EUROPEAN PATENT SPECIFICATION

Date of publication of patent specification: 25.03.92
Application number: 85106917.9
Date of filing: 04.06.85

Preparation of (trifluoromethyl) pyridines.

Priority: 08.06.84 US 618806
Date of publication of application: 11.12.85 Bulletin 85/50
Publication of the grant of the patent: 25.03.92 Bulletin 92/13
Designated Contracting States: BE CH DE FR GB IT LI NL SE

References cited:
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GB-A- 1 272 475
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Description

The present invention relates to a method of preparing (trifluoromethyl)pyridine compounds by reacting (trichloromethyl)pyridine compounds with anhydrous hydrogen fluoride in the absence of a catalyst.

Fluorination of (trichloromethyl)pyridine compounds has been carried out by vapor phase fluorination which requires the use of high temperatures. Such vapor phase reactions suffer from disadvantages including, for example, energy costs associated with elevating the temperature of the reactants, the decomposition of starting materials and end products associated with high temperature vapor phase reaction systems and, furthermore, low conversion and/or low selectivities to the desired (trifluoromethyl)pyridine products. See, for example, Japanese Kokai Tokkyo Koho 80 85,564, 27 June 1980, Appl. 78/158,979, 22 December 1978 and U.S. Patents 4,266,064 and 4,288,599.

U.S. Patent 4,184,041 discloses a method of preparing (trifluoromethyl)pyridine compounds by reacting a (trichloromethyl)pyridine compound with gaseous hydrogen fluoride at a temperature from 0°-50°C. While this method may produce small quantities of (trifluoromethyl)pyridine compounds, it is an unacceptable commercial means for producing (trifluoromethyl)pyridine compounds.

According to EP-A-107 866 a mixture of 2,3-dichloro-5-(trifluoromethyl)pyridine with 3-chloro-2-fluoro-5-(trifluoromethyl)pyridine is prepared by treating 2,3-dichloro-5-(trichloromethyl)pyridine with antimony trifluoride.

GB-A-1 272 475 discloses the preparation of certain fluoropyridines from the corresponding chloropyridines, especially pentachloropyridine, by treatment with hydrogen fluoride in the liquid phase at temperatures of above 100°C and pressures of above 100 psig (793 kPa).

It is clearly evident that a more efficient method of preparing (trifluoromethyl)pyridine compounds is desirable in order to commercially produce such compounds.

Subject matter of the present invention is a process for preparing 2,3-dichloro-5-(trifluoromethyl)pyridine according to claim 1.

Preferred embodiments are subject matter of claims 2 to 5.

In accordance with the present invention, 3-chloro-2-fluoro-5-(trifluoromethyl)pyridine is prepared in a liquid phase halogen (fluorine-chlorine) exchange reaction from 2,3-dichloro-5-(trichloromethyl)pyridine in the absence of a catalyst. In a second step, 2,3-dichloro-5-(trifluoromethyl)pyridine is prepared by treating the reaction mixture containing 3-chloro-2-fluoro-5-(trifluoromethyl)pyridine with HCl with or without a catalyst.

The first step of the present method is conducted by contacting the (trichloromethyl)pyridine compound with anhydrous hydrogen fluoride in the absence of a catalyst under liquid phase conditions sufficient to form the desired (trifluoromethyl)pyridine compound.

The compounds prepared by the process of this invention are useful as intermediates in the manufacture of herbicides.

The present method provides a commercially efficient means of producing (trifluoromethyl)pyridine compounds in a liquid phase reaction system. The liquid phase condition provides a reaction where the desired (trifluoromethyl)pyridine compounds are produced in a selective manner and in a reasonable time.

Additionally, the present liquid phase reaction may be run continuously by the addition of starting materials to a reaction vessel while the desired (trifluoromethyl)pyridine product, which generally has a boiling point less than the temperature at which the reaction is conducted, is collected by the condensation of (trifluoromethyl)pyridine vapors.

