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(54) Title: PROCESS FOR PRODUCING TOLUIDINE COMPOUND

(57) Abstract: Because fluazinam is excellent as an active ingredient of pesticides and highly useful, it is desired to produce it efficiently in a proper form with simple operations at low cost in an environmentally friendly manner. The desired product is obtained in good yields with simple operations by using industrially advantageous reaction systems by a process comprising (1) a step of reacting ACTF and DCDNBTF in the presence of an alkali component a tertiary alcohol as a solvent and (2) a step of neutralizing or acidifying the reaction mixture with an acid.

DESCRIPTION

PROCESS FOR PRODUCING TOLUIDINE COMPOUND

BACKGROUND OF THE INVENTION

TECHNICAL FIELD

The present invention relates to a process for producing 3-chloro-N-(3-chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine as an active ingredient of pesticides (common name: fluazinam).

BACKGROUND ART

USP 4,331,670 (Patent Document 1) discloses a process for producing 3-chloro-N-(3-chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine which comprises reacting 2-amino-3-chloro-5-trifluoromethylpyridine and 2,4-dichloro-3,5-dinitrobenzotrifluoride in the presence of a base and a solvent and discloses alkali metal hydroxides, carbonates and hydrides or alkaline earth metal hydroxides and carbonates as examples of the base and aprotic polar solvents such as dimethylformamide, dimethyl sulfoxide, tetrahydrofuran (THF), sulfolane and dioxane as examples of the solvent.

WO 2007/060662 (Patent Document 2) discloses the use of methyl isobutyl ketone (MIBK) as the solvent in the above-mentioned process disclosed in USP 4,331,670

(Patent Document 1). Patent Document 2 discloses that a higher yield is attained when the presence of water, which is hardly miscible with MIBK, in the reaction is minimized to decrease the hydrolysis by-product and that the presence of a high concentration of water resulting from the reaction or attributed to the reagents increases the hydrolysis by-product and thereby decreases the yield. Patent Document 2 also discloses that the ratio of the solvent to the reactant should be larger than about 10%w/v and that the solvent is preferably pure MIBK (for example, with a purity of about 98%) or recycled MIBK with a water content of less than 2%, and that in the production of fluazinam as the desired product described in Example 2, the reaction was carried out by adding solid KOH (3.5 mol eq.) to a mixture of 2-amino-3-chloro-5-trifluoromethylpyridine, 2,4-dichloro-3,5-dinitrobenzotrifluoride and a MIBK azeotrope containing 1.6% water.

Patent Document 1: USP 4,331,670

Patent Document 2: WO 2007/060662

DISCLOSURE OF THE INVENTION

Because fluazinam is excellent as an active ingredient of pesticides and highly useful, it is desired to produce fluazinam efficiently in a proper form with simple operations at low cost in an environmentally friendly manner. Especially, there is a demand for

processes preferable from the viewpoints of the cost for industrial production, simplicity of reaction procedures and safety.

Through their extensive research on the reaction conditions and reaction procedures for more efficient and industrially advantageous production of 3-chloro-N-(3-chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine, the present inventors found that the use of a tertiary alcohol such as tertiary butyl alcohol, optionally with the intentional use of a substantial amount of water, carries various advantages and allows a high yield of the desired product, leads to an excellent reaction yield and is favorable for post-reaction operations such as isolation, purification and recovery of the product and accomplished the present invention on the basis of these discoveries.

Namely, the present invention provides the following.

[1] A process for producing 3-chloro-N-(3-chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine, which comprises (1) a step of reacting 2-amino-3-chloro-5-trifluoromethylpyridine and 2,4-dichloro-3,5-dinitrobenzotrifluoride in the presence of an alkali component selected from the group consisting of hydroxides and carbonates of alkali metals and hydroxides and carbonates of alkaline earth metals as a basic substance and a tertiary alcohol as a solvent, and (2) a

step of neutralizing or acidifying a mixture containing 3-chloro-N-(3-chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine as the reaction product and the solvent with an acid.

[2] The process according to [1], wherein the basic substance is sodium hydroxide or potassium hydroxide.

[3] The process according to [1] or [2], wherein the solvent is tertiary butyl alcohol.

[4] The process according to any one of [1] to [3], wherein the acid is hydrochloric acid.

