehyde by mixing a base, carbon dioxide, the α -ketoaldehyde and a compound represented by formula (2-1):



wherein

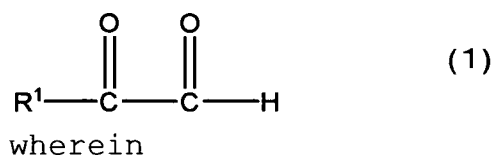
R^2 is an alkyl group optionally having a substituent or an aryl group optionally having a substituent;

R^3 and R^4 are independently an alkyl group optionally having a substituent or an aryl group optionally having a substituent, or R^3 and R^4 combine together to form a divalent hydrocarbon group optionally having a substituent or a group of $-\text{CH}=\text{N}-$ optionally having a substituent;

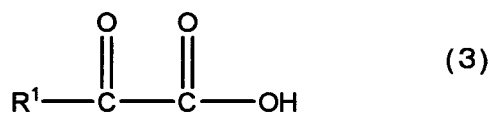
Y is a group of $-\text{S}-$ or $-\text{N}(\text{R}^5)-$, in which R^5 is an alkyl group optionally having a substituent or an aryl group optionally having a substituent, or R^5 combines together with R^4 to form a divalent hydrocarbon group optionally having a substituent; and

X^- is an anion.

[2] The process according to the above item [1], wherein the α -ketoaldehyde is a compound represented by formula (1):

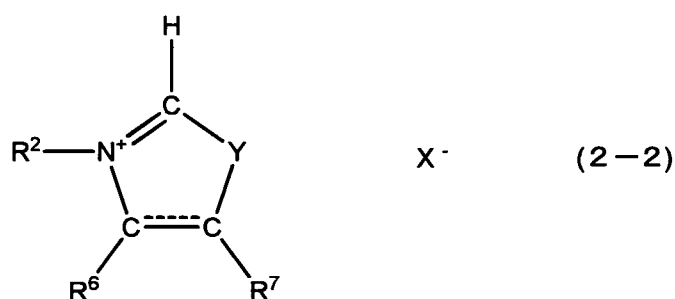


R^1 is a hydrocarbon group optionally having a substituent or a heteroaryl group optionally having a substituent, and wherein the α -ketocarboxylic acid is a compound represented by formula (3):



wherein R^1 means the same as defined above.

[3] The process according to the above item [1] or [2], wherein the compound represented by the formula (2-1) is a compound represented by formula (2-2):



5 wherein

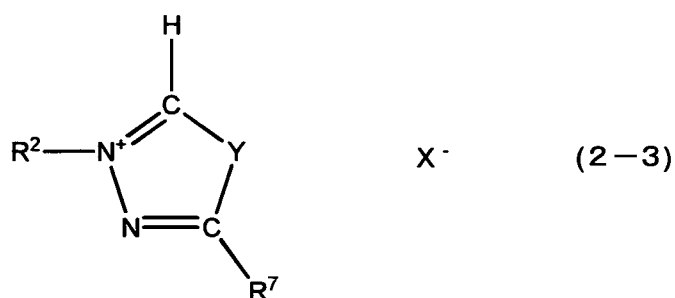
R^2 and Y mean the same as defined above;

R^6 and R^7 are independently a hydrogen atom, an alkyl group optionally having a substituent or an aryl group optionally having a substituent, or R^6 and R^7 are bonded to each other to form a ring together with carbon atoms to which they attach, or R^7 combines together with R^5 to form a divalent hydrocarbon group optionally having a substituent;

$\text{C} \equiv \text{C}$ represents a carbon-carbon single bond or a carbon-carbon double bond; and

15 X^- means the same as defined above,

or a compound represented by formula (2-3):



wherein

R^2 and Y mean the same as defined above;

R^7 is a hydrogen atom, an alkyl group optionally having a substituent or an aryl group optionally having a substituent, or R^7 combines together with R^5 to form a divalent hydrocarbon group optionally having a substituent; and

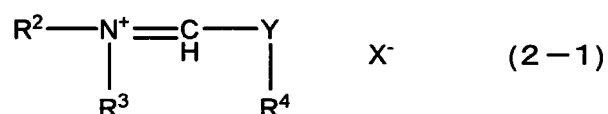
X^- means the same as defined above.

[4] The process according to the above item [3], wherein the compound represented by the formula (2-1) is a compound represented by the formula (2-2).

[5] The process according to the above item [4], wherein in the formula (2-2) Y is a group of $-N(R^5)-$, R^2 and R^5 are independently a 2,6-disubstituted phenyl group, R^6 and R^7 are both a hydrogen atom, and $C \equiv C$ represents a carbon-carbon double bond.

[6] The process according to any one of the above items [1] to [5], wherein the base is at least one base selected from the group consisting of organic bases, alkali metal carbonates and alkaline earth metal carbonates.

[7] A process for producing an α -ketocarboxylic acid, comprising a step of oxidizing an α -ketoaldehyde in the presence of carbon dioxide and a compound obtained by bringing a base into contact with a compound represented by formula (2-1):



wherein

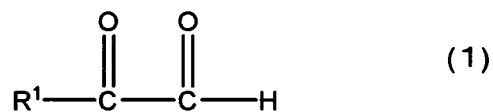
R^2 is an alkyl group optionally having a substituent or an aryl group optionally having a substituent;

R^3 and R^4 are independently an alkyl group optionally having a substituent or an aryl group optionally having a substituent, or R^3 and R^4 combine together to form a divalent hydrocarbon group optionally having a substituent or a group of $-\text{CH}=\text{N}-$ optionally having a substituent;

Y is a group of $-\text{S}-$ or $-\text{N}(\text{R}^5)-$, in which R^5 is an alkyl group optionally having a substituent or an aryl group optionally having a substituent, or R^5 combines together with R^4 to form a divalent hydrocarbon group optionally having a substituent; and

X^- is an anion.

[8] The process according to the above item [7], wherein the α -ketoaldehyde is a compound represented by formula (1):

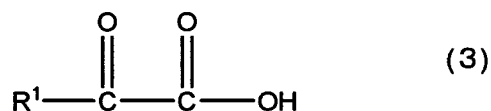


wherein

R¹ is a hydrocarbon group optionally having a substituent or a heteroaryl group optionally having a substituent,

and wherein the α-ketocarboxylic acid is a compound

5 represented by formula (3):

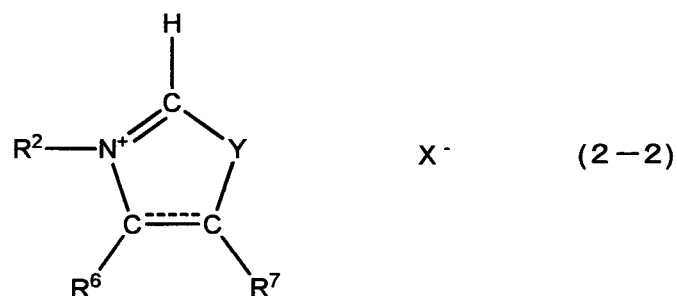


wherein R¹ means the same as defined above.

[9] The process according to the above item [7] or [8],

wherein the compound represented by the formula (2-1) is a

compound represented by formula (2-2):



10 wherein

R² and Y mean the same as defined above;

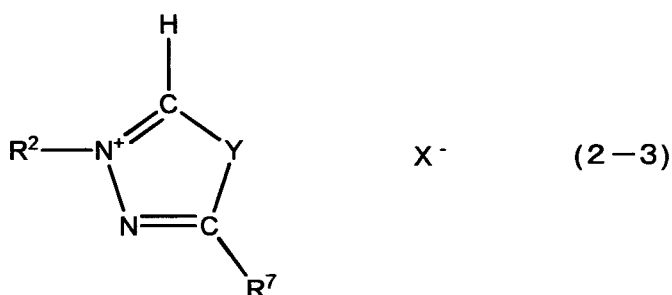
R⁶ and R⁷ are independently a hydrogen atom, an alkyl group optionally having a substituent or an aryl group optionally having a substituent, or R⁶ and R⁷ are bonded to each other

15 to form a ring together with carbon atoms to which they attach, or R⁷ combines together with R⁵ to form a divalent hydrocarbon group optionally having a substituent;

$\text{C}\equiv\text{C}$ represents a carbon-carbon single bond or a carbon-carbon double bond; and

X^- means the same as defined above,

or a compound represented by formula (2-3):



5 wherein

R^2 and Y mean the same as defined above;

R^7 is a hydrogen atom, an alkyl group optionally having a substituent or an aryl group optionally having a substituent, or R^7 combines together with R^5 to form a
 10 divalent hydrocarbon group optionally having a substituent;
 and

X^- means the same as defined above.

