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KIND ATTN:
S. K. Roy (Asst. Controller of Patents and Designs)

By Email, Fax and Courier

Dated: March 10, 2010

To,
The Controller of Patents & Designs,
Patent Office,
DELHI

Dear Sir,

Re: Submission of Written Submissions pursuant to hearing on February 19, 2010:
Patent application no. 5301/ DELNP/ 2006

[Ref: Pre-grant opposition representation filed by Cipla Ltd.]

We act for Tibotec Pharmaceuticals Ltd., the Applicants for Patent application no. 5301/DELNP/ 2006.

In pursuance of the hearing conducted on February 19, 2010 in abovementioned matter, as directed, we submit herewith Applicant's Written Submissions with relevant annexures

We request the above document be taken on record and oblige.

11389

Yours faithfully,

Gowree Gokhale
of Nishith Desai Associates
(Patent agent representing Tibotec Pharmaceuticals)

12/3/10

Enclosures: Copy of Written Submissions + Annexures I to VI

ORIGINAL SET.

BEFORE THE CONTROLLER OF PATENTS, DELHI

IN THE MATTER OF:
THE PATENTS ACT 1970,
THE PATENTS RULES 2003

IN THE MATTER of a representation
under Section 25(1) read with Rule 55

IN THE MATTER OF:
Indian Application No.5301/DELNP/2006 dated March 10, 2010
Applicant's Representation By: Ms. Gowree Gokhale, Ms. Rajeshwari Hariharan
Hearing conducted on: February 19, 2010

CIPLA LIMITED **...OPPONENT**

VERSUS

TIBOTEC PHARMACEUTICALS **...APPLICANT**

WRITTEN SUBMISSIONS ON BEHALF OF THE APPLICANT PURSUANT TO HEARING CONDUCTED ON FEBRUARY 19, 2010

The Applicant herein submits as under:

I. **The invention:**

The invention of the present application is a unique process of preparing diastereomerically pure (3R, 3aS, 6aR)hexahydro-furo[2,3-b]furan-3-ol, [compound of formula **(6)**], in high yield and purity.

The Applicant herein had developed a general process for preparing compound of formula (6) starting from compound (1), which broad process is disclosed in WO03/022853 (D1), the closest prior art. The process disclosed by D1 first prepares

compound (3) which is transformed to compound (4) which in turn is reduced, subject to intramolecular cyclisation to obtain compound (6).

The inventors of the present application surprisingly found that the compound of formula (6) could be produced in higher yield and purity, when one of the intermediates, compound of formula (4), i.e. (3aR,4S,6as) 4-methoxy-tetrahydro-furo[2,3-b] furan-3-ol , is converted to an α-epimer (wherein all the β isomers are also converted to the α-epimer), and this epimerically pure intermediate is converted to compound of formula (6).

Thus, the invention as claimed comprises at least following inventive steps:

a) Identifying the fact that preparation of compound of formula (4) in methyl acetal form would eventually help in obtaining compound (6) in high yield and purity at the same time;
b) Identifying the fact that when compound (4) is prepared in methyl acetal form, a stereo-centre comes into play at 4^{th} position of carbon atom; thus giving rise to 2 diastereomers (α and β);
c) That the α isomer of compound of formula(4)should be crystallized and purified;
d) Identifying the fact that all β-isomer of the compound of formula (4) should be converted to α-isomer by epimerization and then further crystallized and purified;
e) That the crystalline α isomer of formula (4) should be isolated, subjected to reduction and intramolecular cylisation to obtain formula (6) in high yield and purity.

Claims:

The Applicants have filed revised claims, annexed as **Annexure I**.

II. ***Anticipation***:

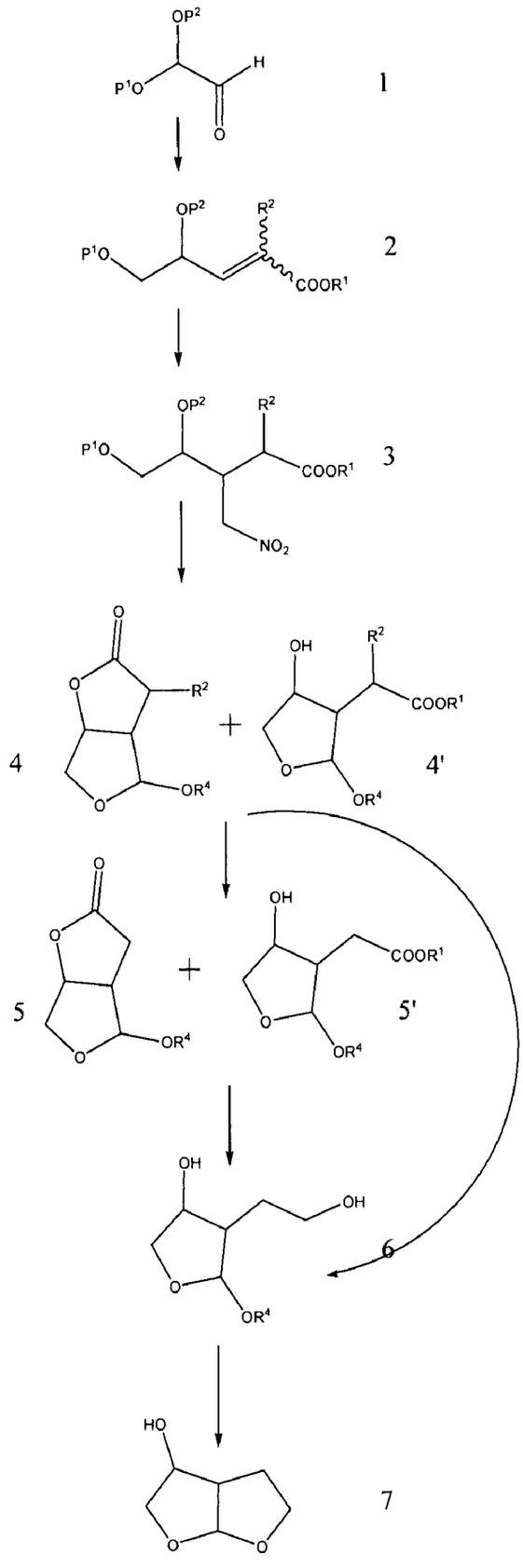
Although this ground has been pleaded in the opposition, the same has been explicitly withdrawn during the arguments. Accordingly, no arguments were lead on this issue, which require rebuttal.

III. Obviousness:

The Opponent had argued that the claims of the subject application are obvious in view of D1 (WO 03/22853).

Present application Vs. D1:

The Document D1 is drawn to a general process of preparation of a compound of formula 7 (which corresponds to compound of formula 6 of the subject application). The document D1 discloses at scheme 1, page 11 (figure 2), that the compound of formula (1) is converted to (2), which is converted to (3). The compound of formula (3) is converted to compounds of formula (4) and a by-product (4'). It is pertinent to note that compounds (4) and (4') are different compounds and not isomers of each other. If the R^2 of the formula (4) is $COOR^3$, a further decarboxylation step produces compounds (5) and (5'). Compounds (4) and (4') and (5) and (5') are then converted to compounds of formula (6), which is converted to formula (7) (equivalent to formula (6) of the subject application).



Scheme 1 of Document D1

In this regard, the Opponent has argued that:

- The chiral centre at C4-position was but obvious;
- Once chiral centre is known/obvious to exist, only 2 diastereomers are possible: α and β;
- It is obvious to convert one to the other – these steps of purification and crystallization are routine and hence obvious.

The Opponent also referred to compound III.5 at pg. 34 lines 15-18 to the argument to show that recrystallisation did occur even in D1.

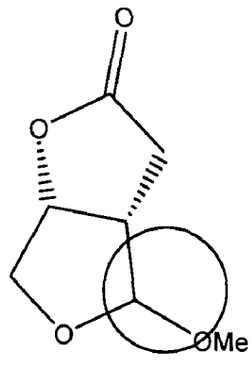
With respect, it is submitted that the arguments of the Opponent are technically incorrect, flawed and result from pure hindsight. The Opponent, at the time of filing the opposition already had the benefit of the present invention and using the invention as a basic blueprint is endeavouring to somehow fit D1 over it to show that the invention was covered by D1.

Compound III.5:

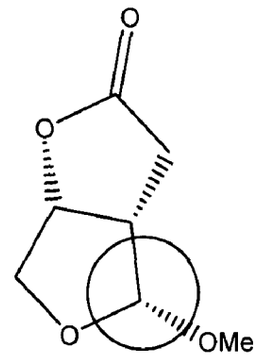
The document D1 does not disclose at any instance, that there is a chiral carbon at position 4 of the formula (4) and that it would have any role to play in influencing the synthesis – both qualitatively (purity) and quantitatively (yield) – of final compound (6).

a) Chiral centre at position 4 of compound (4):

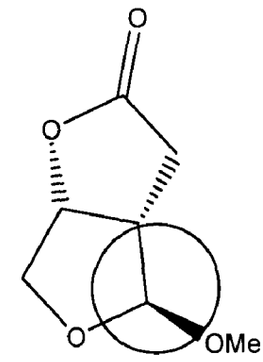
As mentioned above, D1 discloses compound III.5 at page 32 as a part of the scheme of example III, wherein only 2 chiral centres are identified; the chiral centre at position -4- is not identified, clearly showing that the inventors had no knowledge about the existence or the importance of the stereochemistry of the same.



