

## SPECIFICATION

Process for producing pyridine derivatives having a trifluoromethyl group at  $\beta$ -position thereof

5 The present invention relates to a process for producing a pyridine derivative having a trifluoromethyl group at the  $\beta$ -position thereof directly from  $\beta$ -picoline. More particularly, it relates to a process for  
10 producing such a pyridine derivative by a vapor phase reaction of  $\beta$ -picoline with chlorine and hydrogen fluoride, if necessary in the presence of a specific metal fluoride catalyst.

Pyridine derivatives having a trifluoromethyl  
15 group at the  $\beta$ -position thereof can be converted into important compounds having excellent physiological activities and have been used as important intermediates for agricultural chemicals and medicines. 2-Chloro-5-trifluoromethyl-  
20 pyridine in particular is an important intermediate in the synthesis of herbicides, insecticides and fungicides. Therefore, there is a need for an industrial process for producing such compounds by mass production in an economical manner.

25 Not many processes have hitherto been developed for producing these derivatives, since the importance of such compounds has only recently been fully appreciate.

It has been found that the chlorination of the  
30 methyl group of  $\beta$ -picoline is difficult in the production of  $\beta$ -trichloromethylpyridine which has an analogous structure to the above pyridine derivatives (e.g. HELVETICA CHIMICA ACTA vol. 59, Fase 1, Nr. 19-20, 1976). Therefore, it would be expected that  
35 the production of said pyridine derivative from  $\beta$ -picoline would be difficult.

Recently processes have been proposed to produce said pyridine derivatives for example in European Patent Specification 0000483 and PCT specification WO/79/00094. In these publications only  
40 experimental small scale processes are disclosed. For example in WO 79/00094, there is disclosed a process for producing chloro- $\beta$ -trifluoromethylpyridines in which:

45 (1) chlorine gas is fed into a solution of  $\beta$ -picoline in carbon tetrachloride under ultraviolet radiation at 80°C for 3 hours to produce chloro  $\beta$ -trichloromethylpyridines at a yield of less than 10% and

(2) chloro  $\beta$ -trifluoromethylpyridines are produced by reacting the chloro  $\beta$ -trichloromethylpyridines with antimony trifluoride in a liquid phase  
50 at 140 to 145°C for 1 hour or reacting the chloro  $\beta$ -trichloromethylpyridines with hydrogen fluoride in a liquid phase at 200°C for 10 hours in an autoclave.

55 This process, however, has the following disadvantages.

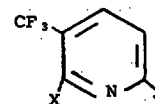
(1) it takes a long time for the chlorination and the fluorination;

(2) the chlorination does not proceed smoothly and produces a large quantity of by-products with a low yield of the desired product, and the purification and the separation steps required are complicated;

(3) antimony trifluoride is expensive and causes difficulties treatment of waste solutions, and an  
65 autoclave is required for the reaction with hydrogen

fluoride.

The present invention is based on the finding that the pyridine derivatives having a trifluoromethyl group at  $\beta$ -position thereof can be obtained by a  
70 single-step vapor phase reaction of  $\beta$ -picoline with chlorine and hydrogen fluoride. The invention provides a process for producing a pyridine derivative having the formula



wherein X and Y respectively represent a hydrogen or chlorine atom, which process comprises reacting  
75  $\beta$ -picoline with chlorine and hydrogen fluoride by a vapor phase reaction in the presence or absence of a catalyst of one or more metal fluorides selected from the fluorides of aluminium, chromium, iron, nickel,  
80 cobalt and manganese. The reaction velocity is increased in the presence of the specific metal fluoride, so that the reaction conditions can be mild and the pyridine derivatives can be produced easily in high yield in a continuous process.

85 A diluent can be used. Typical diluents include organic solvents such as halohydrocarbons, e.g. carbon tetrachloride, chloroform, methylene chloride and F-112 ( $\text{CFCl}_2.\text{CFCl}_2$ ) or F-113 ( $\text{CF}_2\text{Cl}.\text{CFCl}_2$ ) and inert gases such as nitrogen, argon  
90 or helium. The diluent has the functions of controlling combustion, carbonization and the formation of tar by-products and also acts as a heat sink.

In the process of the present invention, the feeding of the starting materials and, the diluent when used can be carried out as in a conventional vapor phase  
95 reaction. For example,  $\beta$ -picoline, chlorine, hydrogen fluoride and the diluent can be simultaneously or separately fed or a mixture of  $\beta$ -picoline and the diluent and a mixture of chlorine and hydrogen  
100 fluoride can be fed simultaneously, sequentially or separately.

