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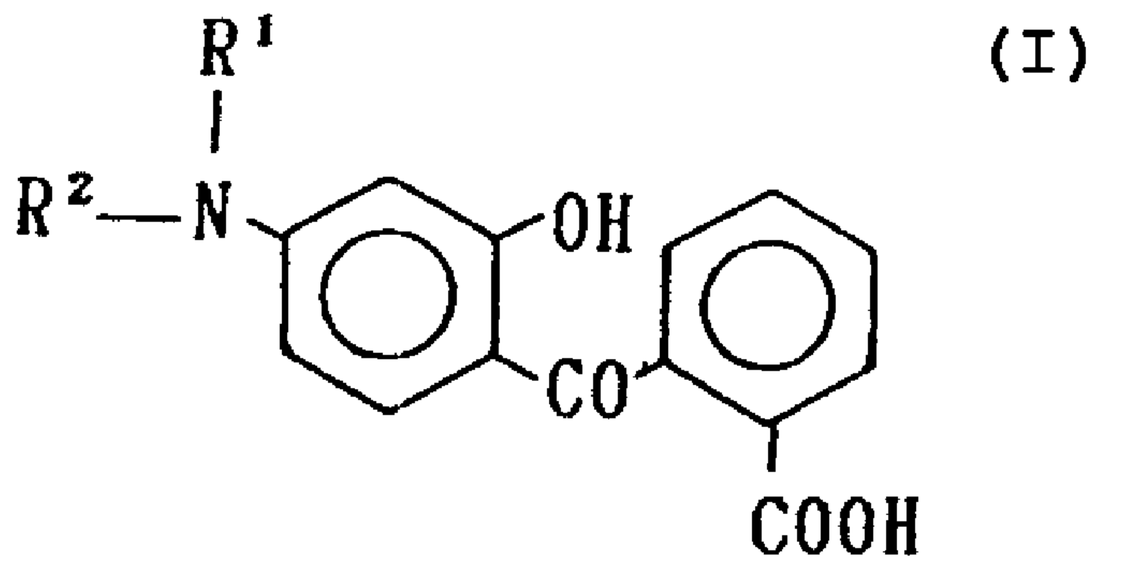
(54) Title: METHOD OF PRODUCING KETO ACIDS



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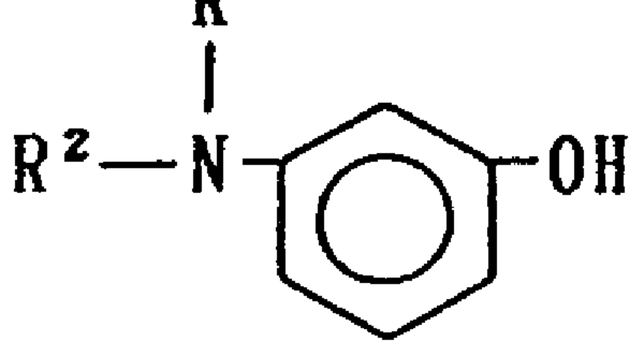

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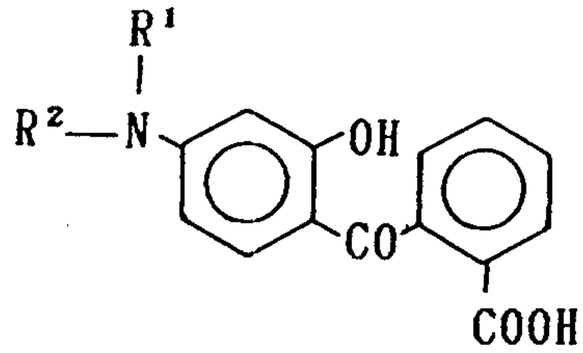
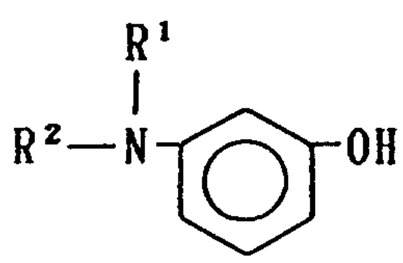
(57) Abrégé/Abstract:
An improvement in a method of producing a keto acid having the general formula of (see formula I) wherein R^1 and R^2 independently represent an alkyl of 1-6 carbons or a cycloalkyl of 4-8 carbons, in an organic solvent, which comprises reacting a m-aminophenol having the general formula of (see formula II) wherein R^1 and R^2 are the same as above, with phthalic anhydride, the improvement comprising depositing the resultant keto acid in the solvent while effecting the reaction in a slurry.