III. 5 of D1



Beta (4) of subj appln



Alpha (4) of subj appln

III.5 vs. (4)

Further, this is fortified by the Applicant's expert Dr. Hartmut Zinser, who points out (in his affidavit dated 24.04.2009) that in determining the stereochemistry of the compound of formula 6, the bonds at 3a and 6a, play a major role. The stereochemistries of these bonds are retained at 3a and 6a positions of formula (6), (see pink color bonds at **Annexure II**). The stereochemistry of the bond at position 3 of formula (6), is formed during the reaction of compound (3) and not as a result of the stereochemistry of formula (4). The methyl acetal at position 4, of the formula (4) (indicated by pink color) is not involved in the stereochemistry of compound of formula (6), hence there is no incentive for the person to locate and explore the chiral at position-4 and develop a certain epimer of formula (4).

A very important aspect is that D1 teaches that the compound of formula 7 may exist as four stereoisomers (7.1 – 7.4) (at intervening paras of page 9 and 10) of which only compound 7.1 is active. It states that these stereoisomers can be obtained by varying the stereocentres at compound of formula 3, which in turn is obtained from compound of formula 1. (See page 19, lines 21-31, page 22, lines 1 to 8, page 23, lines 1 to 5 and page 24, lines 20 to 25 of document D1).

A specific example of preparation of compound 7.1 can be found at page 32. Compound III.5 prepared as per this scheme corresponds compound (4) of the subject application.

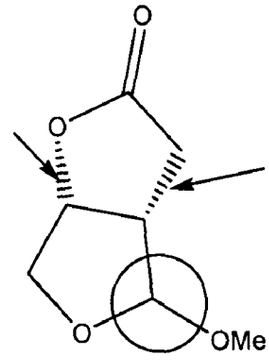


figure: III.5 of Document D1

It is noteworthy that in compound III.5 only 2 chiral centres (represented by the arrow) are shown. Had the inventors known of the existence or importance of the chiral centre at carbon-position-4- (encircled in the figure) and the fact that it would have to be explored; the same would have been depicted, just as all other chiral centres of III.5 and other compounds are depicted.

b) Obvious of diastereomers:

In response to the argument that chiral centres are obvious and so are isomers, it is submitted that:

i) technically, if a compound is represented with straight lines (and not hashed lines) it is assumed that the chirality of these centres are not critical (where no hashed lines exist) or that the carbon at these positions are achiral;

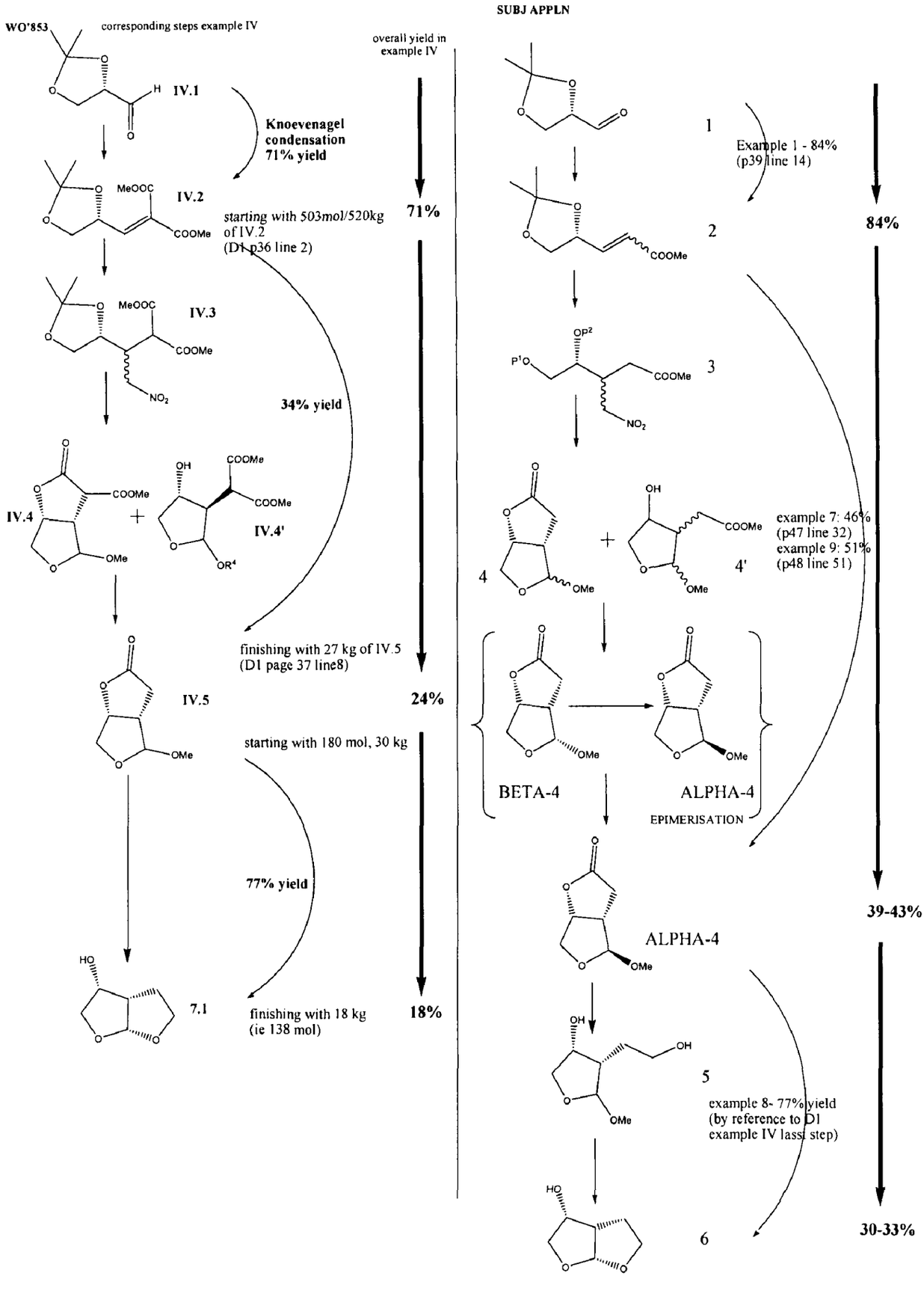
ii) the legal position consistent with the above is that an isomers is not deemed to be obvious if that specific member is not disclosed by prior art. As examples are T_1048/92 (para 21. and 2.5) and T_1046/97 (para 2.1.1.4 and 2.1.1.6, page 7 last paras) wherein this position has been upheld. These decisions have been annexed hereto as **Annexure V** and **Annexure VI** respectively.

c) Epimerization and crystallisation:

In response to the argument that these are routine and obvious steps, it is submitted that such terms may be known in chemistry. The crucial point of difference (as against D1) is that it is the inventors of the subject application who found that racemic compound (4) should be isolated, that too in methyl acetal form. In fact, it is the Applicant who after intensive research found that certain impurities accumulate when compound of formula (4) is prepared and these impurities get carried over to compound of formula (6), thus

affecting the yield and purity of compound of formula (6) and also minimizes the loss of the compound of formula (4) by innovative use of the epimerization reaction, wherein even the less crystalline epimer β is recovered. This finding nowhere features in the document D1.

Further, the expert Dr. Harmut points out (in his Affidavit at para 43) the importance of using the methyl acetal form of the compound of formula (4) by drawing attention to example II of document D1, wherein the methyl acetal form is not crystallisable and hence not suitable in the present invention. It is the inventors of present application who found that epimer α of compound (4) should be subjected to crystallisation and if such epimer is crystallized and purity etc. increased, and yield (and overall manufacturability) of final product (6) is substantially increased. D1 shows an overall yield of 30-33%.


WO'853
corresponding steps example IV
overall yield in example IV
IV.1
Knoevenagel condensation 71% yield
IV.2
71%
starting with 503mol/520kg of IV.2
(D1 p36 line 2)
IV.3
34% yield
IV.4
IV.4'
finishing with 27 kg of IV.5
(D1 page 37 line8)
IV.5
24%
starting with 180 mol, 30 kg
77% yield
7.1
finishing with 18 kg
(ie 138 mol)
18%
SUBJ APPLN
1
Example 1 - 84%
(p39 line 14)
2
84%
3
4
4'
example 7: 46%
(p47 line 32)
example 9: 51%
(p48 line 51)
BETA-4
ALPHA-4
EPIMERISATION
39-43%
ALPHA-4
5
example 8- 77% yield
(by reference to D1
example IV last step)
6
30-33%

This understanding of identifying compound of formula (4) as an isolatable unit, epimerization into its isomers and selective crystallization of one epimer is unique to subject application.