The amounts of chlorine and hydrogen fluoride used are not critical and depend upon the amount of  
105  $\beta$ -picoline used as the starting material, the formation of pyridine derivatives and the kind of reactor. They are suitably in ranges of 2 to 15 moles, preferably 2.5 to 10 moles of chlorine and 2 to 60 moles, preferably 2.5 to 10 moles of hydrogen fluoride based on 1 mole of  $\beta$ -picoline. The amount of  
110 diluent is usually in a range of 3 to 70 mole based on 1 mole of  $\beta$ -picoline. The reaction temperature is usually in a range of 300 to 600°C preferably 350 to 500°C and the residence time of the reaction mixture in the reaction zone is usually in a range of 0.5 to 50  
115 seconds, preferably 1 to 30 seconds.

When the specific metal fluoride catalyst is used, the reaction velocity is increased so that the reaction conditions can be mild and the yield of the product is remarkably increased. The desired product can be  
120 produced by the reaction in the absence of the catalyst, but the reaction velocity is relatively slow. In the latter case, if the reaction velocity is increased, abnormal reactions such as side reactions, decompositions and carbonizations are easily caused. On

the other hand, the reaction in the presence of the catalyst can be performed in mild reaction conditions as regards reaction temperature, amounts of chlorine and hydrogen fluoride and residence time while still giving the desired product in high yield. Therefore, it is highly desirable to use the catalyst in an industrial process.

The fluorides of aluminum, chromium, iron, nickel, cobalt or manganese which can be used as the catalyst include chromium (II) fluoride ( $\text{CrF}_2$ ), chromium (III) fluoride ( $\text{CrF}_3$ ) and chromium (IV) fluoride ( $\text{CrF}_4$ ) as chromium fluorides; iron (II) fluorides ( $\text{FeF}_2$ ) and iron (III) fluoride ( $\text{FeF}_3$ ) as iron fluorides; nickel (II) fluoride ( $\text{NiF}_2$ ) and nickel (III) fluoride ( $\text{NiF}_3$ ) as nickel fluorides; manganese (II) fluoride ( $\text{MnF}_2$ ), manganese (III) fluoride ( $\text{MnF}_3$ ) and manganese (IV) fluoride ( $\text{MnF}_4$ ) as manganese fluorides; cobalt (II) fluoride ( $\text{CoF}_2$ ) and cobalt (III) fluoride ( $\text{CoF}_3$ ) as cobalt fluorides and aluminum (III) fluoride ( $\text{AlF}_3$ ) as the aluminum fluoride.

One or more of the fluorides can be used. Among these catalytic components, a fluoride of chromium, iron or aluminum is preferably used for an industrial process.

Usually the catalytic component is admixed with a carrier such as activated carbon, activated alumina and aluminum (III) fluoride and the mixture is formed into granules or pellets of the desired size and fed into the reaction zone. The catalytic component comprising the specific metal fluoride can be fed into the reactor so as to place it in the reaction zone. It is also possible to feed a precursor of the catalyst in the form of a metal or alloy or a metal oxide, chloride, hydroxide or carbonate or a hydrate thereof, into the reactor and then feed hydrogen fluoride gas to react with the precursor to form the desired fluoride *in situ* in the reaction zone. For example, a carrier of alumina or aluminum (III) fluoride supporting a precursor, for example a metal oxide or chloride such as ferric chloride or chromous trioxide, is fed into the reactor and hydrogen fluoride is fed at a reaction temperature of 200 to 500°C to convert the metal compound into the corresponding metal fluoride before the main reaction.

The process of the present invention can be carried out in any suitable reaction system, but in practice, it is preferable to carry out the reaction in the presence of a fixed bed or a fluidized bed of the solid catalyst in the reaction zone. The best method comprises fluidizing a suspension of the solid catalyst in a mixed gas containing the starting materials  $\beta$ -picoline, chlorine and hydrogen fluoride, the reaction product, hydrogen chloride and the diluent. The amount of the catalytic component is not critical but is usually in a molar ratio 0.001 to 3 based on  $\beta$ -picoline.

In the process of the present invention, the chlorination and the fluorination may occur sequentially or simultaneously. Of the various reactions involved, the conversion of the methyl group of  $\beta$ -picoline into a trifluoromethyl group may predominate or may proceed alongside the selective introduction of a chlorine atom at the  $\alpha$ -position (2- and/or 6-position) of the pyridine ring. When a chlorine atom is introduced at the  $\alpha$ -position of the pyridine ring, it is

easy to introduce a chlorine atom at the 6-position in comparison with the 2-position.

The reaction mixture obtained by the above-mentioned reaction contains various intermediates which are not yet converted into the desired products together with the desired pyridine derivatives.

On the other hand, certain side-reactions introducing chlorine atoms at the  $\beta$ -,  $\gamma$ -positions or the  $\alpha$ - and  $\beta$ -positions of the pyridine ring may occur to some extent besides the main reaction.

