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(71) Applicant(s)
Zeneca Limited

(Incorporated in the United Kingdom)

15 Stanhope Gate, LONDON, W1Y 6LN, United Kingdom

(72) Inventor(s)
Paul John de Fraine
Martin Charles Bowden
Patrick McNeilly

(74) Agent and/or Address for Service
Malcolm John Houghton
Zeneca Agrochemicals, Intellectual Property Dept., PO Box 3538, Jealott's Hill Research Station, BRACKNELL, Berkshire, RG42 6YA, United Kingdom

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C2C CAA CAB CKS CMD CPP CTT CUT C1531 C20Y C200 C204 C21X C215 C247 C25Y C250 C251 C280 C305 C31Y C311 C313 C326 C339 C34Y C342 C351 C352 C355 C36Y C364 C366 C367 C368 C386 C387 C388 C40Y C401 C43X C490 C574 C62X C62Y C624 C625 C628 C65X C655 C676 C678 C694 C695 C761 C762
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None

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(54) CHEMICAL PROCESS

(57) 6-Trifluoro-, 6-chlorodifluoro- and 6-difluoromethyl-2-hydroxypyridines are prepared by decarboxylating the corresponding nicotinic acid at a temperature above 190°C at normal atmospheric pressure. 6-Trifluoro-, 6-chlorodifluoro- and 6-difluoromethyl-2-hydroxy-nicotinic acids are novel compounds and are prepared by hydrolyzing the corresponding nicotinic acid ester or amide or the corresponding nitrile. The pyridines are useful chemical intermediates in the preparation of agricultural products.

A process for the preparation of a compound of formula

$$CF_2XCOCH{=}CHOR^3$$

is also disclosed.

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CHEMICAL PROCESS

This invention relates to a chemical process and more particularly to a novel process for preparing 6-trifluoro-, 6-chlorodifluoro- and 6-difluoromethyl-2-hydroxypyridines which are useful chemical intermediates in the manufacture of agricultural pesticides. The invention also relates to novel intermediates for preparing these pyridines and to a method for the preparation of the intermediates.

The compound 6-trifluoromethyl-2-hydroxypyridine (and its tautomer 6-trifluoromethylpyridone), is known as an intermediate in the manufacture of various agricultural pesticides, such as herbicides and insecticides. Hitherto, it has been prepared, for example, by the trifluoromethylation of 2-hydroxypyridine with bromotrifluoromethane (EP-A-0206951) and by the hydrolysis of 6-trifluoromethyl-2-chloropyridine (US 3787420, US 3711486, US 3705170, US 3682936, US 3609158).

It is also known that halopyridinecarboxylic acids lose carbon dioxide at elevated temperatures to give halopyridines (The Chemistry of Heterocyclic Compounds : Pyridine and its Derivatives, Part Two, [1961], E. Klingsberg (editor), 342-343).

According to the present invention, there is provided a process for preparing a compound of formula (I)[1] wherein X is H, F or Cl, which comprises heating a compound of formula (II) wherein X is as defined above at a temperature above 190°C at normal atmospheric pressure.

The compound (I) may exist in the form of its pyridone tautomer, or in admixture with it. Any reference herein to compound (I) should be taken as a reference to either tautomeric form or mixtures thereof in any proportion.

In the invention process, decarboxylation of compound (II) takes place at a temperature above 190°C either as a melt or in a high boiling, inert organic solvent. The temperature will usually be in the range of 195°C to 300°C, for example, 200°C to 260°C, and typically from 230°C to 250°C. If an organic solvent is used, the solvent will have a boiling point above the decarboxylation temperature and will be inert, ie. unreactive, towards compound (II) and the decarboxylated product. Typically, the solvent will be an aromatic or heteroaromatic

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[1] See Chemical Formulae at the end of this specification for chemical structures.

compound from which the end product can be conveniently separated at the end of the decarboxylation process, for instance by dissolution of a salt of it in water. Where separation of the end product is by dissolution of a salt (eg an alkali metal salt) in water, the solvent will need to be insoluble or only slightly soluble in water. Other methods of separation, for example, by evaporation of the solvent, may also be used where convenient. Examples of suitable solvents are *N*-methyl- pyrrolidone (boiling point (bp) 202°C), *N*-*N*-diethylaniline (bp 217°C), 1,3-dimethylimidazolidinone (bp 224-226°C) and diphenylether (bp. 253°C). A preferred solvent is quinoline (bp 240°C).