Recrystallisation:

The "recrystallisation" at pg. 34 lines 15-16 of D1 refers to a racemate and not individual epimer of (4). It may be noted that the process starts at pg. 32 with a scheme to page 35, line 3 and at pg. 34 lines 15-16 compound III.5 is prepared which is recrystallised. There is however no instruction for isolation. Hence, this para refers to recrystallisation of compound III.5 [corresponding to compound (4) of subject application] with no indication as to the stereochemistry at position 4. There are numerous instances in history wherein racemates are found unsuitable (e.g. administration of Thalidomide racemic mixture resulted in deformed children making the company withdraw the products the epimer is now used for leprosy). Thus, the term "recrystallisation" at pg. 34 of D1 is of no importance. At best, it may refer to crystals of racemic compound (4).

In addition, contrary to the objectives of the present invention, the recrystallisation disclosed in D1 is for analytical purposes only.

Thus, as can be seen from the above, the invention lies in the following:

i) identifying the centre C-4, of formula (4) that could be modified
ii) selecting the acetal form of (4) such that the epimer is crystallisable, i.e, methyl acetal (4);
iii) converting all β epimer of compound (4) to α epimer of compound (4);
iv) isolating and crystallizing the α epimer of formula (4) to obtain pure α;
v) using the pure and high yield α epimer of formula (4) to obtain formula (6) in higher yield and purity.

No motivation from D1:

It is submitted that since D1 does not even refer to the stereochemistry / chiral centre of the carbon at C(4). This coupled with the fact that this centre has no role to play in stereochemistry of compound (6) [i.e. compound (7) of D1], makes it clear that there is no incentive for a skilled person to be interested in the stereochemistry of C-4 and explore the centre, attempt to isolate epimers, if any therein.. Conclusions about presence of isomers at this position can come only from sheer hindsight analysis.

Assuming but not admitting, that it is possible for a skilled person in the art to guess that the carbon-4 of formula (4) is chiral, there is however nothing in D1 that would guide a skilled person as to which form compound of formula (4) should be isolated, i.e. as methyl acetal form, ethyl acetal form or any other form. It was argued that a choice of methyl acetal form is one of the choices from D1 as R2 in D1 may be any alkyl. In this regard it is noteworthy that the Applicant did try to prepare the ethoxy form of compound of formula (4); however, the same would not crystallize out. It was not possible to obtain crystalline compound formula (4) and obtain pure compound (6) (re. intervening paragraph of pg. 4 and pg.5 of specification).

Further, there is nothing in D1 that would incentivise the skilled person to identify the epimers of compound of formula (4) and crystallize in such a manner that all beta epimer is converted into alpha epimer and expect that this process would result in compound of formula (6) in high yield. As this Tribunal is aware, whether a compound would be obtained in high yield or not cannot be speculated by merely observing a chemical formula; actual experiments are required.

Therefore, the invention as claimed **is not** "a logical next step" so as to readily suggest itself to a person skilled in the art.

An invention can be considered obvious if it would naturally occur to a person skilled in the art. The test is:
"*The material question to be considered is, whether the alleged discovery lies so much out of the track of what was known before as not naturally to suggest itself to a person thinking on the subject*" [Patent Law by Narayanan, Edition IV, page 404] annexed hereto as **Annexure III**".

In the present case, a skilled person has to make numerous assumptions to arrive at the invention as claimed viz. assumption of chiral centre, existence of epimers, epimerization, selective crystallization of one epimer and a ready expectation that these steps would result in compound (6) in high yield and purity. Such a large number of assumptions weigh against the fact the invention claimed is obvious.

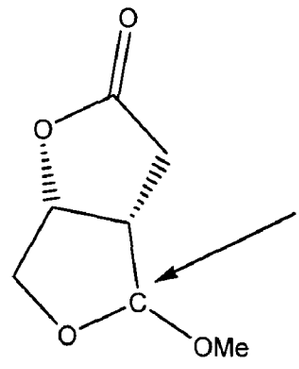
Finally, it is submitted that in instances where the case is absolutely clear on obviousness, should it be refused.

"*Under s. 64(1)(f) obviousness and lack of inventive step is also available as a ground for revocation of a patent by petition before High Court. In opposition proceedings under s. 25(1) (e) and 25(2) (e) it must be shown that the invention "clearly" does not involve any inventive step while there is no such qualification under s.64(1)(f). Hence, if the matter is in doubt, the Controller may allow the grant leaving the question to be finally decided, when an occasion arises, by the High court*" [Patent Law by Narayanan, Edition IV, page 213]

Natu's Affidavit:

The Opponent has relied upon an affidavit executed by Dr. Natu in support of their ground of obviousness. It is submitted that firstly Dr. Natu is not an average person skilled in the art since he has never dealt with anti-HIV compounds or the chemistry of preparation of such compounds. Further, Dr. Natu has not performed a single experiment to test whether the invention is obvious or not or whether the process as claimed does produce compound of formula (6) in high yield or not. Dr. Natu has simply gone through the documents and made speculatory conclusions. It is a well known fact that scientific evidence can be taken by the Controller/ Tribunal for scientific assistance or to understand scientific facts; however, the actual conclusion as to whether an invention is obvious or not has to be arrived at by the Tribunal and not Dr. Nathu.

The entire affidavit of Dr. Natu and the conclusions based therein is based on the premise that compound of formula (4) is an ether (page 21 para 28), whereas in reality, the said compound is an acetal compound – thus belonging to a substantially distinct/different class of compounds. At page 21, Dr. Natu has stated *"I say that a look at the compound of formula 4 of the applicant's invention clarifies that the third chiral carbon atom is bonded to a methoxy group, which makes the compound* ***an ether*** *(which have the general formula R-O-R)……".* The said compound of formula (4) is represented herebelow and relevant extract from the textbook Organic Chemistry by Morrison and Boyd is attached herewith as **Annexure IV**.



Accordingly, it is submitted that the invention is not obvious and is inventive.

IV. **Not an invention:**

It was submitted by the opponents that matter of the subject application is not an invention. However, they used the arguments as above and hence the reply as above is reiterated.

V. **Insufficiency:**

It was argued by the Opponent that the yield, the critical factor of the invention is not illustrated in the specification. However, the applicants demonstrated that yield is indeed provided in the specification and when compared with the examples of that of the prior art, namely Document D1, the yield is significantly higher. The yield is depicted in scheme 3, (along with specific reference to the page number of the specification from where the yield is calculated)

In conclusion, it is submitted that apart from bald allegations and frivolous objections, the Opponent has not been able to dislodge the fact that the subject application possess inventive merit.

In this regard, it is submitted that patent law only requires the applicant to give sufficient guidance in the specification so that the invention as claimed can be made by a person skilled in the art without any difficulty and without recourse to external aids. Such general guidance is provided in ample amount in the specification.

Thus, the invention as claimed has been sufficiently described and illustrated.

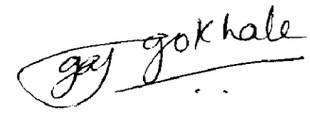
Case laws cited by the Opponent:

The opponents cited several case laws, alleging that the subject matter is not –inventive. Since the subject matter is herein inventive, the case laws do not apply.

In view of the above, it is prayed that the pre-grant opposition filed be rejected and the application may be allowed to proceed to grant.

Dated this 10th day of March 2010

Agents of the Applicants



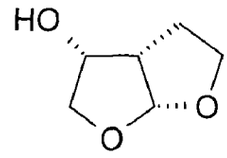
Gowree Gokhale
of Nishith Desai Associates

To,
The Controller of Patents
The Patent Office
New Delhi

Annexure I: Revised Claims filed with the Office on February 18, 2010
Annexure II: Scheme
Annexure III: Extracts from P. Narayanan referred to in this submission
Annexure IV: Extracts from Organic Chemistry by Morrison and Boyd
Annexure V: T_1048/92
Annexure VI: *T_1046/97*

We Claim:

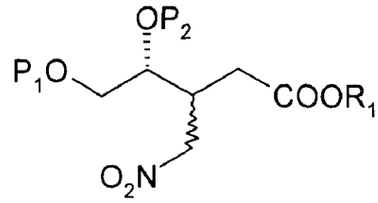
1. A method for the synthesis of (3R,3aS,6aR)hexahydro-furo[2,3-b]furan-3-ol having the structure of formula (6),



(6)

which comprises the steps of:

a) treating intermediate of formula (3) with a base and subsequently with an acid in the presence of methanol;



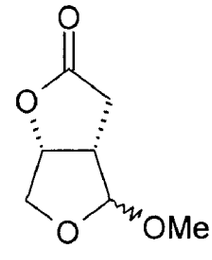
(3)

wherein

P^1 and P^2 are each independently a hydrogen, a hydroxy-protecting group or may together form a vicinal-diol protecting group,

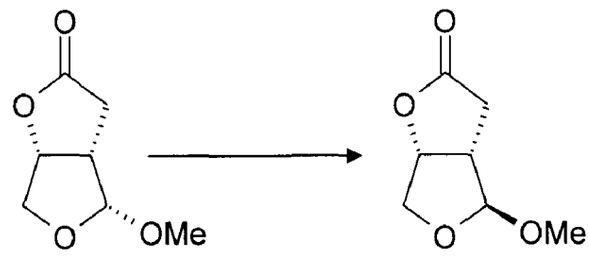
R^1 is alkyl, aryl or aralkyl;

resulting in intermediates of formula (4);



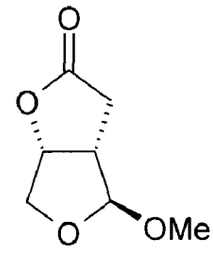
(4)

b) epimerizing with acid the intermediate of formula β-(4) into the intermediate of formula α-(4);



β-(4) α-(4)

c) crystallizing with a solvent intermediate of formula α-(4); and



α-(4)

d) reducing intermediate of formula α-(4) with a suitable reducing agent and applying an intramolecular cyclization reaction to obtain compound of formula (6).

