METHOD FOR PRODUCING PHENYLACETAMIDE COMPOUND

PROCÉDÉ DE PRODUCTION D’UN COMPOSÉ PHÉNYLACÉTAMIDE

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**Description**

**TECHNICAL FIELD**

[0001] The present invention relates to a method for producing a phenylacetamide compound.

**BACKGROUND ART**

[0002] WO 95/27693 discloses that a 2-substituted phenyl-N-alkylacetamide compound having an alkoxy group at the 2-position typified by 2-[2-(2,5-dimethylphenoxy)methyl]phenyl]-2-hydroxy-N-methylacetamide is useful as an agricultural fungicide, and also discloses, as a method for producing the compound, a method in which methyl 2-[2-(2,5-dimethylphenoxy)methyl]phenyl]-2-hydroxyacetate is reacted with methyl iodide to obtain methyl 2-[2-(2,5-dimethylphenoxy)methyl]phenyl]-2-methoxyacetate, and then the methyl 2-[2-(2,5-dimethylphenoxyethyl)phenyl]-2-methoxyacetate is reacted with methylamine to obtain 2-[2-(2,5-dimethylphenoxyethyl)phenyl]-2-methoxy-N-methylacetamide.


**DISCLOSURE OF THE INVENTION**

[0004] The present invention provides

1. a method for producing a phenylacetamide compound represented by formula (1):

   \[
   \begin{align*}
   &OR^4 \\
   &\text{Q} \\
   &\text{CON} \\
   &\text{R}^2 \\
   &\text{R}^5 \\
   &\text{Ar}
   \end{align*}
   \]  

   wherein Q represents a hydrogen atom or a halogen atom, R^2 represents a hydrogen atom or an alkyl group having 1 to 4 carbon atoms, R^4 represents an alkyl group having 1 to 4 carbon atoms, Ar represents an unsubstituted or substituted phenyl group, the optional substituent being selected from the group consisting of alkyl groups having 1 to 4 carbon atoms and halogen atoms, R^5 represents R^4 when R^2 is a hydrogen atom, and R^5 represents a hydrogen atom when R^2 is an alkyl group having 1 to 4 carbon atoms; comprising

   reacting a mandelonitrile compound represented by formula (6):

   \[
   \begin{align*}
   &\text{OH} \\
   &\text{Q} \\
   &\text{CN} \\
   &\text{O} \\
   &\text{Ar}
   \end{align*}
   \]  

   wherein Q represents a hydrogen atom or a halogen atom, and Ar represents an unsubstituted or substituted phenyl group, the optional substituent being selected from the group consisting of alkyl groups having 1 to 4 carbon atoms and halogen atoms; with an alcohol compound represented by formula (7):

   \[
   \begin{align*}
   &\text{R}^1\text{-OH}
   \end{align*}
   \]
wherein \( R^1 \) represents an alkyl group having 1 to 4 carbon atoms; and an acid, and then reacting the resulting product with water to obtain an acetic acid ester compound represented by formula (4):

\[
\text{O} \quad \text{Q} \quad \text{COOR}^1 \\
\text{O} \quad \text{Ar}
\]

wherein Q represents a hydrogen atom or a halogen atom, Ar represents an unsubstituted or substituted phenyl group, the optional substituent being selected from the group consisting of alkyl groups having 1 to 4 carbon atoms and halogen atoms, and \( R^1 \) represents an alkyl group having 1 to 4 carbon atoms; reacting the acetic acid ester compound represented by formula (4), with an amine compound represented by formula (5):

\[
R^2\text{-NH}_2 
\]

wherein \( R^2 \) represents a hydrogen atom or an alkyl group having 1 to 4 carbon atoms; to obtain a phenylacetamide compound represented by formula (2):

\[
\text{O} \quad \text{Q} \quad \text{CON} \quad \text{R}^2 \\
\text{O} \quad \text{Ar} \\
\text{H}
\]

wherein Q, \( R^2 \) and Ar have the same meanings as defined above; and reacting the phenylacetamide compound represented by formula (2) with a dialkyl sulfate represented by formula (3):

\[
\text{O} \quad \text{S} \quad \text{O} \\
\text{O} \quad \text{R}^4 \\
\text{O} \quad \text{R}^4
\]

wherein \( R^4 \) has the same meaning as defined above; in the presence of a base;

[2] the production method according to [1], wherein \( R^2 \) is a hydrogen atom;

[3] the production method according to [1] or [2], wherein Ar is a 2,5-dimethylphenyl group or a 2-methylphenyl group;

[4] the production method according to [1] or [2], wherein Ar is a 2,5-dimethylphenyl group;

[5] the production method according to any one of [1] to [4], wherein \( R^4 \) is a methyl group;

[6] the production method according to any one of [1] to [5], wherein the base is an alkali metal hydroxide;

[7] the production method according to any one of [1] to [6], wherein the reaction of the acetic acid ester compound represented by formula (4) with the amine compound represented by formula (5) is carried out in the presence of
an alcohol solvent having 1 to 4 carbon atoms.

BEST MODE FOR CARRYING OUT THE INVENTION

[0005] In the phenylacetamide compound represented by formula (2) (hereinafter abbreviated to an acetamide compound (2)), Q represents a hydrogen atom or a halogen atom.

\[
\begin{align*}
\text{OH} & \quad \text{CON} \\
\text{Q} & \quad \text{H} \\
\text{O} & \quad \text{Ar}
\end{align*}
\]

Q is preferably a hydrogen atom.

[0006] Examples of the halogen atom include a fluorine atom, a chlorine atom, a bromine atom and an iodine atom. Q is preferably a hydrogen atom.

[0007] R² in formula (2) represents a hydrogen atom or an alkyl group having 1 to 4 carbon atoms. Examples of the alkyl group having 1 to 4 carbon atoms include a methyl group, an ethyl group, a propyl group, an isopropyl group, a butyl group, a sec-butyl group, an isobutyl group and a tert-butyl group, and a methyl group is preferred. R² is preferably a hydrogen atom.

[0008] Ar represents an unsubstituted or substituted phenyl group. The substituent is selected from alkyl groups having 1 to 4 carbon atoms, such as a methyl group, an ethyl group, a propyl group, an isopropyl group, a butyl group, an isobutyl group and a tert-butyl group; and halogen atoms such as a fluorine atom and a chlorine atom. There is no particular limitation on the number of substituents, and the number of substituents is preferably 1 to 3, more preferably 1 or 2, and particularly preferably 2.