A catalyst, for example a transition metal catalyst such as copper, may be used to assist reaction.

In a typical process, the compound (II) is added with stirring to a pre-warmed solvent and any water present distilled off as the temperature is raised above 100°C. When quinoline is used as the solvent, the reaction temperature is raised, for example, to about 235°C and held at that temperature for several hours, for instance around 4 hours, according to batch size, catalyst usage, acceptable degree of decarboxylation, etc. When decarboxylation is as complete as desired, the temperature is reduced to near ambient temperature, and a further solvent, such as toluene, added, followed by aqueous caustic solution.

Any particulate material is filtered out and the aqueous layer separated. The product can then be isolated as a precipitated solid by acidification of the aqueous layer. Keeping the pH of the acidified layer between 5.5 and 6.5 during isolation of the product has been found to give an advantage in terms of product quality.

Where compound (II) is 6-chlorodifluoro- or 6-difluoromethyl-2-hydroxynicotinic acid, i.e. where X is H or Cl, the decarboxylation process is best performed in the absence of a solvent.

The starting material, compound (II), is a novel compound, as is its pyridone tautomer and any mixtures thereof. This compound forms another aspect of the present invention together with a process for its preparation.

Accordingly, as part of this invention, there is also provided a process for the preparation of a compound of formula (II) which comprises treating a compound of the formula (III) wherein Y is a carboxylic acid ester, amide or cyano group, with an inorganic acid or base and, where a base is used, acidifying the metal salt of the product so formed.

In the compound (III), Y is suitably a carboxylic acid ester group COOR wherein R is a lower alkyl group, an amide group $CONR^1R^2$ wherein R^1 and R^2 are independently hydrogen or lower alkyl, or a cyano group. Lower alkyl is used herein to include C_{1-6} alkyl, conveniently C_{1-4} alkyl, for example methyl and ethyl. Typically, R is ethyl and R^1 and R^2 are both hydrogen.

The compound (III) is conveniently hydrolysed to the nicotinic acid by refluxing in concentrated hydrochloric acid or in sulphuric acid. Alternatively, it may be refluxed in an alkali metal hydroxide, for instance, sodium or potassium hydroxide, followed by acidification of the alkali metal salt of the nicotinic acid so formed. The reaction time will depend on batch size and other factors, but 2 to 6 hours will usually be sufficient.

When hydrochloric acid is used, hydrogen chloride is conveniently removed at the end of reaction by distillation and the product isolated by solvent extraction or filtration. When sulphuric acid or a base is used, the product is isolated by filtration, after acidification in the latter case.

Therefore, in another aspect of the present invention there is provided a process for preparing a compound of formula (I) wherein X is H, F or Cl, which comprises the steps :

(a) preparing a compound (II) wherein X is as defined above, by treating a compound of the formula (III) as previously defined with an inorganic acid or base, and where a base is used, acidifying the metal salt of the product so formed; and

(b) heating the product of (a) at a temperature above 190°C at normal atmospheric pressure.

The compound of formula (III) wherein X is F and a method for its preparation are known in the literature. R W Lang and P F Wenk describe the general method set out in Scheme A in *Helv. Chim. Acta.* 1988, 71(3), 596-601. This method can also be used to make the compound III wherein X is H or Cl. Thus, in compounds (IV), (V), (VI), and (VII) in Scheme A, X is H, F or Cl, R^3 is lower alkyl as previously defined, for example, methyl, ethyl or *n*-butyl, and Y is as previously defined.