2. A method as claimed in claim 1 wherein P^1 and P^2 together form a dialkyl methylene radical.

3. A method as claimed in claims 1 and 2 wherein the conversion of compounds of formula (3) into compounds of formula (4) is performed with a base selected from the group of sodium methoxide, lithium methoxide, DBU or TMG or mixtures thereof.

4. A method as claimed in claims 1 to 3, wherein the acid employed in the conversion of compounds of formula (3) into compounds of formula (4) is concentrated sulphuric acid.

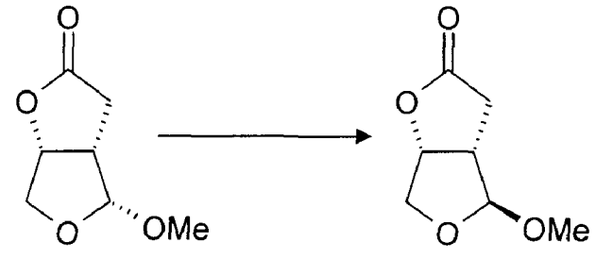
5. A method as claimed in claims 1 to 4 wherein the epimerization of compound of formula β-(4) to compound of formula α-(4) and crystallization of compound of formula α-(4) occur simultaneously.

6. A method as claimed in claim 5, wherein the simultaneous epimerization of compound of formula β-(4) to compound of formula α-(4) and the crystallization of compound of formula α-(4) is performed in methanol in the presence of an acid by evaporation or partial evaporation of the methanol.

7. A method as claimed in claims 1 to 6 wherein crystallization of compound of formula α-(4) is performed in an alcohol.

8. A method according to claim 7 wherein the alcohol is isopropanol, t-amyl alcohol or t-butanol.

9. A method as claimed in claims 1 to 7, wherein the conversion of compound of formula β-(4) into the compound of formula α-(4) which comprises an epimerization with acid.



β-(4) α-(4)

10. A method as claimed in claims 1 to 9 wherein epimerization of compound of formula β-(4) into compound of formula α-(4) is performed with 0.05 to1.5 equivalents of $MeSO_3H$ in methanol.

11. A method as claimed in claims 1 to 10 wherein the epimerization is performed at a temperature between 40°C and reflux temperature.

12. An intermediate having the formula α-(4) prepared by process of claim 1.

13. An intermediate having the formula β-(4) prepared by process of claim 1.

14. An intermediate with formula α-(4) in crystalline form prepared by process of claim 1.

Dated this 18th day of February 2010

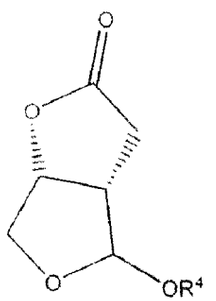
Signature:

Gowree Gokhale
Of Nishith Desai Associates
Constituted Patent Agent for the applicant

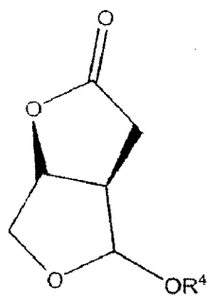
ANNEXURE II

Example II

PAGE 23



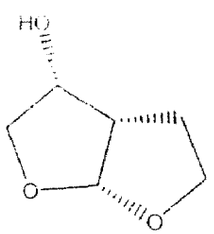
4a/II.3



4b

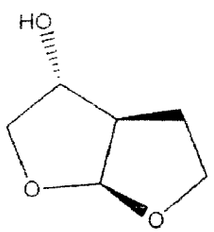
INVOLVED IN STEREOCHEMICAL REACTION

NOT INVOLVED IN STEREO REACTION



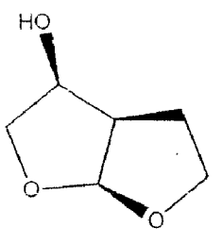
7.1

3R,3aS,6aR



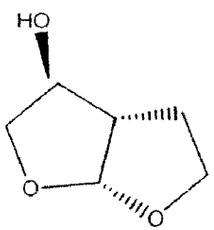
7.2

3R,3aR,6aS



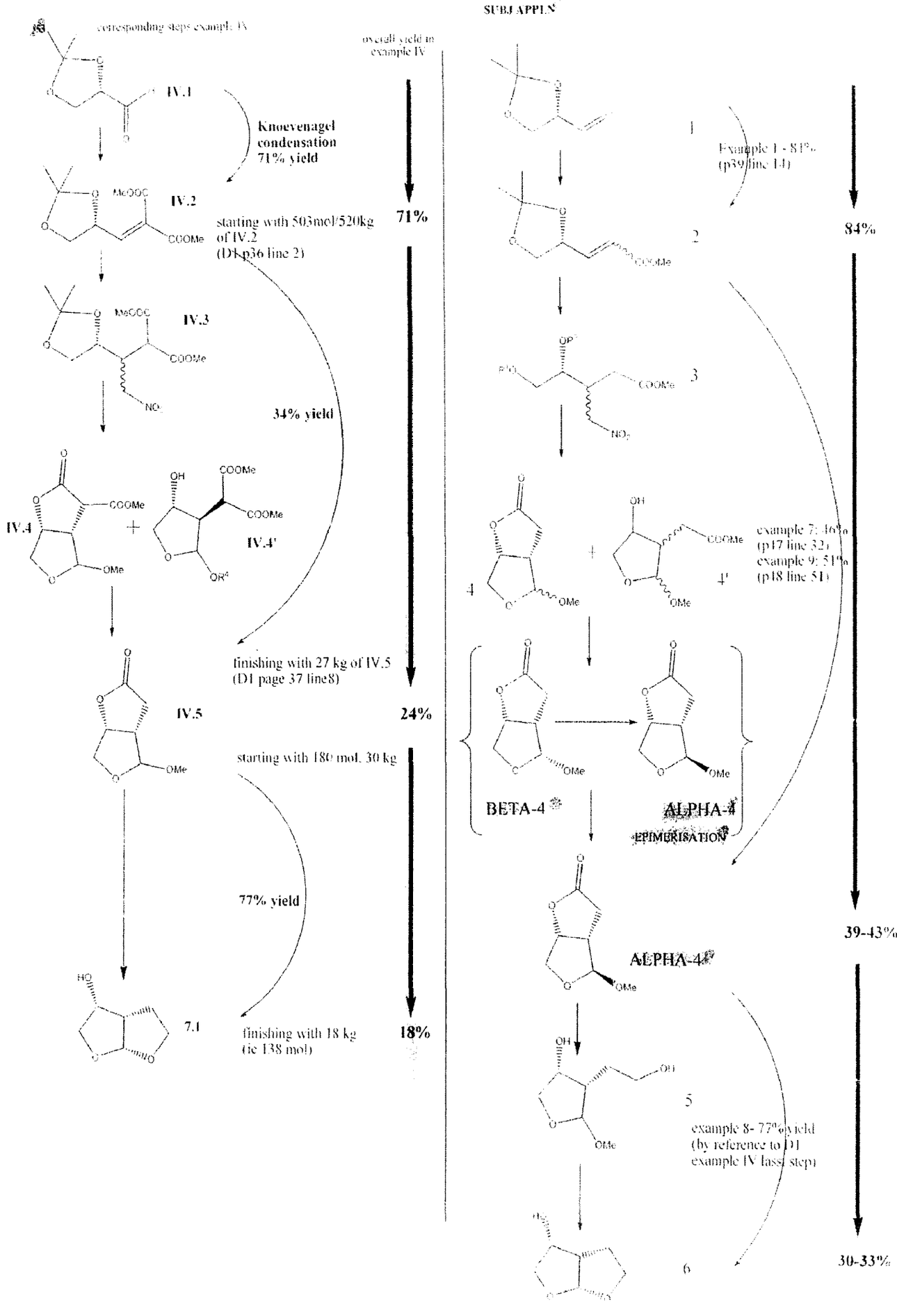
7.3

3S,3aR,6aS



7.4

3S,3aS,6aR


corresponding steps example IV
overall yield in example IV
IV.1
Knoevenagel condensation 71% yield
IV.2
71%
starting with 503mol/520kg of IV.2 (D1 p36 line 2)
IV.3
34% yield
IV.4
IV.4'
finishing with 27 kg of IV.5 (D1 page 37 line8)
IV.5
24%
starting with 180 mol, 30 kg
77% yield
7.1
finishing with 18 kg (ie 138 mol)
18%
1
Example 1 - 81% (p39/line 14)
2
84%
3
4
4'
example 7: 46% (p17 line 32)
example 9: 51% (p18 line 51)
BETA-4
ALPHA-4
EPIMERISATION
ALPHA-4
39-43%
5
example 8- 77% yield (by reference to D1 example IV last step)
6
30-33%