The hydrogen fluoride employed as the source of fluorine in this invention is introduced into the reaction as hydrogen fluoride (anhydrous). The hydrogen fluoride is bubbled into the reaction as a gas or fed into the reaction as a liquid. Hydrogen fluoride (anhydrous) has a boiling point of 19.5°C and the liquid and gas consist of associated molecules. In the practice of the present invention, hydrogen fluoride is supplied at a ratio of at least 3 mols per mol of mono(trichloromethyl)pyridine compound and preferably an excess of this amount is employed.

The reaction is conducted under liquid phase conditions at a temperature of 170° to 200°C, preferably at a temperature between 180°C and 190°C. The halogen exchange reaction is typically conducted in the presence of agitation sufficient to maintain an essentially homogeneous mixture of the reactants and at a pressure of at least 200 psig (1480 kPa), preferably at a pressure of 200 to 300 psig (1480 to 2170 kPa), and most advantageously at a pressure of 240 to 260 psig (1755 to 1895 kPa).

In conducting the reaction, the order of addition of the reactants is not critical. Preferably, the hydrogen fluoride is added to the (trichloromethyl)pyridine compound with stirring, until the reaction is completed, generally in from 1 to 50 hours. The exact time that the reaction is complete will vary depending on a variety of factors, such as temperature, HF flow rate, degree of agitation and pressure. The hydrogen
fluoride is fed into the reaction mixture as a liquid or, alternatively, may be bubbled or sparged into the reaction mixture as a gas.

Higher pressures and higher hydrogen fluoride flow rates tend to decrease the reaction time. However, the use of excessive hydrogen fluoride flow rates presents several disadvantages, i.e., refluxing of liquid hydrogen fluoride tends to reduce temperature and removal and/or recovery of the excess hydrogen fluoride can be costly and/or troublesome. Flow rates of from 0.15 to 0.45 mol/hr/mol starting pyridine preferably 0.22 to 0.31 mol/hr/mol starting pyridine are advantageously employed.

In the second process step this invention, 2,3-dichloro-5-(trifluoromethyl)pyridine is prepared by reacting the 3-chloro-2-fluoro-5-(trifluoromethyl)pyridine with anhydrous HCl at a temperature of 100° to 200° C with or without the presence of a catalyst. When no catalyst is employed in this step, pressures of from 5 psig to 400 psig (135.8 to 2960.56 kPa), preferably from 25 psig to 200 psig (274 to 1480 kPa) may be used. When catalysts such as Lewis acid catalysts are employed, pressures of from 1 to 3 atmospheres (100 to 300 kPa), preferably from 1.2-1.4 atmospheres (120 to 140 kPa) and most preferably about 1.3 atmospheres (130 kPa), are used.

The following example further illustrates the invention. No attempt has been made to balance any chemical equations described herein.

**Example**

![Chemical Reaction](image)

A charge of 1209.5 grams of 99 percent 2,3-dichloro-5-trichloromethylpyridine (4.52 mol) was placed in a 1-liter Hasteloy-C reactor (Parr pressure vessel) equipped for agitation and fitted with condensers, heater, pressure control and hydrogen fluoride feed. The reactor was sealed, heating and agitation begun and the pressure was held between 190-210 psig (1411.33 to 1549.22 kPa) with nitrogen. When 193° C was reached about 46 grams of hydrogen fluoride (HF) was added after which HF feed was continued at an average rate of 20 grams per hour (1.00 mol/hr/4.52 mol pyridine) while holding the temperature at 186° C, pressure at 243 psig (1753.4 kPa) condensers at 12°-17° C. In 38 hours the product analyzed 83.8 wt. percent 3-chloro-2-fluoro-5-(trifluoromethyl)pyridine and 8.0 percent of 2,3-dichloro-5-(trifluoromethyl)-pyridine by GLC.

In a second step, the reactor was depressurized and flushed with nitrogen after which 5 mol percent of FeCl3 was added, the pressure was held at 0-5 psig (100-135.8 kPa), temperatures at 138°-170° C and anhydrous HCl was fed at a constant rate to produce 2,3-dichloro-5-(trifluoromethyl)pyridine (90 percent yield) in 23 hours. The overall yield was 85 percent in a total reaction time of 61 hours.