ABSTRACT OF THE DISCLOSURE

An improvement in a method of producing a keto acid having the general formula of



wherein R^1 and R^2 independently represent an alkyl of 1-6 carbons or a cycloalkyl of 4-8 carbons, in an organic solvent, which comprises reacting a m-aminophenol having the general formula of



wherein R^1 and R^2 are the same as above, with phthalic anhydride, the improvement comprising depositing the resultant keto acid in the solvent while effecting the reaction in a slurry.

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METHOD OF PRODUCING KETO ACIDS

Field of the Invention

This invention relates to a method of producing keto acids.

Keto acids are useful intermediates for the production of fluoran compounds used as dyestuff in pressure- or heat-sensitive recording.

Description of the Prior Art

The keto acids have hitherto been produced by the reaction of an N,N-dialkyl-m-aminophenol with phthalic anhydride in a molar ratio of phthalic anhydride to N,N-dialkyl-m-aminophenol of 0.5-2 both dissolved in an inactive organic solvent such as toluene, xylene or tetrahydrofuran at a temperature of 80-150℃. However, the method provides a considerable amount of Rhodamines known as red dyes by the reaction of the resultant keto acids with the N,N-dialkyl-m-aminophenol, thereby to reduce the yield of the keto acids, as well as to make it difficult to obtain high purity keto acids.

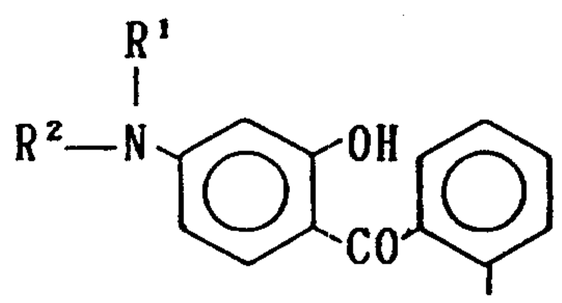
To solve the above problem, there has been proposed a method in which an aqueous solution of an alkali metal hydroxide such as sodium hydroxide is added to the resultant reaction mixture, the reaction mixture is heated to decompose by-produced Rhodamines to alkali metal salts of the keto acid, the alkali metal salt of the keto acid is crystallized and then dissolved again in water, and then the salt is neutralized in water to recover the keto acid, as disclosed

in Japanese Patent Application Laid-open No. 62-70350. However, the method needs a many number of steps, and in addition, the method produces a large amount of neutralization waste water.

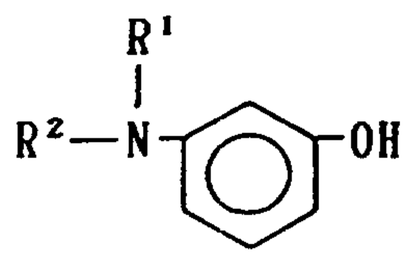
Brief Summary of the Invention

It is, therefore, an object of the invention to provide a method of producing keto acids of high purity in high yield by the reaction of an N,N-dialkyl-m-aminophenol with phthalic anhydride while suppressing undesirable by-production of Rhodamines.

The invention provides an improvement in a method of producing a keto acid having the general formula of



wherein R^1 and R^2 independently represent an alkyl of 1-6 carbons or a cycloalkyl of 4-8 carbons, in an organic solvent, which comprises reacting a m-aminophenol having the general formula of



wherein R^1 and R^2 are the same as above, with phthalic anhydride, the improvement comprising depositing the resultant keto acid in the organic solvent while effecting the reaction in a slurry.