In the process of the present invention, reaction conditions suitable for the particular pyridine derivative required can be selected from the ranges mentioned above so as to obtain efficiently the desired pyridine derivative. For example, when 2-chloro-5- (and 3-) trifluoromethylpyridine is produced, it is preferable to use chlorine and hydrogen fluoride at molar ratios of 3.5 to 7 and 3 to 10 based on  $\beta$ -picoline respectively, reacting them at a temperature of 350 to 450°C for a residence time of 1 to 20 seconds. As a result, the reaction mixture contains 40 to 60 wt.% of 2-chloro-5-trifluoromethylpyridine, 5 to 20 wt.% of 2-chloro-3-trifluoromethylpyridine, 10 to 50 wt.% of 2,6-dichloro-3-trifluoromethylpyridine, 5 to 35 wt.% of  $\beta$ -trifluoromethylpyridine and 5 to 15 wt.% of other compounds such as  $\beta$ -chlorodifluoromethylpyridine, 2,5-dichloro-3-trifluoromethylpyridine, 2-chloro-5-chlorodifluoromethylpyridine and 2,3-dichloro-5-trifluoromethylpyridine.

When 2,6-dichloro-3-trifluoromethylpyridine is produced, the reaction is preferably performed under severe reaction conditions with a high proportion of chlorine, high reaction temperature or longer residence time in comparison with those used to produce 2-chloro-5- (and 3-) trifluoromethylpyridine.

When  $\beta$ -trifluoromethylpyridine is produced, the reaction is preferably carried out under mild reaction conditions with a lower proportion of chlorine, lower reaction temperature or shorter residence time in comparison with those used to produce 2-chloro-5- (and 3-) trifluoromethylpyridines.

Among the pyridine derivatives, mono- or di-chlorotrifluoromethylpyridines and especially 2-chloro-5-trifluoromethylpyridine are useful as the intermediates for agricultural chemicals. The process of the present invention is especially effective for the production of these pyridine derivatives.

In the specification, the term 'chloro  $\beta$ -trifluoromethylpyridines' means mono- and/or di-chloro  $\beta$ -trifluoromethylpyridines and the term 'chloro  $\beta$ -perchlorofluoromethylpyridines' means mono- and/or di-chloro  $\beta$ -perchlorofluoromethylpyridines.

Usually, gaseous materials containing the fluorinated products such as the pyridine derivatives as the main products and the unreacted hydrogen fluoride, chlorine, intermediates, hydrogen chloride as a by-product and the diluent are discharged from the reactor. The pyridine derivatives are separated as a liquid mixture through a suitable cooling and condensing device.

In the separation, it is possible to liquefy the desired pyridine derivatives, the intermediates, hyd-

rogen fluoride and some of the hydrogen chloride by cooling the gaseous reaction mixture and to treat the separated liquid phase by adding water. The liquid mixture usually contains  $\beta$ -trifluoromethylpyridine, 2-chloro-5-trifluoromethylpyridine, 2-chloro-3-trifluoromethylpyridine, and 2,6-dichloro-3-trifluoromethylpyridine. For example, the pyridine derivatives can be obtained at the yield of higher than 80%. When the intermediates such as the chloro  $\beta$ -perchlorofluoromethylpyridines, which are not converted into the desired pyridine derivatives remain in the liquid mixture, they can be recycled to the reaction zone after separating and recovering them with the unreacted material or the diluent. The resulting pyridine derivative can be purified by a conventional purifying treatment such as extraction, distillation or crystallization whereby a single pyridine derivative such as 2-chloro-5-trifluoromethylpyridine having high purity can be obtained.

When 2-chloro-5-trifluoromethylpyridine is produced at high yield, the following process is advantageous for an industrial purpose. In this process, the reaction conditions are selected so as to increase the yield of 2-chloro-5-trifluoromethylpyridine regardless of the production of 2-chloro-3-trifluoromethylpyridine and 2,6-dichloro-3-trifluoromethylpyridine.

In such reaction conditions, the resulting liquid mixture usually contains 40 to 60% of 2-chloro-5-trifluoromethylpyridine, 5 to 20% of 2-chloro-3-trifluoromethylpyridine, and 5 to 25% of 2,6-dichloro-3-trifluoromethylpyridine.

From the liquid mixture, 2-chloro-5-trifluoromethylpyridine is separated at high yield.

The residue obtained by the separation of 2-chloro-5-trifluoromethylpyridine contains 0 to 3% of 2-chloro-5-trifluoromethylpyridine, 10 to 35% of 2-chloro-3-trifluoromethylpyridine, and 10 to 50% of 2,6-dichloro-3-trifluoromethylpyridine.