ANNEXURE III

PATENT LAW by P. Narayanan IV Edition

Refusal in clear cases

cl. (*b*) or having regard to what was used in India before the priority date of theclaim."[4]

The question whether the invention claimed is obvious and clearly does not involve any inventive step be decided having regard to prior publication or prior user. No account is to be taken of any secret user.[5] The prior publications are those mentioned in cl. (*b*), namely: (*i*) specifications filed in pursuance of applications for patents made in India after 1st January 1912 but before the priority date of claim: (*ii*) any other document published in India or elsewhere before the priority date of the claim. This will include books and foreign specifications. In determining the issue of obviousness both the Controller and the High Court are entitled to make use of their own knowledge and experience of the relevant scientific and technical background to the subject-matter of the alleged invention.[6]

There is a similar ground of revocation, see s. 64(1)(*f*) and paras 16–73 to 16–131.

8–63 Refusal only in clear cases. Under s. 64(1)(*f*) obviousness and lack of inventive step is also available as a ground for revocation of a patent by petition before the High Court. In opposition proceedings under s. 25(1)(*e*) and 25(2)(*e*) it must be shown that the invention "clearly" does not involve any inventive step while there is no such qualification under s. 64(1)(*f*). This shows that if the matter is in doubt, the Controller may allow the grant leaving the question to be finally decided, when an occasion arises, by the High Court.

Referring to the corresponding provisions of the U.K. Act,[7] Diplock, L.J. observed:[8] "This difference in phraseology of the corresponding paragraphs in s. 14 and s. 32 reflects the difference in the character of the proceedings upon opposition to the grant of a patent and in an action for the revocation of a patent. The effect of the former is to dismiss the applicants' Claim *in limine* in pursuance of the public policy, inherent in the adoption of a system of granting only 'examined patents', that the register shall not be cluttered up with patents which would be certain to be revoked by the court in a revocation action. To allow such patents to be granted would not only place

4 This is a new ground of objection. It follows closely the wording of s. 14(1)(*e*) of the U.K. Act of 1949. There was no parallel provision either in the Indian Act of 1911 or in the U.K. Act of 1907. There is a similar ground of revocation under s. 64(1)(*f*), see paras 16–73 to 17–131.

5 Section 25(3).

6 See *Johns Manville Corporation's Patent* [1967] RPC 479 at 491.

7 Sections 14(1)(*e*) and 32(1)(*f*) of the U.K. Patents Act 1949 correspond to ss. 25(1)(*e*) and 64(1)(*f*) respectively of the Indian Act. The material portions in both sections are identical.

8 *General Electric Co.'s Appln.* [1964] RPC 413 at 452, 453. In *Esso Research and Engineering Co.'s Appln.* [1972] RPC 624 at 634 it was observed by Graham, J. that the exact nature of the distinction to be drawn between the test of obviousness for opposition purposes and the test for purposes of revocation proceeding in the High Court is not very easy to ascertain.

PATENT LAW by P. Narayanan IV Edition

Obviousness

Other formulations of the test. The test is whether what is claimed is "so obvious that it could at once occur to anyone acquainted with the subject and desirous of accomplishing the end."[6]

"The material question to be considered is, whether the alleged discovery lies so much out of the track of what was known before as not naturally to suggest itself to a person thinking on the subject."[7]

The words "obvious" and "Inventive Step" involve questions of fact and degree which must be answered in accordance with the general policy of the Patents Act to reward and encourage invention without inhibiting improvements of existing technology by others. The question is therefore whether in accordance with this policy the patent discloses something sufficiently inventive to deserve the grant of a monopoly.[8]

In *Beecham Group Ltd.'s (Amoxycillin) Appln.*[9] Buckley, L.J. citing previous decisions observed:

> "It is clearly established that, for a particular step or process to be obvious for the purpose of either section, it is not necessary to establish that its success is clearly predictable. It will suffice if it is shown that it would appear to anyone skilled in the art but lacking inventive capacity that to try the step or process would be worthwhile. Worthwhile to what end? It must in my opinion be shown to be worth trying in order to solve some recognised problem or meet some recognised end. The uninventive expert should not be supposed to be attempting to discover something new, that is, to be striving for inventiveness. Having been shown what was disclosed by the prior art, he must be supposed to be attempting to solve some problem or fulfil some need which has not been resolved or satisfied by the prior art but which appears to his uninventive mind to be possibly capable of solution or satisfaction by taking the step or doing the thing under consideration. If on carrying out his test he finds that the new step has the sort of consequence he had hoped but in an unexpectedly high degree, this would or might not mean that the new step was inventive or other than obvious, it might merely mean that a new and obvious step has solved the problem or met the need unexpectedly well. The question would, I think, be one of degree. If, on the other hand, the new step produces some unexpected result productive of an improvement or benefit of an unexpected kind

6 Lord Herschell in *Siddell* v *Vickers* (1890)7 RPC 292 at 304 (HL) quoted in *Windsurfing* v *Tabur* [1985] RPC 59 at 73 (CA).

7 *Savage* v *Harris* (1896)13 RPC 364 at 370 (CA) quoted in *Windsurfing* v *Tabur* [1985] RPC 59 at 73 (CA).

8 *Societe Technique De Pulverisation Step* v *Emson Europe* [1993] RPC 513 (CA) at 519. See the comments made on the subject at the same page.

9 [1980] RPC 261 at 290-291. See p. 291 for cases of obviousness where the objective was known and the suggested means or instrument for achieving it was known and the question was whether it was obvious that the latter would achieve the former, or at least that it would be worth trying to see if it would do so.

PATENT LAW by P. Narayanan IV Edition

10. EVIDENCE

Expert

18–118 Number of witnesses. For the purpose of Evidence Act no fixed number of witnesses is needed to prove a fact: even the testimony of but one witness is sufficient, if that witness can be believed.[10]

Affidavit evidence on obviousness. For a well drafted affidavit in support of obviousness attack see *Johns-Manville Corporation's Patent* [1967] RPC 479.

18–119 Expert evidence. In an action for infringement it is necessary to examine each patent separately and to ascertain first what the patented invention really is; and, secondly, whether the defendants have used that invention. The nature of the invention must be ascertained from the specification, the interpretation of which is for the Judge, and not for any expert. The Judge may, and indeed generally must, be assisted by expert evidence to explain technical terms, to show the practical working of machinery described or drawn, and to point out what is old and what is new in the specification. Expert evidence is also admissible, and is often required to show the particulars in which an alleged invention has been used by an alleged infringer, and the real importance of whatever differences there may be between the plaintiff's invention and whatever is done by the defendant. But the nature of the invention for which a patent is granted must be ascertained from the specification, and has to be determined by the Judge and not by any expert or other witness.[11]

Expert witnesses–duties and responsibilities. In the *Ikarian Reefer* case [1993] FSR 563 at 565, Crosswell, J. summarised the duties and responsibilities of expert witnesses as follows:

1. Expert evidence presented to the court should be, and should be seen to be, the independent product of the expert uninfluenced as to form of content by the exigencies of litigation—*Whitehouse* v *Jordan* (1981)1 WLR 246 at 256 (Lord Wilberforce).
2. An expert witness should provide independent assistance to the court by way of objective unbiased opinion in relation to matters within his expertise: *Polivitte Ltd.* v *Commercial Union Assurance* (1987)1 Lloyds' Rep. 379 at 386, Garland, J. and Re J. (1990) FCR 193, Cazalet, J. An expert witness in the High Court should never assume the role of an advocate.
3. An expert witness should state the facts or assumptions upon which his opinion is based. He should not omit to consider material facts which could detract from the concluded opinion (Re J., *supra*).
4. An expert witness should make it clear when a particular question or issue falls outside his expertise.

10 *Bombay Agarwal* v *Ramchand* AIR 1953 Nag 154 at 159.
11 Lindley, L.J. in *Brooks* v *Steel & Currie* (1897)14 RPC 46 at 73.

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5. If an expert's opinion is not properly researched because he considers that insufficient data is available, then this must be stated with an indication that the opinion is no more than a provisional one (Re J., *supra*). In cases where an expert witness, who has prepared a report, could not assert that the report contained the truth, the whole truth and nothing but the truth without some qualification, that qualification should be stated in the report, *Derby & Co. Ltd.* v *Weldon. The Times*, 9th November 1990 per Slaughton, L.J.
6. If, after exchange of reports, an expert witness changes his view on a material matter having read the other sides' expert's report or for any other reason, such change of view should be communicated (through legal representatives) to the other side without delay and when appropriate to the court.
7. Where expert evidence refers to photographs, plans, calculations, analysis measurements, survey reports or other similar documents these must be provided to the opposite party at the same time as the exchange of reports.