[10] The process according to the above item [9], wherein
 the compound represented by the formula (2-1) is a compound
 15 represented by the formula (2-2).

[11] The process according to the above item [10], wherein
 in the formula (2-2) Y is a group of $-\text{N}(\text{R}^5)-$, R^2 and R^5 are
 independently a 2,6-disubstituted phenyl group, R^6 and R^7
 are both a hydrogen atom, and $\text{C}\equiv\text{C}$ represents a carbon-
 20 carbon double bond.

[12] The process according to any one of the above items [7] to [11], wherein the base is at least one base selected from the group consisting of organic bases, alkali metal carbonates and alkaline earth metal carbonates.

5 [0007]

According to the present invention, a new process for producing an α -ketocarboxylic acid can be provided.

MODES FOR CARRYING OUT THE INVENTION

10 [0008]

Hereinafter, the present invention will be described in detail.

[0009]

There is no limit in selection of the α -ketoaldehyde for use in the present invention if it is an aldehyde having a carbonyl group at α -position. As the α -ketoaldehyde, it is preferable to use a compound represented by the formula (1). Hereinafter, the compound represented by the formula (1) is sometimes referred to as a compound (1).

20 [0010]

As to R^1 in the formula (1), the hydrocarbon group optionally having a substituent may be an alkyl group optionally having a substituent, an alkenyl group optionally having a substituent and an aryl group

optionally having a substituent.

[0011]

As to R¹, the alkyl group may be linear or branched C₁-C₁₂ alkyl groups such as a methyl group, an ethyl group, a propyl group, an isopropyl group, a butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group, a pentyl group and a decyl group; and C₃-C₁₂ cycloalkyl groups such as a cyclopropyl group, a 2,2-dimethylcyclopropyl group, a cyclopentyl group, a cyclohexyl group and a menthyl group.

[0012]

Examples of the substituent which the alkyl group may have include a group selected from the following Group 1:

<Group 1>

- a C₁-C₁₀ alkoxy group optionally having a fluorine atom;
- a C₇-C₂₀ aralkyloxy group optionally having a C₁-C₁₀ alkoxy group;
- a C₇-C₂₀ aralkyloxy group having a C₆-C₁₀ aryloxy group;
- a C₆-C₁₀ aryloxy group optionally having a C₁-C₁₀ alkoxy group;
- a C₆-C₁₀ aryloxy group having a C₆-C₁₀ aryloxy group;
- a C₂-C₁₀ acyl group optionally having a C₁-C₁₀ alkoxy group;
- a C₁-C₁₀ alkylthio group;
- a C₂-C₁₀ alkoxycarbonyl group; and
- a halogen atom.

[0013]

In the Group 1, examples of the C₁-C₁₀ alkoxy group optionally having a fluorine atom include a methoxy group, an ethoxy group, a propoxy group, an isopropoxy group, a butoxy group, an isobutoxy group, a sec-butoxy group, a tert-butoxy group and a trifluoromethyloxy group.

Examples of the C₇-C₂₀ aralkyloxy group optionally having a C₁-C₁₀ alkoxy group include a benzyloxy group, a 4-methylbenzyloxy group and a 4-methoxybenzyloxy group.

Examples of the C₇-C₂₀ aralkyloxy group having a C₆-C₁₀ aryloxy group include a 3-phenoxybenzyloxy group.

Examples of the C₆-C₁₀ aryloxy group optionally having a C₁-C₁₀ alkoxy group include a phenoxy group, a 2-methylphenoxy group, a 4-methylphenoxy group and a 4-methoxyphenoxy group.

Examples of the C₆-C₁₀ aryloxy group having a C₆-C₁₀ aryloxy group include a 3-phenoxyphenoxy group.

Examples of the C₂-C₁₀ acyl group optionally having a C₁-C₁₀ alkoxy group include an acetyl group, a propionyl group, a benzylcarbonyl group, a 4-methylbenzylcarbonyl group, a 4-methoxybenzylcarbonyl group, a benzoyl group, 2-methylbenzoyl group, a 4-methylbenzoyl group and 4-methoxybenzoyl group.

Examples of the C₁-C₁₀ alkylthio group include a methylthio group, an ethylthio group and an isopropylthio

group.

Examples of the C₂-C₁₀ alkoxy carbonyl group include a methoxy carbonyl group and an ethoxy carbonyl group.

Examples of the halogen atom include a fluorine atom,
5 a chlorine atom and a bromine atom.

[0014]

Examples of the alkyl group having a group selected from Group 1 include a chloromethyl group, a fluoromethyl group, a trifluoromethyl group, a methoxymethyl group, an
10 ethoxymethyl group, a methoxyethyl group, a methoxycarbonylmethyl group, a 1-ethoxycarbonyl-2,2-dimethyl-3-cyclopropyl group and a 2-methylthioethyl.

[0015]

As to R¹, the alkenyl group may be linear or branched
15 C₂-C₁₂ alkenyl groups such as a vinyl group, a 1-propenyl group, 1-butenyl group, 2-methyl-1-propenyl group; and C₃-C₁₂ cycloalkenyl group such as 1-cyclohexenyl group.

Examples of the substituent which the alkenyl group may have include a group selected from the above Group 1.

20 [0016]

Examples of the alkenyl group having a group selected from Group 1 include a 2-chlorovinyl group and a 2-trifluoromethylvinyl group.

[0017]

25 As to R¹, the aryl group may be C₆-C₂₀ aryl groups such

as a phenyl group, a 2-methylphenyl group, a 4-methylphenyl group, a 1-naphthyl group, a 2-naphthyl group and a styryl group.

[0018]

5 Examples of the substituent which the aryl group may have include a group selected from the following Group 2:

<Group 2>

a C₁-C₁₀ alkoxy group optionally having a fluorine atom or a C₁-C₁₀ alkoxy group;

10 a C₆-C₁₀ aryloxy group optionally having a C₁-C₁₀ alkoxy group;

a C₆-C₁₀ aryloxy group having a C₆-C₁₀ aryloxy group;

a C₂-C₁₀ acyl group optionally having a C₁-C₁₀ alkoxy group;

a C₁-C₆ alkylenedioxy group;

15 a nitro group; and

a halogen atom.

[0019]

In the Group 2, examples of the C₁-C₁₀ alkoxy group optionally having a fluorine atom or a C₁-C₁₀ alkoxy group
20 include a methoxy group, an ethoxy group, a propoxy group, an isopropoxy group, a butoxy group, an isobutoxy group, a sec-butoxy group, a tert-butoxy group, a pentyloxy group, a cyclopentyloxy group, fluoromethoxy group, a trifluoromethoxy group, a methoxymethoxy group, an
25 ethoxymethoxy group and a methoxyethoxy group.

Examples of the C₆-C₁₀ aryloxy group optionally having a C₁-C₁₀ alkoxy group include a phenoxy group, a 2-methylphenoxy group, a 4-methylphenoxy group and a 4-methoxyphenoxy group.

5 Examples of the C₆-C₁₀ aryloxy group having a C₆-C₁₀ aryloxy group include a 3-phenoxyphenoxy group.

 Examples of the C₂-C₁₀ acyl group optionally having a C₁-C₁₀ alkoxy group include an acetyl group, a propionyl group, a benzylcarbonyl group, a 4-methylbenzylcarbonyl group and a 4-methoxybenzylcarbonyl group.

10

 Examples of the C₁-C₆ alkylenedioxy group include a methylenedioxy group and an ethylendioxy group.

 Examples of the halogen atom include a fluorine atom and a chlorine atom.

15 [0020]

 Examples of the aryl group having a group selected from Group 2 include a 4-chlorophenyl group, a 4-methoxyphenyl group and a 3-phenoxyphenyl group.

[0021]

20 As to R¹, the heteroaryl group may be C₄-C₁₀ heteroaryl group which has at least one hetero atom such as a nitrogen atom, an oxygen atom and a sulfur atom. The specific examples of the heteroaryl group include a 2-pyridyl group, a 3-pyridyl group, a 4-pyridyl group, a 2-furyl group, a 3-furyl group, a 5-methyl-2-furyl group and 2-chloro-3-

25

pyridinyl group.