[5] The process according to any one of [1] to [3], wherein the acid is sulfuric acid.

[6] The process according to any one of [1] to [5], wherein in the step (1), water is present in a sufficient amount to substantially dissolve the alkali component.

[7] The process according to any one of [1] to [6], wherein in the step (1), a 35-50% sodium hydroxide aqueous solution or a corresponding amount of a mixture of a sodium hydroxide aqueous solution, solid sodium hydroxide and water is present in an amount of at least 2 mol, preferably 6 to 10 mol, in relation to 1 mol of 2-amino-3-chloro-5-trifluoromethylpyridine.

[8] The process according to any one of [1] to [7], wherein in the step (1), water is present in an amount of at least 7%, preferably 14.8 to 79%, particularly preferably 20 to 40%, in relation to the total of water and the solvent.

[9] The process according to any one of [1] to [8], wherein in the step (1), 2,4-dichloro-3,5-dinitrobenzotrifluoride is used in an amount of from 0.8 to 1.2 mol, preferably 1 to 1.05 mol, in relation to 1 mol of 2-amino-3-chloro-5-trifluoromethylpyridine.

[10] The process according to any one of [1] to [9], wherein the solvent is used in an amount of from 50 to 1000 g, preferably 100 to 700 g, in relation to 100 g of 2-amino-3-chloro-5-trifluoromethylpyridine.

[11] The process according to any one of [1] to [5], wherein in the step (2), the mixture containing 3-chloro-N-(3-chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine as the reaction product and the solvent is separated, and the organic phase is neutralized or acidified with the acid.

[12] The process according to any one of [1] to [5] and [11], wherein in the step (2), the pH is adjusted to 2 to 7, preferably 5 to 6, with the acid.

[13] The process according to any one of [1] to [5], [11] and [12], wherein in the step (2), the mixture containing 3-chloro-N-(3-chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine as the reaction product and the solvent is mixed with water and then neutralized or acidified with the acid to precipitate crystals of the product.

[14] The process according to any one of [1] to [5] and [11] to [13], wherein in the step (2), the crystals are

precipitated in the presence of α-crystals of the reaction product as a seed.

[15] A method for purifying 3-chloro-N-(3-chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine as a product, which comprises washing precipitated crystals with hydrous isopropanol to obtain the product in a purer form with less contaminants.

[16] The method according to [15], wherein the precipitated crystals are washed with water before they are washed with hydrous isopropanol.

[17] A method for drying a product, which comprises drying 3-chloro-N-(3-chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine as a product under a reduced pressure.

[18] The method for drying a product according to [17], wherein the drying is carried out under a reduced pressure of at most 300 mmHg.

[19] The method for drying a product according to [17], wherein the drying is carried out under a reduced pressure of at most 200 mmHg.

[20] The method for drying a product according to any one of [17] to [19], wherein the drying is carried out at a temperature of 115°C or below.

[21] The method for drying a product according to any one of [17] to [19], wherein the drying is carried out at a temperature of 70°C or below.

[22] A process for producing 3-chloro-N-(3-chloro-5-

trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine or a salt thereof, which comprises reacting 2-amino-3-chloro-5-trifluoromethylpyridine and 2,4-dichloro-3,5-dinitrobenzotrifluoride in the presence of an alkali component selected from the group consisting of sodium hydroxide and potassium hydroxide and a tertiary alcohol as a solvent.

According to the present invention, in production of 3-chloro-N-(3-chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine by reacting 2-amino-3-chloro-5-trifluoromethylpyridine and 2,4-dichloro-3,5-dinitrobenzotrifluoride, it is possible not only to obtain the desired product in excellent yields by using industrially advantageous reaction systems through simple procedures, but also to isolate and purify the desired product efficiently and industrially advantageously. The process of the present invention gives a high yield of the desired product and is therefore advantageous over conventional processes in industrial applicability. Further, it is an extremely excellent industrial process from the viewpoints of cost, operations and safety.

Other objects, features, advantages and aspects of the present invention would be clear to a person skilled in the art from the following description. However, it should be understood that the following description and specific examples in the present specification illustrate preferable embodiments of the present invention just for

the sake of explanation. From the teachings of the following description and the rest of the present specification, a person skilled in the art would readily understand various possible changes and/or revisions (modifications) within the intention in the present invention and the scope of the present invention disclosed in the present specification. All the patent documents and reference documents referred to in the present specification are referred to for the sake of explanation, and their contents should be understood to be incorporated in the present specification as part of the present specification.

