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Anmeldenummer / Filing No / N° de la demande : 83 307 212.7

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Bezeichnung der Erfindung: Preparation of (trifluoromethyl)pyridines

Title of invention:

Titre de l'invention :

Klassifikation / Classification / Classement : C07D 213/61

ENTSCHEIDUNG / DECISION

vom / of / du 31 May 1989

Anmelder / Applicant / Demandeur : The Dow Chemical Company

Patentinhaber / Proprietor of the patent /
Titulaire du brevet :

Einsprechender / Opponent / Opposant :

Stichwort / Headword / Référence : (Trifluoromethyl)pyridines/DOW

EPÜ / EPC / CBE Article 56

Schlagwort / Keyword / Mot clé : "Inventive step - state of the art,
reassessment - unexpected effect"

Leitsatz / Headnote / Sommaire

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Boards of Appeal

Office européen
des brevets

Chambres de recours



Case Number : T 456/88 - 3.3.2

D E C I S I O N
of the Technical Board of Appeal
of 31 May 1989

Appellant : The Dow Chemical Company
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Decision under appeal : Decision of Examining Division 005
of the European Patent Office
notified on 13 April 1988 refusing
European patent application
No. 83 307 212.7 pursuant to
Article 97(1) EPC

Composition of the Board :

Chairman : P. Lançon
Members : S. Schödel
R. Schulte

Summary of Facts and Submissions

I. European patent application No. 83 307 212.7, filed on 25 November 1983 and published under No. 110 690, was refused by a decision of the Examining Division notified on 13 April 1988. The decision was based on claims 1-6 filed on 27 August 1987 and claims 7-10 filed on 12 February 1987. Claim 1, of which an inaccurate version was reproduced in the decision, was directed to a method of preparing a trifluoromethyl substituted pyridine compound from the corresponding trichloromethyl substituted pyridine.

II. The reason given for the refusal was lack of inventive step of the claimed subject-matter in view of the documents:

(A) = US-A-4 266 064

(B) = EP-A-63 872

(C) = US-A-4 184 041 [similar to (D) = DE-A-2 812 607].

The problem arising out of (A), which document was considered to be the most relevant state of the art and which taught the first real industrial process, was to find an economic method for the fluorination of a trichloromethylpyridine with HF, without the disadvantages of the known catalytic vapour phase process (e.g. corrosiveness of HF and HCl).

According to the Examining Division, it was obvious to try the fluorination catalysts disclosed in (A) in a liquid phase reaction system at a lower temperature. Such liquid phase and vapour phase processes were presented in the prior art without one being favoured over the other (in

particular (C), (D); (B)) and were therefore considered to be equivalent.

Consequently, the skilled person could have expected that the catalytic process known from (A) could be carried out in the liquid phase and that this would also lead to good results.

The lower yields of desired products, the higher amount of by-products and longer reaction times associated with the liquid phase process cancelled out any economic advantages vis-à-vis the prior art process. The feature "in the absence of a diluent" seemed to be of no relevance and, therefore, non-essential.

In the absence of any unexpected advantage, the grant of a patent was not justified.

III. A Notice of Appeal against this decision was lodged by the Appellant on 11 June 1988, the fee being paid on the same day. A Statement of Grounds and an amended Claim 1 were filed on 11 August 1988.

The amended Claim 1 differs from Claim 1 forming the basis of the decision to refuse, in that the feature "at a temperature of below 250°C" has been inserted. The claim now reads as follows:

"A method of preparing a trifluoromethyl substituted pyridine compound from a trichloromethyl substituted pyridine compound containing one or two trichloromethyl groups, which trichloromethyl pyridine compound may be substituted with one or more other substituents which do not affect the halogen exchange reaction, which process comprises contacting the trichloromethyl pyridine compound in the liquid phase with HF, characterized in that the

reaction is carried out at a temperature of below 250°C in the absence of a diluent and in the presence of a catalytic amount of FeCl₂, FeCl₃, NbCl₅, TaCl₅, WCl₆, SnCl₄, TiCl₄ or mixtures thereof, SbF₃, FeF₂, FeF₃, AgF, KF, CrF₂ or mixtures thereof, optionally in combination with a phosphorus halide."

IV. The Appellant has argued substantially as follows:

Document (A), although itself relating to a vapour phase process of fluorinating a chloro-β-trichloromethylpyridine, referred in its statement of prior art to three liquid phase processes, none of which had been applied industrially; this had to be interpreted as teaching away from the possibility of using further liquid phase processes.

Had such liquid phase options been obvious to the authors of (A), they would surely have claimed them in (A); the omission of any mention of them was persuasive of non-obviousness.

The argument of "equivalence" of liquid phase and vapour phase processes derived from the teaching of (C) was based on obsolete prior art; the more recent perspective was given by (A), which had been filed two years after (C).

The claimed process had the advantages of:

- significantly lower temperature, resulting in substantial energy savings;
- no diluent to be separated from the reaction products;
- HF being less corrosive and less dangerous in the liquid phase than in the vapour phase.