[0022]

Examples of the compound (1) include phenylglyoxal, 4-chlorophenylglyoxal, 2-methylphenylglyoxal, 4-fluorophenylglyoxal, 2-methoxyphenylglyoxal, 2,4-dichlorophenylglyoxal, 2-nitrophenylglyoxal, 2-naphthylglyoxal, 2-pyridineglyoxylaldehyde, methylglyoxal, ethylglyoxal, n-propylglyoxal, isopropylglyoxal, cyclohexylglyoxal, 4-(methylthio)-2-oxo-1-butanal, vinylglyoxal and styrylglyoxal.

As the compound (1), a commercially available product may be used. And also the compound (1) can be synthesized according to a known method, such as a method in which ketoalcohol is oxygen oxidized in the presence of a metal catalyst. Such method can be found in JP 2000-336055 A, for example.

[0023]

The step of oxidizing an α -ketoaldehyde (hereinafter sometimes referred to as "the present reaction") may be carried out by mixing a base, carbon dioxide, an α -ketoaldehyde and a compound represented by the formula (2-1). The present reaction may be carried out in the presence of carbon dioxide and a compound obtained by bringing a base into contact with a compound represented by the formula (2-1).

[0024]

Hereinafter, the compound represented by the formula (2-1) (hereinafter sometimes referred to as a compound (2-1)) for use in the present invention is described.

5 [0025]

As to R^3 and R^4 in the formula (2-1), the alkyl group may be linear or branched C_1 - C_{12} alkyl groups such as a methyl group, an ethyl group, a propyl group, an isopropyl group, a butyl group, an isobutyl group, a sec-butyl group, 10 a tert-butyl group, a pentyl group and a decyl group; and C_3 - C_{12} cycloalkyl groups such as a cyclopropyl group, a 2,2-dimethylcyclopropyl group, a cyclopentyl group, a cyclohexyl group and a menthyl group.

[0026]

15 Examples of the substituent which the alkyl group may have include a group selected from the following Group 3:

<Group 3>

a C_6 - C_{10} aryl group optionally having a C_1 - C_{10} alkoxy group;

a C_1 - C_{10} alkoxy group optionally having a fluorine atom;

20 a benzyloxy group optionally having at least one group selected from the group consisting of C_1 - C_{10} alkoxy group, C_1 - C_{10} alkyl group and C_6 - C_{10} aryloxy group;

a C_6 - C_{10} aryloxy group optionally having a C_1 - C_{10} alkoxy group;

25 a C_6 - C_{10} aryloxy group optionally having a C_6 - C_{10} aryloxy

group;

a C₂-C₁₀ acyl group optionally having a C₁-C₁₀ alkoxy group;

a carboxy group; and

a fluorine atom.

5 [0027]

In the Group 3, examples of the C₆-C₁₀ aryl group optionally having a C₁-C₁₀ alkoxy group include a phenyl group, a naphthyl group, 4-methylphenyl group and 4-methoxyphenyl group.

10 Examples of the C₁-C₁₀ alkoxy group optionally having a fluorine atom include a methoxy group, an ethoxy group, a propoxy group, an isopropoxy group, a butoxy group, an isobutoxy group, a sec-butoxy group, a tert-butoxy group and a trifluoromethyloxy group.

15 Examples of the benzyloxy group optionally having at least one group selected from the group consisting of C₁-C₁₀ alkoxy group, C₁-C₁₀ alkyl group and C₆-C₁₀ aryloxy group include a benzyloxy group, a 4-methylbenzyloxy group, a 4-methoxybenzyloxy group and a 3-phenoxybenzyloxy group.

20 Examples of the C₆-C₁₀ aryloxy group optionally having a C₁-C₁₀ alkoxy group include a phenoxy group, a 2-methylphenoxy group, a 4-methylphenoxy group and a 4-methoxyphenoxy group.

25 Examples of the C₆-C₁₀ aryloxy group having a C₆-C₁₀ aryloxy group include a 3-phenoxyphenoxy group.

Examples of the C₂-C₁₀ acyl group optionally having a C₁-C₁₀ alkoxy group include an acetyl group, a propionyl group, a benzylcarbonyl group, a 4-methylbenzylcarbonyl group, a 4-methoxybenzylcarbonyl group, a benzoyl group, 2-methylbenzoyl group, a 4-methylbenzoyl group and 4-methoxybenzoyl group.

[0028]

Examples of the alkyl group having a group selected from Group 3 include a fluoromethyl group, a trifluoromethyl group, a methoxymethyl group, an ethoxymethyl group, a methoxyethyl group, a benzyl group, a 4-fluorobenzyl group, a 4-methylbenzyl group, a phenoxyethyl group, a 2-oxopropyl group, a 2-oxobutyl group, a phenacyl group and a 2-carboxyethyl group.

[0029]

As to R³ and R⁴ in the formula (2-1), the aryl group may be C₆-C₁₀ aryl groups such as a phenyl group, a 2-methylphenyl group, a 4-methylphenyl group and a naphthyl group.

Examples of the substituent which the aryl group may have include a group selected from the above Group 2.

[0030]

Examples of the aryl group having a group selected from Group 2 include a 4-chlorophenyl group and 4-methoxyphenyl group.

[0031]

In the formula (2-1), R^3 and R^4 may combine together to form a divalent hydrocarbon group optionally having a substituent or a group of $-CH=N-$ optionally having a

5 substituent. Examples of the divalent hydrocarbon group include an ethylene group, a vinylidene group, a cyclopentane-1,2-diyl group, a cyclohexane-1,2-diyl group and an o-phenylene group. Examples of the substituent

which the divalent hydrocarbon group may have include an
10 alkyl group optionally having a substituent and an aryl group optionally having a substituent. Examples of the substituent which the group of $-CH=N-$ may have include an alkyl group optionally having a substituent and an aryl group optionally having a substituent. Examples of the

15 alkyl group include linear or branched C_1 - C_{12} alkyl groups such as a methyl group, an ethyl group, a propyl group, an isopropyl group, a butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group, a pentyl group and a decyl group; and C_3 - C_{12} cycloalkyl groups such as a cyclopropyl
20 group, a 2,2-dimethylcyclopropyl group, a cyclopentyl group, a cyclohexyl group and a menthyl group. Examples of the aryl group include C_6 - C_{10} aryl groups such as a phenyl group, a 2-methylphenyl group, a 4-methylphenyl group and a naphthyl group.

25 [0032]

As to R^2 and R^5 in the formula (2-1), the alkyl group may be linear or branched C_1 - C_{12} alkyl groups such as a methyl group, an ethyl group, a propyl group, an isopropyl group, a butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group, a pentyl group, a tert-pentyl group and a decyl group; and C_3 - C_{12} cycloalkyl groups such as a cyclopropyl group, a 2,2-dimethylcyclopropyl group, a cyclopentyl group, a cyclohexyl group, a menthyl group and an adamantyl group.

10 [0033]

Examples of the substituent which the alkyl group may have include a group selected from the following Group 4:

<Group 4>

a C_6 - C_{10} aryl group optionally having a C_1 - C_{10} alkoxy group;

15 a C_1 - C_{10} alkoxy group optionally having a fluorine atom;

a C_7 - C_{20} aralkyloxy group optionally having a C_1 - C_{10} alkoxy group;

a C_7 - C_{20} aralkyloxy group having a C_6 - C_{10} aryloxy group;

20 a C_6 - C_{10} aryloxy group optionally having a C_1 - C_{10} alkoxy group;

a C_6 - C_{10} aryloxy group having a C_6 - C_{10} aryloxy group; and

a C_2 - C_{10} acyl group optionally having a C_1 - C_{10} alkoxy group.

[0034]

25 In the Group 4, examples of the C_6 - C_{10} aryl group optionally having a C_1 - C_{10} alkoxy group include a phenyl

group, a naphthyl group, 4-methylphenyl group and 4-methoxyphenyl group.

Examples of the C₁-C₁₀ alkoxy group optionally having a fluorine atom include a methoxy group, an ethoxy group, a propoxy group, an isopropoxy group, a butoxy group, an isobutoxy group, a sec-butoxy group, a tert-butoxy group and a trifluoromethyloxy group.

Examples of the C₇-C₂₀ aralkyloxy group optionally having a C₁-C₁₀ alkoxy group include a benzyloxy group, a 4-methylbenzyloxy group and a 4-methoxybenzyloxy group.