Detailed Description of the Invention

The m-aminophenol wherein both R^1 and R^2 are alkyls of 1-6 carbons used in the invention includes, for example, N,N-dimethyl-m-aminophenol, N,N-diethyl-m-aminophenol, N,N-di-n-propyl-m-aminophenol, N,N-di-isopropyl-m-aminophenol, N,N-di-n-butyl-m-aminophenol, N-methyl-N-ethyl-m-aminophenol, N-ethyl-N-isopropyl-m-aminophenol, N-ethyl-N-n-butyl-m-aminophenol and N-ethyl-N-isoamyl-m-aminophenol. The m-aminophenol wherein one of R^1 and R^2 is a cycloalkyl may be exemplified by N-ethyl-N-cyclohexyl-m-aminophenol.

For the reaction of the m-aminophenol derivative as above mentioned with phthalic anhydride, the latter is used usually in an amount of 0.7-2 moles per mole of the m-aminophenol derivative. The reaction is effected in a controlled amount of an organic solvent so that the resultant keto acid deposits in the solvent thereby to form a slurry, and the reaction is allowed to proceed in such a slurry. Strictly speaking, the amount of the solvent used is determined so that the resultant keto acid deposits in the solvent and thus the reaction proceeds in a slurry of the keto acid in the solvent. However, the amount of the solvent is usually in the range of 0.5-3 parts by weight in relation to one part by weight of the m-aminophenol derivative used.

The organic solvent used includes, for example, an aromatic hydrocarbon of 6-10 carbons such as benzene, toluene or xylene, an aliphatic hydrocarbon of 8-12 carbons such as octane, isooctane or decane, a halogenated hydrocarbon of 2-8 carbons, aliphatic, cycloaliphatic or aromatic, such as perchlene or chlorobenzene, ethers such as tetrahydrofuran, dibutyl ether or diphenyl ether, among which are especially preferred aromatic hydrocarbons or ethers.

By way of example, when the reaction of N,N-di-n-

butyl-m-aminophenol with phthalic anhydride is carried out in an aromatic hydrocarbon such as benzene, toluene or xylene, the preferred amount of the solvent is in the range of 0.5-2 parts by weight in relation to one part by weight of the N,N-di-n-butyl-m-aminophenol.

The reaction is effected at an elevated temperature, preferably at a temperature in the range of 60-120℃ for a period of 4-40 hours, although the reaction temperature and time are not critical. After the reaction, the reaction mixture is cooled usually to normal temperature, preferably to a temperarture of 0-35℃, most preferably to 10-30℃, depending upon the solvent used, or a bad solvent such as a saturated hydrocarbons is added to the reaction mixture, to effect primary crystallization of the resultant keto acid.

The resultant crude crystals are then dissolved under heating in an aliphatic alcohol of 1-4 carbons and then secondary crystallization is effected. The secondary crystallization may be effected at the same temperature range as in the primary crystallization. The secondary crystallization enables to obtain a high purity keto acid which contains substantially no Rhodamine impurities.

There may be used as the alcohol for the secondary crystallization solvent, for example, methanol, ethanol, propanols such as isopropanol or butanols such as n-butanol. There may also be used a mixture of the alcohol with water, or a mixture of the alcohol with a hydrocarbon solvent, preferably an aromatic hydrocarbon of 6-10 carbons such as toluene or xylene, or an aliphatic hydrocarbon of 5-10 carbons such as pentane, hexane or heptane.

The crude crystals may be dissolved in the alcohol under an elevated pressure, usually under a pressure of several atmospheric pressures, and then the solution may be cooled to effect the secondary crystallization.

Further according to the invention, after the reaction,

an aliphatic alcohol of 1-4 carbons may be added to the reaction mixture and then primary crystallization may be effected. The addition of the aliphatic alcohol to the reaction mixture enables selective dissolution of Rhodamines so that the slurry is kept in a good state from which the resultant crystals can be collected by filtration easily.

As above set forth, the reaction of the m-aminophenol derivative with phthalic anhydride is carried out in a controlled amount of an organic solvent to allow the resultant keto acid to deposit in the solvent and the reaction to proceed in a slurry according to the invention. Thus, the by-production of undesirable Rhodamines is effectively suppressed to improve the selectivity of the reaction to the keto acid. In addition, there is obtained a high purity keto acid which contains substantially no Rhodamine impurities by effecting secondary crystallization of the resultant keto acid out of the alcohol.