[0009] Examples of the substituted phenyl group include a 2-methylphenyl group, a 3-methylphenyl group, a 4-methylphenyl group, a 2,3-dimethylphenyl group, a 2,4-dimethylphenyl group, a 2,5-dimethylphenyl group, a 2,6-dimethylphenyl group, a 3,4-dimethylphenyl group, a 3,5-dimethylphenyl group, a 2,4,6-trimethylphenyl group, a 2-ethylphenyl group, a 3-ethylphenyl group, a 4-ethylphenyl group, a 2,3-diethylphenyl group, a 2,4-diethylphenyl group, a 2,5-diethylphenyl group, a 2,6-diethylphenyl group, a 3,5-diethylphenyl group, a 2,4,6-triethylphenyl group, a 2-propylphenyl group, a 3-propylphenyl group, a 4-propylphenyl group, a 2,4-dipropylphenyl group, a 2,5-dipropylphenyl group, a 2,6-dipropylphenyl group, a 2,4,6-tripropylphenyl group, a 2-isopropylphenyl group, a 3-isopropylphenyl group, a 4-isopropylphenyl group, a 2,4-diisopropylphenyl group, a 2,5-diisopropylphenyl group, a 2,6-diisopropylphenyl group, a 2,4,6-triisopropylphenyl group, a 2-butylphenyl group, a 3-butylphenyl group, a 4-butylphenyl group, a 2,4-dibutylphenyl group, a 2,5-dibutylphenyl group, a 2,6-dibutylphenyl group, a 2,4,6-tributylphenyl group, a 2-isobutylphenyl group, a 3-isobutylphenyl group, a 4-isobutylphenyl group, a 2,4-diisobutylphenyl group, a 2,5-diisobutylphenyl group, a 2,6-diisobutylphenyl group, a 2,4,6-triisobutylphenyl group, a 2-(tert-butyl)phenyl group, a 3-(tert-butyl)phenyl group, a 4-(tert-butyl)phenyl group, a 2,5-di-(tert-butyl)phenyl group, a 2,4-di-(tert-butyl)phenyl group, a 2,6-di-(tert-butyl)phenyl group, a 2-fluorophenyl group, a 4-fluorophenyl group, a 2,4-difluorophenyl group, a 2,4,6-trifluorophenyl group, a pentafluorophenyl group, a 2-chlorophenyl group, a 4-chlorophenyl group, a 2,4-dichlorophenyl group, a 2,4,6-trichlorophenyl group, and a pentachlorophenyl group. Among these groups, a 2,5-dimethylphenyl group and a 2-methylphenyl group are preferred, and a 2,5-dimethylphenyl group is more preferred.

[0010] Examples of the acetamide compound (2) include

- 2-hydroxyacetamide compounds such as
  2-[2-(phenoxymethyl)phenyl]-2-hydroxyacetamide,
  2-[2-(2-methoxyethyl)phenyl]-2-hydroxyacetamide,
  2-[2-(3-methoxyethyl)phenyl]-2-hydroxyacetamide,
  2-[2-(4-methoxyethyl)phenyl]-2-hydroxyacetamide,
  2-[2-(2-ethylphenoxymethyl)phenyl]-2-hydroxyacetamide,
  2-[2-(4-ethylphenoxymethyl)phenyl]-2-hydroxyacetamide,
  2-[2-(2-isopropylphenoxymethyl)phenyl]-2-hydroxyacetamide,
  2-[2-(4-isopropylphenoxymethyl)phenyl]-2-hydroxyacetamide,
  2-[2-(2-tert-butylphenoxymethyl)phenyl]-2-hydroxyacetamide,
  2-[2-(4-tert-butylphenoxymethyl)phenyl]-2-hydroxyacetamide,
2-[2-(2,4-dimethylphenoxymethyl)phenyl]-2-hydroxyacetamide,
2-[2-(2,5-dimethylphenoxymethyl)phenyl]-2-hydroxyacetamide,
2-[2-(2,6-dimethylphenoxymethyl)phenyl]-2-hydroxyacetamide,
2-[2-(3,5-dimethylphenoxymethyl)phenyl]-2-hydroxyacetamide,
2-[2-(2,4-diethylphenoxymethyl)phenyl]-2-hydroxyacetamide,
2-[2-(2,5-diethylphenoxymethyl)phenyl]-2-hydroxyacetamide,
2-[2-(6-diethylphenoxymethyl)phenyl]-2-hydroxyacetamide,
2-[2-(2,6-diisopropylphenoxymethyl)phenyl]-2-hydroxyacetamide,
2-[2-(2,4,5-trimethylphenoxymethyl)phenyl]-2-hydroxyacetamide,
2-[2-(2,4,6-trimethylphenoxymethyl)phenyl]-2-hydroxyacetamide,
2-[2-(3,4,5-trimethylphenoxymethyl)phenyl]-2-hydroxyacetamide,
2-[2-(2,4-diethylphenoxymethyl)-3-chlorophenyl]-2-hydroxyacetamide,
2-[2-(2-methylphenoxymethyl)-3-chlorophenyl]-2-hydroxyacetamide,
2-[2-(2,5-diethylphenoxymethyl)-4-chlorophenyl]-2-hydroxyacetamide,
2-[2-(2-methylphenoxymethyl)-4-chlorophenyl]-2-hydroxyacetamide,
2-[2-(2,5-diethylphenoxymethyl)-5-chlorophenyl]-2-hydroxyacetamide,
2-[2-(2-methylphenoxymethyl)-5-chlorophenyl]-2-hydroxyacetamide,
2-[2-(2,5-diethylphenoxymethyl)-6-chlorophenyl]-2-hydroxyacetamide,
2-[2-(2-methylphenoxymethyl)-6-chlorophenyl]-2-hydroxyacetamide,
2-[2-(2,5-diethylphenoxymethyl)-4-chlorophenyl]-2-hydroxyacetamide,
2-[2-(2-ethylphenoxymethyl)-4-chlorophenyl]-2-hydroxyacetamide,
2-[2-(2,5-diisopropylphenoxymethyl)-4-chlorophenyl]-2-hydroxyacetamide, and
2-[2-(2-isopropylphenoxymethyl)-4-chlorophenyl]-2-hydroxyacetamide;
2-hydroxy-N-methylacetamide compounds such as
2-[2-(2-methylphenoxymethyl)-3-chlorophenyl]-2-hydroxyacetamide,
2-[2-(2,5-dimethylphenoxymethyl)-4-chlorophenyl]-2-hydroxyacetamide,
2-[2-(2,5-dimethylphenoxymethyl)-5-chlorophenyl]-2-hydroxyacetamide,
2-[2-(2,5-dimethylphenoxymethyl)-6-chlorophenyl]-2-hydroxyacetamide,
2-[2-(2,4,5-trimethylphenoxymethyl)phenyl]-2-hydroxyacetamide,
2-[2-(2,4,6-trimethylphenoxymethyl)phenyl]-2-hydroxyacetamide,
2-[2-(3,4,5-trimethylphenoxymethyl)phenyl]-2-hydroxyacetamide,
2-[2-(2,5-dimethylphenoxymethyl)-3-chlorophenyl]-2-hydroxyacetamide,
2-[2-(2-methylphenoxymethyl)-3-chlorophenyl]-2-hydroxyacetamide,
2-[2-(2,5-dimethylphenoxymethyl)-4-chlorophenyl]-2-hydroxyacetamide,
2-[2-(2-methylphenoxymethyl)-4-chlorophenyl]-2-hydroxyacetamide,
2-[2-(2,5-dimethylphenoxymethyl)-5-chlorophenyl]-2-hydroxyacetamide,
2-[2-(2-methylphenoxymethyl)-5-chlorophenyl]-2-hydroxyacetamide,
2-[2-(2,5-dimethylphenoxymethyl)-6-chlorophenyl]-2-hydroxyacetamide,
2-[2-(2-methylphenoxymethyl)-6-chlorophenyl]-2-hydroxyacetamide,
2-[2-(2,5-diethylphenoxymethyl)-4-chlorophenyl]-2-hydroxyacetamide,
2-[2-(2-ethylphenoxymethyl)-4-chlorophenyl]-2-hydroxyacetamide,
2-[2-(2,5-diisopropylphenoxymethyl)-4-chlorophenyl]-2-hydroxyacetamide, and
2-[2-(2-isopropylphenoxymethyl)-4-chlorophenyl]-2-hydroxyacetamide;
Among these compounds, a 2-hydroxyacetamide compound and a 2-hydroxy-N-methylacetamide compound are preferred.