Video recordings are like photograph and could be interpreted with the assistance of expert evidence.[1]

18–120 Lord Tomlin observed in *British Celanese Ltd.* v *Courtaulds Ltd.*:[2] An expert "is entitled to give evidence as to the state of the art at any given time. He is entitled to explain the meaning of any technical terms used in the art. He is entitled to say whether in his opinion that which is described in the specification on a given hypothesis as to its meaning is capable of being carried into effect by a skilled worker. He is entitled to say what at a given time to him as skilled in the art a given piece of apparatus or a given sentence on any given hypothesis as to its meaning would have taught or suggested to him. He is entitled to say whether in his opinion a particular operation in connection with the art could be carried out and generally to give any explanation required as to facts of a scientific kind.

He is not entitled to say nor is counsel entitled to ask him what the specification means, nor does the question become any more admissible if it takes the form of asking him what it means to him as an engineer or as a chemist. Nor is he entitled to say whether any given step or alteration is obvious, that being a question for the court."

18–121 Evidence of common knowledge. A person who can give evidence as to common knowledge must be one properly informed in the art. He should not have an excess of any peculiar or special sort of knowledge. But what he is telling must be what he has acquired in his ordinary practice as a man engaged in the art.[3]

1 *Vax Appliances* v *Hoover* [1991] FSR 307 following dictum of Lord Reid in *Van der Lely* v *Bamfords* [1963] RPC 61.
2 (1935)52 RPC 171 at 196 (HL).
3 *British Celanese Ltd.* v *Courtaulds Ltd.* (1933)50 RPC 63 at 90 (Clauson, J. in the course of arguments).

ANNEXURE IV

SIXTH EDITION

Organic Chemistry

Robert Thornton Morrison
Robert Neilson Boyd
New York University

PEARSON
Prentice

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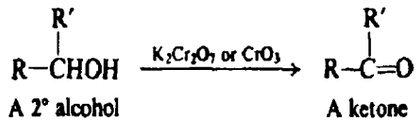
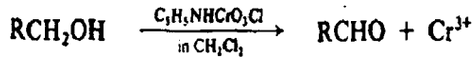
Oxidation of alcohols to the aldehyde or ketone stage is usually accomplished by the use of Cr(VI) in one of the forms described above. Oxidation of secondary alcohols to ketones is generally straightforward.



A 2° alcohol — A ketone

Because aldehydes are susceptible to further oxidation, the conversion of primary alcohols to aldehydes can be troublesome. One of the best and most convenient reagents for this purpose is pyridinium chlorochromate ($C_5H_5NH^+CrO_3Cl^-$) formed by the reaction between chromic acid and pyridinium chloride (Sec. 30.11).



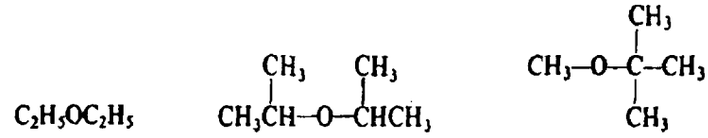
Later on, we shall encounter two reagents used to oxidize alcohols of special kinds: (a) *hypohalite* (Sec. 18.21), and (b) *periodic acid* (Sec. 18.22).

ETHERS

6.16 Structure and nomenclature of ethers

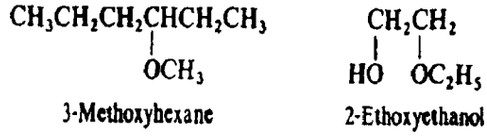
Ethers are compounds of the general formula R—O—R, Ar—O—R, or Ar—O—Ar. (Ar is phenyl or some other aromatic group.)

To name ethers we usually name the two groups that are attached to oxygen, and follow these names by the word *ether*:



Diethyl ether — Diisopropyl ether — *tert*-Butyl methyl ether

If one group has no simple name, the compound may be named as an *alkoxy* derivative:



3-Methoxyhexane — 2-Ethoxyethanol

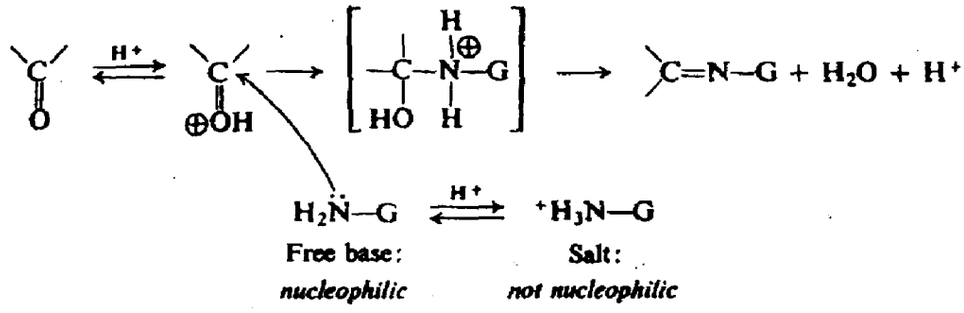
If the two groups are identical, the ether is said to be *symmetrical* (e.g., *diethyl ether, diisopropyl ether*); if different, *unsymmetrical* (e.g., *tert-butyl methyl ether*).

needed, the basic reagents are liberated from their salts in the presence of the carbonyl compound by addition of a base, usually sodium acetate.

$$C_6H_5NHNH_3^+Cl^- + CH_3COO^-Na^+ \rightleftharpoons C_6H_5NHNH_2 + CH_3COOH + Na^+Cl^-$$

Phenylhydrazine hydrochloride	Sodium acetate	Phenylhydrazine	Acetic acid
Stronger acid	*Stronger base*	*Weaker base*	*Weaker acid*

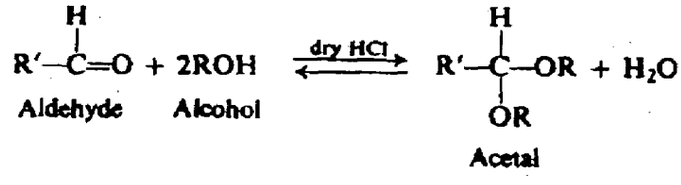
It is often necessary to adjust the reaction medium to just the right acidity. Addition involves nucleophilic attack by the basic nitrogen compound on carbonyl carbon. Protonation of carbonyl oxygen makes carbonyl carbon more susceptible to nucleophilic attack; in so far as the carbonyl compound is concerned, then, addition will be favored by high acidity. But the ammonia derivative, $H_2N—G$, can also undergo protonation to form the ion, $^+H_3N—G$, which lacks unshared electrons and is no longer nucleophilic; in so far as the nitrogen compound is concerned, then, addition is favored by low acidity. The conditions under which



addition proceeds most rapidly are thus the result of a compromise: the solution must be acidic enough for an appreciable fraction of the carbonyl compound to be protonated, but not so acidic that the concentration of the free nitrogen compound is too low. The exact conditions used depend upon the basicity of the reagent, and upon the reactivity of the carbonyl compound.

18.12 Addition of alcohols. Acetal formation

Alcohols add to the carbonyl group of aldehydes in the presence of anhydrous acids to yield **acetals**:



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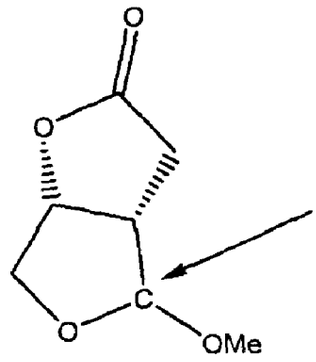
AFFIDAVIT OF MR. NATU

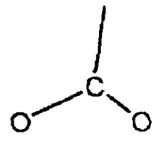
Page 21 of Affidavit, para 28.

"I say that a look at the compound of formula 4 of the applicant's invention clarifies that the third chiral carbon atom is bonded to a methoxy group, which makes the compound ***an ether*** *(which have the general formula R-O-R), ..."*

The structure is presented below:



The third chiral carbon (at position 4, as indicated by expert can be simplified as below.



The formula is RO-C-OR, and R-O-R, hence it is an acetal and not ether.

ANNEXURE V

KRS

BESCHWERDEKAMMERN DES EUROPÄISCHEN PATENTAMTS | BOARDS OF APPEAL OF THE EUROPEAN PATENT OFFICE | CHAMBRES DE RECOURS DE L'OFFICE EUROPEEN DES BREVETS

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D E C I S I O N
of 5 December 1994

Case Number: T 1048/92 - 3.3.1

Application Number: 88304016.4

Publication Number: 0294934

IPC: C07D 499/00

Language of the proceedings: EN

Title of invention:
Diasteriomeric 5R, 6S-6-(1R-hydroxyethyl)-2-(cis-1-oxo-3-thiolanylthio)-2-penem-3-carboxylic acids

Applicant:
PFIZER INC.