BEST MODE FOR CARRYING OUT THE INVENTION

It is necessary to carry out the above-mentioned step (1) at a sufficient alkali concentration, preferably at the highest possible alkali concentration or under high alkali conditions. As the basic substance, alkali components such as hydroxides and carbonates of alkali metals, hydroxides and carbonates of alkaline earth metals may be mentioned, and specifically, sodium hydroxide, potassium hydroxide, sodium carbonate, potassium carbonate, sodium hydrogen carbonate, potassium hydrogen carbonate, calcium hydroxide, magnesium hydroxide, calcium carbonate and magnesium carbonate may be mentioned. Sodium hydroxide, potassium hydroxide, calcium hydroxide and magnesium hydroxide are preferably

mentioned. An alkali selected from the group consisting of sodium hydroxide and potassium hydroxide is preferred for industrial use. Sodium hydroxide is particularly preferred because it is industrially available at low prices. For simplicity, the present invention will be described in reference to sodium hydroxide as a typical example of the basic substance, although other basic substances may be used instead of sodium hydroxide.

In the step (1), the alkali component may be present in an amount of at least 5 g in relation to 100 g of a tertiary alcohol, although there are no particular restrictions. For example, at least 5 g, preferably at least 8 g, particularly preferably at least 10 g, of sodium hydroxide may be present in the reaction system in relation to 100 g of a tertiary butyl alcohol. In typical cases, the reaction system contains from 10 to 50 g, preferably from 12 to 30 g, particularly preferably from 13 to 20 g, of an alkali such as sodium hydroxide, in relation to 100 g of tertiary butyl alcohol as the solvent.

In the step (1), it is possible and preferred to incorporate water in an amount enough to substantially dissolve the alkali. In the step (1), at least 2 mol, preferably from 6 to 10 mol, of an alkali component, for example, at least 2 mol, preferably from 6 to 10 mol, of a 30-50% sodium hydroxide aqueous solution, or the corresponding amounts of an alkali such as sodium

hydroxide and water, may be present in the reaction system in relation to 1 mol of 2-amino-3-chloro-5-trifluoromethylpyridine. The concentration of the alkali aqueous solution such as the above-mentioned sodium hydroxide aqueous solution in the reaction solution is preferably from 35 to 50%, particularly preferably from 37 to 48%. The aqueous solution or the corresponding amounts of an alkali such as sodium hydroxide and water may be incorporated into the reaction system by using an alkali aqueous solution such as a sodium hydroxide aqueous solution preliminarily prepared at a predetermined concentration, of course. When a material containing water such as a recycled solvent is used for the reaction, a solid alkali such as sodium hydroxide and water may be used by allowing for the water in the material so that the above-mentioned aqueous solution is obtained in the reactor, and the present invention covers such a case. For example, the concentration of an alkali aqueous solution such as a sodium hydroxide aqueous solution in the reaction system may be raised as long as an alkali such as sodium hydroxide does not remain in the crystalline or solid form in the reaction system at the time of isolation of the desired product.

In the step (1), although the reaction may be carried out without water in the reaction system, the reaction is carried out preferably in a reaction system containing a substantial amount of water. The

substantial amount of water contained in the reaction system means an amount sufficient not to leave the alkali such as sodium hydroxide in the crystalline or solid form so that the alkali does not have to be separated by solid-liquid separation such as filtration or dissolved by adding water when the desired product is isolated after the reaction. For example, at least 7%, preferably from 14.8 to 79%, of water may be present in relation to the total of water and the solvent, and typically, from 20 to 40%, of water is present.

In the step (1), from 0.8 to 1.2 mol of 2,4-dichloro-3,5-dinitrobenzotrifluoride may be used in relation to 1 mol of 2-amino-3-chloro-5-trifluoromethylpyridine. Preferably, from 1 to 1.05 mol of 2,4-dichloro-3,5-dinitrobenzotrifluoride may be used in relation to 1 mol of 2-amino-3-chloro-5-trifluoromethylpyridine. The reaction (1) is a condensation reaction between 2-amino-3-chloro-5-trifluoromethylpyridine and 2,4-dichloro-3,5-dinitrobenzotrifluoride, and the two starting materials are preferably used in a ratio within the above-mentioned range by allowing for slight loss of the latter, though they are used in equimolar amounts in theory. Nevertheless, their ratio may fall outside the above-mentioned range.