Further according to the invention, the alcohol may be recovered from the the secondary crystallization mother liquor, and if necessary, the alcohol is completely removed, to provide a residual solid which contains the keto acid. The solid is then dissolved in an inactive organic solvent which can be used as a reaction solvent, and the thus resultant solution may be added to the reaction mixture, and the mixture is then cooled to effect primary crystallization. This results in a remarkable improvement in yield of keto acid.

The amount of undesirable Rhodamines by-produced in the reaction is small according to the invention, and thus the rate of the Rhodamines to the keto acid in the mother liquor after the secondary crystallization is very small. Therefore, according to the invention, the solvent in the mother liquor is exchanged with an organic solvent which can be used as a reaction solvent, and the resultant solution containing the keto acid can be advantageously

used for primary crystallization together with the reaction mixture, thereby to increase the yield of the keto acid.

The invention will now be described in more detail with reference to examples, however, the invention is not limited to the examples.

Example 1

An amount of 165 g (1.0 mole) of N,N-diethyl-m-aminophenol, 170.3 g (1.15 mole) of phthalic anhydride and 206 g of xylene were placed in a reactor, and stirred for 7 hours at 115℃ while allowing the resultant keto acid (4-N,N-diethylamino-2-hydroxy-2'-carboxybenzophenone) to deposit in the reaction mixture and the reaction to proceed in a slurry.

After the reaction, 247 g of xylene were added to the reaction mixture, and the mixture was cooled gradually to 20℃ so that the keto acid crystalized out. The crystals were collected by filtration and washed with 577 g of n-butanol to provide 303.9 g of crude crystals.

An amount of 1486 g of n-butanol was added to the crystals and heated to dissolve the crystals therein, and then the mixture was cooled to 20℃ gradually. The resultant crystals were collected by filtration and dried to provide 291.9 g of high purity keto acid (4-N,N-diethylamino-2-hydroxy-2'-carboxybenzophenone). The amount of Rhodamines in the keto acid was found to be not more than 0.1% by liquid chromatographic analysis. The yield was 93.1 mol %.

Example 2

After the reaction, n-butanol was added to the reaction mixture in place of xylene, and otherwise in the same manner as in Example 1, crude crystals were obtained.

An amount of 1486 g of n-butanol was added to 303.6 g

of the crystals and heated to dissolve the crystals therein, and then the mixture was cooled to 20℃ gradually. The resultant pale yellow crystals were collected by filtration and dried to provide 291.5 g of high purity keto acid (4-N,N-diethylamino-2-hydroxy-2'-carboxybenzophenone).

There was detected no Rhodamines in the keto acid by liquid chromatographic analysis. The yield was 93.5 mol %.

Example 3

The reaction was effected in toluene in place of xylene, and after the reaction methanol was added in place of xylene to the reaction mixture, and the mixture was cooled gradually to 20℃ so that the keto acid crystalized out and the crystals were washed with methanol, and otherwise in the same manner as in Example 1.

An amount of 913 g of methanol was added to 304.5 g of the crude crystals and heated to 113℃ under a pressure of 3 Kg/cm^2 to completely dissolve the crystals therein, and then the mixture was cooled to 20℃ gradually. The resultant pale yellow crystals were collected by filtration and dried to provide 295.3 g of high purity keto acid (4-N,N-diethylamino-2-hydroxy-2'-carboxybenzophenone).

There was detected no Rhodamines in the keto acid by liquid chromatographic analysis. The yield was 94.3 mol %.

Example 4

An amount of 221 g (1.0 mole) of N,N-di-n-butyl-m-aminophenol, 177.7 g (1.2 mole) of phthalic anhydride and 220 ml of xylene were placed in a reactor, and stirred for 7 hours at 100℃ while allowing the resultant keto acid (4-N,N-di-n-butylamino-2-hydroxy-2'-carboxybenzophenone) to deposit in the reaction mixture and the reaction to proceed in a slurry.

After the reaction, 220 ml of xylene were added to the reaction mixture, and the mixture was cooled gradually

to 20℃ so that the keto acid crystalized out. The crystals were collected by filtration and washed with 80 ml of xylene twice.