Examples of the C₇-C₂₀ aralkyloxy group having a C₆-C₁₀ aryloxy group include a 3-phenoxybenzyloxy group.

Examples of the C₆-C₁₀ aryloxy group optionally having a C₁-C₁₀ alkoxy group include a phenoxy group, a 2-methylphenoxy group, a 4-methylphenoxy group and a 4-methoxyphenoxy group.

Examples of the C₆-C₁₀ aryloxy group having a C₆-C₁₀ aryloxy group include a 3-phenoxyphenoxy group.

Examples of the C₂-C₁₀ acyl group optionally having a C₁-C₁₀ alkoxy group include an acetyl group, a propionyl group, a benzylcarbonyl group, a 4-methylbenzylcarbonyl group, a 4-methoxybenzylcarbonyl group, a benzoyl group, 2-methylbenzoyl group, a 4-methylbenzoyl group and 4-methoxybenzoyl group.

[0035]

Examples of the alkyl group having a group selected from Group 4 include a methoxymethyl group, an ethoxymethyl group, a methoxyethyl group, a benzyl group, 4-fluorobenzyl group, a 4-methylbenzyl group, a phenoxymethyl group, a 2-oxopropyl group, 2-oxobutyl group and a phenacyl group.

[0036]

As to R^2 and R^5 in the formula (2-1), the aryl group may be C_6 - C_{20} aryl groups such as a phenyl group, a naphthyl group, a 2-methylphenyl group, a 4-methylphenyl group, a 2,6-dimethylphenyl group, a 2,4,6-trimethylphenyl group and a 2,6-diisopropylphenyl group.

[0037]

Examples of the substituent which the aryl group may have include a group selected from the following Group 5:

15 <Group 5>

a C_1 - C_{10} alkoxy group optionally having a fluorine atom or a C_1 - C_{10} alkoxy group; and
a halogen atom.

[0038]

20 In the Group 5, examples of the C_1 - C_{10} alkoxy group optionally having a fluorine atom or a C_1 - C_{10} alkoxy group include a methoxy group, an ethoxy group, a propoxy group, an isopropoxy group, a butoxy group, an isobutoxy group, a sec-butoxy group, a tert-butoxy group, a pentyloxy group, a
25 cyclopentyloxy group, fluoromethoxy group, a

trifluoromethoxy group, a methoxymethoxy group, an ethoxymethoxy group and a methoxyethoxy group.

Examples of the halogen atom include a fluorine atom and a chlorine atom.

5 [0039]

Examples of the aryl group having a group selected from Group 5 include a 4-chlorophenyl group, a 4-methoxyphenyl group and a 2,6-dichlorophenyl group.

[0040]

10 In the formula (2-1), R^4 and R^5 may combine together to form a divalent hydrocarbon group optionally having a substituent. Examples of the divalent hydrocarbon group include polymethylene groups such as an ethylene group, a trimethylene group and a tetramethylene group, a vinylidene
15 group, a cyclopentane-1,2-diyl group, a cyclohexane-1,2-diyl group and an o-phenylene group. Examples of the substituent which the divalent hydrocarbon group may have include an alkyl group optionally having a substituent and an aryl group optionally having a substituent. Examples of
20 the alkyl group include linear or branched C_1 - C_{12} alkyl groups such as a methyl group, an ethyl group, a propyl group, an isopropyl group, a butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group, a pentyl group and a decyl group; and C_3 - C_{12} cycloalkyl groups such as a
25 cyclopropyl group, a 2,2-dimethylcyclopropyl group, a

cyclopentyl group, a cyclohexyl group and a menthyl group. Examples of the aryl group include C₆-C₁₀ aryl groups such as a phenyl group, a 2-methylphenyl group, a 4-methylphenyl group and a naphthyl group.

5 [0041]

In the formula (2-1), the anion represented by X⁻ may be halide ion such as a chloride ion, a bromide ion and an iodide ion; alkanesulfonate ions optionally having a fluorine atom, such as a methanesulfonate and a trifluoromethanesulfonate; acetate ions optionally having a halogen atom, such as a trifluoroacetate and a trichloroacetate; a nitrate ion; a perchlorate ion; tetrahaloborate ions such as a tetrafluoroborate and a tetrachloroborate; hexahalophosphate ions such as a hexafluorophosphate; hexahaloantimonate ions such as a hexafluoroantimonate and a hexachloroantimonate; pentahalostannate ions such as a pentafluorostannate and a pentachlorostannate; and tetraarylborate ion optionally having a substituent, such as a tetraphenylborate, a tetrakis(pentafluorophenyl)borate, a tetrakis[3,5-bis(trifluoromethyl)phenyl]borate.

[0042]

The compound (2-1) is preferably a compound represented by the formula (2-2) (hereinafter sometimes referred to as a compound (2-2)) or a compound represented

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by the formula (2-3) (hereinafter sometimes referred to as a compound (2-3)), more preferably a compound (2-2).

[0043]

The present reaction is carried out preferably by
5 mixing the compound (2-2) or (2-3), a base, carbon dioxide
and an α -ketoaldehyde. More preferably, the present
reaction is carried out by mixing the compound (2-2), a
base, carbon dioxide and an α -ketoaldehyde. In addition,
the present reaction is carried out preferably in the
10 presence of carbon dioxide and a compound obtained by
bringing a base into contact with the compound (2-2) or (2-
3), more preferably in the presence of carbon dioxide and a
compound obtained by bringing a base into contact with the
compound (2-2).

15 Hereinafter, the compounds (2-2) and (2-3) will be
described.

[0044]

In the formulae (2-2) and (2-3), R^2 and Y mean the
same as defined in the formula (2-1). When Y is a group of
20 $-N(R^5)-$ in the formulae (2-2) and (2-3), R^5 means the same
as defined in the formula (2-1). X^- means the same as
defined in the formula (2-1).

[0045]

In the formulae (2-2) and (2-3), Y is preferably a
25 group of $-N(R^5)-$.

[0046]

In the formula (2-2), it is preferred that at least one of R^2 and R^5 is a bulky group. More preferably, R^2 and R^5 are both a bulky group. R^2 and R^5 may be the same group
5 or may be a different group from each other.

[0047]

As to R^2 and R^5 , examples of the bulky group include C_4 - C_{12} tertiary alkyl groups such as a tert-butyl group and a tert-pentyl group; C_3 - C_{10} cycloalkyl groups such as a
10 cyclopropyl group, a 2,2-dimethylcyclopropyl group, a cyclopentyl group, a cyclohexyl group, a menthyl group and an adamantyl group; phenyl groups having substituents at least on 2-position and 6-position, i.e. 2,6-disubstituted phenyl group, such as a 2,6-dimethylphenyl group, a 2,6-
15 dichlorophenyl group, 2,4,6-trimethylphenyl group and 2,6-diisopropylphenyl group; and naphthyl groups having a C_1 - C_{10} alkyl group at 2-position, such as a 2-methylnaphthyl group. As the substituent included in 2,6-disubstituted phenyl group, a C_1 - C_{12} alkyl group and halogen atoms are
20 exemplified.

The bulky group is preferably a tert-butyl group, a tert-pentyl group, a cyclohexyl group, an adamantyl group or a 2,6-disubstituted phenyl group, more preferably a 2,6-disubstituted phenyl group, still more preferably a 2,6-
25 diisopropylphenyl group.

[0048]

As to R^6 in the formula (2-2) and R^7 in the formulae (2-2) and (2-3), the alkyl group may be linear or branched C_1 - C_{10} alkyl groups such as a methyl group, an ethyl group, a propyl group, an isopropyl group, a butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group, a pentyl group and a decyl group; and C_3 - C_{10} cycloalkyl groups such as a cyclopropyl group, a 2,2-dimethylcyclopropyl group, a cyclopentyl group, a cyclohexyl group and a menthyl group.

Examples of the substituent which the alkyl group may have include a group selected from the above Group 3.

Examples of the alkyl group having a group selected from Group 3 include a fluoromethyl group, a trifluoromethyl group, a methoxymethyl group, an ethoxymethyl group, a methoxyethyl group, a benzyl group, a 4-fluorobenzyl group, a 4-methylbenzyl group, a phenoxymethyl group, a 2-oxopropyl group, a 2-oxobutyl group, a phenacyl group and a 2-carboxyethyl group.

[0049]

As to R^6 in the formula (2-2) and R^7 in the formulae (2-2) and (2-3), the aryl group may be C_6 - C_{10} aryl groups such as a phenyl group, a 2-methylphenyl group, a 4-methylphenyl group and a naphthyl group.