In the step (1), from 50 to 1000 g, preferably from 100 to 700 g, of a solvent may be used in relation to 100

g of 2-amino-3-chloro-5-trifluoromethylpyridine. The solvent used in the process of the present invention is selected from tertiary alcohols (such as tertiary butyl alcohol and tertiary amyl alcohol). The use of such a solvent is not only suitable for attaining a higher yield in the reaction (1) but also greatly simplifies the operations up to recovery of the desired product in the process of the present invention. Such a solvent is miscible with water or forms a low-boiling azeotrope with water.

The reaction procedure in the step (1) such as the order in which the starting materials and the solvent are fed into the reactor is determined considering that the reaction is exothermic and that 2,4-dichloro-3,5-dinitrobenzotrifluoride is susceptible to hydrolysis. The best procedure comprises firstly feeding 2-amino-3-chloro-5-trifluoromethylpyridine and a given amount of a solvent into the reactor, mixing them, then feeding an alkali aqueous solution such as a sodium hydroxide aqueous solution and/or an alkali such as solid sodium hydroxide, if necessary further adding a solvent and/or water for adjustment of the basicity of the resulting solution, mixing the resulting solution, cooling the resulting mixture to 5-30°C for a while and feeding 2,4-dichloro-3,5-dinitrobenzotrifluoride dissolved in the solvent. The procedure may be appropriately modified in view of the prices of the starting reaction materials to

be used and the reaction conditions.

The reaction temperature for the reaction is from 10 to 40°C, preferably from 15 to 35°C. The reaction time is about from 0.5 to 5 hours, preferably about from 1.0 to 3.5 hours. The reaction may be carried out under an atmosphere of an inert gas such as nitrogen or argon. The progress and completion of the reaction can be monitored by instrumental analysis such as HPLC. After completion of the reaction, the reaction mixture is neutralized or acidified with an acid in order to inactivate the excess base in the reaction mixture and liberate the free reaction product from its salt with an alkali such as sodium.

In the step (2), an acid is used to neutralize or acidify the reaction mixture obtained after completion of the reaction (1). The acid is preferably hydrochloric acid or sulfuric acid in view of their industrial availability, though any acid at any concentration may be used as long as it can neutralize or acidify the reaction mixture after completion of the reaction (1). The acid is used in such an amount that it can neutralize or acidify the reaction mixture. When the acid is used at a high concentration, water may be added to the reactor in advance. For example, in the step (2), the reaction mixture obtained after the step (1) may be adjusted to pH 2-7, preferably pH 5-6.

Further, in the step (2), the reaction mixture

obtained after the step (1) may be neutralized or acidified directly, or the organic phase separated from the reaction mixture may be neutralized or acidified. In the process of the present invention, because the reaction product is formed in the form of an alkali salt such as a sodium salt and migrates into the organic phase, there is no loss of the product at the time of separation of the reaction mixture after the reaction. Addition of water to the reactor before the separation removes the excess sodium hydroxide or the salt resulting from the reaction such as sodium chloride and is favorably keeps down the volume of the reaction system at the time of the subsequent neutralization or acidification of the organic phase.

In the step (2), 3-chloro-N-(3-chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine as the reaction product crystallizes in water upon neutralization or acidification of the mixture containing it and the solvent.

The solvent in the step (2) is the same solvent as used in the step (1). The solvent may be removed by distillation at a temperature of from 10 to 65°C, optionally under reduced pressure. The removed solvent is typically recovered as the water azeotrope and may be recycled in the process of the present invention.

Crystals of the desired product obtained in the present invention such as crystals of 3-chloro-N-(3-

chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine (common name: fluazinam) are a known compound disclosed in The Pesticide Manual Thirteenth Edition and the like and are light yellow crystals having a melting point of 115-117°C, called α-crystals. A different form of crystals having a lower melting point is called β-crystals. Stable production of α-crystals is demanded from the viewpoint of manufacturing control.

In the step (2), crystallization may be carried out in the presence of α-crystals of the product as a seed.

