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**D E C I S I O N**  
**of 13 December 2005**

**Case Number:** T 0912/03 - 3.3.01

**Application Number:** 99940396.7

**Publication Number:** 1114042

**IPC:** C07D 311/76

**Language of the proceedings:** EN

**Title of invention:**  
Process for preparing 3-Isochromanone

**Applicant:**  
Syngenta Limited

**Opponent:**  
-

**Headword:**  
3-Isochromanone/SYNGENTA

**Relevant legal provisions:**  
EPC Art. 123(2), 54, 56

**Keyword:**  
"Amendments - allowable (yes) - directly and unambiguously disclosed"  
"Novelty (yes) - claimed process not specifically disclosed";  
"Inventive step (yes) - non obvious improved process over the structurally most closely related process disclosed in the prior art"

**Decisions cited:**  
-

**Catchword:**  
-



Case Number: T 0912/03 - 3.3.01

**D E C I S I O N**  
of the Technical Board of Appeal 3.3.01  
of 13 December 2005

**Appellant:**

Syngenta Limited  
European Regional Centre  
Priestley Road  
Surrey Research Park  
Guildford  
Surrey GU2 7YH (GB)

**Representative:**

Osborn, Martin Keith  
Syngenta Limited  
Intellectual Property Department

Jealott's Hill International Research  
Center  
P.O. Box No. 3538  
Bracknell  
Berkshire RG42 6EY (GB)

**Decision under appeal:**

Decision of the Examining Division of the  
European Patent Office posted 14 February 2003  
refusing European application No. 99940396.7  
pursuant to Article 97(1) EPC.

**Composition of the Board:**

**Chairman:** A. J. Nuss  
**Members:** P. F. Ranguis  
R. T. Menapace

## Summary of Facts and Submissions

- I. The present appeal lies from the decision of the Examining Division to refuse the European patent application No. 99 940 396.7 (European publication No. 1 114 042) under Article 97(1) EPC.
- II. The refused set of claims according to the main request contained ten claims. Claim 1, the sole independent claim, read as follows:

"1. A process for the preparation of 3-isochromanone which comprises contacting an o-xylene- $\alpha,\alpha'$ -dihalide with carbon monoxide in the presence of a palladium catalyst and N,N-diisopropylethylamine in a liquid medium comprising water and a tertiary alcohol, the molar ratio of N,N-diisopropylethylamine:o-xylene- $\alpha,\alpha'$ -dihalide being in the range of 10:1 to 1:1 and the molar ratio of water:tertiary alcohol being in the range of 1:1 to 20:1."

- III. The Examining Division considered in its decision that the claimed subject-matter was novel over document

(1) EP-A- 834 497

given that this document did not disclose unambiguously a process for preparing 3-isochromanone involving N,N-diisopropylethylamine as an hydrogen halide capturing agent.

However, document (1) disclosed that the reaction could be run by using any basic compounds able to capture hydrogen halides and among those, inorganic bases or

amine derivatives. It followed that the claimed subject-matter was to be regarded as a selection over document (1) and the technical problem to be solved could only be seen in the provision of an improved process for making 3-isochromanone vis-à-vis the disclosure of document (1).

The data provided by the Applicant (now Appellant) in order to show the presence of an unexpected effect based on a better yield obtained by the N,N-diisopropylethylamine vis-à-vis the amine derivatives disclosed in document (1) could not be accepted given that those amines did not represent the closest state of the art. In view of document (1), the teaching of which was to be considered as a whole, the best yields were obtained with calcium hydroxide and any proper comparison should have been made between N,N-diisopropylethylamine and the said inorganic base.

Since no improved effect had been shown over calcium hydroxide, the claimed subject-matter did not involve an inventive step.

IV. At the Oral proceedings before the Board which took place on 13 December 2005, the Appellant submitted as sole request a set of nine claims. Claim 1, the sole independent claim, reads as follows:

"1. A process for the preparation of 3-isochromanone which comprises contacting an o-xylene- $\alpha,\alpha'$ -dihalide with carbon monoxide in the presence of a palladium catalyst and N,N-diisopropylethylamine in a liquid medium comprising water and a tertiary alcohol which is 2-methyl butan-2-ol or 2,3-dimethylbutane-2,3-diol, the

molar ratio of N,N-diisopropylethylamine:o-xylene- $\alpha,\alpha'$ -dihalide being in the range of 5:1 to 2:1 and the molar ratio of water:tertiary alcohol being in the range of 1:1 to 10:1."