An amount of 320 g of the resultant crude crystals was added to 1250 g of methanol. The mixture was heated to dissolve the crystals in the methanol, and then the mixture was cooled to 20℃ gradually to effect recrystallization of the keto acid. The resultant crystals were collected by filtration and washed with 100 g of cold methanol twice followed by drying the crystals to provide 255 g of high purity keto acid (4-N,N-di-n-butylamino-2-hydroxy-2'-carboxybenzophenone).

There was detected no Rhodamines in the keto acid by liquid chromatographic analysis. The yield was 69.0 mol %.

Example 5

The reaction was effected in toluene in place of xylene, and otherwise in the same manner as in Example 4 to provide 258 g of high purity keto acid (4-N,N-di-n-butylamino-2-hydroxy-2'-carboxybenzophenone).

There was detected no Rhodamines in the keto acid by liquid chromatographic analysis. The yield was 69.8 mol %.

Example 6

The crystals of keto acid (4-N,N-di-n-butylamino)-2-hydroxy-2'-carboxybenzophenone) obtained in Example 4 were recrystallized, collected by filtration, and washed with cold methanol. The mother liquor was distilled to recover methanol.

An amount of 220 ml of xylene was added to the distillation bottom containing the keto acid to dissolve the keto acid therein.

The resultant solution was added to the same reaction mixture as obtained in Example 1 and then primary crystallization was effected, followed by working in the

same manner as in Example 1, there were obtained 299 g of pale yellow crystals of high purity keto acid (4-N,N-di-n-butylamino-2-hydroxy-2'-carboxybenzophenone).

There was detected no Rhodamines in the keto acid by liquid chromatographic analysis. The yield was 81 mol % based on the N,N-di-n-butyl-m-aminophenol used.

Example 7

An amount of 207 g (1.0 mole) of N-ethyl-N-isoamyl-m-aminophenol, 177.6 g (1.2 mole) of phthalic anhydride and 300 g of diphenyl ether were placed in a reactor, and stirred for 35 hours at 60℃ while allowing the resultant keto acid (4-N-ethyl-N-isoamylamino-2-hydroxy-2'-carboxybenzophenone) to deposit in the reaction mixture and the reaction to proceed in a slurry.

The conversion rate of N-ethyl-N-isoamyl-m-aminophenol was 66%; the yield of keto acid (4-N-ethyl-N-isoamylamino-2-hydroxy-2'-carboxybenzophenone) was 65%; and the yield of Rhodamines was 1%.

After the reaction, the reaction mixture was cooled to 30℃ so that the keto acid crystalized out, and the crystals were collected by filtration. An amount of 1700 ml of a mixture of methanol/water (75/25 in volume ratio) was added to 230 g of the crystals and heated to dissolve the crystals therein. The mixture was then cooled gradually to 20℃ to effect recrystallization and the resultant crystals were collected by filtration.

The amount of Rhodamines in the keto acid was found to be not more than 0.1% by liquid chromatographic analysis.

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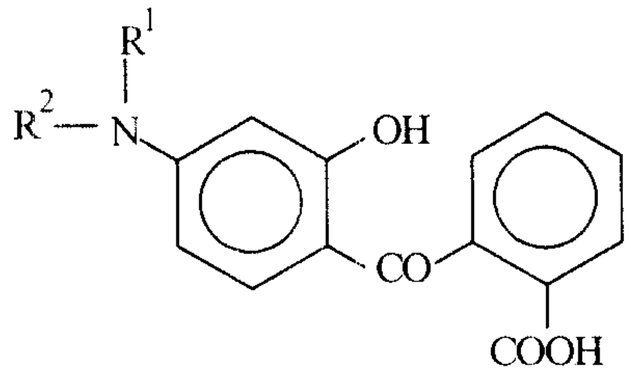
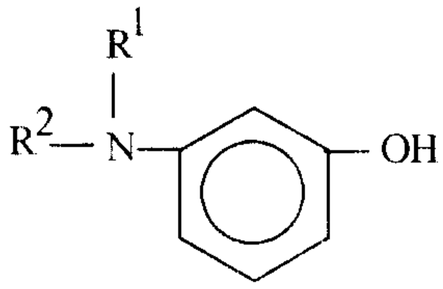
CLAIMS:

1. A method of producing a keto acid having the general formula:



wherein R^1 and R^2 independently represent an alkyl group of 1-6 carbons or a cycloalkyl group of 4-8 carbons, in an organic solvent, which comprises:

reacting a m-aminophenol having the general formula:



wherein R^1 and R^2 are the same as above, with phthalic anhydride, in an organic solvent in an amount of 0.5-3 parts by weight per part by weight of the m-aminophenol,

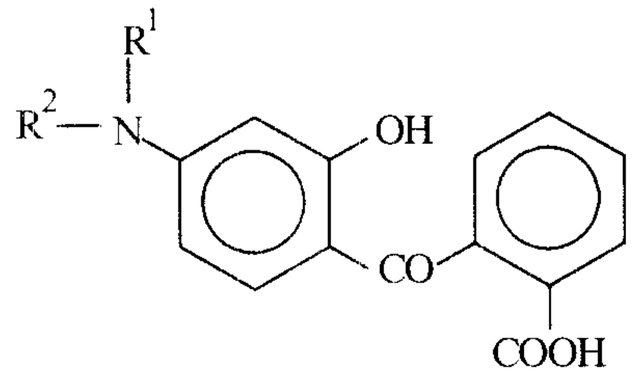
wherein the resultant keto acid is deposited in the solvent while effecting the reaction in a slurry.

2. The method as claimed in claim 1, wherein phthalic anhydride is used in an amount of 0.7-2 moles per mole of the m-aminophenol.

3. The method as claimed in claim 1 or 2, wherein the organic solvent is benzene, toluene or xylene.

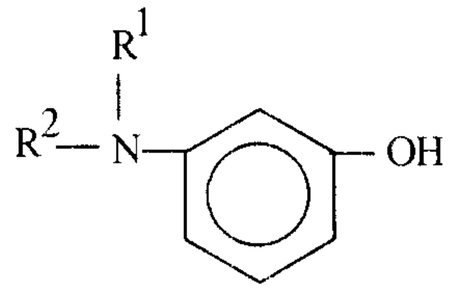
4. The method as claimed in claim 1 or 2, wherein the organic solvent is diphenyl ether.

5. A method of producing a keto acid having the general formula:



wherein R^1 and R^2 independently represent an alkyl group of 1-6 carbons or a cycloalkyl group of 4-8 carbons, which comprises:

reacting a m-aminophenol having the general formula:



wherein R^1 and R^2 are the same as above, with phthalic anhydride at an elevated temperature in an organic solvent in an amount of 0.5-3 parts by weight per part, by weight of the m-aminophenol, wherein:

a) the resultant keto acid is deposited in the solvent while effecting the reaction in a slurry to obtain a reaction mixture;

b) the reaction mixture is cooled to effect primary crystallization to provide crude crystals of the keto acid;

c) the crude crystals are dissolved in an aliphatic alcohol of 1-4 carbons, or a mixture of the

alcohol with water, or a mixture of the alcohol with a hydrocarbon solvent;

d) secondary crystallization is effected from the alcohol or the mixture;

e) the alcohol or the mixture is recovered from the resultant crystallization mother liquor; and

f) the recovered keto acid is added to the reaction mixture for use in the primary crystallization.

6. The method as claimed in claim 5, wherein the aliphatic alcohol is methanol or butanol.

7. The method as claimed in claim 5 or 6, wherein after the reaction, an aliphatic alcohol of 1-4 carbons is added to the reaction mixture, and then the primary crystallization is effected.

8. The method as claimed in claim 7, wherein the aliphatic alcohol is methanol or butanol.

9. The method as claimed in any one of claims 5 to 8, wherein the hydrocarbon solvent is an aromatic hydrocarbon of 6-10 carbons.

10. The method as claimed in any one of claims 5 to 8, wherein the hydrocarbon solvent is an aliphatic hydrocarbon of 5-10 carbons.