When the residue is hydrogenated, chlorine atom on the pyridine ring is easily substituted by a hydrogen atom to produce  $\beta$ -trifluoromethylpyridine. The hydrogenation can for example be carried out as a catalytic reaction of the chloro  $\beta$ -trifluoromethylpyridine with hydrogen in the presence of a specific catalyst. The catalyst can be a platinum, palladium, nickel, copper or silver type catalyst.

The reaction can be carried out in the liquid or vapor phase. For example, water, alcohols, ethers, aromatic hydrocarbons can be used in a liquid phase reaction. The reaction temperature is usually in a range of 50 to 200°C in the liquid phase reaction or 150 to 400°C in the vapor phase reaction. In the reaction, the trifluoromethyl group of the chloro  $\beta$ -trifluoromethylpyridines is not disconnected, and only chlorine atom is selectively substituted by a hydrogen atom whereby  $\beta$ -trifluoromethylpyridine can be produced at high yield. Therefore  $\beta$ -trifluoromethylpyridine having high purity can be produced at high yield by applying a conventional purifying treatment such as filtration, extraction or distillation. The  $\beta$ -trifluoromethylpyridine is recycled to the chloro  $\beta$ -trifluoromethylpyridine production stage so as to reuse it. The  $\beta$ -trifluoromethyl-

pyridine can be easily converted into the chloro  $\beta$ -trifluoromethylpyridines by feeding the  $\beta$ -trifluoromethylpyridine with  $\beta$ -picoline as a mixture or separately. The intermediates which are not converted into the chloro  $\beta$ -trifluoromethylpyridines in the chlorination and fluorination of  $\beta$ -picoline can be also converted into the chloro  $\beta$ -trifluoromethylpyridines by treating them in the hydrogenation and then recycling them to the chloro  $\beta$ -trifluoromethylpyridine production stage.

The present invention will be further illustrated by the following examples.

#### EXAMPLE 1:

A stainless steel reaction tube having an inner diameter of 42 mm and a length of 1250 mm as a reaction zone was used. A stainless steel preheating tube having an inner diameter of 20 mm and a length of 500 mm was used for a preheating of hydrogen fluoride and chlorine. A stainless steel preheating tube having an inner diameter of 30 mm and a length of 500 mm was used for a preheating of  $\beta$ -picoline and carbon tetrachloride.

The reaction tube and the preheating tubes were covered by each electric heater and each insulator so as to control the temperature outwardly and they were respectively placed in slant positions.

Into the reaction tube, 47 g. (0.5 mole) of  $\beta$ -picoline and 770 g. (5 mole) of carbon tetrachloride which were preheated to 230°C and 181 g. (2.55 mole) of chlorine and 520 g. (26 mole) of hydrogen fluoride which were preheated to 300°C were respectively fed during about 100 minutes at substantially constant flow rate to carry out a vapor phase reaction at 430°C. A residence time of the reaction mixture in the reaction zone was about 5 seconds.

The gas discharged from the reaction tube was condensed by passing it through a water scrubbing column and a caustic alkali scrubbing column. The resulting oily product was separated and washed with water and dehydrated over sodium sulfate and then carbon tetrachloride was distilled off under a reduced pressure to obtain 77 g. of an oily product. The oily product was analyzed by gas chromatography with a temperature programmer. In the recovered organic materials, the chloro  $\beta$ -trifluoromethylpyridines were obtained at a ratio of 60.5 wt.% and the intermediates such as the chloro  $\beta$ -perchlorofluoromethylpyridines were obtained at a ratio of about 40 wt.%. The result of the analysis of the oily product by the gas chromatography is shown in the following table 1.

#### EXAMPLE 2:

In the reaction tube used in Example 1, 28 g. (0.3 mole) of  $\beta$ -picoline and 277 g. (1.8 mole) of carbon tetrachloride which were preheated to 250°C and 149 g. (2.1 mole) of chlorine and 30 g. (1.5 mole) of hydrogen fluoride which were preheated to 300°C were fed during 30 minutes. The vapour phase reaction was carried out at a reaction temperature of 410°C and a residence time of the reaction mixture of 9.5 seconds.

The gas discharged from the reaction tube was treated as the process of Example 1 to obtain 44 g. of an oily product. The result of the analysis of the oily product by the gas chromatography is shown in the

following table 1.

The data of the other components in the table

show a percent of a total of compounds such as the chloro  $\beta$  - perchlorofluoromethylpyridines.