Examples of the substituent which the aryl group may

have include a group selected from the above Group 2.

Examples of the aryl group having a group selected from Group 2 include a 4-chlorophenyl group and a 4-methoxyphenyl group.

5 [0050]

In the formula (2-2), R^6 and R^7 may be bonded to each other to form a ring together with carbon atoms to which they attach. Examples of such a ring include a cyclopentane ring, a cyclohexane ring and a benzene ring.

10 [0051]

In the formula (2-2), preferably, R^6 and R^7 are independently a hydrogen atom or an alkyl group optionally having a substituent, more preferably, R^6 and R^7 are both a hydrogen atom.

15 [0052]

In the formulae (2-2) and (2-3), R^5 and R^7 may combine together to form a divalent hydrocarbon group optionally having a substituent. Examples of the divalent hydrocarbon group include polymethylene groups such as an ethylene group, a trimethylene group and a tetramethylene group, a vinylidene group, a cyclopentane-1,2-diyl group, a cyclohexane-1,2-diyl group and an o-phenylene group. Examples of the substituent which the divalent hydrocarbon group may have include an alkyl group optionally having a substituent and an aryl group optionally having a

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substituent. Examples of the alkyl group include linear or branched C₁-C₁₂ alkyl groups such as a methyl group, an ethyl group, a propyl group, an isopropyl group, a butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group, a pentyl group and a decyl group; and C₃-C₁₂ cycloalkyl groups such as a cyclopropyl group, a 2,2-dimethylcyclopropyl group, a cyclopentyl group, a cyclohexyl group and a menthyl group. Examples of the aryl group include C₆-C₁₀ aryl groups such as a phenyl group, a 2-methylphenyl group, a 4-methylphenyl group and a naphthyl group.

[0053]

In the formula (2-2), $\text{C}=\text{C}$ preferably represents a carbon-carbon double bond.

[0054]

The specific examples of the compound (2-2) include 1,3-di-tert-butylimidazolium chloride, 1,3-di-tert-butylimidazolinium chloride, 1,3-dicyclohexylimidazolium chloride, 1,3-dicyclohexylimidazolinium chloride, 1,3-diadamantylimidazolium chloride, 1,3-diadamantylimidazolinium chloride, 1,3-diphenylimidazolium chloride, 1,3-diphenylimidazolinium chloride, 1,3-bis[(2,6-diisopropyl)phenyl]imidazolium chloride, 1,3-bis[(2,6-diisopropyl)phenyl]imidazolinium chloride, 1,3-bis[(2,4,6-trimethyl)phenyl]imidazolium chloride, 1,3-bis[(2,4,6-

trimethyl)phenyl]imidazolinium chloride,
4,5-dimethyl-1,3-bis[(2,4,6-trimethyl)phenyl]imidazolium
chloride, 4,5-dimethyl-1,3-bis[(2,4,6-
trimethyl)phenyl]imidazolinium chloride, 4,5-dimethyl-1,3-
5 bis[(2,6-diisopropyl)phenyl]imidazolium chloride, 4,5-
dimethyl-1,3-bis[(2,6-diisopropyl)phenyl]imidazolinium
chloride, 4,5-dichloro-1,3-bis[(2,6-
diisopropyl)phenyl]imidazolium chloride, 4,5-dichloro-1,3-
bis[(2,6-diisopropyl)phenyl]imidazolinium chloride, 4,5-
10 diphenyl-1,3-bis[(2,4,6-trimethyl)phenyl]imidazolium
chloride, 4,5-diphenyl-1,3-bis[(2,4,6-
trimethyl)phenyl]imidazolinium chloride,
4,5-difluoro-1,3-bis[(2,6-diisopropyl)phenyl]imidazolium
chloride, 4,5-difluoro-1,3-bis[(2,6-
15 diisopropyl)phenyl]imidazolinium chloride, 4-methyl-1,3-
bis[(2,4,6-trimethyl)phenyl]imidazolium chloride, 4-methyl-
1,3-bis[(2,4,6-trimethyl)phenyl]imidazolinium chloride,
1,3-bis[(2,6-dichlor)phenyl]imidazolium chloride, 1,3-
bis[(2,6-dichlor)phenyl]imidazolinium chloride, 1-tert-
20 butyl-3-phenylimidazolium chloride, 1-tert-butyl-3-
phenylimidazolinium chloride, 1-cyclohexyl-3-[(2,6-
diisopropyl)phenyl]imidazolium chloride, 1-cyclohexyl-3-
[(2,6-diisopropyl)phenyl]imidazolinium chloride, 1-phenyl-
3-[(2,4,6-trimethyl)phenyl]imidazolium chloride, 1-phenyl-
25 3-[(2,4,6-trimethyl)phenyl]imidazolinium chloride, 1-tert-

butyl-3-[(2,6-diisopropyl)phenyl]imidazolium chloride, 1-
tert-butyl-3-[(2,6-diisopropyl)phenyl]imidazolinium
chloride, 1-tert-butyl-3-[(2,4,6-
trimethyl)phenyl]imidazolium chloride, 1-tert-butyl-3-
5 [(2,4,6-trimethyl)phenyl]imidazolinium chloride, 3-(2,6-
diisopropyl)phenyl-4,5-dimethylthiazolium chloride, 3-
phenyl-4,5-dimethylthiazolium chloride, 3-benzylthiazolium
chloride and 3-(2,4,6-trimethyl)phenyl-4,5-
dimethylthiazolium chloride.

10 [0055]

The specific examples of the compound (2-3) include
1,4-dimethyl-1H-1,2,4-triazol-4-ium chloride, 1,3,4-
triphenyl-1H-1,2,4-triazol-4-ium chloride and 6,7-dihydro-
2-pentafluorophenyl-5H-pyrrolo[2,1-c]-1,2,4-triazolium
15 chloride.

[0056]

In addition, as the compounds (2-2) and (2-3), the
compounds in which "chloride" of the above compounds is
substituted by "iodide", "bromide", "methanesulfonate",
20 "trifluoromethanesulfonate", "nitrate", "perchlorate",
"tetrafluoroborate", "tetrachloroborate",
"hexafluorophosphate", "hexafluoroantimonate",
"hexachloroantimonate", "pentafluorostannate",
"pentachlorostannate", "tetraphenylborate",
25 "tetrakis(pentafluorophenyl)borate" or "tetrakis[3,5-

bis(trifluoromethyl)phenyl]borate" are exemplified.

[0057]

As the compound (2-1), a commercially available product may be used. And also the compound (2-1) can be
5 synthesized according to the methods described in J. Organometallic. Chem. Soc., 606, 49 (2000), J. Organometallic. Chem. Soc., 73, 2784 (2008), or the like.

[0058]

The amount of the compound (2-1) to be used is
10 preferably from 0.001 to 0.5 mol, more preferably from 0.01 to 0.3 mol per mole of α -ketoaldehyde.

[0059]

The base for use in the present reaction is preferably at least one base selected from the group consisting of
15 organic bases, alkali metal carbonates and alkaline earth metal carbonates.

[0060]

Examples of the organic bases include tertiary amine such as triethylamine, trioctylamine, diisopropylethylamine
20 and 4-dimethylaminopyridine; nitrogen-containing alicyclic compounds such as 1,8-diazabicyclo[5.4.0]-7-undecene and 1,5,7-triazabicyclo[4.4.0]-5-decene; nitrogen-containing aromatic compounds such as pyridine and imidazole; and alkali metal alkoxide such as sodium methoxide and sodium
25 ethoxide.

Examples of the alkali metal carbonates include sodium carbonate, sodium bicarbonate, potassium carbonate, potassium bicarbonate, lithium carbonate and lithium bicarbonate.

5 Examples of the alkaline earth metal carbonates include magnesium carbonate and calcium carbonate.

As the base for use in the present reaction, the organic bases are more preferable.

[0061]

10 The amount of the base to be used is usually from 0.001 to 3 mol, preferably from 0.001 to 0.5 mol, more preferably from 0.01 to 0.3 mol per mole of α -ketoaldehyde.

[0062]

15 The carbon dioxide for use in the present reaction may be in either form of gaseous carbon dioxide, a solid carbon dioxide (i.e. dry ice) or supercritical carbon dioxide. The gaseous carbon dioxide may be diluted with an inert gas such as nitrogen.