In the first stage of Scheme A, trifluoro-, chlorodifluoro- or difluoroacetic anhydride (IV) optionally in a convenient solvent such as chloroform, is added gradually to a stirred mixture of the alkyl vinyl ether (V), pyridine and a compatible solvent, conveniently chloroform, maintaining the temperature between 0 and 20°C. The reaction mixture is then stirred at 20-25°C. When no further reaction takes place, the reaction mixture is quenched

with water, the product extracted from the aqueous layer with a convenient solvent such as dichloromethane and the product (VI) isolated by evaporation of the solvent. As an alternative to the use of a separate solvent such as chloroform, additional quantities of an alkyl vinyl ether may be employed. Thus, the chloroform used may be replaced by an equal volume of an alkyl vinyl ether. This has advantages in terms of recovery and recycling of the alkyl vinyl ether solvent.

Although this stage of the process as described in the literature gives the product in an acceptable yield and purity under dilute concentrations, for example 2% w/v, at higher concentrations necessary for commercial production (eg. 20% w/v), lower yields are obtained and the product (VI) is of poorer quality and unstable. It has been found that this instability is associated with an excess of the acetic anhydride (IV). Thus, according to a further aspect of the present invention there is provided an improved process for the preparation of a compound of formula (VI) which comprises contacting an alkyl vinyl ether of formula (V) wherein R^3 is lower alkyl with a stoichiometric amount of an acetic anhydride (IV) in a convenient solvent and in the presence of pyridine.

By stoichiometric amount of an acetic anhydride is meant approximately 1 mole of the acetic anhydride (IV) for each mole used of the alkyl vinyl ether (V).

The amount of pyridine may vary, for example, from 0.3 mole/mole to 1 mole/mole of the alkyl vinyl ether (V). Suitably, 1 mole of pyridine for each mole of (V) is used.

A convenient solvent is a chlorinated alkane, such as a chlorinated methane, for example chloroform or dichloromethane. The amount used is such that the process is carried out at a concentration of from 15% w/v to 25% w/v, typically 15-20% w/v, ie. 15-20g vinyl ether substrate per 100 ml of solvent.

The temperature of reaction is maintained below 30°C, preferably between 20°C to 25°C once mixing of the ingredients is complete.

The second stage of Scheme A is conveniently carried out by adding the compound (VII) wherein Y is as previously defined, to an alkali metal alkoxide dissolved in an alcohol, suitably sodium methoxide in methanol or sodium ethoxide in ethanol, with cooling to control the associated exotherm. Once the exotherm has subsided, the first stage product (VI) is added and the mixture heated under reflux. The reaction may be quenched with hydrochloric acid and the product mass extracted with a suitable solvent such as ethyl acetate. The solution is then dried and the solvent removed by evaporation. Alternatively, the reaction

mixture is drowned into water, the methanol removed by distillation and the precipitated product filtered off and dried.

The addition of a second solvent, such as *N,N*-dimethylformamide, to the alcohol allows the reaction to be carried out at higher concentrations, up to, for example, 20% w/v, avoiding solidification of the reaction mass.

Examples of the compound (VII) are cyanoacetamide, malonamide and ethyl malonate monoamide. Malonamide is particularly suitable. When an ester is used, ie. when Y in formula (VII) is a carboxylic acid ester group, the value of Y in the compound (III) produced in the second stage of Scheme A may be the same or different depending on the choice of metal alkoxide used in the process. For instance, where ethyl malonate monoamide (VII, Y=COOEt) is used in conjunction with sodium methoxide, the compound (III) obtained may be in the form of the methyl ester (III, Y=COOMe).

Therefore, in yet another aspect of the present invention there is provided a process which comprises the steps :

(i) preparing a compound of the formula (VI) as previously defined by contacting an alkyl vinyl ether of formula (V) as previously defined with a stoichiometric amount of an acetic anhydride (IV) as previously defined in a convenient solvent in the presence of pyridine;

(ii) preparing a compound of the formula (III) as previously defined by reacting the product of (i) with a compound of formula (VII) as previously defined in the presence of an alkyl metal alkoxide in an alcohol solvent;

(iii) preparing a compound of formula (II) wherein X is H, F or Cl by treating the product of (ii) with an inorganic acid or base, and where a base is used, acidifying the metal salt of the product so formed; and

(iv) heating the product of (iii) at a temperature above 190°C at normal atmospheric pressure to obtain a compound of formula (I) wherein X is H, F or Cl.