In the dialkyl sulfate represented by formula (3) (hereinafter abbreviated to a dialkyl sulfate (3)), \( R^4 \) represents an alkyl group having 1 to 4 carbon atoms.

Examples of the alkyl group having 1 to 4 carbon atoms include a methyl group, an ethyl group, a propyl group, an isopropyl group, a butyl group, a sec-butyl group, an isobutyl group, and a tert-butyl group, and a methyl group is preferred.

Examples of the dialkyl sulfate (3) include dialkyl sulfates having a linear alkyl group, such as dimethyl sulfate, diethyl sulfate, dipropyl sulfate and dibutyl sulfate; and dialkyl sulfates having a branched alkyl group, such as diisopropyl sulfate and diisobutyl sulfate, and dialkyl sulfates having a linear alkyl group are preferred, and dimethyl sulfate is more preferred.

As such dialkyl sulfates (3), commercially available dialkyl sulfates or those produced by a known method may be used.

The amount of the dialkyl sulfate (3) used is usually from 1 to 20 mol, and preferably from 1 to 10 mol, based on 1 mol of the acetamide compound (2).

The reaction of the acetamide compound (2) with the dialkyl sulfate (3) is carried out in the presence of a base. Examples of the base include alkali metal hydroxides such as sodium hydroxide and potassium hydroxide; and alkaline earth metal hydroxides such as barium hydroxide and calcium hydroxide, and alkali metal hydroxides are preferred, and sodium hydroxide is more preferably.

The amount of the base used is usually from 2 to 50 mol, and preferably from 2 to 20 mol, based on 1 mol of the acetamide compound (2).

The reaction of the acetamide compound (2) with the dialkyl sulfate (3) is usually carried out in the presence of a solvent inert in the reaction. Examples of the solvent include alcohol solvents such as methanol and ethanol; aromatic hydrocarbon solvents such as toluene and xylene; ether solvents such as diethyl ether and tetrahydrofuran; and water. These solvents may be used alone, two or more kinds of solvents may be used in combination. Among these solvents, aromatic hydrocarbon solvents are preferred, and toluene or xylene is more preferred. There is no particular limitation on the amount of the solvents used, and it is preferably from 0.5 to 100 parts by weight, and more preferably from 1 to 20 parts by weight, based on 1 part by weight of the acetamide compound (2).

The reaction of the acetamide compound (2) with the dialkyl sulfate (3) is carried out by mixing the acetamide compound (2), the dialkyl sulfate (3) and the base, and there is no particular limitation on the mixing order of these components. For example, the dialkyl sulfate (3) and the base may be simultaneously added to the acetamide compound (2) adjusted to reaction temperature, or the base may be added to the acetamide compound (2) adjusted to reaction temperature and then the dialkyl sulfate (3) may be added. Among these, it is preferred that the base is added to the acetamide compound (2) adjusted to reaction temperature, and then the dialkyl sulfate (3) may be added. There is no particular limitation on the time of the base and the dialkyl sulfate (3) added.

The reaction temperature is usually from 0 to 70°C, and preferably from 10 to 50°C. The reaction time depends on the reaction temperature, and is usually from 0.5 to 20 hours, and preferably from 1 to 10 hours.

The progress of the reaction can be recognized by general analytical means such as high-performance liquid chromatography and gas chromatography.

After completion of the reaction, for example, the obtained reaction mixture may be washed with water or an aqueous acid solution such as diluted hydrochloric acid, and then concentrated to obtain a phenylacetamide compound represented by formula (1) (hereinafter abbreviated to a phenylacetamide compound (1)).
wherein Q, R2, R4 and Ar have the same meanings as defined above; R5 represents R4 when R2 is a hydrogen atom and R5 represents a hydrogen atom when R2 is an alkyl group having 1 to 4 carbon atoms. The phenylacetamide compound (1) thus obtained may be further purified by general purification means such as column chromatography.

[0023] When the acetamide compound (2) wherein R2 is an alkyl group having 1 to 4 carbon atoms is used, the phenylacetamide compound (1) is obtained wherein a hydroxyl group at the 2-position is alkylated and a nitrogen atom on the amide moiety is not alkylated. When the acetamide compound (2) wherein R2 is a hydrogen atom is used, the phenylacetamide compound (1) is obtained wherein a hydroxyl group at the 2-position is alkylated and a nitrogen atom on the amide moiety is also monoalkylated. The method of the present invention is advantageous because the phenylacetamide compound (1) wherein a hydroxyl group at the 2-position is alkylated and a nitrogen atom on the amide moiety is also monoalkylated is obtained in one step when the acetamide compound (2) wherein R2 is a hydrogen atom is used. Also, the phenylacetamide compound wherein a nitrogen atom on the amide moiety is dialkylated is scarcely generated as a by-product, when the acetamide compound (2) wherein R2 is a hydrogen atom is used. Furthermore, a phenylacetamide compound wherein a nitrogen atom on the amide moiety is alkylated is scarcely generated as a by-product, even when the acetamide compound (2) wherein R2 is an alkyl group having 1 to 4 carbon atoms is used. Accordingly, the objective phenylacetamide compound (1) can be obtained in good yield. Also, the phenylacetamide compound (1) having good purity can be easily obtained because of less by-products.