Opponent:

Headword:
Penem derivatives/PFIZER

Relevant legal provisions:
EPC Art. 54(1), 111(1)

Keyword:
"Implicit disclosure of steric configuration (no)"
"Remittal"

Decisions cited:
T 0012/81, T 0181/82, T 0296/87, T 0012/90, T 0658/91

Catchword:

Case Number: T 1048/92 - 3.3.1

D E C I S I O N
of the Technical Board of Appeal 3.3.1
of 5 December 1994

Appellant: PFIZER INC.
235 East 42nd Street
New York, N.Y. 10017 (US)

Representative: Moore, James William, Dr.
Pfizer Limited
Ramsgate Road
Sandwich
Kent CT13 9NJ (GB)

Decision under appeal: **Decision of the Examining Division of the European Patent Office dated 6 July 1992 refusing European patent application No. 88 304 016.4 pursuant to Article 97(1) EPC.**

Composition of the Board:

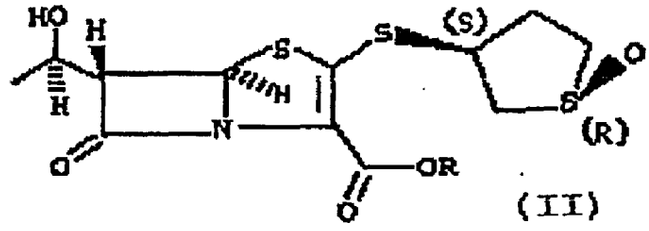
Chairman: A. Jahn
Members: R. K. Spangenberg
J. A. Stephens-Ofner

Summary of Facts and Submissions

I. The appeal was filed on 1 August 1992 and the appropriate fee was paid at the same date. It lies against the decision of the Examining Division of 6 July 1992 refusing European patent application No. 88 304 016.4, filed on 4 May 1988 and published under No. 0 294 934.

II. The decision under appeal was based on amended application documents, including three sets of claims for different Contracting States. The first set of claims for all designated Contracting States except GR and ES contained six claims, the first of them reading as follows:

"A penem having the absolute stereochemical formula:



(II)

wherein R is hydrogen or a radical forming an ester hydrolysable under physiological conditions; or a pharmaceutically acceptable cationic salt thereof when R is hydrogen."

Claim 2 related to the compounds according to Claim 1 wherein R is either hydrogen or pivaloylmethyl.

The sole ground of refusal was that the subject-matter of the above two claims was not novel with respect to the content of document

(1) EP-A 0 130 025.

The Examining Division held that this document implicitly disclosed the compound of the above claims wherein R was hydrogen, since this compound was one of only two possible stereoisomers comprised by Claim 6 of document (1) and since it was expressly stated in the description of this patent application that "various optically active isomers" of the compounds described therein were possible and that the "invention embraces such optically active isomers". It further held that these optically isomers could be prepared by a skilled person at the priority date of the application, so that the disclosure in document (1) was sufficient to make these compounds available to the public.

III. The Appellant (the Applicant) submitted that the objection raised under Article 54(1) EPC was based on a misinterpretation of the disclosure of document (1), since Claim 6 of that document related to a 50:50 mixture of two diastereomers and the statement in the description referred to by the Examining Division was a standard one which was included as a matter of law to alert possible infringers to the fact that separated isomeric forms are regarded as falling within the scope of the claims. From the point of view of science, it did not add anything to what the skilled chemist already knew, i. e. that various optical isomers were

theoretically possible. Furthermore, the skilled chemist would not have recognised the mixture of stereoisomers disclosed in Claim 6 of document (1) as the same compound as either of its component diastereomers, as is evident from the fact that these products were given different Registry Numbers in Chemical Abstracts. Referring, inter alia, to decisions T 181/82, T 296/87 and T 12/81, he submitted that the compounds according to the present application were to be regarded as chemical entities different from those disclosed in document (1) and were therefore novel.

IV. The Appellant requested that the decision under appeal be set aside and a patent be granted on the basis of "the latest set of claims on file", i. e. the sets of claims underlying the decision under appeal. In the alternative, he requested that a question be referred to the Enlarged Board of Appeal.

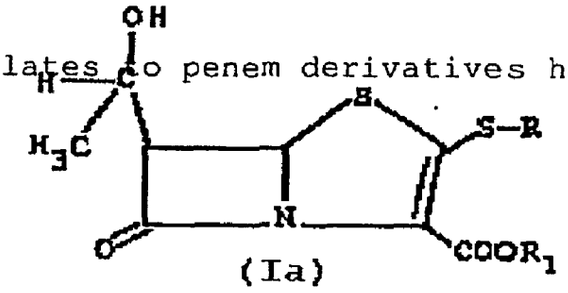
Reasons for the Decision

1. The appeal is admissible.

2. The sole issue to be decided in these appeal proceedings is that of the novelty of the subject-matter of Claims 1 and 2 in respect of the disclosure in document (1). In the Board's judgment these claims relate to substantially pure compounds which are not contaminated by significant amounts of stereoisomers.

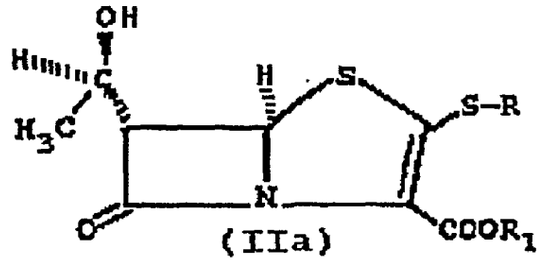
2.1 On that basis, the only question to be decided is whether the individual stereochemical configuration of the compounds according to the present Claims 1 and 2 has been made available to the public by that disclosure. The Board holds, in accordance with the consistent jurisprudence of the Boards of Appeal, that the novelty of such an individual chemical configuration can only be denied if there is an unambiguous disclosure of this very configuration in the form of a technical teaching (see in particular T 181/82, OJ EPO 1984, 401, No. 8 of the reasons, and T 296/87, OJ EPO 1990, 195, Nos. 6 and 7 of the reasons). It is thus not sufficient that the configuration in question belongs conceptually to a disclosed class of possible configurations, without any pointer to the individual member. It is further clear that, if such a configuration is novel , it constitutes a "new element" in the sense of decisions T 12/81 (OJ EPO 296, No. 14.2 of the reasons, and T 12/90 of 23 August 1990 (not published in OJ EPO, No. 2.6 of the reasons), conferring novelty to any group of individual chemical compounds having this feature in common. It is therefore to be examined whether the common stereochemical configuration of the presently claimed compounds is disclosed in document (1).

2.2. Document (1) relates to penem derivatives having the formula Ia



(Ia)

in which R_1 is hydrogen or an ester group which can be hydrolysed **in vivo** and R has a great number of different meanings, comprising acyclic radicals such as 2-(methylsulfinyl)ethyl as well as cyclic radicals such as **1-oxo-3-thiolanyl** and 3-thianyl (page 1, line 10 to page 2, line 6. The description then indicates that compounds of the following formula IIa



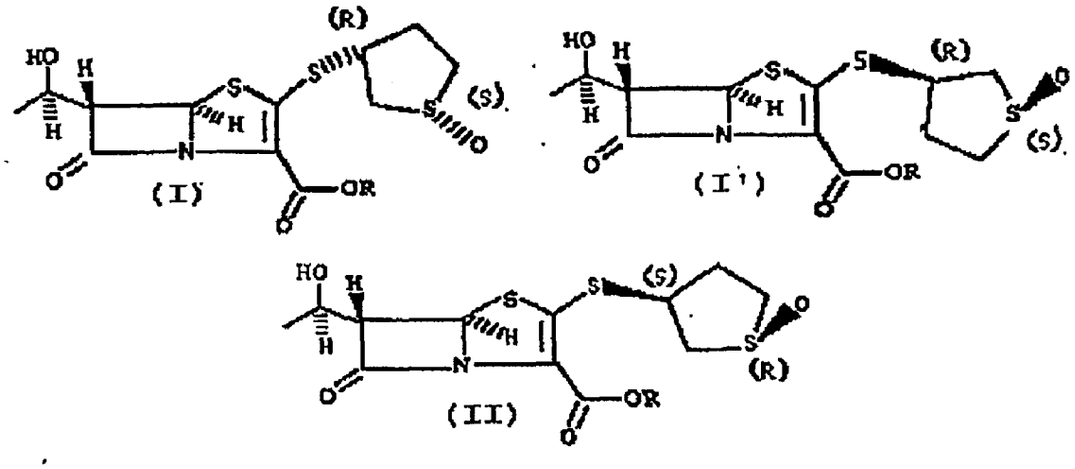
(IIa)

in which R and R_1 have the same meanings as in formula Ia "were included within the scope of the present invention" (page 2, lines 20 to 24). The description then goes on and states on page 4, lines 7 to 10: "As will be appreciated, various optically active isomers of the new compounds are possible. The present

invention embraces such optically active isomers as well as mixtures thereof."

Claim 6 relates to a compound of the above formula IIa wherein R is **cis**-1-oxo-3-thiolanyl.