The compound (III) wherein X is H and Y is as previously defined may also be prepared by the reduction of the corresponding compound (III) wherein X is Cl, for example, in a suitable solvent in the presence of zinc dust. The reduction may be assisted by sonication in an ultra-sonic bath. The compound (II) wherein X is H may also be prepared either from a compound (III) wherein X is H by the method described earlier or by the reduction of the compound (II) wherein X is Cl, for example, in a suitable solvent in the presence of zinc dust.

The following Examples illustrate the invention. Unless otherwise stated, magnesium sulphate was used to dry solutions, solutions were concentrated under reduced pressure, reactions involving water-sensitive reagents were performed under an atmosphere of nitrogen and solvents were dried before use, where appropriate.

EXAMPLE 1

Preparation of 2-hydroxy-6-trifluoromethylpyridine by decarboxylation of 2-hydroxy-6-trifluoronicotinic acid.

Quinoline (2949g, 96%, 21.92 mol) was charged to split-neck reaction flask fitted with a reflux condenser and thermometer and heated to 60°C by means of an isomantle. 2-Hydroxy-6-trifluoromethylnicotinic acid obtained by the method of Example 11 (2710g, 83.6%, 10.94 mol) was charged to the flask and the solution heated to 235°C with agitation using a mechanical agitator. Above 100°C, water present in the nicotinic acid was distilled off. The reaction liquors were held for 4 hours at 235°C, decarboxylation being monitored by HPLC analysis of samples of the reaction liquors taken at intervals. The contents of the flask were then cooled to room temperature. Toluene (9600g, 99%) was charged to the flask, followed by caustic solution (1650g, 47%) and water (10500g). The liquors were agitated for 30 minutes at 30-40°C and then passed through a filter to remove black particulate material. The liquors were then allowed to settle before the lower aqueous layer was separated off. Water (5200g) and caustic soda (826g, 47%) were added to the toluene layer and the mixture was agitated for 15 minutes, allowed to settle and the lower aqueous layer was again separated off. The combined aqueous layers were heated to 45-50°C and washed with toluene (7000g, 99%). The upper toluene layer was separated off and carbon 'Norit CN4' (88g) was charged to the aqueous layer. The liquors were agitated for 1 hour and then screened through a filter. Hydrochloric acid (4240g, 36%, 41.82 mol) was charged to the filtrates, precipitating the product. The liquors were stirred overnight at room temperature and then filtered. The solid was washed with 2 x 1kg of water and deliquored before discharging. Yield 1489.3g at 100%wt (83.5% theory yield).

EXAMPLES 2-10

Further preparations of 2-hydroxy-6-trifluoromethylpyridine by decarboxylation of 2-hydroxy-6-trifluoronicotinic acid.

In a similar manner to Example 1, the following Examples were carried out.

Example No.	Scale (g nicotinic acid)	Concentration (% w/v)	Solvent	Conditions	Yield %
2	5.1	-	None	2.5hr at 250°C	79
3	2	13	*N*-methyl-pyrrolidone	6 hr at 206°C	9*
4	2	50	*N,N*-diethyl-aniline	4 hr at 217°C	3.5*
5	2	50	Diphenyl ether	4 hr at 259°C	20*
6	1	50	Quinoline	4 hr at 235°C with copper catalyst	100*
7	1	50	Quinoline	4 hr at 235°C	100*
8	2	50	1,3-dimethyl imidazol-idinone	10 hr at 225°C	90*
9	12	75	Quinoline	3 hr at 200-205°C	100*
10	9.7	75	Quinoline	3 hr at 235°C	74.9

* = % conversion

EXAMPLE 11

Preparation of 2-hydroxy-6-trifluoromethylnicotinic acid by the hydrolysis of 2-hydroxy-6-trifluoromethylnicotinamide.

Water (7600kg) was charged to a split-neck reaction flask fitted with a reflux condenser, thermometer, and mechanical agitator. Sulphuric acid (1859g, 98%, 18.579 mol) was added dropwise to the stirred water followed by 2-hydroxy-6-trifluoromethylnicotinamide obtained by the method of Example 16 (1380g, 92.5%, 6.193 mol). The reaction liquors were heated to reflux (104°C) and held for 6 hours. A sample was taken for end of reaction analysis. The batch was cooled to room temperature and held for 1 hour before filtering the precipitate. The solid was washed with 2 x 1000g water. The solid was pulled free of liquors under vacuum before discharging.