11. The method as claimed in claim 9, wherein the aromatic hydrocarbon is toluene or xylene.

12. The method as claimed in claim 10, wherein the aliphatic hydrocarbon is hexane.

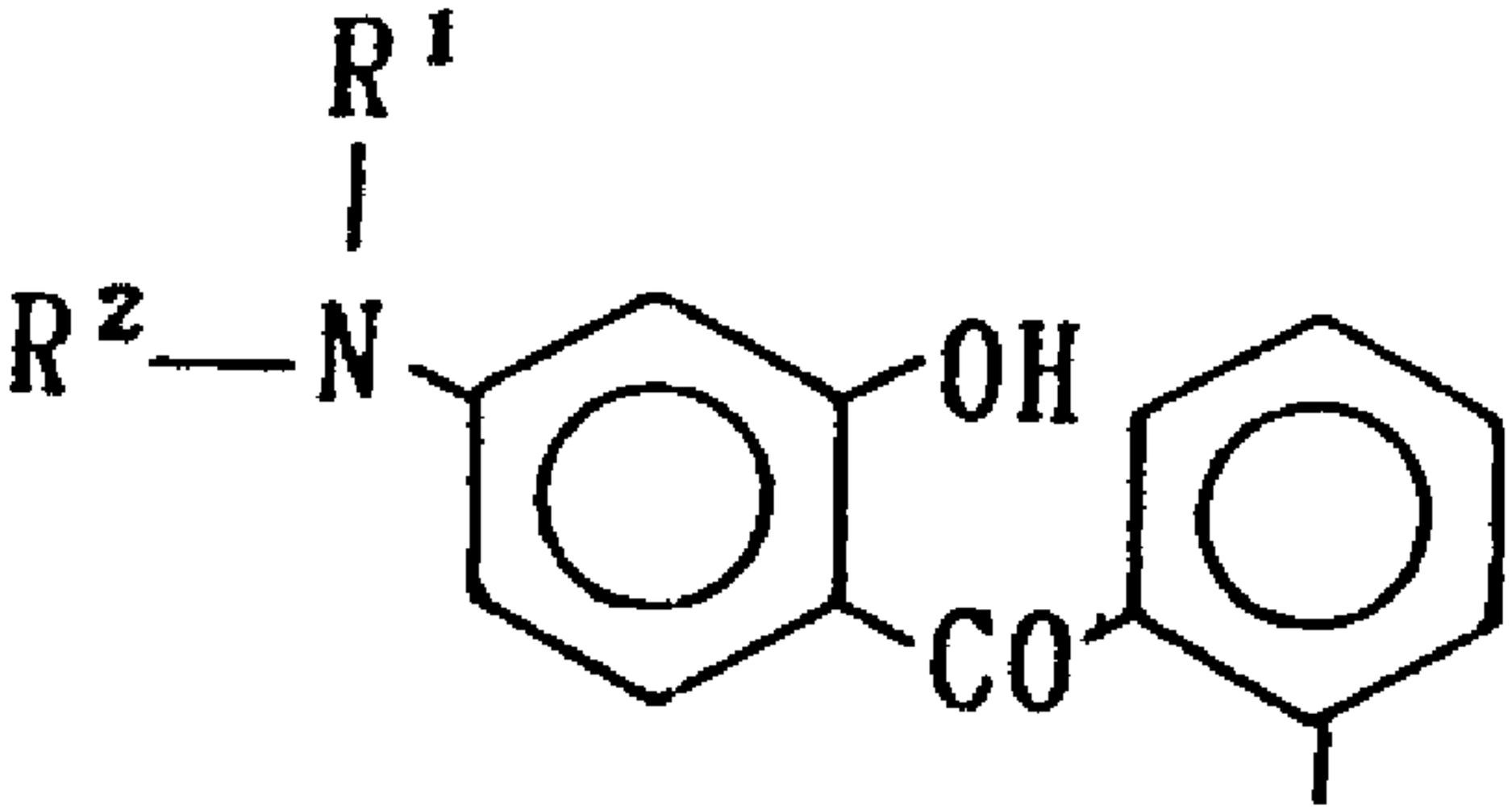
13. The method as claimed in any one of claims 5 to 12, wherein the crude crystals are dissolved in the alcohol or the mixture under an elevated pressure.

14. The method as claimed in any one of claims 5 to 13, wherein the reaction is effected at a temperature in the range of 60-120°C.

SMART & BIGGAR

OTTAWA, CANADA

PATENT AGENTS



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(II)