The crystals precipitated in water in the step (2) can be recovered easily by ordinary filtration.

The crystals of 3-chloro-N-(3-chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine which precipitate in the step (2) may be purified by washing with hydrous isopropanol. In the purification method by washing, the starting material may preliminarily be washed with water before washed with hydrous isopropanol. The water content of the hydrous isopropanol used for the washing may be appropriately selected so as not to substantially dissolve the desired crystals of 3-chloro-N-(3-chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine. Isopropanol (IPA) with a low water content unfavorably dissolves the desired crystals of 3-chloro-N-(3-chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine. Typically, at most 90% aqueous isopropanol,

preferably at most 85% aqueous isopropanol, is used. The hydrous isopropanol is used in an amount of from 50 to 500 g, preferably from 100 to 200 g, in relation to 100 g of crystals of the desired product as the starting material.

The results of washing of the crystals of 3-chloro-N-(3-chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine which precipitate in the step (2) with hydrous isopropanol are described below. When the starting crystals (PhOH derivative, 0.25; impurity 1, 0.63; impurity 2, 0.80; other impurities, 2.27; the desired product, 96.05) were washed with 85% aqueous isopropanol, crystals (PhOH derivative, 0; impurity 1, 0; impurity 2, 0; other impurities, 0.74; the desired product, 99.26) were obtained after the washing. The PhOH derivative means a decomposition product of 2,4-dichloro-3,5-dinitrobenzotrifluoride (DCDNBTF), impurity 1 means 2-amino-3-chloro-5-trifluoromethylpyridine (ACTF), impurity 2 means DCDNBTF, and the desired product means 3-chloro-N-(3-chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine.

The product, 3-chloro-N-(3-chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine, obtained is suitably dried under a reduced pressure to give a highly pure dry product. In the method for drying a product, optimum conditions can be selected appropriately from conditions which do not cause

decomposition of the desired product, and for example, the drying may be carried out under a reduced pressure of at most 300 mmHg, or a reduced pressure of at most 200 mmHg. In the drying method, the product may be dried, for example, at a temperature of 115°C or below, or at a temperature of 70°C or below. The drying method can efficiently provide a stable preparation of the pesticide active ingredient with a good purity.

The crystals thus obtained are formulated with various adjuvants into products in the forms of powders, wettable powders, suspensions.

Now, the present invention will be described in detail with reference to Examples. However, these Examples are mere concrete embodiments for the sake of explanation and by no means limit or restrict the scope of the present invention. It should be understood that the present invention can be carried out in various modes on the basis of the concept in the present specification.

All the Examples were carried out or can be carried out by standard techniques common and conventional to a person skilled in the art.

EXAMPLE 1

24.8 g of 2-amino-3-chloro-5-trifluoromethylpyridine (ACTF) (purity 99%, 0.125 mol) and 96 g of tertiary butyl alcohol were fed into a four-necked flask equipped with a stirrer, a thermometer and a dropping funnel and then

mixed with 15.2 g (0.375 mol) of 99% NaOH with stirring. The resulting mixture was cooled to about 10°C, and 40.48 g of 2,4-dichloro-3,5-dinitrobenzotrifluoride (DCDNBTF) powder (purity 98.3%, 0.131 mol) was added while the temperature was kept at 30°C or below. Then, the reaction was carried out at room temperature for about 3 hours.

After addition of 50 g of water, the reaction mixture was neutralized with 15 g of 70% sulfuric acid until the pH reached 5-6 to precipitate crystals. The reaction solution was cooled until the internal temperature reached about 20°C or below, and the resulting slurry was filtered under a reduced pressure. The resulting cake was washed with 100 g of water and 80 g of 85% aqueous isopropanol (IPA aq.). The resulting yellow crystals were dried at 60°C to give 45.58 g of 3-chloro-N-(3-chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine (mp. 117-119.5°C).

EXAMPLE 2

24.8 g of ACTF (purity 99%, 0.125 mol) and 106.6 g of tertiary butyl alcohol containing 10% water were fed into a four-necked flask equipped with a stirrer, a thermometer and a dropping funnel and then mixed with 80.6 g of a 48% NaOH aqueous solution and 2.6 g of NaOH flakes (purity 99%) with stirring. The resulting mixture was cooled to about 10°C, and 39.60 g of DCDNBTF powder (purity 99.2%, 0.129 mol) was added while the temperature

was kept at 30°C or below. Then, the reaction was carried out at room temperature for about 1 hour.