Yield 1341.13g at 88.27% strength (1183.8g at 100%wt: 92.3% theory yield).

^{1}H NMR(d^6 acetone) δ:7.40(1H,d) 8.60(1H,d), 11.85(2H,br) ppm.

mp 160-162°C (effervescence).

EXAMPLES 12-15

Further preparations of 2-hydroxy-6-trifluoromethylnicotinic acid by the hydrolysis of a compound of the formula (III) where X is F.

In a similar manner to Example 11, the following Examples were carried out.

When hydrochloric acid was used instead of sulphuric acid, hydrogen chloride was removed by distillation at atmospheric pressure at the end of the reaction and the resulting solid product dried under vacuum.

Example No.	Y in Compound (III)	Scale (g of III)	Concentration (% w/v)	Conditions	Yield %
12	COOEt	18	26	3.5 hr reflux in HCl	84
13	$CONH_2$	10	24	2 hr reflux in HCl	>95
14	$CONH_2$	5	16	2 hr reflux in *c* H_2SO_4	87.3
15	$CONH_2$	50	11.5	2 hr reflux in NaOH followed by adjustment of pH to 1	88

EXAMPLE 16

Preparation of 2-hydroxy-6-trifluoromethylnicotinamide.

A dry, nitrogen purged split-neck reaction flask was fitted with a mechanical stirrer, condenser, thermometer and dropping funnel. To the flask was added methanol (6282g) followed by a sodium methoxide/methanol solution (1914g, 30%, 10.6 mol). Malonamide (772g, 98%, 7.41 mol) was charged and the reaction liquors agitated for 15 minutes. (*E*)-4-Ethoxy-1,1,1-trifluoro-3-buten-2-one obtained by the method of Example 21 (1978g, 64.5%, 7.59 mol) was slowly run from the dropping funnel into the reaction flask. The liquors were slowly heated to reflux.

After 2 hours at reflux, the batch was sampled for end of reaction analysis. When the reaction was complete, water (1780g) was added and then HCl (687g, 36%, 6.77 mol) was run in slowly at 45°C. The pH was checked to be between pH 1 - 3. The reaction liquors were stirred overnight at room temperature.

The liquors were heated to reflux and then set for atmospheric distillation of methanol. After distillation, water (9.38kg) was charged and the liquors cooled to 15°C to precipitate the product. The liquors were held at 15°C for 1 hour and then passed through a filter.

The solid was washed with 2 x 1000g water and pulled free of liquors. The solid was discharged giving 1292g of the title product as a 98.6% paste (1274g at 100% wt: 81.1% yield).

EXAMPLES 17-20

These Examples illustrate the preparation of a compound (III) where X is F and Y is CN, $COOC_2H_5$ or $CONH_2$ from (*E*)-4-ethoxy-1,1,1-trifluoro-3-buten-2-one (compound (VI) where X is F) and a compound (VII) where Y is CN, $COOC_2H_5$ or $CONH_2$. The method of preparation used was similiar to the one used in Example 16. The main differences were that sodium ethoxide and ethanol were used instead of sodium methoxide and methanol and the end product was extracted with ethyl acetate after quenching the reaction mass with hydrochloric acid.

The ethyl acetate solution was dried and the solvent removed by rotary evaporation.