20 The amount of the carbon dioxide to be used is preferably one mole or more per mole of α -ketoaldehyde. Although the upper limit of the amount is not limited, it is usually 100 mol or less from the viewpoint of productivity.

[0063]

25 The present reaction may be carried out further in the

presence of a solvent.

There is no limit in selection of the organic solvent if it does not hinder the present reaction. Examples of the solvent include ether solvents such as tetrahydrofuran, methyl-tert-butyl ether, cyclopentyl methyl ether and diisopropyl ether; ester solvents such as ethyl acetate and butyl acetate; aromatic solvents such as toluene and chlorobenzene; nitrile solvents such as acetonitrile and propionitrile; and a mixture thereof.

The amount of the solvent to be used is usually 100 parts by weight or less per part by weight of α -ketoaldehyde, while this amount is not limited.

[0064]

In the present reaction, the order of blending the reactants is not limited. In the preferred embodiment, for example, α -ketoaldehyde, the compound (2-1) and carbon dioxide, optionally a solvent are mixed, and then, a base is added to the resultant mixture. This mixing is preferably carried out under an atmosphere of an inert gas such as nitrogen.

[0065]

The present reaction may be carried out under reduced pressure or normal pressure or increased pressure. Preferably, the present reaction is carried out under normal pressure or increased pressure.

[0066]

A temperature for the present reaction may vary depending on the kind and amount of the compound (2-1) and the base to be used, and is preferably from -20 to 150°C, more preferably from 0 to 100°C. When the reaction temperature is -20°C or higher, the oxidation reaction rate tends to become higher. When the reaction temperature is 150°C or lower, the oxidation reaction can be carried out with a higher selectivity.

10 [0067]

Progress of the present reaction can be confirmed by analytical means such as gas chromatography, high-performance liquid chromatography, thin-layer chromatography, nucleic magnetic resonance spectrum analysis, or infrared absorption spectrum analysis.

15 [0068]

After completion of the reaction, α -ketocarboxylic acid may be brought out by a procedure in which the resultant reaction mixture is optionally neutralized with mineral acid such as sulfuric acid, hydrochloric acid or the like and then concentrated and cooled. Alternatively, α -ketocarboxylic acid may be brought out by a procedure in which an aqueous alkali solution such as aqueous sodium hydroxide is added to the resultant reaction mixture to prepare an aqueous solution of an alkali salt of α -

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ketocarboxylic acid, and then the resulting aqueous alkaline salt solution is washed with a solvent immiscible to water and is then neutralized, and extracted and/or crystallized.

5 The solvent immiscible to water may be ester solvents such as ethyl acetate, and ether solvents such as methyl tert-butyl ether. The amount of the immiscible solvent to be used is not limited.

10 The obtained α -ketocarboxylic acid may be purified by distillation, column chromatography, crystallization or the like.

[0069]

According to the process of the present invention, for example, the following α -ketocarboxylic acids can be
15 produced: benzoylformic acid, 4-chloro-benzoylformic acid, 2-methylbenzoylformic acid, 4-fluoro-benzoylformic acid, 4-methoxy-benzoylformic acid, 2-nitro-benzoylformic acid, 2,4-dichloro-benzoylformic acid, 2-naphthoylformic acid, α -oxo-2-pyridineacetic acid, pyruvic acid, 2-oxobutanoic acid,
20 2-oxopentanoic acid, 3-methyl-2-oxobutanoic acid, α -oxo-cyclohexaneacetic acid, 4-(methylthio)-2-oxo-butanoic acid, 2-oxo-3-butenic acid and 2-oxo-4-phenyl-3-butenic acid.

EXAMPLES

25 [0070]

Hereinafter, the present invention will be described in more detail by way of Examples.

[0071]

(Example 1)

5 A 50 ml schrenck tube equipped with a magnetic rotor was charged with phenylglyoxal monohydrate (260 mg), 1,3-bis[(2,6-diisopropyl)phenyl]imidazolium chloride (50 mg) and tetrahydrofuran (5 g) under a nitrogen atmosphere, and the resulting mixture was stirred while maintaining the
10 temperature of the mixture in a water bath at 25°C. Dry ice (1.0 g) was added to the mixture, and 1,8-diazabicyclo[5,4,0]-7-undecene (23 mg) was further added thereto so as to initiate the reaction, and the mixture was stirred for 2 hours at a room temperature. At 30 minutes
15 and 1 hour following the start of reaction, dry ice (1 g) was added to the reaction mixture, respectively. After completion of the reaction, the solvent was distilled off from the reaction mixture to obtain a yellow solid containing benzoylformic acid.

20 [0072]

Determination of Yield

 Methanol (5 g) was added to the obtained yellow solid, and a 10% hexane solution of trimethylsilyldiazomethane was further added thereto, to obtain methyl benzoylformate.
25 A methanol solution containing the obtained methyl

benzoylformate was analyzed with a gas chromatography internal standard method to determine the yield of methyl benzoylformate from phenylglyoxal. As a result, the yield was 68%. In other words, benzoylformic acid was obtained
5 from phenylglyoxal at a yield of 68% or more.

[0073]

(Example 2)

A 100 ml stainless-steel pressure reaction tube equipped with a magnetic rotor was charged with
10 phenylglyoxal monohydrate (260 mg), 1,3-bis[(2,6-diisopropyl)phenyl]imidazolium chloride (50 mg) and tetrahydrofuran (5 g) under a nitrogen atmosphere, and the resulting mixture was cooled in a dry ice bath at -70°C. After dry ice (2 g) and potassium carbonate (520 mg) were
15 added to the cooled mixture, the pressure reaction tube was sealed. The reaction was carried out by stirring the resulting mixture for 2 hours at 60°C. After completion of the reaction, the solvent was distilled off from the reaction mixture to obtain a yellow solid containing
20 benzoylformic acid.

[0074]

Determination of Yield

Methanol (5 g) was added to the obtained yellow solid, and a 10% hexane solution of trimethylsilyldiazomethane was
25 further added thereto, to obtain methyl benzoylformate.

A methanol solution containing the obtained methyl benzoylformate was analyzed with a gas chromatography internal standard method to determine the yield of methyl benzoylformate from phenylglyoxal. As a result, the yield
5 was 35%. In other words, benzoylformic acid was obtained from phenylglyoxal at a yield of 35% or more.

[0075]

(Example 3)

A 100 ml stainless-steel pressure reaction tube
10 equipped with a magnetic rotor was charged with phenylglyoxal monohydrate (200 mg), 1,3-bis[(2,6-diisopropyl)phenyl]imidazolium chloride (30 mg) and tetrahydrofuran (5 g) under a nitrogen atmosphere, and the resulting mixture was cooled in a dry ice bath at -70°C.
15 After dry ice (2 g) and sodium bicarbonate (50 mg) were added to the cooled mixture, the pressure reaction tube was sealed. The reaction was carried out by stirring the resulting mixture for 6 hours at 60°C. After completion of the reaction, the solvent was distilled off from the
20 reaction mixture to obtain a yellow solid containing benzoylformic acid.

[0076]

Determination of Yield

Methanol (5 g) was added to the obtained yellow solid,
25 and a 10% hexane solution of trimethylsilyldiazomethane was

further added thereto, to obtain methyl benzoylformate. A methanol solution containing the obtained methyl benzoylformate was analyzed with a gas chromatography internal standard method to determine the yield of methyl benzoylformate from phenylglyoxal. As a result, the yield was 50%. In other words, benzoylformic acid was obtained from phenylglyoxal at a yield of 50% or more.

[0077]

(Example 4)

10 A 50 ml schrenck tube equipped with a magnetic rotor was charged with phenylglyoxal monohydrate (260 mg), 1,3-bis[(2,4,6-trimethyl)phenyl]imidazolinium tetrafluoroborate (50 mg) and tetrahydrofuran (5 g) under a nitrogen atmosphere, and the resulting mixture was stirred while
15 maintaining the temperature of the mixture in a water bath at 25°C. Dry ice (1.0 g) was added to the mixture, and 1,8-diazabicyclo[5,4,0]-7-undecene (23 mg) was further added thereto so as to initiate the reaction, and the mixture was stirred for 2 hours at a room temperature. At
20 30 minutes and 1 hour following the start of reaction, dry ice (1 g) was added to the reaction mixture, respectively. After completion of the reaction, the solvent was distilled off from the reaction mixture to obtain a yellow solid containing benzoylformic acid.