V. The Appellant submitted in essence the following arguments:

Document (1) indicated that any bases which functioned as an hydrogen halide capturing agent might be used, including alkali metal inorganic bases, alkaline earth metal inorganic bases and tertiary amines. It was true that the best yields were obtained with the use of calcium hydroxide as the hydrogen halide capturing agent. However, calcium hydroxide was a solid in the reaction mixture. The bulk handling of solids on an industrial scale was a more demanding operation than that of liquids. This was especially important when adding materials to vessels containing toxic, gaseous atmospheres such as carbon monoxide. By contrast N,N-diisopropylethylamine was in a liquid state in the liquid medium. It followed that the comparison was to be made with the liquid tertiary amines disclosed in document (1) and not with calcium hydroxide.

Thus taking document (1) as the closest state of the art, the technical problem to be solved could be seen in the provision of an improved process over the tertiary amine base process as disclosed in document (1).

As evidenced by comparative data provided in the course of the examining proceedings, it was surprisingly discovered that the choice of N,N-diisopropylethylamine

in the molar ratio range with respects to o-xylene- $\alpha,\alpha'$ -dihalide as defined in Claim 1 in combination with specific tertiary alcohols, i.e. 2-methyl butan-2-ol or 2,3-dimethylbutane-2,3-diol, in the molar ratio range with respect of water as defined in Claim 1 gave superior results to other tertiary amine bases in terms of the total yield of 3-isochromanone obtained. Hence the claimed process according to the present request involved an inventive step.

VI. The Appellant requested that the decision under appeal be set aside and a patent be granted on the basis of Claims 1 to 9 as submitted during the oral proceedings before the Board.

VII. At the end of the oral proceedings the decision of the Board was announced.

### **Reasons for the Decision**

1. The appeal is admissible.

#### *Main request*

2. *Amendments - Article 123(2) EPC*

2.1 Compared to Claim 1 as originally filed, present Claim 1 results from the following amendments:

- the catalyst is a palladium catalyst. This amendment finds support on page 2, lines 29 to 31.

- the hindered amine base is N,N-diisopropylethylamine. Such an amendment finds support on page 4, lines 22-23 of the application as originally filed.
  - the added molar ratio of N,N-diisopropylethylamine:o-xylene- $\alpha,\alpha'$ -dihalide is in the range of 5:1 to 2:1. Such an amendment finds support on page 4, lines 29 to 31 of the application as originally filed.
  - the tertiary alcohols are 2-methyl butan-2-ol or 2,3-dimethylbutane-2,3-diol. Such an amendment finds support on page 2, lines 11-12.
  - and the added molar ratio of water:tertiary alcohol is in the range of 1:1 to 10:1, which finds support on page 2, lines 19-20 of the application as originally filed.
- 2.2 The subject-matter of Claims 2, 3, 5 to 9 correspond to the subject-matter of Claims 2, 4 (partially), 11 to 15 of the application as originally filed respectively. The subject-matter of Claim 4 finds support on page 2, lines 22-23 of the application as originally filed.
- 2.3 The amendments are, therefore, directly and unambiguously derivable from the application as originally filed and thus the present claimed subject-matter does not extend beyond the content of the application as originally filed (Article 123(2) EPC).

3. *Novelty - Article 54(1)(2) EPC*

3.1 Document (1) discloses a process for preparing 3-isochromanones by reacting an  $\alpha,\alpha'$ -o-xylene dihalide derivative with carbon monoxide and water in an organic solvent in the presence of a hydrogen halide capturing agent and a catalyst to obtain a reactant and then treating the reactant with an acid (see page 5, lines 40 to 52).