Table 1

|                                                  | Exp. 1 | Exp. 2 |
|--------------------------------------------------|--------|--------|
| 2 - chloro - 5 - trifluoromethylpyridine (%)     | 33.2   | 36.4   |
| 2 - chloro - 3 - trifluoromethylpyridine (%)     | 10.7   | 8.7    |
| 2,6 - dichloro - 3 - trifluoromethylpyridine (%) | 16.6   | 12.8   |
| Other components (%)                             | 39.5   | 42.1   |

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### EXAMPLE 3:

A stainless steel reaction tube having an inner diameter of 42 mm and a length of 1250 mm was used as a reaction zone. A catalyst layer having a length of 250 mm was formed at a distance of 500 mm from the inlet of the reaction tube. A stainless steel preheating tube having an inner diameter of 20 mm and a length of 500 mm was used for a preheating of anhydrous hydrogen fluoride and chlorine. A stainless steel preheating tube having an inner diameter of 20 mm and a length of 500 mm was used for a preheating of  $\beta$  - picoline and carbon tetrachloride. The reaction tube and the preheating tubes were covered by each electric heater and each insulator so as to control the temperature outwardly, and they were respectively placed in slant positions.

In the catalyst packing part of the reaction tube, a mixture of 0.03 mole of chromium (III) fluoride hydrate and 200 g. of active alumina having a particle size of 4 to 6 mm was packed and the reaction tube was heated to 430°C and anhydrous hydrogen fluoride was fed at a rate of 1 g./min. for 2 hours to activate it. Then, 280 g. (3 mole) of  $\beta$  - picoline and 2310 g. (15 mole) of carbon tetrachloride which were preheated to 230°C and 960 g. (13.5 mole) of chlorine and 480 g. (24 mole) of anhydrous hydrogen fluoride which were preheated to 300°C were fed during 290 minutes at the substantially same rates into the reaction tube to carry out a vapor phase reaction at 430°C to react them. The residence time of the reaction mixture in the reaction zone was about 9 seconds.

The gas discharged from the reaction tube was condensed by passing it through a water scrubbing column and a caustic alkali scrubbing column. The oily product was separated and washed with water and dehydrated over sodium sulfate and then, carbon tetrachloride was distilled off under a reduced pressure to obtain 420 g. of an oily product. The oily product was analyzed by a gas chromatography with a temperature programmer. The result is shown in the following table 2.

### EXAMPLE 4:

In the catalyst packing part in the reaction tube used in Example 3, 300 g. of  $\gamma$  - alumina was fed and was activated by the hydrogen fluoride. Then, 465 g. (5 mole) of  $\beta$  - picoline and 3850 g. (25 mole) of carbon tetrachloride which were preheated to 250°C

and 1950 g (27.5 mole) of chlorine and 900 g. (45 mole) of hydrogen fluoride which were preheated to 300°C were respectively fed during about 8 hours at substantially same rates. The vapor phase reaction was carried out at a reaction temperature of 430°C and a residence time of the reaction mixture in the reaction zone was 10.5 seconds.

In accordance with the process of Example 3, the gas discharged from the reaction tube was treated to obtain 708 g. of an oily product.

The result of the analysis of the oily product by the gas chromatography is shown in the following table 2.

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### EXAMPLE 5:

In accordance with the process of Example 4 except using a catalyst supporting 0.1 mole of nickel (II) fluoride hydrate on 200 g. of active carbon having a particle size of 2 to 4 mm., the catalyst was used instead of 300 g. of  $\gamma$  - alumina and the catalytic activation of alumina by anhydrous hydrogen fluoride, the vapor phase reaction was carried out to obtain 300 g. of an oily product.

The result of the analysis of the oily product by the gas chromatography is shown in the following table 2.

The data of the other components in the table show a percent of a total of compounds such as the chloro  $\beta$  - perchlorofluoromethylpyridines.

Table 2

|                                            | Exp. 3 | Exp. 4 | Exp. 5 |
|--------------------------------------------|--------|--------|--------|
| 2-chloro-5-trifluoromethylpyridine (%)     | 54.8   | 51.8   | 48.6   |
| 2-chloro-3-trifluoromethylpyridine (%)     | 13.8   | 18.2   | 17.9   |
| 2,6-dichloro-3-trifluoromethylpyridine (%) | 17.5   | 22.6   | 23.4   |
| Other components (%)                       | 13.9   | 7.4    | 10.1   |

**EXAMPLE 6:**

A vertical reaction tube made of Inconel having a reaction zone of a catalyst fluidized bed (an inner diameter of 82 mm and a height of 1100 mm) was used as a reactor. Two preheating tubes made of Inconel having an inner diameter of 8 mm and a length of 2000 mm for the starting material and the diluent were connected to the reaction tube. The reaction tube and the preheating tubes were covered by each electric heater and each insulator so as to control the temperature outwardly.

The activated catalyst used in Example 3 was pulverised to give a particle diameter of 0.18 to 0.4 mm. In the reaction zone, 1.7 kg. of the product was charged as the catalyst.