[0024] Examples of the phenylacetamide compound (1) thus obtained include

2-[2-(phenoxymethyl)phenyl]-2-methoxy-N-methylacetamide,
2-[2-(2-methylphenoxymethyl)phenyl]-2-methoxy-N-methylacetamide,
2-[2-(3-methylphenoxymethyl)phenyl]-2-methoxy-N-methylacetamide,
2-[2-(4-methylphenoxymethyl)phenyl]-2-methoxy-N-methylacetamide,
2-[2-(2-ethylphenoxymethyl)phenyl]-2-methoxy-N-methylacetamide,
2-[2-(4-ethylphenoxymethyl)phenyl]-2-methoxy-N-methylacetamide,
2-[2-(2-isopropylphenoxymethyl)phenyl]-2-methoxy-N-methylacetamide,
2-[2-(4-isopropylphenoxymethyl)phenyl]-2-methoxy-N-methylacetamide,
2-[2-(2-tert-butylphenoxymethyl)phenyl]-2-methoxy-N-methylacetamide,
2-[2-(4-tert-butylphenoxymethyl)phenyl]-2-methoxy-N-methylacetamide,
2-[2-(2,4-dimethylphenoxymethyl)phenyl]-2-methoxy-N-methylacetamide,
2-[2-(2,5-dimethylphenoxymethyl)phenyl]-2-methoxy-N-methylacetamide,
2-[2-(2,6-dimethylphenoxymethyl)phenyl]-2-methoxy-N-methylacetamide,
2-[2-(3,5-dimethylphenoxymethyl)phenyl]-2-methoxy-N-methylacetamide,
2-[2-(2,4,6-trimethylphenoxymethyl)phenyl]-2-methoxy-N-methylacetamide,
2-[2-(2,5-diethylphenoxymethyl)-4-chlorophenyl]-2-methoxy-N-methylacetamide,
2-[2-(2-ethylphenoxymethyl)-4-chlorophenyl]-2-methoxy-N-methylacetamide,
2-[2-(2,5-diisopropylphenoxymethyl)-4-chlorophenyl]-2-methoxy-N-methylacetamide,
2-[2-(2-isopropylphenoxymethyl)-4-chlorophenyl]-2-methoxy-N-methylacetamide,
2-[2-(2-methylphenoxymethyl)[phenyl]-2-ethoxy-N-ethylacetamide,
2-[2-(2,5-dimethylphenoxymethyl)[phenyl]-2-ethoxy-N-ethylacetamide,
2-[2-(2-methylphenoxymethyl)[phenyl]-2-propoxy-N-propylacetamide,
2-[2-(2,5-dimethylphenoxymethyl)[phenyl]-2-propoxy-N-propylacetamide,
2-[2-(2-methylphenoxymethyl)[phenyl]-2-butoxy-N-butylacetamide, and
2-[2-(2,5-dimethylphenoxymethyl)[phenyl]-2-butoxy-N-butylacetamide.

Among them,
2-[2-(2-methylphenoxymethyl)[phenyl]-2-methoxy-N-methylacetamide and
2-[2-(2,5-dimethylphenoxymethyl)[phenyl]-2-hydroxy-N-methylacetamide are preferred, and
2-[2-(2,5-dimethylphenoxymethyl)[phenyl]-2-methoxy-N-methylacetamide is more preferred.

[0025] The acetamide compound (2) is produced by reacting an acetic acid ester compound represented by formula (4) (hereinafter abbreviated to an acetic acid ester compound (4)):

\[
Q \text{ Ar} \quad \text{(4)}
\]

wherein Q and Ar have the same meanings as defined above, and R^1 represents an alkyl group having 1 to 4 carbon atoms; with an amine compound represented by formula (5) (hereinafter abbreviated to an amine compound (5)):

\[
R^2-NH_2 \quad \text{(5)}
\]

wherein R^2 has the same meaning as defined above.

[0026] Examples of the acetic acid ester compound (4) include methyl 2-hydroxyacetate compounds such as methyl

2-[2-(phenoxyethyl)[phenyl]-2-hydroxyacetate,
methyl -2-[2-(2-methoxyphenoxyethyl)[phenyl]-2-hydroxyacetate,
methyl 2-[2-(3-methoxyphenoxyethyl)[phenyl]-2-hydroxyacetate,
methyl 2-[2-(4-methoxyphenoxyethyl)[phenyl]-2-hydroxyacetate,
methyl 2-[2-(2-ethylphenoxyethyl)[phenyl]-2-hydroxyacetate,
methyl 2-[2-(2-ethylphenoxyethyl)[phenyl]-2-hydroxyacetate,
methyl 2-[2-(3,5-diethylphenoxyethyl)[phenyl]-2-hydroxyacetate,
methyl 2-[2-(2,4-diethylphenoxyethyl)[phenyl]-2-hydroxyacetate,
methyl 2-[2-(2,5-diethylphenoxyethyl)[phenyl]-2-hydroxyacetate,
methyl 2-[2-(2,6-diethylphenoxyethyl)[phenyl]-2-hydroxyacetate,
methyl 2-[2-(3,5-diethylphenoxyethyl)[phenyl]-2-hydroxyacetate,
methyl 2-[2-(2,4-diethylphenoxyethyl)[phenyl]-2-hydroxyacetate,
methyl 2-[2-(2,5-diethylphenoxyethyl)[phenyl]-2-hydroxyacetate,
methyl 2-[2-(2,6-diethylphenoxyethyl)[phenyl]-2-hydroxyacetate,
methyl 2-[2-(2,5-diethylphenoxyethyl)[phenyl]-2-hydroxyacetate,
methyl 2-[2-(2,6-diethylphenoxyethyl)[phenyl]-2-hydroxyacetate,
methyl 2-[2-(3,5-diethylphenoxyethyl)[phenyl]-2-hydroxyacetate,
methyl 2-[2-(2,4,5-trimethylphenoxyethyl)[phenyl]-2-hydroxyacetate,
methyl 2-[2-(2,4,6-trimethylphenoxyethyl)[phenyl]-2-hydroxyacetate,
methyl 2-[2-(2,5,6-trimethylphenoxyethyl)[phenyl]-2-hydroxyacetate,
methyl 2-[2-(2,4,5-trimethylphenoxyethyl)[phenyl]-2-hydroxyacetate,
methyl 2-[2-(2,4,6-trimethylphenoxyethyl)[phenyl]-2-hydroxyacetate,
methyl 2-[2-(3,4,5-trimethylphenoxyethyl)[phenyl]-2-hydroxyacetate,
2-[2-(2,5-dimethylphenoxy)methyl]-3-chlorophenyl]-2-hydroxyacetate,
methyl 2-[2-(2-methylphenoxy)methyl]-3-chlorophenyl]-2-hydroxyacetate,
methyl 2-[2-(2,5-dimethylphenoxy)methyl]-4-chlorophenyl]-2-hydroxyacetate,
methyl 2-[2-(2-methylphenoxy)methyl]-4-chlorophenyl]-2-hydroxyacetate,
methyl 2-[2-(2,5-dimethylphenoxy)methyl]-5-chlorophenyl]-2-hydroxyacetate,
methyl 2-[2-(2-methylphenoxy)methyl]-5-chlorophenyl]-2-hydroxyacetate,
methyl 2-[2-(2,5-diethylphenoxy)methyl]-4-chlorophenyl]-2-hydroxyacetate,
methyl 2-[2-(2-ethylphenoxy)methyl]-4-chlorophenyl]-2-hydroxyacetate, and
methyl 2-[2-(2,5-diisopropylphenoxy)methyl]-4-chlorophenyl]-2-hydroxyacetate, and
methyl 2-[2-(2-isopropylphenoxy)methyl]-4-chlorophenyl]-2-hydroxyacetate; ethyl 2-hydroxyacetate compounds
such as ethyl
2-[2-(2-methylphenoxy)methyl]phenyl]-2-hydroxyacetate, and ethyl
2-[2-(2,5-dimethylphenoxy)methyl]phenyl]-2-hydroxyacetate; propyl 2-hydroxyacetate compounds such as propyl
2-[2-(2-methylphenoxy)methyl]phenyl]-2-hydroxyacetate, and propyl
2-[2-(2,5-dimethylphenoxy)methyl]phenyl]-2-hydroxyacetate; isopropyl 2-hydroxyacetate compounds such as iso-
propyl
2-[2-(2-methylphenoxy)methyl]phenyl]-2-hydroxyacetate, and isopropyl
2-[2-(2,5-dimethylphenoxy)methyl]phenyl]-2-hydroxyacetate; butyl 2-hydroxyacetate compounds such as butyl
2-[2-(2-methylphenoxy)methyl]phenyl]-2-hydroxyacetate, and butyl
2-[2-(2,5-dimethylphenoxy)methyl]phenyl]-2-hydroxyacetate; isobutyl 2-hydroxyacetate compounds such as isobutyl
2-[2-(2-methylphenoxy)methyl]phenyl]-2-hydroxyacetate; tert-butyl 2-hydroxyacetate compounds such as tert-butyl
2-[2-(2-methylphenoxy)methyl]phenyl]-2-hydroxyacetate, and tert-butyl
2-[2-(2,5-dimethylphenoxy)methyl]phenyl]-2-hydroxyacetate; isobutyl 2-hydroxyacetate compounds such as isobutyl
2-[2-(2,5-dimethylphenoxy)methyl]phenyl]-2-hydroxyacetate; and the like. Among these compounds, methyl
2-[2-(2-methylphenoxy)methyl]phenyl]-2-hydroxyacetate and methyl
2-[2-(2,5-dimethylphenoxy)methyl]phenyl]-2-hydroxyacetate are preferred, and methyl
2-[2-(2,5-dimethylphenoxy)methyl]phenyl]-2-hydroxyacetate is more preferred.