25 [0078]

Determination of Yield

Methanol (5 g) was added to the obtained yellow solid, and a 10% hexane solution of trimethylsilyldiazomethane was further added thereto, to obtain methyl benzoylformate.

5 A methanol solution containing the obtained methyl benzoylformate was analyzed with a gas chromatography internal standard method to determine the yield of methyl benzoylformate from phenylglyoxal. As a result, the yield was 9%. In other words, benzoylformic acid was obtained
10 from phenylglyoxal at a yield of 9% or more. 55% of phenylglyoxal used as the starting material was recovered.

[0079]

(Example 5)

A 100 ml stainless-steel pressure reaction tube
15 equipped with a magnetic rotor was charged with phenylglyoxal monohydrate (260 mg), 1,3-bis[(2,6-diisopropyl)phenyl]imidazolinium chloride (50 mg) and tetrahydrofuran (5 g) under a nitrogen atmosphere, and the resulting mixture was cooled in a dry ice bath at -70°C.
20 After dry ice (2 g) and 1,8-diazabicyclo[5,4,0]-7-undecene (23 mg) were added to the cooled mixture, the pressure reaction tube was sealed. The reaction was carried out by stirring the resulting mixture for 2 hours at 25°C. After completion of the reaction, the solvent was distilled off
25 from the reaction mixture to obtain a yellow solid

containing benzoylformic acid.

[0080]

Determination of Yield

Methanol (5 g) was added to the obtained yellow solid,
5 and a 10% hexane solution of trimethylsilyldiazomethane was
further added thereto, to obtain methyl benzoylformate.
A methanol solution containing the obtained methyl
benzoylformate was analyzed with a gas chromatography
internal standard method to determine the yield of methyl
10 benzoylformate from phenylglyoxal. As a result, the yield
was 7%. In other words, benzoylformic acid was obtained
from phenylglyoxal at a yield of 7% or more. 45% of
phenylglyoxal used as the starting material was recovered.

[0081]

15 (Example 6)

A 100 ml stainless-steel pressure reaction tube
equipped with a magnetic rotor was charged with
phenylglyoxal monohydrate (200 mg), 1,4-dimethyl-1H-1,2,4-
triazol-4-ium iodide (25 mg) and tetrahydrofuran (3 g)
20 under a nitrogen atmosphere, and the resulting mixture was
cooled in a dry ice bath at -70°C. After dry ice (2 g) and
triethylamine (10 mg) were added to the cooled mixture, the
pressure reaction tube was sealed. The reaction was
carried out by stirring the resulting mixture for 6 hours
25 at 60°C. After completion of the reaction, the solvent was

distilled off from the reaction mixture to obtain a yellow solid containing benzoylformic acid.

[0082]

Determination of Yield

5 Methanol (5 g) was added to the obtained yellow solid, and a 10% hexane solution of trimethylsilyldiazomethane was further added thereto, to obtain methyl benzoylformate. A methanol solution containing the obtained methyl benzoylformate was analyzed with a gas chromatography
10 internal standard method to determine the yield of methyl benzoylformate from phenylglyoxal. As a result, the yield was 25%. In other words, benzoylformic acid was obtained from phenylglyoxal at a yield of 25% or more.

[0083]

15 (Example 7)

 A 100 ml stainless-steel pressure reaction tube equipped with a magnetic rotor was charged with phenylglyoxal monohydrate (200 mg), 6,7-dihydro-2-pentafluorophenyl-5H-pyrrolo[2,1,c]-1,2,4-triazolium
20 tetrafluoroborate (27 mg) and tetrahydrofuran (3 g) under a nitrogen atmosphere, and the resulting mixture was cooled in a dry ice bath at -70°C. After dry ice (2 g) and 1,8-diazabicyclo[5,4,0]-7-undecene (10 mg) were added to the cooled mixture, the pressure reaction tube was sealed. The
25 reaction was carried out by stirring the resulting mixture

for 6 hours at 40°C. After completion of the reaction, the solvent was distilled off from the reaction mixture to obtain a yellow solid containing benzoylformic acid.

[0084]

5 Determination of Yield

Methanol (5 g) was added to the obtained yellow solid, and a 10% hexane solution of trimethylsilyldiazomethane was further added thereto, to obtain methyl benzoylformate. A methanol solution containing the obtained methyl benzoylformate was analyzed with a gas chromatography internal standard method to determine the yield of methyl benzoylformate from phenylglyoxal. As a result, the yield was 10%. In other words, benzoylformic acid was obtained from phenylglyoxal at a yield of 10% or more.

15 [0085]

(Example 8)

A 100 ml stainless-steel pressure reaction tube equipped with a magnetic rotor was charged with phenylglyoxal monohydrate (200 mg), 3-(2,6-diisopropyl)phenyl-4,5-dimethylthiazolium chloride (21 mg) and tetrahydrofuran (3 g) under a nitrogen atmosphere, and the resulting mixture was cooled in a dry ice bath at -70°C. After dry ice (2 g) and 1,8-diazabicyclo[5,4,0]-7-undecene (11 mg) were added to the cooled mixture, the pressure reaction tube was sealed. The reaction was carried out by

stirring the resulting mixture for 6 hours at 60°C. After completion of the reaction, the solvent was distilled off from the reaction mixture to obtain a yellow solid containing benzoylformic acid.

5 [0086]

Determination of Yield

Methanol (5 g) was added to the obtained yellow solid, and a 10% hexane solution of trimethylsilyldiazomethane was further added thereto, to obtain methyl benzoylformate.

10 A methanol solution containing the obtained methyl benzoylformate was analyzed with a gas chromatography internal standard method to determine the yield of methyl benzoylformate from phenylglyoxal. As a result, the yield was 9%. In other words, benzoylformic acid was obtained
15 from phenylglyoxal at a yield of 9% or more.

[0087]

(Example 9)

A 100 ml stainless-steel pressure reaction tube equipped with a magnetic rotor was charged with
20 methylglyoxal (150 mg), 1,3-bis[(2,6-diisopropyl)phenyl]imidazolium chloride (50 mg) and tetrahydrofuran (3 g) under a nitrogen atmosphere, and the resulting mixture was cooled in a dry ice bath at -70°C. After dry ice (2 g) and 1,8-diazabicyclo[5,4,0]-7-undecene
25 (11 mg) were added to the cooled mixture, the pressure

reaction tube was sealed. The reaction was carried out by stirring the resulting mixture for 2 hours at 25°C. After completion of the reaction, the solvent was distilled off from the reaction mixture to obtain a yellow solid
5 containing pyruvic acid.

[0088]

Determination of Yield

Methanol (5 g) was added to the obtained yellow solid, and a 10% hexane solution of trimethylsilyldiazomethane was
10 further added thereto, to obtain methyl pyruvate. A methanol solution containing the obtained methyl pyruvate was analyzed with a gas chromatography internal standard method to determine the yield of methyl pyruvate from methylglyoxal. As a result, the yield was 2%. In other
15 words, pyruvic acid was obtained from methylglyoxal at a yield of 2% or more.

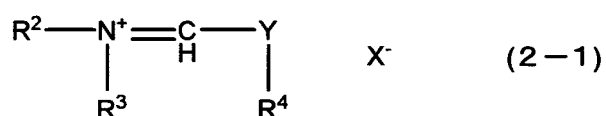
INDUSTRIAL APPLICABILITY

[0089]

20 The present invention is useful as a process for producing the α -ketocarboxylic acids which are known as useful compounds for an intermediate in the preparation of pharmaceuticals and agrichemicals since the α -ketocarboxylic acids can be converted to α -amino acids by
25 reductive amination.