**Claims**

1. A process for preparing 2,3-dichloro-5-(trifluoromethyl)pyridine which is characterized by contacting 2,3-dichloro-5-(trichloromethyl)pyridine with at least a stoichiometric amount of anhydrous hydrogen fluoride in the liquid phase at a temperature of 170 to 200° C and a pressure of at least 1480 kPa to obtain a mixture containing 3-chloro-2-fluoro-5-(trifluoromethyl)pyridine as a major component and subsequently contacting the mixture with anhydrous hydrogen chloride at a temperature of 100 to 200° C and a pressure of from 136 to 2960 kPa, optionally in the presence of a Lewis acid catalyst and a pressure of from 100 to 300 kPa.

2. A process of claim 1 wherein the temperature of the hydrogen fluoride contact is from 180 to 190° C.

3. A process of claim 1 or 2 wherein the pressure of the hydrogen fluoride contact is from 200 to 300 psig (1480 to 2170 kPa).
4. A process of any of claims 1 to 3 wherein a Lewis acid catalyst is added to the mixture contacted with hydrogen chloride.

5. A process of claim 4 wherein the Lewis acid catalyst is ferric chloride.

Revendications

1. Procédé de préparation de 2,3-dichloro-5-(trifluorométhyl)pyridine, caractérisé en ce qu'on met la 2,3-dichloro-5-(trichlorométhyl)pyridine au contact d'au moins une quantité stoechiométrique de fluorure d'hydrogène anhydre, en phase liquide, à une température de 170 à 200 °C et sous une pression d'au moins 1480 kPa, pour obtenir un mélange renfermant de la 3-chloro-2-fluoro-5-(trifluorométhyl)-pyridine, comme composant majeur, et en ce qu'on met ensuite ce mélange au contact de chlorure d'hydrogène anhydre, à une température de 100 à 200 °C et sous une pression de 136 à 2960 kPa, éventuellement en présence d'un catalyseur acide de Lewis et sous une pression de 100 à 300 kPa.

2. Procédé de la revendication 1, dans lequel la température, lors du contact avec le fluorure d'hydrogène, est comprise entre 180 et 190 °C.

3. Procédé de la revendication 1 ou 2, dans lequel la pression, lors du contact avec le fluorure d'hydrogène, est comprise entre 1480 et 2170 kPa (200 et 300 psig).

4. Procédé de l'une quelconque des revendications 1 à 3, dans lequel on ajoute un catalyseur acide de Lewis au mélange mis en contact avec le chlorure d'hydrogène.

5. Procédé de la revendication 4, dans lequel le catalyseur acide de Lewis est le chlorure ferrique.

Patentansprüche

1. Verfahren zur Herstellung von 2,3-Dichlor-5-(trifluormethy1)pyridin, dadurch gekennzeichnet, daß man 2,3-Dichlor-5-(trichlormethy1)pyridin mit mindestens einer stöchiometrischen Menge an wasserfreiem Fluorwasserstoff in der Flüssigphase bei einer Temperatur von 170 bis 200 °C und einem Druck von mindestens 1480 kPa kontaktiert, um eine Mischung zu erhalten, die 3-Chlor-2-fluor-5-(trifluormethyl)-pyridin als eine Hauptkomponente enthält, und anschließend die Mischung mit wasserfreiem Chlorwasserstoff bei einer Temperatur von 100 bis 200 °C und einem Druck von 136 bis 2960 kPa kontaktiert, gegebenenfalls in Gegenwart eines Lewissäure-Katalysators und einem Druck von 100 bis 300 kPa.

2. Verfahren nach Anspruch 1, worin die Temperatur des Fluorwasserstoff-Kontakts von 180 bis 190 °C ist.

3. Verfahren nach Anspruch 1 oder 2, worin der Druck des Fluorwasserstoff-Kontakts von 200 bis 300 psig (1480 bis 2170 kPa) ist.

4. Verfahren nach einem der Ansprüche 1 bis 3, worin ein Lewissäure-Katalysator zu der mit Chlorwasserstoff kontaktierten Mischung gegeben wird.