The catalyst to be used includes palladium catalysts (see page 6, line 22). Tert-butyl alcohol and 2-methyl-2-butyl alcohol may be used as a solvent (see page 7, line 34). As substance functioning as a hydrogen halide capturing agent, metal inorganic bases, alkaline earth metal inorganic bases and tertiary amines can be used. The tertiary amines include pyridine, triethylamine, trimethylamine, and tri-n-butylamine. The amount of the base to be used is 1 to 10 molar equivalents to the reaction substrate (see page 7, lines 14 to 16)

3.2 Although the N,N-diisopropylethylamine base is generically encompassed by the term "tertiary amine", the Board concurs with the Examining Division and the Appellant that such a specific base does not emerge unambiguously from the generic definition disclosed in document (1). This document is also silent with respect to the molar ratio water:alcohol as far as the process involves a tertiary amine as an hydrogen halide capturing agent. The subject-matter of Claim 1 is, therefore, novel over document (1).

3.3 Neither in the international proceedings nor in the Examining proceedings was other prior art cited.



4. *Inventive step - Article 56 EPC*

- 4.1 Document (1) discloses a process for preparing 3-isochromanones by reacting an  $\alpha,\alpha'$ -o-xylene dihalide derivative with carbon monoxide and water in a tertiary alcohol as a solvent in the presence of a palladium catalyst and an hydrogen halide capturing agent such as alkali metal inorganic bases, alkaline earth metal inorganic bases and tertiary amines, in a molar ratio base:o-xylene- $\alpha,\alpha'$ -dihalide ranging from 10:1 to 1:1, encompassing, therefore, the claimed subject-matter. As a consequence, in view of the disclosure of document (1), there must be for the skilled person an expectation of the retention of the same activity, namely obtaining 3-isochromanone, in implementing the process as defined in Claim 1. Unless evidence refutes this assumption by showing that the claimed process is associated with an improvement, the presumption prevails that the process represents only a predictable effect and is, therefore, obvious. The onus is on the Appellant to refute this inference based on the information so far available. If he chooses to give evidence by comparative tests, these must be carried out in respect of the relevant closest state of the art.
- 4.2 It becomes, therefore, critical to determine the terms of the comparison to assess whether or not an improvement can or cannot be acknowledged.

To resolve this question, the Board follows the principle laid down *inter alia* in decision T 181/82 (OJ EPO 1984, 401, point 4) according to which, where comparative tests are submitted as evidence of an

unexpected effect, there must be the closest possible structural approximation in a comparable type of use to the subject-matter claimed.

The Board, in that respect, does not share the opinion of the Examining Division which stated that the comparison should rely on calcium hydroxide which was the preferred hydrogen halide capturing agent according to document (1). Indeed, calcium hydroxide is an inorganic base solid in the reaction mixture which as such differs essentially from an amine base like N,N,-diisopropylethylamine which is liquid in the implementation of the process for preparing 3-isochromanone. In the Board's judgment, N,N,-diisopropylethylamine being liquid in the liquid medium, the comparison has to be made with a prior art involving an hydrogen halide capturing agent being a liquid in the reaction mixture if already known. Since document (1) discloses tertiary amines which are liquid, they must be considered as the closest hydrogen halide capturing agent to which the claimed invention must be compared. In particular, N,N,-diisopropylethylamine being an aliphatic tertiary amine, it seems appropriate to compare it with aliphatic tertiary amines having the most closely related structure disclosed in document (1), namely triethylamine and tri-n-butylamine.

- 4.3 To this end, the Appellant submitted in the course of the Examining proceedings experimental evidence intended to demonstrate the superior yield obtained in performing the process according to Claim 1 over the closest state of the art.

Three different tertiary amines, i.e. N,N-diisopropylethylamine, triethylamine and tri-n-butylamine were used in the presence of 2-methyl butan-2-ol in the conditions of the claimed process, i.e. molar ratio tertiary amine:o-xylene- $\alpha,\alpha'$ -dihalide of 3, molar ratio water: 2-methyl butan-2-ol of 6.6. The yield is of 80.0% with N,N-diisopropylethylamine, 70.17% with triethylamine and 38.5% with tri-n-butylamine.