The finding that the invention was obvious was thus based on hindsight.

- V. The Appellant requests in substance that the decision of the Examining Division be set aside, that the application be allowed to proceed to grant on the basis of Claim 1 filed with the Statement of Grounds on the 11 August 1988, Claims 2-6 filed on 27 August 1987 and Claims 7-10 filed on 12 February 1987; also that the appeal fee be reimbursed.

Reasons for the Decision

1. The appeal complies with Articles 106 to 108 and Rule 64 EPC and is, therefore, admissible.
2. There is no formal objection to the present claims since they do not contain subject-matter which extends beyond the content of the application as filed (Article 123(2) EPC).

The amendments introduced into Claim 1 during the proceedings as to the reaction temperature and the catalysts are clearly derivable from the original description (cf page 4, paragraph 2 to page 5, paragraph 3). The insertion "in the absence of a diluent", which is a "minus" feature, is also on balance acceptable having regard to the statement on page 5, paragraph 4 and the examples. Claims 2 and 4-10 correspond essentially to the identically numbered original claims. The feature of Claim 3 is supported by the description on page 5, line 2.

3. The application in suit relates to a method for producing (trifluoromethyl)pyridine compounds by contacting an unsubstituted or substituted (trichloromethyl)pyridine having one or two trichloromethyl groups with HF in the liquid phase. The resulting (trifluoromethyl)pyridine compounds are important intermediates in the production of agricultural chemicals.

Liquid phase processes of this type are known, in particular from

(A') = WO 79/00094

which document is referred to in (A) and represents, in the Board's view, the closest state of the art. In (A'), a process is described for the preparation of 2-chloro- and 2,3(2,5)-dichloro-5(3)-trifluoromethylpyridines, which process comprises heating the corresponding (trichloromethyl) pyridines with HF at 200°C. The reactants are contacted with each other in the absence of a diluent with stirring in an autoclave. The reaction time is ten hours. No indication is given as to the yield.

Experiments under similar conditions show that no substantial fluorination takes place, and that even at longer reaction times only trace amounts of the desired (trifluoromethyl)pyridine derivative are obtained. This process has therefore not been industrially applied (cf. (A'), Examples 5, 7, 20b; (A), column 1, line 56; specification, Example 5, runs 1, 1a; Declaration of Dr Fung, filed on 16 July 1986, Experiments I, III).

4. The technical problem underlying the application in suit was therefore to improve this prior art process.

The solution to this problem essentially consists in carrying out the known fluorination in the presence of a catalytic amount of a metal halide or a metal halide/phosphorus halide catalyst, under liquid phase reaction conditions, and, optionally, under superatmospheric pressure.

It is clear from the experimental results that the technical problem has been solved by the measures applied. Only when a catalyst of the claimed type is present do the gross yield of the fluorinated product and the proportion of the desired trifluoromethyl compound in the crude product significantly increase

(cf. Declaration of Dr. Fung, filed on 16 July 1986, Experiments II and III; specification, Examples 1, 3 and 5, runs 1, 1a). Thus:

Starting material	Reaction conditions	Catalyst	Yield of desired product - TFP***	Yield of fluorinated by-products
2,3-DC1-TC1P*	200°C/90h	-	0.2% of crude product ⁺	97.9% of crude product ⁺
2,3-DC1-TC1P*	175°C/14h	FeCl ₃	85g = 47% of theoretical	41.8% of crude product ⁺
2,6-DC1-TC1P**	180°C/19.5h	FeCl ₃	125g = 70% of theoretical	-

* 2,3-dichloro-5-(trichloromethyl)pyridine

** 2,6-dichloro-5-(trichloromethyl)pyridine

*** corresponding (trifluoromethyl)pyridine

+ gas-liquid chromatography

In the majority of the examples given in the specification, the desired (trifluoromethyl)pyridine is the predominant reaction product (cf Example 4, runs 1-8, 10, 14-18; Example 5, runs 2-4, 6-8).

At elevated pressures a further level of improved yield is obtained (cf Examples 9, 10 and 19).

An additional increase in yield can also be obtained by a simple "back chlorination" of the ring-fluorinated by-products as is outlined in present Claims 7 and 8 and in Examples 11-16.

5. None of the documents cited discloses a liquid phase fluorinating process having the particularity of using specific catalysts as set out in present Claim 1. The subject-matter of this claim is therefore novel under Article 54(2) EPC. Since novelty was not disputed, it need not be discussed further.

6. It remains, therefore, to examine whether or not the claimed solution to the technical problem as stated above was obvious in the light of the cited prior art.
 - 6.1 The method as claimed in present Claim 1 essentially differs from the "basic" process for the preparation of (trifluoromethyl)pyridines known from (A') in that the fluorination is carried out in the presence of a catalyst, this being either a specific metal chloride (derived from Fe, Nb, Ta, W, Sn, Ti; type 1 catalysts), or a specific metal fluoride (derived from Sb, Fe, Ag, K, Cr; type 2 catalysts). Also acceptable as a catalyst is a combination of such metal halides with a phosphorous halide (type 3 catalysts). Superatmospheric pressure, instead of being an obligatory feature, is now an optional one (cf present Claim 5).
 - 6.2 Neither of these modifications is disclosed or suggested in (A') nor in any of the other documents cited.