[0007] Examples of the amine compound (5) include ammonia and monoalkylamines such as methylamine, ethylamine,
propylamine, isopropylamine, butylamine, isobutylamine and tert-butylamine, and methylamine is preferred.
[0008] As such amine compound (5), commercially available amine compounds or those produced by a known method
may be used.
[0009] The amount of the amine compound (5) used is usually from 1 to 10 mol, and preferably from 1 to 6 mol, based
on 1 mol of the acetic acid ester compound (4).
[0030] The reaction of the acetic acid ester compound (4) with the amine compound (5) is usually carried out in the
presence of a solvent in the reaction. Examples of the solvent include alcohol solvents having 1 to 4 carbon atoms,
such as methanol and ethanol; aromatic hydrocarbon solvents such as toluene and xylene; ether solvents such as diethyl
ether and tetrahydrofuran; and water. These solvents may be used alone, or two or more kinds of solvents may be used in
combination. Among these solvents, aromatic hydrocarbon solvents, alcohol solvents having 1 to 4 carbon atoms and
mixed solvents thereof are preferred, and alcohol solvents having 1 to 4 carbon atoms and mixed solvents of alcohol
solvents having 1 to 4 carbon atoms with aromatic hydrocarbon solvents are more preferred. There is no particular
limitation on the amount of the solvent used, and it is usually from 0.5 to 100 parts by weight, and preferably from 1 to
10 parts by weight, based on 1 part by weight of the acetic acid ester compound (4).
[0031] The reaction temperature is usually from 0 to 100°C, and preferably from 20 to 60°C. The reaction time depends
on the reaction temperature, and is usually from 0.5 to 100 hours, and preferably from 1 to 50 hours. The progress of
the reaction can be recognized by general analytical methods such as high-performance liquid chromatography and gas
chromatography.
[0032] The reaction of the acetic acid ester compound (4) with the amine compound (5) is usually carried out by mixing
both compounds. There is no particular limitation on the mixing order and, for example, there is exemplified a method
in which the amine compound (5) is usually added to the acetic acid ester compound (4) over 0.5 to 100 hours, and
preferably over 1 to 50 hours.
[0033] After completion of the reaction, the obtained reaction mixture contains the acetamide compound (2). The
reaction mixture may be used in the above reaction of the acetamide compound (2) with the dialkyl sulfate (3) directly
or after washing. Alternatively, the acetamide compound (2) may be separated from the reaction mixture by concentration,
crystallization or the like, and the acetamide compound (2) thus separated may be used in the above reaction of the
acetamide compound (2) with the dialkyl sulfate (3). The acetamide compound (2) thus separated may be further purified
by general purification means such as column chromatography.

[0034] The acetic acid ester compound (4) is produced by reacting a mandelonitrile compound represented by formula (6) (hereinafter abbreviated to a mandelonitrile compound (6)):

![Formula 6](image)

wherein Q and Ar have the same meanings as defined above; with an alcohol compound represented by formula (7) (hereinafter abbreviated to an alcohol compound (7)):

\[ \text{R}^1\text{-OH} \] (7)

wherein \( \text{R}^1 \) has the same meaning defined above; and an acid, and then reacting the obtained product with water.

[0035] Examples of the mandelonitrile compound (6) include

- 2-(phenoxyethyl)mandelonitrile,
- 2-(2-methoxyethyl)mandelonitrile,
- 2-(3-methoxyethyl)mandelonitrile,
- 2-(4-methoxyethyl)mandelonitrile,
- 2-(2-ethylphenoxyethyl)mandelonitrile,
- 2-(4-ethylphenoxyethyl)mandelonitrile,
- 2-(2-isopropylphenoxyethyl)mandelonitrile,
- 2-(4-isopropylphenoxyethyl)mandelonitrile,
- 2-(2-tert-butylphenoxyethyl)mandelonitrile,
- 2-(4-tert-butylphenoxyethyl)mandelonitrile,
- 2-(2,4-dimethylphenoxyethyl)mandelonitrile,
- 2-(2,5-dimethylphenoxyethyl)mandelonitrile,
- 2-(2,6-dimethylphenoxyethyl)mandelonitrile,
- 2-(3,5-dimethylphenoxyethyl)mandelonitrile,
- 2-(2,4-diethylphenoxyethyl)mandelonitrile,
- 2-(2,5-diethylphenoxyethyl)mandelonitrile,
- 2-(2,6-diethylphenoxyethyl)mandelonitrile,
- 2-(2,5-diisopropylphenoxyethyl)mandelonitrile,
- 2-(2,6-diisopropylphenoxyethyl)mandelonitrile,
- 2-(2,4,5-trimethylphenoxyethyl)mandelonitrile,
- 2-(2,4,6-trimethylphenoxyethyl)mandelonitrile,
- 2-(3,4,5-trimethylphenoxyethyl)mandelonitrile,
- 2-(2,5-dimethylphenoxyethyl)-3-chloromandelonitrile,
- 2-(2-methoxyethyl)-3-chloromandelonitrile,
- 2-(2,5-dimethylphenoxyethyl)-4-chloromandelonitrile,
- 2-(2-methoxyethyl)-4-chloromandelonitrile,
- 2-(2,5-dimethylphenoxyethyl)-5-chloromandelonitrile,
- 2-(2-methoxyethyl)-5-chloromandelonitrile,
- 2-(2,5-dimethylphenoxyethyl)-6-chloromandelonitrile,
- 2-(2-methoxyethyl)-6-chloromandelonitrile,
- 2-(2,5-diethylphenoxyethyl)-4-chloromandelonitrile,
- 2-(2-ethylphenoxyethyl)-4-chloromandelonitrile,
- 2-(2-ethylphenoxyethyl)-4-chloromandelonitrile,
- 2-(2,5-diisopropylphenoxyethyl)-4-chloromandelonitrile,
- 2-(2-isopropylphenoxyethyl)-4-chloromandelonitrile.