25 g of water was added to the reaction mixture, and the aqueous phase which separated out as the lower layer was removed. 54 g of water was added to the tertiary butyl alcohol layer, and then 70% sulfuric acid was added dropwise for neutralization until the pH reached 5-6 to precipitate crystals. After addition of 50 g of water, the tertiary butyl alcohol was removed by distillation under reduced pressure (150 mmHg) until the internal temperature reached 60°C. The residue was cooled slowly to an internal temperature of about 20°C, and the resulting slurry was filtered under a reduced pressure. The resulting cake was washed with 100 g of water and 80 g of 85% IPA aq.. The resulting yellow crystals were dried at 60°C to give 45.00 g of 3-chloro-N-(3-chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine.

EXAMPLE 3

24.8 g of ACTF (purity 99%, 0.125 mol) and 106.6 g of tertiary butyl alcohol containing 10% water were fed into a four-necked flask equipped with a stirrer, a thermometer and a dropping funnel and mixed with 80.6 g of a 48% NaOH aqueous solution and 2.6 g of NaOH flakes (purity 99%) with stirring. The resulting mixture was cooled to about 20°C, and 40.0 g of DCDNBTF powder (purity 98.3%, 0.129 mol) was added while the temperature

was kept at 30°C or below. Then, the reaction was carried out at a temperature between 20°C and 30°C for about 1 hour.

73.7 g of water was added to the reaction mixture, and the aqueous layer which separated out was removed. The tertiary butyl alcohol layer was heated in a warm water bath, and 5% sulfuric acid was gradually added dropwise (about 1.0 mL/min) for neutralization until the pH reached 5-6 to precipitate crystals, while the temperature was kept at 55°C-60°C. When crystals started to precipitate (at pH = about 8), 0.05 g of α-crystals were added as a seed. After the dropwise addition, the crystals were aged at 55°C-60°C for 30 minutes with stirring.

The reaction solution was cooled to an internal temperature of 20°C or below, and the resulting slurry was filtered under a reduced pressure. The resulting cake was washed with 101.7 g of water and 66.6 g of 85% isopropanol (IPA) aq. The resulting yellow crystals were dried at 60°C to give 42.0 g of 3-chloro-N-(3-chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine.

EXAMPLE 4

19.9 g of ACTF (purity 99%, 0.10 mol) and 85.2 g of tertiary butyl alcohol containing 10% water were fed into a four-necked flask equipped with a stirrer, a thermometer and a dropping funnel and mixed with 64.5 g

of a 48% NaOH aqueous solution and 2.1 g of NaOH flakes (purity 99%) with stirring. The resulting mixture was cooled to about 20°C, and 32.0 g of DCDNBTF powder (purity 98.3%, 0.103 mol) was added while the temperature was kept at 30°C or below. Then, the reaction was carried out at a temperature between 20°C and 30°C for about 1 hour.

59.0 g of water was added to the reaction mixture, and the aqueous layer which separated out was removed. 10% sulfuric acid was heated to 60°C and mixed with 0.04 g of α-crystals as a seed. The tertiary alcohol layer was gradually added dropwise (about 1.0 mL/min) for neutralization while the temperature was kept at 55°C-60°C until the pH reached 5-6 to precipitate crystals. After the dropwise addition, the crystals were aged at 55°C-60°C for 30 minutes with stirring.

The reaction solution was cooled to an internal temperature of 20°C or below, and the resulting slurry was filtered under a reduced pressure. The resulting cake was washed with 81.4 g of water and 53.3 g of 85% isopropanol (IPA) aq. The resulting yellow crystals were dried at 60°C to give 34.4 g of 3-chloro-N-(3-chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine.

INDUSTRIAL APPLICABILITY

The present invention makes it possible to

efficiently obtain a highly pure preparation of a pesticide active ingredient, fluazinam, in good yields and in an industrially advantageous manner and makes it possible to isolate and purify the desired product from the reaction system for its synthesis and obtain a dry preparation of the desired product efficiently at low cost with simple operations. Therefore, the process of the present invention is an industrially excellent process.