Example No.	Y in Compound (VII)	Scale (g of VI)	Concentration (% w/v)	Conditions	Yield %
17	CN	25	10	2 hr reflux in ethanol	59
18	$COOC_2H_5$	10	4	2 hr reflux in ethanol	78
19	$CONH_2$	10	20	*N,N*-dimethyl-formamide/-ethanol (4/1) 80°C for 2 hr	62
20	$CONH_2$	10	10	2 hr reflux in ethanol	80

EXAMPLE 21

Preparation of (*E*)-4-ethoxy-1,1,1-trifluoro-3-buten-2-one

A dry, nitrogen purged 3-split-neck reaction flask was fitted with an overhead stirrer, dropping funnel and thermometer. Chloroform (9954g) was added to the flask and cooled to 10°C. Ethyl vinyl ether (1373g, 99%, 18.854 mol) was run slowly into the flask from the dropping funnel followed by pyridine (1505g, 99%, 18.854 mol). The solution was cooled to 5°C and trifluoroacetic anhydride (4000g, 99%, 18.854 mol) was added over 3.75 hours from the dropping funnel while maintaining the temperature below 20°C. After stirring for 30 minutes at 20-25°C, water (9370g) was added, stirring continued for another 30 minutes, and the reaction mixture then allowed to settle for 15 minutes. The upper aqueous layer and

lower organic layer were separated and the organic layer washed with water (2 x 7000g) and separated. Chloroform was distilled from the washed organic layer at ca. 100 mbar at a temperature up to 40°C. The still residue was discharged giving the title product (3260g, 85%, 87.9% theory yield).

By comparison, similar experiments showed that using 2 mol trifluoroacetic anhydride 1 mol ethyl vinyl ether at a concentration of 20% w/v and 1.4 mol trifluoroacetic anhydride to 1 mol ethyl vinyl ether at a concentration of 16% w/v gave a product of low purity which decomposed.

EXAMPLE 22

Preparation of 6-chlorodifluoromethylpyrid-2-one.

Pyridine (24g) was added to a solution of ethyl vinyl ether (22g) in chloroform (75ml) under nitrogen keeping the temperature below 10°C. Chlorodifluoroacetic anhydride (75g) was added over 90 minutes keeping the temperature below 20°C. The reaction mixture was stirred for 16 hours then quenched with water. The chloroform layer was washed with water, dried and concentrated to give (*E*)-ethoxy-1,1,1-chlorodifluorobuten-2-one (50.2g, 91% yield) as an orange liquid; ^{1}H NMR (270MHz): δ 1.43(3H,t), 4.12(2H,q), 5.89(1H,d), 7.90(1H,d) ppm.

Malonamide (27.5g) was added to a solution of sodium methoxide in methanol [prepared from sodium (8.7g) and methanol (300ml)]. After 15 minutes (*E*)-ethoxy-1,1,1-chlorodifluorobuten-2-one (50.2g) was added and the reaction mixture heated to reflux for 2 hours. After cooling the reaction mixture was concentrated then diluted with water, acidified with concentrated hydrochloric acid and the precipitate filtered off, washed with water and dried to give 6-chlorodifluoromethyl-2-hydroxynicotinamide (48.8g, 81% yield) as a white solid mp. 230-232 °C; ^{1}H NMR (270MHz): δ 7.29(1H,brm), 8.03(1H,brs), 8.38(2H,d), 13.6(1H,brs) ppm.

6-Chlorodifluoromethyl-2-hydroxynicotinamide (48.5g) was heated in dilute sulphuric acid (36ml in 250ml water) for 12 hours. The reaction was concentrated to about half the volume and cooled in ice, and the precipitate filtered, washed with water and air dried to give 6-chlorodifluoromethyl-2-hydroxynicotinic acid (48.1g, 98% yield) as a pale brown solid mp.131-3°C; ^{1}H NMR (270MHz): δ 7.36(1H,d), 8.33(1H,d) ppm.

6-Chlorodifluoromethyl-2-hydroxynicotinic acid (1.1g) was heated to 250°C for 10 minutes until the effervescence had ceased. On cooling it was taken up in ethyl acetate and

the organic phase washed with saturated sodium bicarbonate solution. The combined organic phase was dried, decolourised with activated charcoal and concentrated to give 6-chlorodifluoromethyl-pyrid-2-one (0.41g, 47% yield) as an off white solid; ^{1}H NMR (270MHz): δ 6.89(2H,m), 7.12(1H,t), 13.5(1H,brs) ppm.

