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Bezeichnung der Erfindung:
Title of invention:
Titre de l'invention : Halogenating compounds and a process for their production

Klassifikation / Classification / Classement : C 07 F 9/14

ENTSCHEIDUNG / DECISION

vom / of / du 31 October 1986

Anmelder / Applicant / Demandeur : Eli Lilly & Co.

Patentinhaber / Proprietor of the patent /
Titulaire du brevet :

Einsprechender / Opponent / Opposant :

Stichwort / Headword / Référence :

EPÜ / EPC / CBE
Article 52(1), 54 and 56 EPC

Kennwort / Keyword / Mot clé :

Novelty - Disclaimer - State of the art implied by disclosure
Inventive Step

Leitsatz / Headnote / Sommaire

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Case Number : T 197 /84

D E C I S I O N
of the Technical Board of Appeal 3.3.2
of 31 October 1986

Appellant : Eli Lilly & Co.
307, East McCarty Street
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Representative : McVey, Kenneth William Henry
Erl Wood Manor
Windlesham, Surrey
GB

Decision under appeal : **Decision of Examining Division 009 of the European Patent Office dated 20 March 1984 refusing European patent application No 80 300 282.3 pursuant to Article 97(1) EPC**

Composition of the Board :

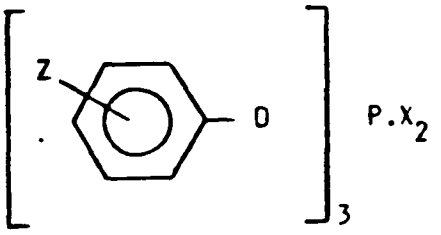
Chairman : P. Lançon
Member : G. Szabo
Member : R. Schulte

I

Summary of Facts and Submissions

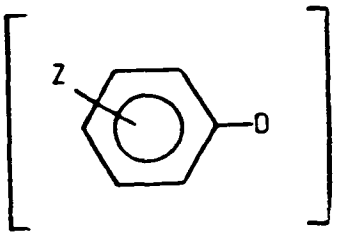
I. European patent application No. 80 300 282.3 filed on 31 January 1980 and published on 3 September 1980, with publication No. 15 079, claiming priority of the prior application on 1 February 1979 (US-8469) was refused by the Examining Division 009 of the European Patent Office dated 20 March 1984. The decision was based on Claims 1 to 17. Claim 1 was worded as follows:

"A halogenating compound of the general formula



(I)

which is the kinetically controlled product of the reaction of equivalent amounts of a triaryl phosphite of the formula



(II)

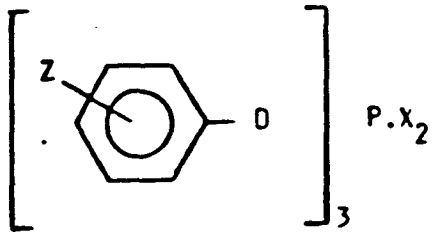
and chlorine or bromine in a substantially anhydrous inert organic solvent wherein in the above formulae Z is hydrogen, halo, C_1-C_4 alkyl or C_1-C_4 alkoxy, and X is Cl or Br."

II. The reason for the refusal was, **inter alia**, that the subject-matters of Claim 1 and of others lack novelty. The cited state of the art, i.e. (A) R. Anschütz et al, Annalen

d. Chemie, 1889, 353, 112, (B) W. Autenrieth et al, Berichte, 1908, 41, 155-157, and (C) H.N. Rydon, et al, J. Chem. Soc., 1956, 3043-3056, in particular pages 3053 and 3054, disclosed the reaction of m- and p-toluyl and phenyl phosphite with chlorine as well as with bromine. The reactions must have directly though unknowingly led to the "kinetically controlled" products according to Claim 1 before these transitional materials spontaneously converted themselves into the thermodynamically stable isomers. The former were therefore made available to the public without any restriction. The mere discovery that such freshly prepared temporary "intermediates" had advantageous properties could not render them novel. To limit them "for use as a halogenating agent" would be no effective limitation to that use, since this could not alter the fact that the same entity already existed in the state of the art.