It is clear that the present invention can be practiced in other modes than those described herein or in the Examples. In view of the teachings herein, many revisions and/or variations on the present invention are possible and fall within the scope of the claims attached hereto.

The entire disclosures of Japanese Patent Application No. 2007-202362 filed on August 2, 2007 and Japanese Patent Application No. 2008-037635 filed on February 19, 2008 including specifications, claims and summaries are incorporated herein by reference in their entireties.

CLAIMS

1. A process for producing 3-chloro-N-(3-chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine, which comprises (1) a step of reacting 2-amino-3-chloro-5-trifluoromethylpyridine and 2,4-dichloro-3,5-dinitrobenzotrifluoride in the presence of an alkali component selected from the group consisting of hydroxides and carbonates of alkali metals and hydroxides and carbonates of alkaline earth metals as a basic substance and a tertiary alcohol as a solvent, and (2) a step of neutralizing or acidifying a mixture containing 3-chloro-N-(3-chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine as the reaction product and the solvent with an acid.

2. The process according to Claim 1, wherein the basic substance is sodium hydroxide or potassium hydroxide.

3. The process according to Claim 1, wherein the solvent is tertiary butyl alcohol.

4. The process according to Claim 1, wherein the acid is hydrochloric acid.

5. The process according to Claim 1, wherein the acid is sulfuric acid.

6. The process according to Claim 1, wherein in the step (1), water is present in a sufficient amount to substantially dissolve the alkali component.

7. The process according to Claim 1, wherein in the step (1), a 35-50% sodium hydroxide aqueous solution or a

corresponding amount of a mixture of a sodium hydroxide aqueous solution, solid sodium hydroxide and water is present in an amount of at least 2 mol in relation to 1 mol of 2-amino-3-chloro-5-trifluoromethylpyridine.

8. The process according to Claim 1, wherein in the step (1), water is present in an amount of at least 7% in relation to the total of water and the solvent.

9. The process according to Claim 1, wherein in the step (1), 2,4-dichloro-3,5-dinitrobenzotrifluoride is used in an amount of from 0.8 to 1.2 mol in relation to 1 mol of 2-amino-3-chloro-5-trifluoromethylpyridine.

10. The process according to Claim 1, wherein the solvent is used in an amount of from 50 to 1000 g in relation to 100 g of 2-amino-3-chloro-5-trifluoromethylpyridine.

11. The process according to Claim 1, wherein in the step (2), the mixture containing 3-chloro-N-(3-chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine as the reaction product and the solvent is separated, and the organic phase is neutralized or acidified with the acid.

12. The process according to Claim 1, wherein in the step (2), the pH is adjusted to 2 to 7 with the acid.

13. The process according to Claim 1, wherein in the step (2), the mixture containing 3-chloro-N-(3-chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine as the reaction product and the solvent is

mixed with water and then neutralized or acidified with the acid to precipitate crystals of the product.

14. The process according to Claim 1, wherein in the step (2), the crystals are precipitated in the presence of α-crystals of the reaction product as a seed.

15. A method for purifying 3-chloro-N-(3-chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine as a product, which comprises washing precipitated crystals with hydrous isopropanol to obtain the product in a purer form with less contaminants.

16. The method according to Claim 15, wherein the precipitated crystals are washed with water before they are washed with hydrous isopropanol.

17. A method for drying a product, which comprises drying 3-chloro-N-(3-chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine as a product under a reduced pressure.

18. The method for drying a product according to Claim 17, wherein the drying is carried out under a reduced pressure of at most 300 mmHg.

19. The method for drying a product according to Claim 17, wherein the drying is carried out under a reduced pressure of at most 200 mmHg.

20. The method for drying a product according to Claim 17, wherein the drying is carried out at a temperature of 115°C or below.

21. The method for drying a product according to Claim

17, wherein the drying is carried out at a temperature of 70°C or below.

22. A process for producing 3-chloro-N-(3-chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine or a salt thereof, which comprises reacting 2-amino-3-chloro-5-trifluoromethylpyridine and 2,4-dichloro-3,5-dinitrobenzotrifluoride in the presence of an alkali component selected from the group consisting of sodium hydroxide and potassium hydroxide and a tertiary alcohol as a solvent.