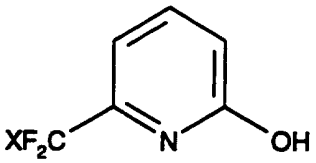
EXAMPLE 23

Preparation of (*E*)-4-ethoxy-1,1,1-trifluoro-3-buten-2-one

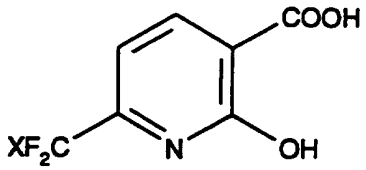
Pyridine (37.5g) and ethyl vinyl ether (159.9g) were charged to a dry 500ml flask and cooled to less than 5°C with agitation. Trifluoroacetic anhydride (100g) was run into the flask from a dropping funnel over 2.5 hours maintaining a temperature of less than 15°C. The reaction mixture was stirred for a further hour at 20-25°C before washing with water (3 x 125ml). The separated organic layer was found to contain 71.86g of the title product on analysis (90.7% theory yield). Ethyl vinyl ether was removed by atmospheric distillation.

CHEMICAL FORMULAE

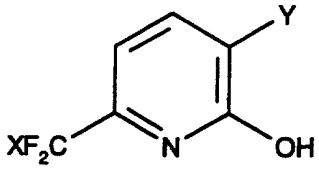
(As in Description)



(I)

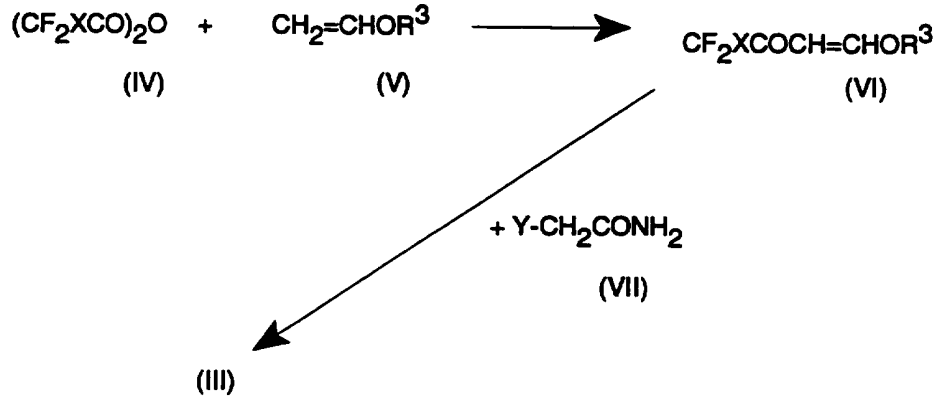


(II)



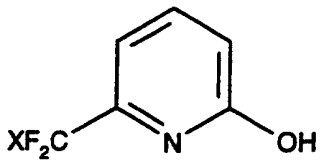
(III)

Scheme A



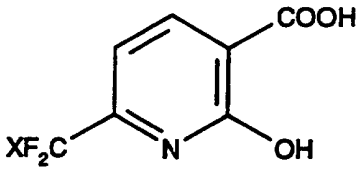
CLAIMS

1. A process for preparing a compound of formula (I):



(I)

wherein X is H, F or Cl, which comprises heating a compound of formula (II):



(II)

wherein X is H, F or Cl, at a temperature above 190°C at normal atmospheric pressure.

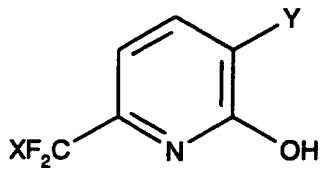
2. A process according to claim 1 wherein the temperature is in the range of 195°C to 300°C.

3. A process according to claim 1 or 2 wherein the compound of formula (II) is in molten form.

4. A process according to claim 1 or 2 wherein the compound of formula (II) is in a high boiling, inert organic solvent.

5. A process for preparing a compound of formula (I) as defined in claim 1 which comprises the steps :

(a) preparing a compound of formula (II) as defined in claim 1 by treating a compound of formula (III):



(III)

wherein X is H, F or Cl and Y is a carboxylic acid ester, amide or cyano group, with an inorganic acid or base, and where a base is used, acidifying the metal salt of the product so formed; and

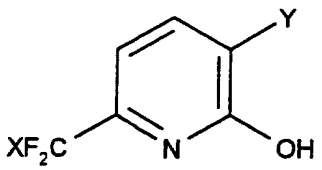
(b) heating the product of (a) at a temperature above 190°C at normal atmospheric pressure.