Among these compounds, 2-(2-methoxyethyl)mandelonitrile and 2-(2,5-dimethoxyethyl)mandelonitrile are preferred, and
2-(2,5-dimethylphenoxymethyl)mandelonitrile is more preferred.

Examples of the alcohol compound (7) include methanol, ethanol, 1-propanol, 2-propanol, 1-butanol, and 2-butanol, and methanol is preferred.

Examples of the acid include sulfuric acid, hydrogen chloride and p-toluenesulfonic acid, and hydrogen chloride is preferred. The amount of the acid used is usually from 1 to 10 mol, and preferably from 1 to 5 mol, based on 1 mol of the mandelonitrile compound (6). Such an acid may be used by mixing with the alcohol compound (7). In particular, it is preferred to use a solution obtained by dissolving hydrogen chloride in the alcohol compound (7). The content of the hydrogen chloride in the solution obtained by dissolving hydrogen chloride in the alcohol compound (7) is preferably from 20 to 60 parts by weight, and more preferably from 40 to 55 parts by weight, based on 100 parts by weight of the solution. When hydrogen chloride is used as the acid, the amount of the hydrogen chloride used is preferably from 1 to 5 mol, more preferably from 1.2 to 3 mol, and particularly preferably from 1.2 to 2.5 mol, based on 1 mol of the mandelonitrile compound (6).

Examples of the organic solvent include aromatic hydrocarbon solvents such as benzene, toluene, xylene and chlorobenzene; aliphatic hydrocarbon solvents such as hexane and heptane; alicyclic hydrocarbon solvents such as cyclopentane and cyclohexane; ketone solvents such as methyl ethyl ketone and methyl isobutyl ketone; and ether solvents such as diethylether, dibutylether, tetrahydrofuran and tetrahydropyrany. These solvents may be used alone, or two or more kinds of solvents may be used in combination. Among these solvents, aromatic hydrocarbon solvents are preferred. The amount of the organic solvent used is usually from 0.5 to 10 parts by weight, and preferably from 1 to 5 parts by weight, based on 1 part by weight of the mandelonitrile compound (6).

The reaction temperature is usually from -20 to 50°C, and preferably from 0 to 30°C. The reaction time depends on the reaction temperature, and is usually from 0.5 to 20 hours, and more preferably over 1 to 10 hours.

The progress of the reaction can be recognized by general analytical means such as high-performance liquid chromatography and gas chromatography.

EXAMPLES

The present invention will be described in more detail below by way of Examples, but the invention is not limited thereto. The analysis was carried out using high-performance liquid chromatography according to an internal standard method.

Example 1 (Reference)

A xylene solution containing 0.33 g of 2-[2-(2,5-dimethylphenoxymethyl)phenyl]-2-hydroxyacetamide was adjusted to 20°C with stirring. To the xylene solution, 1.2 g of a 48% by weight aqueous sodium hydroxide solution was added dropwise over 1 hour, followed by 0.70 g of dimethyl sulfate over 1 hour. The obtained mixture was stirred at 20°C for 5 hours to obtain a reaction mixture containing 2-[2-(2,5-dimethylphenoxymethyl)phenyl]-2-methoxy-N,N'-dimethylacetamide.

To the obtained reaction mixture, 1.3 g of water was added. The obtained mixture was heated to 50°C, and the water layer was then removed. The obtained organic layer was washed at 50°C with 1.3 g of 5% by weight hydrochloric acid. The obtained organic layer was washed at 50°C with 1.3 g of water. The obtained organic layer was concentrated to obtain 0.36 g (content: 96.5%) of 2-[2-(2,5-dimethylphenoxymethyl)phenyl]-2-methoxy-N-methylacetamide.

The formation of 2-[2-(2,5-dimethylphenoxymethyl)phenyl]-2-methoxy,N,N'-dimethylacetamide was not recognized.

Example 2a

First, 255.9 g (content: 93% by weight) of 2-(2,5-dimethylphenoxymethyl)mandelonitrile was mixed with 469.0 g of xylene. The obtained mixture was adjusted to 7°C with stirring. To the mixture, 160.1 g of a 47% by weight hydrogen chloride/methanol solution was added dropwise over 2 hours. The obtained mixture was stirred and maintained at 7°C for 2 hours to obtain a reaction mixture containing 1-[2-(2,5-dimethylphenoxymethyl)phenyl]-1-hydroxy-2-methoxy th-
neiminium chloride.

[0047] To the obtained reaction mixture, 320.1 g of water was added dropwise at 7°C over 1 hour. The obtained mixture was stirred and maintained at 50°C for 1 hour, and 312.6 g of an organic layer was then separated. The content of methyl 2-[2-(2,5-dimethylphenoxymethyl)phenyl]-2-hydroxyacetate in the organic layer was 82.4% by weight, and the yield was 96.2%.

Example 2b

[0048] Then, 30.0 g (content: 25% by weight) of the organic layer containing methyl 2-[2-(2,5-dimethylphenoxymethyl)phenyl]-2-hydroxyacetate was adjusted to 50°C with stirring. To the layer, 5.8 g of a 40% by weight methylamine/methanol solution was added dropwise over 1 hour. The obtained mixture was stirred and maintained at 50°C for 10 hours to obtain a reaction mixture containing 2-[2-(2,5-dimethylphenoxymethyl)phenyl]-2-hydroxy-N-methylacetamide.

[0049] The obtained reaction mixture was concentrated under reduced pressure conditions to remove low-boiling components. The residue was adjusted to 50°C, and washed with 7.7 g of water and then with 7.7 g of a 5% by weight aqueous sulfuric acid solution to obtain 31.5 g of a solution (content: 23.8% by weight) containing 2-[2-(2,5-dimethylphenoxymethyl)phenyl]-2-hydroxy-N-methylacetamide. Yield: 100%.