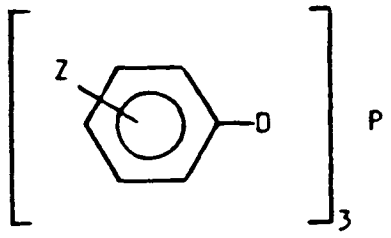
III. The Applicants filed an appeal against this decision on 14 May 1984 with the payment of the fee, and submitted a statement of Grounds on 23 July 1984. Later in the proceedings before the Board the claims on file were replaced with a new set I, and auxiliary sets II, III, and IV for consideration (25.03.86). Claim 6 of set I was further amended in the letter dated 4 June 1986. Claims 1, 5 and 6 of set I are as follows:

"1. The use of a compound of the general formula



(I)

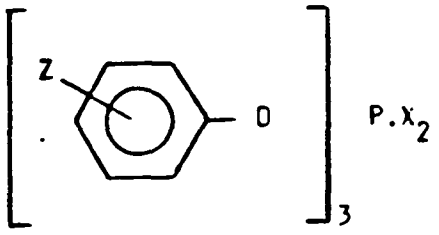
which is the kinetically controlled product of the reaction of equivalent amounts of a triaryl phosphite of the formula



(II)

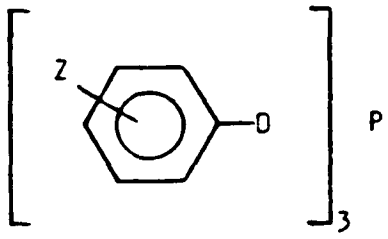
and chlorine or bromine in a substantially anhydrous inert organic solvent where in the above formulae Z is hydrogen, halo, C_1-C_4 alkyl or C_1-C_4 alkoxy and X is Cl or Br, as an agent for halogenating an enol or amido group.

5. A halogenating compound of the general formula



(I)

which is the kinetically controlled product of the reaction of equivalent amounts of a triaryl phosphite of the formula



(II)

and chlorine or bromine in a substantially anhydrous inert organic solvent where the above formulae Z is hydrogen, halo, C_1-C_4 alkyl or C_1-C_4 alkoxy, and X is Cl or Br; provided that when X_2 is Cl_2, Z is not hydrogen, m-CH_3 or p-CH_3, and when X_2 is Br_2, Z is not hydrogen.

6. A halogenation process which comprises (a) preparing a kinetically controlled product of formula (I), as defined in Claim 1, by reacting a triaryl phosphite of formula (II), as defined in Claim 1, and chlorine or bromine in a substantially anhydrous inert organic solvent at a temperature of -70°C to 0°C, and (b) immediately utilising the solution of kinetically controlled product to halogenate a substrate having an enol or amido group, at a temperature within the said temperature range."

IV. The Appellants argued that the use claim was submitted because the Examining Division had suggested that such claims would be allowable (cf. communication of 22 October 1982, page 2). The claim to the compounds **per se** now excluded those disclosed in the prior art and should no more be subjected to objections on grounds of lack of novelty. In view of the non-obvious use thereof, these should also be allowable (cf. communication from the Examining Division dated 29 September 1981, page 3). The rest of the submissions by the Appellant have since become irrelevant in view of the deletion of claims objected to in the decision under appeal.

V. The Appellants request that the decision be set aside and the patent be granted with the revised set of claims, or with one of the auxiliary sets submitted on 25 March 1986.

II

Reasons for the Decision

1. The appeal complies with Articles 106 to 108 and Rule 64 EPC and is, therefore, admissible.

2. Claims 1 to 4 of the various requests are identical sets of use claims formulated on the basis of former compound Claims 1 to 5 in the original disclosure. The indication of purpose, i.e. the use "as an agent for halogenating an enol or amido group" is supported by lines 17 to 22 on page 15. This feature is essential since it specifies the outcome of the use process in relation to the reactants.

3. Claim 5 relates to a novel group of halogenating compounds as such by excluding the four specific compounds incidentally obtained as transitional intermediates in documents (A), (B) and (C). These restrictions of original Claim 1 by the disclaimer, as well as the incorporation of references (A) and (B) by amendment of page 2 of the description, are unobjectionable in the circumstances. The latter amendment merely refers to the closest prior art and represents no addition of new subject-matter contrary to Article 123(2) EPC (cf. "Control circuit/LANSING BAGNALL", T 11/82, OJ 12/1983, 479). The features of the disclaimer are thereby included in the specification itself through implication from the disclosures of the prior art thus referred to. No equivalent positive definition from the same set of remaining compounds can otherwise be derived directly from the text of the specification and the disclaimer is therefore acceptable (cf. "Polyether polyols/ BAYER", T 04/80, OJ 4/1982, 149). Claim 6, as amended, derives support from page 11 of the specification. Claims 7 to 9 are based on page 17, lines 14-18 and page 3, lines 19-21.