6. A process according to claim 5 wherein Y in the compound of formula (III) is a carboxylic acid ester group COOR wherein R is a lower alkyl group, an amide group $CONR^1R^2$ wherein R^1 and R^2 are independently hydrogen or lower alkyl, or a cyano group.

7. A process for preparing a compound of formula (I) wherein X is F or Cl, which comprises the steps:

(i) preparing a compound of the formula $CF_2XCOCH=CHOR^3$, wherein X is H, F or Cl and R^3 is lower alkyl, by contacting an alkyl vinyl ether of formula $CH_2=CHOR^3$ with a stoichiometric amount of an acetic anhydride $(CF_2XCO)_2O$ in a convenient solvent in the presence of pyridine;

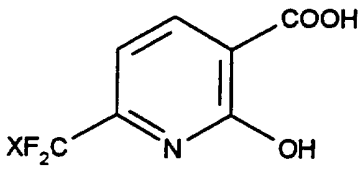
(ii) preparing a compound of the formula (III):



(III)

wherein X is F or Cl and Y is a carboxylic acid ester, amide or cyano group by reacting the product of (i) with a compound of formula $Y\text{-}CH_2CONH_2$ in the presence of an alkyl metal alkoxide in an alcohol solvent;

(iii) preparing a compound of formula (II):



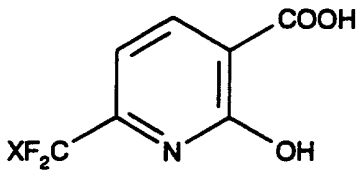
(II)

wherein X is F or Cl, by treating the product of (ii) with an inorganic acid or base, and where a base is used, acidifying the metal salt of the product so formed; and

(iv) heating the product of (iii) at a temperature above 190°C at normal atmospheric pressure.

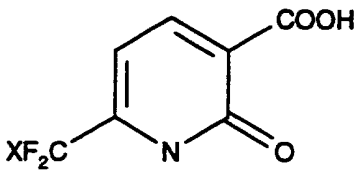
8. An improved process for the preparation of a compound of formula $CF_2XCOCH{=}CHOR^3$, wherein X is H, F or Cl and R^3 is lower alkyl, which comprises contacting an alkyl vinyl ether of formula $CH_2{=}CHOR^3$ with a stoichiometric amount of an acetic anhydride $(CF_2XCO)_2O$ in a convenient solvent and in the presence of pyridine.

9. A compound of formula (II):



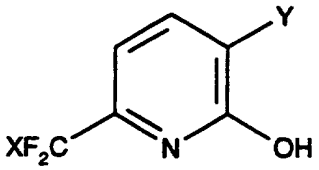
(II)

wherein X is H, F or Cl, or its tautomer of formula :



or any mixture thereof.

10. A process for the preparation of a compound of formula (II) as defined in claim 9, which comprises treating a compound of the formula (III) :



(III)

wherein X is H, F or Cl and Y is a carboxylic acid ester, amide or cyano group, with an inorganic acid or base and, where a base is used, acidifying the metal salt of the product so formed.

The Patent Office

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Application No: GB 9619011.1
Claims searched: 1-7, 9 and 10

Examiner: Dr Carol Davies
Date of search: 26 November 1996

Patents Act 1977
Search Report under Section 17

Databases searched:

UK Patent Office collections, including GB, EP, WO & US patent specifications, in:

UK Cl (Ed.O): C2C (CTT)

Int Cl (Ed.6): C07D

Other: ONLINE: CAS ONLINE

Documents considered to be relevant:

Category	Identity of document and relevant passage	Relevant to claims
	NONE	

X	Document indicating lack of novelty or inventive step	A	Document indicating technological background and/or state of the art.
Y	Document indicating lack of inventive step if combined with one or more other documents of same category.	P	Document published on or after the declared priority date but before the filing date of this invention.
&	Member of the same patent family	E	Patent document published on or after, but with priority date earlier than, the filing date of this application.