CLAIMS

1. A process for producing an α -ketocarboxylic acid,
 comprising a step of oxidizing an α -ketoaldehyde by mixing
 5 a base, carbon dioxide, the α -ketoaldehyde and a compound
 represented by formula (2-1):



wherein

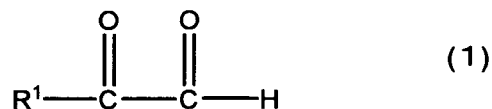
R^2 is an alkyl group optionally having a substituent or an
 aryl group optionally having a substituent;

10 R^3 and R^4 are independently an alkyl group optionally
 having a substituent or an aryl group optionally having a
 substituent, or R^3 and R^4 combine together to form a
 divalent hydrocarbon group optionally having a substituent
 or a group of $-\text{CH}=\text{N}-$ optionally having a substituent;

15 Y is a group of $-\text{S}-$ or $-\text{N}(\text{R}^5)-$, in which R^5 is an alkyl
 group optionally having a substituent or an aryl group
 optionally having a substituent, or R^5 combines together
 with R^4 to form a divalent hydrocarbon group optionally
 having a substituent; and

20 X^- is an anion.

2. The process according to claim 1, wherein the α -
 ketoaldehyde is a compound represented by formula (1):

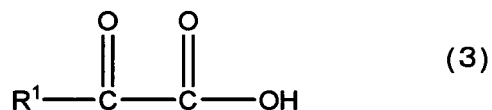


wherein

R^1 is a hydrocarbon group optionally having a substituent
or a heteroaryl group optionally having a substituent,

and wherein the α -ketocarboxylic acid is a compound

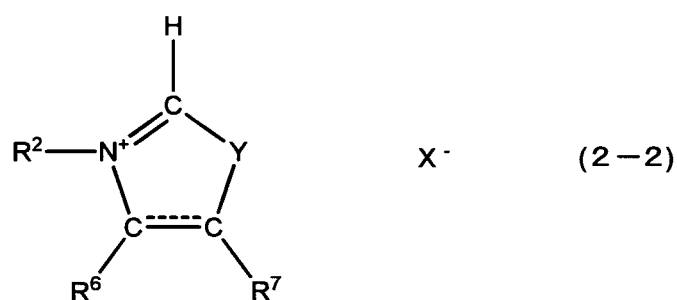
5 represented by formula (3):



wherein R^1 means the same as defined above.

3. The process according to claim 1 or 2, wherein the
compound represented by the formula (2-1) is a compound

10 represented by formula (2-2):



wherein

R^2 and Y mean the same as defined above;

R^6 and R^7 are independently a hydrogen atom, an alkyl group
optionally having a substituent or an aryl group optionally

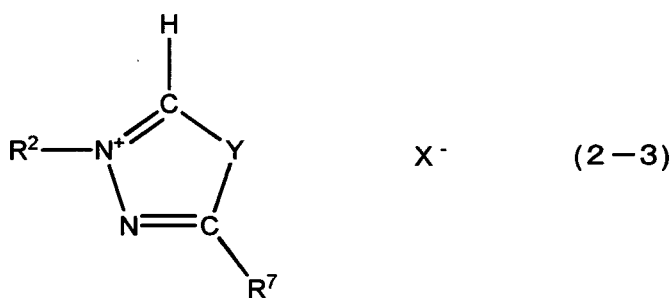
15 having a substituent, or R^6 and R^7 are bonded to each other
to form a ring together with carbon atoms to which they
attach, or R^7 combines together with R^5 to form a divalent

hydrocarbon group optionally having a substituent;

$\text{C}\equiv\text{C}$ represents a carbon-carbon single bond or a carbon-carbon double bond; and

X^- means the same as defined above,

5 or a compound represented by formula (2-3):



wherein

R^2 and Y mean the same as defined above;

R^7 is a hydrogen atom, an alkyl group optionally having a substituent or an aryl group optionally having a substituent, or R^7 combines together with R^5 to form a divalent hydrocarbon group optionally having a substituent; and

10

X^- means the same as defined above.

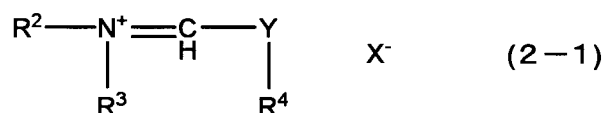
15 4. The process according to claim 3, wherein the compound represented by the formula (2-1) is a compound represented by the formula (2-2).

5. The process according to claim 4, wherein in the formula
20 (2-2) Y is a group of $-\text{N}(\text{R}^5)-$, R^2 and R^5 are independently a

2,6-disubstituted phenyl group, R^6 and R^7 are both a hydrogen atom, and $C \equiv C$ represents a carbon-carbon double bond.

5 6. The process according to claim 1, wherein the base is at least one base selected from the group consisting of organic bases, alkali metal carbonates and alkaline earth metal carbonates.

10 7. A process for producing an α -ketocarboxylic acid, comprising a step of oxidizing an α -ketoaldehyde in the presence of carbon dioxide and a compound obtained by bringing a base into contact with a compound represented by formula (2-1):



15 wherein

R^2 is an alkyl group optionally having a substituent or an aryl group optionally having a substituent;

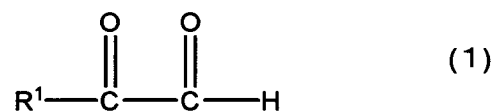
R^3 and R^4 are independently an alkyl group optionally having a substituent or an aryl group optionally having a substituent, or R^3 and R^4 combine together to form a divalent hydrocarbon group optionally having a substituent or a group of $-CH=N-$ optionally having a substituent;

20 Y is a group of $-S-$ or $-N(R^5)-$, in which R^5 is an alkyl

group optionally having a substituent or an aryl group optionally having a substituent, or R⁵ combines together with R⁴ to form a divalent hydrocarbon group optionally having a substituent; and

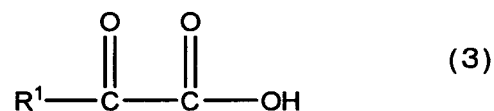
5 X⁻ is an anion.

8. The process according to claim 7, wherein the α-ketoaldehyde is a compound represented by formula (1):



wherein

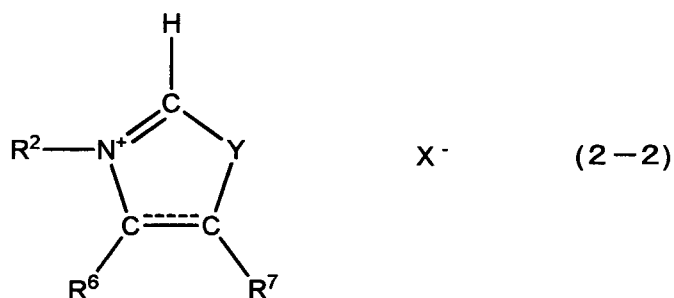
10 R¹ is a hydrocarbon group optionally having a substituent or a heteroaryl group optionally having a substituent, and wherein the α-ketocarboxylic acid is a compound represented by formula (3):



wherein R¹ means the same as defined above.

15

9. The process according to claim 7 or 8, wherein the compound represented by the formula (2-1) is a compound represented by formula (2-2):



wherein

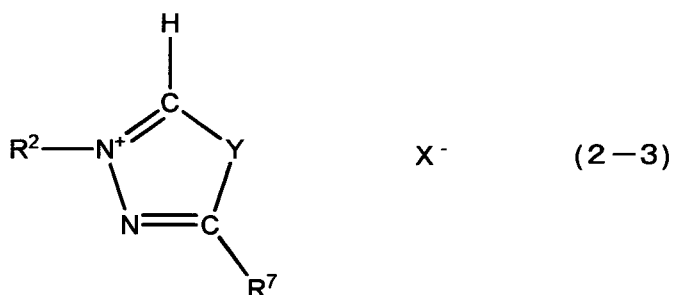
R^2 and Y mean the same as defined above;

R^6 and R^7 are independently a hydrogen atom, an alkyl group optionally having a substituent or an aryl group optionally having a substituent, or R^6 and R^7 are bonded to each other to form a ring together with carbon atoms to which they attach, or R^7 combines together with R^5 to form a divalent hydrocarbon group optionally having a substituent;

$C \equiv C$ represents a carbon-carbon single bond or a carbon-carbon double bond; and

X^- means the same as defined above;

or a compound represented by formula (2-3):



wherein

R^2 and Y mean the same as defined above; and

R^7 is a hydrogen atom, an alkyl group optionally having a substituent or an aryl group optionally having a substituent

substituent, or R^7 combines together with R^5 to form a divalent hydrocarbon group optionally having a substituent; and

X^- means the same as defined above.

5

10. The process according to claim 9, wherein the compound represented by the formula (2-1) is a compound represented by the formula (2-2).

10 11. The process according to claim 10, wherein in the formula (2-2) Y is a group of $-N(R^5)-$, R^2 and R^5 are independently a 2,6-disubstituted phenyl group, R^6 and R^7 are both a hydrogen atom, and $C \equiv C$ represents a carbon-carbon double bond.

15

12. The process according to claim 7, wherein the base is at least one base selected from the group consisting of organic bases, alkali metal carbonates and alkaline earth metal carbonates.