Example 2c

[0050] Then, 31.1 g of the solution containing 2-[2-(2,5-dimethylphenoxymethyl)phenyl]-2-hydroxy-N-methylacetamide obtained in Example 7 was adjusted to 17°C with stirring. To the solution, 7.0 g of a 48% by weight aqueous sodium hydroxide solution was added dropwise over 0.5 hour, followed by 4.2 g of dimethyl sulfate over 2 hours. The obtained mixture was stirred and maintained at 19°C for 5 hours to obtain a reaction mixture containing 2-[2-(2,5-dimethylphenoxymethyl)phenyl]-2-methoxy-N-methylacetamide.

[0051] To the obtained reaction mixture, 7.4 g of water was added. The obtained mixture was heated to 50°C, and an organic layer was obtained at the same temperature. The obtained organic layer was washed at the same temperature with 7.4 g of 5% by weight hydrochloric acid and then with 7.5 g of water to obtain 32.1 g of a solution (content: 24.0% by weight) containing 2-[2-(2,5-dimethylphenoxymethyl)phenyl]-2-methoxy-N-methylacetamide. Yield: 99.1%.

[0052] The obtained solution was concentrated until the content of 2-[2-(2,5-dimethylphenoxymethyl)phenyl]-2-methoxy-N-methylacetamide was 42.5% by weight, and then heated to 60°C. The obtained solution was cooled, and crystals precipitated were separated by filtration, washed with heptane, and dried under reduced pressure conditions to obtain crystals of 2-[2-(2,5-dimethylphenoxymethyl)phenyl]-2-methoxy-N-methylacetamide.

Industrial Applicability

[0053] According to the present invention, a phenylacetamide compound can be produced in a satisfactory yield.

Claims

1. A method for producing a phenylacetamide compound represented by formula (1):

\[
\begin{align*}
\text{OR}^4 & \quad \text{CON} \\
\text{R}^2 & \quad \text{R}^5 \\
\text{Q} & \quad \text{Ar}
\end{align*}
\]

wherein \(Q\) represents a hydrogen atom or a halogen atom, \(R^2\) represents a hydrogen atom or an alkyl group having 1 to 4 carbon atoms, \(R^4\) represents an alkyl group having 1 to 4 carbon atoms, \(Ar\) represents an unsubstituted or substituted phenyl group, the optional substituent being selected from the group consisting of alkyl groups having 1 to 4 carbon atoms and halogen atoms, \(R^5\) represents \(R^4\) when \(R^2\) is a hydrogen atom, and \(R^5\) represents a hydrogen atom when \(R^2\) is an alkyl group having 1 to 4 carbon atoms;
comprising
reacting a mandelonitrile compound represented by formula (6):

\[
\text{OH} \\
\text{CN} \\
\text{O}_{\text{Ar}}
\]

wherein Q represents a hydrogen atom or a halogen atom, and Ar represents an unsubstituted or substituted phenyl group, the optional substituent being selected from the group consisting of alkyl groups having 1 to 4 carbon atoms and halogen atoms;

with an alcohol compound represented by formula (7):

\[
\text{R}^1\text{-OH}
\]

wherein \( R^1 \) represents an alkyl group having 1 to 4 carbon atoms;

and an acid, and then reacting the resulting product with water to obtain an acetic acid ester compound represented by formula (4):

\[
\text{OH} \\
\text{COOR}^1 \\
\text{O}_{\text{Ar}}
\]

wherein Q represents a hydrogen atom or a halogen atom, Ar represents an unsubstituted or substituted phenyl group, the optional substituent being selected from the group consisting of alkyl groups having 1 to 4 carbon atoms and halogen atoms, and \( R^1 \) represents an alkyl group having 1 to 4 carbon atoms;

reacting the acetic acid ester compound represented by formula (4) with an amine compound represented by formula (5):

\[
\text{R}^2\text{-NH}_2
\]

wherein \( R^2 \) represents a hydrogen atom or an alkyl group having 1 to 4 carbon atoms;

to obtain a phenylacetamide compound represented by formula (2):

\[
\text{OH} \\
\text{CON} \\
\text{O}_{\text{Ar}}
\]

wherein Q, \( R^2 \) and Ar have the same meanings as defined above;
and reacting the phenylacetamide compound represented by formula (2) with a dialkyl sulfate represented by formula (3):

\[
\begin{align*}
\text{R}^4 & \quad \text{O} \\
\text{O} & \quad \text{S} \\
\text{S} & \quad \text{O} \\
\text{O} & \quad \text{R}^4
\end{align*}
\]

wherein \( \text{R}^4 \) has the same meaning as defined above; in the presence of a base.

2. The production method according to claim 1, wherein \( \text{R}^2 \) is a hydrogen atom.

3. The production method according to claim 1, wherein \( \text{Ar} \) is a 2,5-dimethylphenyl group or a 2-methylphenyl group.

4. The production method according to claim 1, wherein \( \text{Ar} \) is a 2,5-dimethylphenyl group.

5. The production method according to claim 1, wherein \( \text{R}^4 \) is a methyl group.

6. The production method according to claim 1, wherein the base is an alkali metal hydroxide.

7. The production method according to claim 1, wherein the reaction of the acetic acid ester compound represented by formula (4) with the amine compound represented by formula (5) is carried out in the presence of an alcohol solvent having 1 to 4 carbon atoms.

**Patentansprüche**

1. Ein Verfahren zur Herstellung einer Phenylacetamidverbindung, dargestellt durch Formel (1):

\[
\begin{align*}
\text{O} & \quad \text{R}^4 \\
\text{CON} & \quad \text{R}^2 \\
\text{OR}^4 & \quad \text{Ar} \\
\text{Q} & \quad \text{R}^5
\end{align*}
\]

wobei \( \text{Q} \) für ein Wasserstoffatom oder ein Halogenatom steht, \( \text{R}^2 \) für ein Wasserstoffatom oder eine Alkylgruppe mit 1 bis 4 Kohlenstoffatomen steht, \( \text{R}^4 \) für eine Alkylgruppe mit 1 bis 4 Kohlenstoffatomen steht, \( \text{Ar} \) für eine unsubstituierte oder substituierte Phenylgruppe steht, wobei der optionale Substituent aus der Gruppe bestehend aus Alkylgruppen mit 1 bis 4 Kohlenstoffatomen und Halogenatomen ausgewählt ist, \( \text{R}^5 \) für \( \text{R}^4 \) steht, wenn \( \text{R}^2 \) ein Wasserstoffatom ist, und \( \text{R}^5 \) für ein Wasserstoffatom steht, wenn \( \text{R}^2 \) eine Alkylgruppe mit 1 bis 4 Kohlenstoffatomen ist; umfassend
Umsetzen einer Mandelonitrilverbindung, dargestellt durch Formel (6):
wobei Q für ein Wasserstoffatom oder ein Halogenatom steht und Ar für eine unsubstituierte oder substituierte Phenylgruppe steht, wobei der optionale Substituent aus der Gruppe bestehend aus Alkylgruppen mit 1 bis 4 Kohlenstoffatomen und Halogenatomen ausgewählt ist; mit einer Alkoholverbindung, dargestellt durch Formel (7):