- 4.4 These results show that N,N-diisopropylamine in a process for preparing 3-isochromanone as defined in Claim 1 provides an improvement in terms of the yield of 3-isochromanone obtained over two tertiary amine bases explicitly indicated in document (1), i.e. triethylamine and tri-n-butylamine.
- 4.5 The Board, therefore, concurs with the Appellant that the technical problem to be solved may be seen in the provision of an improved process over the tertiary amine base process disclosed in document (1).
- 4.6 As the solution to this problem, the claimed subject-matter proposes a process involving N,N-diisopropylamine as hydrogen halide capturing agent for preparing 3-isochromanone in the conditions as defined in Claim 1.
- 4.7 The next step is to verify whether or not the technical problem is solved within the whole claimed area.
- 4.7.1 The application as originally filed discloses eight experimental methods (examples 2 to 9) for performing the process according to the claimed subject-matter in

- the presence of 2-methyl butan-2-ol. The molar ratio N,N-diisopropylamine:o-xylene- $\alpha,\alpha'$ -dihalide ranges from 2.8 to 3.13 and the molar ratio water: 2-methyl butan-2-ol ranges from 2.1 to 9.8. The yields of 3-isochromanone are no lower than 75.4% (see example 2).
- 4.7.2 Furthermore, the experimental data submitted before the Examining Division show that a yield of 3-isochromanone of 81.04% is obtained when replacing 2-methyl-2-butyl alcohol by 2,3-dimethyl-2,3-butanediol in a molar ratio N,N-diisopropylamine:o-xylene- $\alpha,\alpha'$ -dihalide of 3 and molar ratio water: 2,3-dimethyl-2,3-butanediol of 6.6.
- 4.7.3 In view of the above, the Board accepts that an improved yield is obtained by the use of N,N-diisopropylamine in lieu of triethylamine or tri-n-butylamine and that this improvement is upheld in using either 2-methyl butan-2-ol or 2,3-dimethyl-2,3-butanediol or by varying the molar ratios N,N-diisopropylamine:o-xylene- $\alpha,\alpha'$ -dihalide and water: alcohol within the ranges as defined in Claim 1. The technical problem is, therefore, solved within the whole claimed area.
- 4.8 It remains to be decided whether or not the proposed solution to the problem underlying the invention is obvious in view of the cited prior art. The question arises whether or not it would have been obvious to select N,N-diisopropylethylamine as an hydrogen halide capturing agent in order to achieve a better yield in a process for preparing 3-isochromanone.

4.8.1 Document (1) merely lists among the tertiary amines to be used as hydrogen halide capturing agent three specific aliphatic amines, triethylamine, trimethylamine, and tri-n-butylamine. Furthermore, document (1) does not include any examples involving the use of tertiary amines. From these findings, the person skilled in the art can obtain no indication which would have led him to try with a reasonable expectation of success N,N-diisopropylamine in order to obtain 3-isochromanone with a better yield and, as a result, solve the above defined technical problem. Indeed, the skilled person would have at most expected to obtain more or less the same yield whatever the tertiary amine used. Hence it was not obvious to choose N,N-diisopropylamine for achieving a significantly better yield in the preparation of 3-isochromanone.

4.8.2 It follows that the subject-matter of Claim 1 involves an inventive step. The same applies to dependent Claims 2 to 9 which represent particular embodiments of the subject-matter of Claim 1.

5. *Remittal to the first instance - Article 111(1) EPC*

Although the Board has come to the conclusion that the present request is to be allowed, it is noted that the description still needs to be put into conformity with the claims of the present request. Therefore, having regard to the fact that the function of the Boards of Appeal is primarily to give a judicial decision upon the correctness of the earlier decision taken by the first instance, the Board exercises its discretion under Article 111(1) EPC to remit the case to the first instance in order for the description to be adapted to

the allowable claimed subject-matter according to the present request.

## **Order**

### **For these reasons it is decided that:**

1. The decision under appeal is set aside.
2. The case is remitted to the Department of first instance with the order to grant a patent with the claims 1 to 9 as submitted during the oral proceedings before the Board.

The Registrar:

The Chairman:

P. Cremona

A. Nuss