The reactor was heated at 430°C and  $\beta$ -picoline was fed at a rate of 3.6 g./min. and nitrogen gas was fed at a rate of 11.3 l/min. through the preheating tube and chlorine gas was fed at a rate of 2.8 l/min. and anhydrous hydrogen fluoride was fed at a rate of 2.5 l/min. through the other preheating tube. They were respectively fed into the reaction tube as the mixed gases at about 200°C. to react them for about 5 hours. The residence time of the reaction mixture in the reaction zone was about 7 seconds.

The gas discharged from the reactor was treated as the process set forth in Example 3 to obtain 1680 g. of an oily product.

The result of the analysis of the oily product by the gas chromatography with a temperature programmer is shown in the table 3.

**EXAMPLE 7:**

In accordance with the process of Example 6 except that  $\beta$ -picoline was fed at a rate of 2.38 g./min.; 3-trifluoromethylpyridine was fed at a rate of 1.88 g./min. and nitrogen gas was fed at a rate of 11.3 l/min. and also chlorine gas was fed at a rate of 2.8 l/min. and anhydrous hydrogen fluoride was fed at a rate of 2.5 l/min. to react them for about 3 hours, the reaction was carried out. The residence time of the reaction mixture in the reaction zone was about 7 seconds.

The gas discharged from the reactor was treated by the process as set forth in Example 3 to obtain 1090 g. of an oily product.

The result of the analysis of the oily product by the gas chromatography is shown in table 3.

The data of the other components in the table show a percent of a total of compounds such as the

chloro  $\beta$ -perchlorofluoromethylpyridines.

Table 3

|                                            | Exp. 6 | Exp. 7 |
|--------------------------------------------|--------|--------|
| 2-chloro-5-trifluoromethylpyridine (%)     | 51.5   | 56.4   |
| 2-chloro-3-trifluoromethylpyridine (%)     | 6.6    | 9.6    |
| 2,6-dichloro-3-trifluoromethylpyridine (%) | 25.1   | 18.3   |
| Other components (%)                       | 16.8   | 15.7   |

**EXAMPLE 8:****(1) Production of chloro  $\beta$ -trifluoromethylpyridines:**

A vertical reaction tube made of Inconel having a reaction zone of a catalyst fluidized bed (an inner diameter of 151 mm and a height of 1440 mm) was used as a reactor. Two preheating tubes made of Inconel having an inner diameter of 40 mm and a length of 1500 mm for the starting materials and the diluent were connected to the reaction tube. The reaction tube and the preheating tubes were covered by each electric heater and each insulator so as to control the temperature outwardly.

A mixture of 970 g. of chromium (III) fluoride hydrate and 12 kg. of active alumina having a particle size of 0.18 to 0.4 mm was charged into the catalyst packing part. The reaction tube was heated at 430°C and anhydrous hydrogen fluoride was fed at a rate of 20 l/min. for 3 hours to activate it.

The reactor was heated at 430°C and  $\beta$ -picoline was fed at a rate of 17 g./min, nitrogen gas was fed at a rate of 41 l/min. through the preheating tube and chlorine gas was fed at a rate of 21 l/min. and anhydrous hydrogen fluoride was fed at a rate of 21 l/min. through the other preheating tube. They were respectively fed into the reaction tube as the mixed gases at about 200°C to react them for about 100 hours. The activated catalyst was continuously fed and discharged at a rate of 3 kg./hour during the

reaction. The residence time of the reaction mixture in the reaction zone was about 2.5 seconds.

The gas discharged from the reactor was passed through a water scrubbing column and a caustic alkali scrubbing column. The oily product was separated and washed with water to obtain 160 kg. of the oily mixture of chloro  $\beta$ -trifluoromethylpyridines. The oily product was purified to obtain 72 kg. of 2-chloro-5-trifluoromethylpyridine. After separating by-products with a distillation, 72 kg. of the mixture of chloro  $\beta$ -trifluoromethylpyridines containing 2.6% of 2-chloro-5-trifluoromethylpyridine, 13% of 2-chloro-3-trifluoromethylpyridine and 50% of 2,6-dichloro-3-trifluoromethylpyridine was obtained as the residue obtained by the separation of the object compound.

(2) *Production of  $\beta$ -trifluoromethylpyridine:*

In a 100 liter autoclave, 13.5 kg. of the mixture of the chloro  $\beta$ -trifluoromethylpyridines, 14 kg. of triethylamine, 15 liters of water and 65 g. of 2% palladium on carbon were charged. Hydrogen gas was introduced into the autoclave. The catalytic reduction was carried out at a reaction temperature of 75°C for 120 minutes under a hydrogen pressure of 20 kg./cm<sup>2</sup>. After the reaction, the catalyst was separated by a filtration and a small amount of dilute hydrochloric acid was added to the filtrate to adjust pH to 3.5. The oil phase was separated and distilled to obtain 8.4 kg. of an oily product ( $\beta$ -trifluoromethylpyridine:  $\beta$ -difluoromethylpyridine = 9:1). A small amount of a dilute aqueous solution of sodium hydroxide was added to an alkaline condition and 12.3 kg. of triethylamine was recovered.