\[ R^1\text{-OH} \quad (7) \]

wobei \( R^1 \) für eine Alkylgruppe mit 1 bis 4 Kohlenstoffatomen steht; und einer Säure und anschließendes Umsetzen des entstandenen Produktes mit Wasser, um eine Essigsäureester-verbinding, dargestellt durch Formel (4), zu erhalten:

\[ \text{OH} \]
\[ \text{Q} \]  
\[ \text{Ar} \]
\[ \text{COOR}^1 \]
\[ \text{(4)} \]

wobei Q für ein Wasserstoffatom oder ein Halogenatom steht, Ar für eine unsubstituierte oder substituierte Phenylgruppe steht, wobei der optionale Substituent aus der Gruppe bestehend aus Alkylgruppen mit 1 bis 4 Kohlenstoffatomen und Halogenatomen ausgewählt ist, und \( R^1 \) für eine Alkylgruppe mit 1 bis 4 Kohlenstoffatomen steht; Umsetzen der Essigsäureester-verbinding, dargestellt durch Formel (4), mit einer Aminverbindung, dargestellt durch Formel (5):

\[ R^2\text{-NH}_2 \quad (5) \]

wobei \( R^2 \) für ein Wasserstoffatom oder eine Alkylgruppe mit 1 bis 4 Kohlenstoffatomen steht; um eine Phenylacetamid-verbinding, dargestellt durch Formel (2), zu erhalten:

\[ \text{OH} \]
\[ \text{Q} \]  
\[ \text{Ar} \]
\[ \text{CON} \]
\[ \text{H} \]
\[ \text{(2)} \]

wobei Q, \( R^2 \) und Ar die vorstehend definierten Bedeutungen aufweisen; und Umsetzen der Phenylacetamid-verbinding, dargestellt durch Formel (2), mit einem Dialkylsulfat, dargestellt durch Formel (3):
wobei R₄ die vorstehend definierte Bedeutung aufweist; in Gegenwart einer Base.

2. Das Herstellungsverfahren gemäß Anspruch 1, wobei R² ein Wasserstoffatom ist.

3. Das Herstellungsverfahren gemäß Anspruch 1, wobei Ar eine 2,5-Dimethylphenylgruppe oder eine 2-Methylphenylgruppe ist.

4. Das Herstellungsverfahren gemäß Anspruch 1, wobei Ar eine 2,5-Dimethylphenylgruppe ist.

5. Das Herstellungsverfahren gemäß Anspruch 1, wobei R⁴ eine Methylgruppe ist.

6. Das Herstellungsverfahren gemäß Anspruch 1, wobei die Base ein Alkalimetallhydroxid ist.

7. Das Herstellungsverfahren gemäß Anspruch 1, wobei die Umsetzung der Essigsäureesterverbindung, dargestellt durch Formel (4), mit der Aminverbindung, dargestellt durch Formel (5), in Gegenwart eines alkoholischen Lösungsmittels mit 1 bis 4 Kohlenstoffatomen durchgeführt wird.

Revendications

1. Procédé de production d’un composé de phénylacétamide représenté par la formule (1):

![Diagram](3)

dans laquelle Q représente un atome d’hydrogène ou un atome d’halogène, R² représente un atome d’hydrogène ou un groupe alkyle ayant de 1 à 4 atomes de carbone, R⁴ représente un groupe alkyle ayant de 1 à 4 atomes de carbone, Ar représente un groupe phényle non substitué ou substitué, le substituant éventuel étant choisi dans le groupe constitué de groupes alkyle ayant de 1 à 4 atomes de carbone et d’atomes d’halogène, R⁵ représente R⁴ lorsque R² est un atome d’hydrogène, et R⁵ représente un atome d’hydrogène lorsque R² est un groupe alkyle ayant de 1 à 4 atomes de carbone ; comprenant la réaction d’un composé de mandélonitrile représenté par la formule (6) :
dans laquelle Q représente un atome d’hydrogène ou un atome d’halogène, et Ar représente un groupe phényle non substitué ou substitué, le substituant éventuel étant choisi dans le groupe constitué de groupes alkyle ayant de 1 à 4 atomes de carbone et d’atomes d’halogène ; avec un composé d’alcool représenté par la formule (7) :

\[
R^1\text{-OH} \quad (7)
\]
dans laquelle \( R^1 \) représente un groupe alkyle ayant de 1 à 4 atomes de carbone ; et un acide, et la réaction subséquente du produit résultant avec de l’eau pour obtenir un composé d’ester d’acide acétique représenté par la formule (4) :

\[
\begin{align*}
\text{OH} & \\
\text{Ar} & \\
\text{Q} & \\
\end{align*} \quad (4)
\]
dans laquelle Q représente un atome d’hydrogène ou un atome d’halogène, Ar représente un groupe phényle non substitué ou substitué, le substituant éventuel étant choisi dans le groupe constitué de groupes alkyle ayant de 1 à 4 atomes de carbone et d’atomes d’halogène, et \( R^1 \) représente un groupe alkyle ayant de 1 à 4 atomes de carbone ; la réaction du composé d’ester d’acide acétique représenté par la formule (4) avec un composé d’amine représenté par la formule (5) :

\[
\begin{align*}
\text{R}^2\text{-NH}_2 & \\
\end{align*} \quad (5)
\]
dans laquelle \( R^2 \) représente un atome d’hydrogène ou un groupe alkyle ayant de 1 à 4 atomes de carbone ; pour obtenir un composé de phénylacétamide représenté par la formule (2) :

\[
\begin{align*}
\text{OH} & \\
\text{Ar} & \\
\text{Q} & \\
\text{R}^2 & \\
\text{H} & \\
\end{align*} \quad (2)
\]
dans laquelle Q, \( R^2 \) et Ar ont les mêmes significations que définies ci-dessus ; et la réaction du composé de phénylacétamide représenté par la formule (2) avec un sulfate de dialkyle représenté par la formule (3) :
dans laquelle $R^4$ a la même signification que définie ci-dessus ; en présence d’une base.

2. Procédé de production selon la revendication 1, dans lequel $R^2$ est un atome d’hydrogène.

3. Procédé de production selon la revendication 1, dans lequel $Ar$ est un groupe 2,5-diméthylphényle ou un groupe 2-méthylphényle.

4. Procédé de production selon la revendication 1, dans lequel $Ar$ est un groupe 2,5-diméthylphényle.

5. Procédé de production selon la revendication 1, dans lequel $R^4$ est un groupe méthyle.

6. Procédé de production selon la revendication 1, dans lequel la base est un hydroxyde de métal alcalin.

7. Procédé de production selon la revendication 1, dans lequel la réaction du composé d’ester d’acide acétique représenté par la formule (4) avec le composé d’amine représenté par la formule (5) est réalisée en présence d’un solvant d’alcool ayant de 1 à 4 atomes de carbone.
REFERENCES CITED IN THE DESCRIPTION

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Patent documents cited in the description

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