6.2.1 The document (A) is concerned with a vapour phase process. In this, 2-chloro-3(5)-trichloromethylpyridine and 2,6-dichloro-3-trichloromethylpyridine are converted to the corresponding (trifluoromethyl)pyridines in high yield by reacting with HF in the presence of a metal fluoride catalyst (13 separate species derived from Cr, Fe, Mn, Ni, Co, Al) and a diluent. The temperature applied ranges from 300°-500°C. Among the catalytic compounds disclosed, the fluorides of chromium, iron or aluminium are preferably used for industrial purposes (cf. Claim 1; column 3, paragraphs 1 and 2).

There is no pointer for the skilled man to test the usefulness (activity) of any of these vapour phase catalysts in the liquid phase system of (A') with a view to a possible improvement.

6.2.2 Documents (B) and (C) although also relating to the preparation of (trifluoromethyl)pyridines, contribute equally little to the solution of the technical problem.

Both disclose and exemplify a different kind of fluorination method using KF, SbF₃ or a trifluoromethyl derivative and not HF as a fluorinating agent, as is obligatory in the present case (cf. (B), Claims 1 and 5; (C) preparations (1) and (2)). There is no hint to apply SbF₃ in quantities lower than stoichiometric, in an HF fluorination.

6.2.3 Accordingly, it was the Appellant's own initiative to have modified the liquid phase process of (A') in such a way as to arrive at the claimed subject-matter, i.e. a working process which allows the production of the desired intermediates on a larger scale. In this respect the new process can also be seen as a competitive alternative to the existing vapour phase process of (A).

The technical advantages associated with working under liquid-phase conditions (lower temperature, absence of diluent) have already been pointed out (cf. item IV, paragraph 4). As to the gross yield of fluorinated products as well as the yield of the desired (trifluoromethyl)-pyridine derivatives, the results obtained could not have been predicted and must, therefore, be regarded as surprising (cf. section 4 above).

- 6.3 The arguments put forward in the decision under appeal are, in contrast to this, not conclusive.

In particular, the finding of "equivalence" between liquid phase and vapour phase fluorination leading to the "obvious transferability" of the known gas phase catalysts to the liquid reaction system of (A'), upon which the decision for refusal is mainly based, results from a misinterpretation of the technical teaching of (C) and finds no support in the passage relied upon (cf. column 2, paragraph 2). At this point there is neither a reference to a fluorination method using HF as fluorinating agent nor to a catalyst of any kind.

The above assertion is therefore of no relevance to the evaluation of the actual situation in the present case.

As to the alleged "transferability", a closer analysis reveals that none of the catalysts of the claimed types 1 and 3 is so much as mentioned in document (A) and consequently the question of transfer of these cannot arise. The same is true of SbF_3 , AgF and KF , which belong to the type 2 catalysts (cf. section 6.1).

Indeed, of all the catalysts disclosed in (A), only three, namely CrF_2 , FeF_2 and FeF_3 are common to the claimed subject-matter and have the additional quality of

functioning in the liquid phase. Of the remainder, at least one species - MnF_3 - has been found not to work in the liquid phase; furthermore, $AlCl_3$ is inactive (cf. (A), column 3, paragraphs 1 to 3; specification, Example 4, run 11; Example 5, run 9).

Thus the three "transferred" catalysts represent a narrow selection and the position taken by the Examining Division in this respect amounts to a "hindsight" analysis, not giving any reason why the skilled person should have made such a selection. In the absence of any indication of additional activity in these species, one cannot assume that the practitioner would have made an effort in this area (cf. T 2/83, OJ EPO 1984, 265).

The reasoning given in the decision under appeal, even starting out from (A), therefore, does not support the finding under Article 56 EPC.

- 6.4 From the above it is clear that the subject-matter of Claim 1 under discussion cannot be derived in an obvious manner from the cited state of the art and involves an inventive step as required by Article 56 EPC. The claim is therefore patentable. This applies also mutatis mutandis to dependent Claims 2-10 which relate to further elaborations of the process specified in Claim 1.
7. With regard to the Appellant's request for oral proceedings, it was confirmed on enquiry that this was only intended for the case that the Board would decide unfavourably to the Appellant on the substantive issue.
8. The Appellant's request for reimbursement of the appeal fee has not been reasoned. The Board cannot find a substantial procedural violation within the meaning of Rule 67 EPC. An

error in interpreting a document cannot be regarded as a procedural violation. The success of the appeal in itself does not justify repayment of the appeal fee.

Order

For these reasons, it is decided that:

- (1) The decision of the Examining Division is set aside.
- (2) The case is remitted to the Examining Division for grant of a patent on the basis of Claims 1-10 on file.
- (3) The request for reimbursement of the appeal fee is refused.

The Registrar:

The Chairman:

F. Klein

P. Lançon