4. Although such products are advantageously prepared in solution and are used without delay to avoid the risk of substantial conversion to the thermodynamically stable but less active state, their characteristics have been identified in distinction to the stable version (cf. Tables

I and II pages 8 and 10). As it cannot be excluded that the same products might be presented in a solvent-free form, it would be unjust to exclude these from protection and to limit the claim to specific solutions.

5. The closest state of the art is represented by (B) and (C) which describe certain reactions of triaryl phosphites with chlorine and bromine leading to the appropriate complexes, i.e. to the four thermodynamically stable compounds (Z=H, m-Me, or p-Me with $X_2=Cl_2$, and Z=H with $X_2=Br_2$) through the appropriate kinetically controlled transitional stage, as we now know. These stable halogen-containing complexes or adducts were known to have halogenating properties (cf. the formation of alkyl halides on alcoholysis, together with phenol as a by-product in (C), p. 3049, Table 3.). The technical problem in relation to this prior art was to provide improved and more specific halogenating agents and processes for the treatment of enols and amido-groups with reduced amounts of phenol as a by-product. The solution of the problem comprises the provision of the so-called kinetically controlled triphenyl phosphite chlorine and bromine complexes, analogue to those transitionally formed in the prior art, as defined in Claim 5, and the use of both the known and the additionally provided kinetically controlled compounds in halogenation reactions with the said enols and amido-compounds (rest of the claims).

6. Claim 5 to the complexes themselves now excludes the transitionally obtained variants in the prior art. This was necessary since the latter became available to the public at least in respect of their use for spontaneous conversion into the stable isomer, and cannot therefore enjoy absolute protection. Those excluded, therefore, lack novelty as such

but could be incorporated in claims to new uses and related processes, since none of the particular reactions with enols or amides were disclosed in any of the documents cited in the proceedings. All claims are therefore novel.

7. It was recognised that by working under appropriate conditions, e.g. for instance in anhydrous, inert organic solvents at substantially reduced temperatures (e.g. from -70°C to 0°C) the half life of the claimed transitional compounds could be enhanced. The resulting isomers are apparently quite specifically reactive, and high yields were for instance obtained with 3-hydroxy and 7-substituted-amido-cephems leading to important antibiotic products (cf. Examples 3 to 5 and 7 to 9, respectively). The enhanced specificity of these agents have also been shown in hydrolysis and alcoholysis tests, which suggested that contrary to the thermodynamically stable variants no phenol by-product is provided (see Table I on page 8 of the specification, and (C), pages 3047 to 3049, Tables 1 to 3). The suggested technical problem has therefore been solved.

8. As to the inventive step, there was no disclosure in the state of the art recommending the use of the known thermodynamically stable variants for the purposes of particularly treating enols or amido-groups, let alone to take particular measures to use the prepared compounds immediately, i.e. without delay for any of such purposes. Even if one were to assume that the person skilled would have attributed some halogenating properties to any transitional isomers in view of the loosely complexed chlorine or bromine content of the agent and of the halogenation of **saturated** alcohols in the alcoholysis of the stable isomers in the prior art, there was no reason to suspect that the phenolic by-products were to disappear and that good results would be obtained with the kinetically controlled unstable isomer in the treatment of **unsaturated**

alcohols and amides. There was apparently no knowledge about the transitional stage, and if there had been an assumption that some kind of unstable intermediate precursor existed, this would also have been thought to increase the risk of uncertainty as to the exact reproductibility of results in use. This rather suggests circumstances to be avoided in the absence of knowledge as to how to reduce the instability by introducing a "kinetic control".

9. The improved properties of the claimed agents in a qualitative sense, as well as their impressive capabilities in the specified use could not be foreseen and the subject-matters of Claims 5 and 1, respectively, as well as that of the dependent claims involve an inventive step as unexpected solution of the stated technical problem.

III

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 first instance with the order to grant a patent on the basis of the following documents:

(a) Claim 1 to 9, as presented in set I, received on 25.03.86, and amended in letter received on 07.06.86;

(b) amended pages of the description 1 to 5, 9, 11, 15 and 17, received on 25.03.86; and

(f) rest of pages as originally filed and published.

The Registrar

The Chairman

17.10.

16/10.