(3) *Production of chloro  $\beta$ -trifluoromethylpyridines:*

In accordance with the former step of producing the chloro  $\beta$ -trifluoromethylpyridines except that  $\beta$ -picoline was fed at a rate of 11.3 g./min.; the hydrogenated product was fed at a rate of 8.9 g./min.; nitrogen gas was fed at a rate of 41 l/min.; and also chlorine gas was fed at a rate of 21 l/min. and anhydrous hydrogen fluoride was fed at a rate of 21 l/min. to react them for about 3 hours, the reaction was carried out. The residence time of the reaction mixture in the reaction zone was about 2.5 seconds.

In accordance with the former step of producing the chloro  $\beta$ -trifluoromethylpyridines, the gas discharged from the reactor was treated to obtain 44 kg. of the oily mixture of chloro  $\beta$ -trifluoromethylpyridines.

The product was analyzed by a gas chromatography with a temperature programmer to find that the product contained 58.5% of 2-chloro-5-trifluoromethylpyridine, 11.4% of 2-chloro-3-trifluoromethylpyridine, 16.2% of 2,6-dichloro-3-trifluoromethylpyridine and 13.9% of the other components such as  $\beta$ -trifluoromethylpyridine, 2,5-dichloro-3-trifluoromethylpyridine, 2,3-dichloro-5-trifluoromethylpyridine, chloro  $\beta$ -chlorodifluoromethylpyridines. The product was distilled to obtain 21.9 kg. of the object 2-chloro-5-trifluoromethylpyridine.

**EXAMPLE 9:**

A vertical reaction tube made of Inconel having a catalyst fluidized bed (an inner diameter of 97.1 mm

and a height of 1570 mm) was used as a reactor. Two preheating tubes made of Inconel having an inner diameter of 30 mm and a length of 1,000 mm for the starting materials and the diluent were connected to the reaction tube. The reaction tube and the preheating tubes were covered by each electric heater and each insulator so as to control the temperature outwardly.

A mixture of 277 g. of anhydrous ferric chloride and 2.2 kg. of aluminum (III) fluoride having a particle size of 105 $\mu$ ~250 $\mu$  was charged into the catalyst packing part. The reaction tube was heated at 200°C and anhydrous hydrogen fluoride was fed at a rate of 2.3 l/min. for 1 hour to activate it.

The reactor was heated at 400°C and  $\beta$ -picoline was fed at a rate of 6.8 g./min., nitrogen gas was fed at a rate of 9.9 l/min. through the preheating tube. Chlorine gas was fed at a rate 7.4 l/min. and anhydrous hydrogen fluoride was fed at a rate of 7.4 l/min. through the other preheating tube. They were respectively fed into the reaction tube as the mixed gases at about 200°C to react them for about 30 hours. The activated catalyst was continuously fed and discharged at a rate of 300 g./hour during the reaction. The residence time of the reaction mixture in the reaction zone was about 3.4 seconds.

The gas discharged from the reactor was passed through a water scrubbing column and a caustic alkali scrubbing column. The condensed product was separated and neutralized by an ammonia solution to obtain 19.11 kg. of an oily product by a steam distillation. Further, the oily product was distilled to obtain 1.53 kg. of a forerun containing  $\beta$ -trifluoromethylpyridine as a main component, 9.56 kg. of a main distillate containing 2-chloro-5-trifluoromethylpyridine and 7.62 kg. of a last distillate containing 3.7% of 2-chloro-5-trifluoromethylpyridine, 14.5% of 2-chloro-3-trifluoromethylpyridine, 47.7% of 2,6-dichloro-3-trifluoromethylpyridine and 34.1% of other components.

**EXAMPLE 10:**

In accordance with the production step of the chloro  $\beta$ -trifluoromethylpyridines of the Example 8 except that chlorine gas was fed at a rate of 4.9 l/min., and the reaction was performed at a temperature of 380°C, in the residence time of about 3.9 seconds and for 6 hours, the production was carried out.

The gas discharged from the reactor was condensed through a water scrubbing column and a caustic alkali scrubbing column. Further the condensed product was washed with an aqueous caustic alkali solution and water to obtain 8.2 kg. of an oil. This oil was dried and distilled to obtain 5.8 kg of  $\beta$ -trifluoromethylpyridine.

**EXAMPLES 11-12:**

In accordance with the process of Example 5 except for using respectively a catalyst supporting 0.1 mole of manganese (III) fluoride and a catalyst supporting 0.1 mole of cobalt (II) fluoride, the catalysts were used instead of the catalyst of nickel (II) fluoride, the vapor phase reaction was carried out to obtain respectively 340 g. and 280 g. of an oily product.

The result of the analysis of the oily product by the

gas chromatography is shown in the following table 4 which is represented in the same manner as the table 2.

Table 4

|                                                 | Exp. 11          | Exp. 12          |
|-------------------------------------------------|------------------|------------------|
| Catalyst                                        | MnF <sub>3</sub> | CoF <sub>2</sub> |
| 2-chloro-5-trifluoro-<br>methylpyridine (%)     | 39.7             | 32.2             |
| 2-chloro-3-trifluoro-<br>methylpyridine (%)     | 14.8             | 12.3             |
| 2,6-dichloro-3-trifluoro-<br>methylpyridine (%) | 22.8             | 18.1             |
| Other components (%)                            | 22.7             | 37.4             |

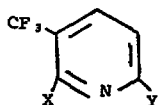
EXAMPLE 13:

- 5 In accordance with the Example 10, except for that chlorine gas was fed at a rate of 16.6 l/min., hydrogen fluoride was fed at a rate of 12.9 l/min.,  $\beta$ -picoline was fed at a rate of 10.5 g./min. and nitrogen gas was fed at a rate of 25.2 l/min., the reaction was performed at a temperature of 440°C, in the residence time of about 3.7 seconds and for 4.5 hours.

- 10 The gas discharged from the reactor was condensed, purified and separated by the same manner as the Example 10 to obtain 3.1 kg. of 2,6-dichloro-3-trifluoromethylpyridine.

CLAIMS

1. A process for producing a pyridine derivative having the formula



- 20 wherein X and Y respectively represent a hydrogen or chlorine atom, which process comprises reacting  $\beta$ -picoline with chlorine and hydrogen fluoride by a vapor phase reaction in the presence or absence of a catalyst of one or more metal fluorides selected from the fluorides of aluminum, chromium, iron, nickel, cobalt and manganese.
2. A process according to claim 1 wherein said reaction is carried out in the presence of a diluent.
3. A process according to claim 1 or claim 2
- 30 wherein said reaction is carried out at 300 to 600°C.
4. A process according to any preceding claim wherein the reaction is carried out in a reaction zone in which the residence time of the reaction mixture is in a range of 0.5 to 50 seconds.
- 35 5. A process according to any preceding claim wherein said pyridine derivative is 2-chloro-3-trifluoromethylpyridine, 2-chloro-5-trifluoromethylpyridine or 2,6-dichloro-3-trifluoromethylpyridine and the said fluoride catalyst is

40 used.

6. A process according to claim 5 wherein said pyridine derivative is 2-chloro-5-trifluoromethylpyridine.

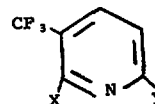
7. A process according to any one of claims 1 to 4
- 45 wherein said pyridine derivative is  $\beta$ -trifluoromethylpyridine and said fluoride catalyst is used.

8. A process according to any preceding claim wherein said catalyst is suspended in solid form in a
- 50 gas flow containing the reaction mixture, and said reaction is carried out in a fluidized condition.

9. A process according to any preceding claim wherein said catalyst is a fluoride of aluminum, iron or chromium.

- 55 10. A process according to claim 1 substantially as herein described with reference to any one of the Examples.

11. A pyridine derivative having the formula



- 60 wherein X and Y each represent a hydrogen or chlorine atom, made by a process according to any preceding claim.

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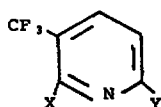
**EXAMPLE 13:**

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**CLAIMS**

1. A process for producing a pyridine derivative having the formula



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2. A process according to claim 1 wherein said reaction is carried out in the presence of a diluent.

3. A process according to claim 1 or claim 2

- 30 wherein said reaction is carried out at 300 to 600°C.

4. A process according to any preceding claim wherein the reaction is carried out in a reaction zone in which the residence time of the reaction mixture is in a range of 0.5 to 50 seconds.

- 35 5. A process according to any preceding claim wherein said pyridine derivative is 2-chloro-3-trifluoromethylpyridine, 2-chloro-5-trifluoromethylpyridine or 2,6-dichloro-3-trifluoromethylpyridine and the said fluoride catalyst is

40 used.

6. A process according to claim 5 wherein said pyridine derivative is 2-chloro-5-trifluoromethylpyridine.

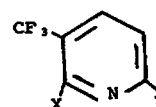
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50 gas flow containing the reaction mixture, and said reaction is carried out in a fluidized condition.

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- 60 wherein X and Y each represent a hydrogen or chlorine atom, made by a process according to any preceding claim.

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