2.3 The chemical formula of Claim 6 of document (1) indicates the specific configurations of the three asymmetric carbon atoms of the penem ring system which are also present in the claimed compounds. In respect of the configurations of the asymmetric atoms of the thiolane ring (the sulphur atom in position 1 and the carbon atom in position 3) this formula additionally indicates that the oxygen atom bound to position 1 and the sulphur atom (carrying the penem ring system) bound to position 3 must be on the same side of the thiolane ring (cis - configuration). This information is however not sufficient to describe unambiguously the absolute steric configuration at the two asymmetric atoms of the thiolane ring, since two different steric configurations exist which satisfy this requirement and which may be represented by the following formulas I or I' (which describe the same configuration, because formula I can be converted in formula I' by rotation of the thiolane ring around the exocyclic C-S-bond) on the one hand, and formula II on the other hand.



The reference, Claim 6 of document (1), taken in isolation, does not unambiguously disclose any one of the above two absolute configurations, although it conceptually comprises both of them.

2.4 In the Board's judgment the above ambiguity is not removed by the disclosure contained in the paragraph on page 4 of document (1) relied upon in the decision under appeal, since this paragraph refers to optical active isomers in general, including a great number of possible diastereomeric and enantiomeric forms, but not to any specific configuration even at the three asymmetric carbon atoms contained in the penem ring system, for which the specific configuration at these three carbon atoms disclosed in Claim 6 is an example. Moreover, there is no indication that this paragraph contains any technical teaching relevant to asymmetric carbon or even sulphur atoms which may be contained in some of the substituents R comprised by formula Ia, corresponding to formula I in document (1). Rather, the skilled reader would consider this paragraph solely in

respect of the essential structural elements of the disclosed class of chemical compounds, i.e. the three asymmetric carbon atoms of the penem ring system. Nevertheless, the Board observes that it does not agree with the Appellant's submission that the above paragraph relating to optically active isomers would not add anything to what the skilled chemist already knew, i.e. that various optical isomers were theoretically possible, since the express statement that such optically active isomers **are embraced by the invention** goes beyond the conceptual information that such isomers are theoretically possible (see also T 658/91 of 14 May 1993, No. 2.4 of the reasons) and is therefore a relevant part of the disclosure of document (1).

2.5 In these circumstances the fact that the disclosure of Claim 6 of document (1) does not embrace more than two possible steric configurations does not take away the novelty of the specific one which is claimed in the present application, because there is no unambiguous technical teaching directed to that configuration in the parts of document (1) relied upon by the Examining Division. Thus the facts of the present case are quite different from the facts underlying decision T 658/91 and are rather similar to those underlying decision T 296/87. For this reason, the novelty of the subject-matter of the present claims cannot be denied on that basis and the decision under appeal must be set aside.

3. However, the Examining Division, having taken the position that the claimed subject-matter lacked novelty

for the above reason, as set out in the decision under appeal, has not yet examined whether other objections might prejudice the requested grant of a patent. It is therefore appropriate to remit the case to the Examining Division for further prosecution, in order to give the Appellant an opportunity to have any such further objections considered by two instances.

Order

For these reasons it is decided that

1. The decision under appeal is set aside.

2. The case is remitted to the Examining Division for further prosecution.

The Registrar: The Chairman:

E. Görgmaier A. Jahn

ANNEXURE VI

BESCHWERDEKAMMERN DES EUROPÄISCHEN PATENTAMTS

BOARDS OF APPEAL OF THE EUROPEAN PATENT OFFICE

CHAMBRES DE RECOURS DE L'OFFICE EUROPEEN DES BREVETS

Internal distribution code:
(A) [ ] Publication in OJ
(B) [X] To Chairmen and Members
(C) [ ] To Chairmen

D E C I S I O N
of 2 December 1999

Case Number: T 1046/97 - 3.3.1

Application Number: 91307624.6

Publication Number: 0472392

IPC: C07D 521/00

Language of the proceedings: EN

Title of invention:
Optically active triazole derivatives and compositions

Applicant:
Zeneca Limited, et al

Opponent:
-

Headword:
Enantiomer/ZENECA

Relevant legal provisions:
EPC Art. 54(1)(2)

Keyword:
"Novelty (yes) - claimed enantiomer not directly and unambiguously disclosed"

Decisions cited:
G 0001/92, T 0181/82, T 0296/87, T 0990/96

Catchword:
"No individualised disclosure of a specific enantiomer by the term "optically-actice forms" (see point 2.1.1.6 of the

reasons)"

Europäisches Patentamt | European Patent Office | Office européen des brevets

Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 1046/97 - 3.3.1

D E C I S I O N
of the Technical Board of Appeal 3.3.1
of 2 December 1999

Appellant: Zeneca Limited et al
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Decision under appeal: **Decision of the Examining Division of the European Patent Office posted 3 June 1997 refusing European patent application No. 91 307 624.6 pursuant to Article 97(1) EPC.**

Composition of the Board:

Chairman: A. J. Nuss
Members: P. Bracke
S. C. Perryman

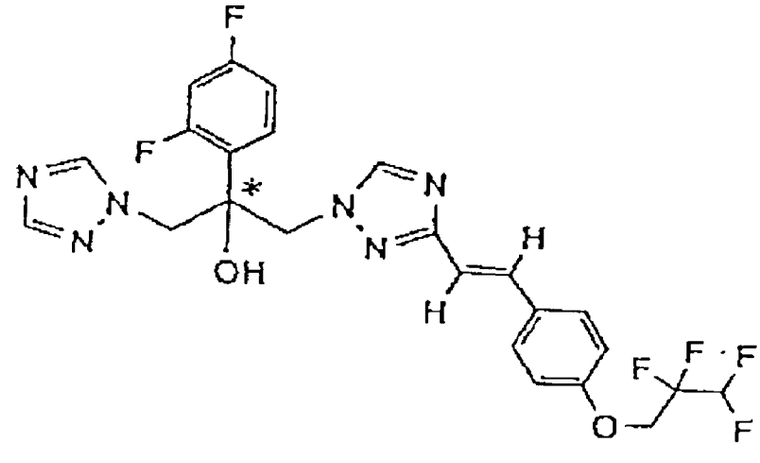
Summary of Facts and Submissions

I. The appeal lies from the Examining Division's decision, dispatched on 3 June 1997, refusing European patent application No. 91 307 624.6, published as EP-A-0 472 392, since the claimed compounds were not considered to be novel.

II. The decision was based on the claims and description as listed in the decision under appeal, namely: Claims 1 to 14 as originally filed and Claims 15 to 17 filed with letter of 10 August 1995 (received 16 August 1995); pages 3 to 20, 22 to 30 and 32 to 42 as originally filed and pages 1, 2, 21 and 31 filed with letter of 10 August 1995.

The independent Claims 1 and 2 read:

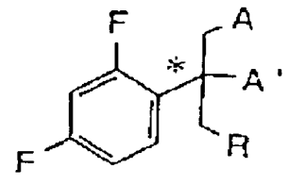
"1. (+)-2-(2,4-difluorophenyl)-1-[3-[(E)-4-(2,2,3,3-tetrafluoropropoxy)styryl]-1H-1,2,4-triazol-1-yl]-3-(1H-1,2,4-triazol-1-yl)propan-2-ol shown in the formula ((+)-I)



((+)-I)

(where * indicates an optically active centre), pharmacologically acceptable salts thereof, solvates thereof and solvates of salts thereof."

"2. (-)- or (+)-2-(2,4-difluorophenyl)propane derivatives shown in the formula (II)



(II)

(where * indicates an optically active centre, point A and A' together are an oxygen atom, or A' is a hydroxy group and A is a hydroxy group, methanesulfonyloxy group or p-toluenesulfonyloxy group, and R is a hydroxy group, acetoxy group, 1H-1,2,4-triazol-1-yl group or 3-[(E)-4-(2,2,3,3-tetrafluoropropoxy)styryl]-1H-1,2,4-triazol-1-yl group, providing that both A and R are not simultaneously hydroxy groups)."

Claims 3 to 9 were dependent on Claim 2; Claims 10 to 14 were related to methods of preparing the enantiomer of formula ((+)-I) and to methods of preparing intermediates used therein; Claims 15, 16 and 17 were related to a pharmaceutical composition comprising the enantiomer of formula ((+)-I), the enantiomer of formula ((+)-I) for use in a method of therapeutic treatment and the use of the enantiomer of formula ((+)-I) for the preparation of a medicament for treating fungal infection in animals including humans respectively.

III. The Examining Division was of the opinion that the claimed enantiomer of formula ((+)-I) was known from document (B), EP-A-0 174 769, since 2-(2,4-difluorophenyl)-1-[3-[(E)-4-(2,2,3,3-tetrafluoropropoxy)styryl]-1H-1,2,4-triazol-1-yl]-3-(1H-1,2,4-triazol-1-yl)propan-2-ol was described in example 11 thereof and since it was stated in document (B) that all optically active forms of the compounds described therein were enclosed in the teaching thereof.

More particularly, since example 11 of document (B) was nothing else than a mixture of enantiomers and since it belongs to the skilled person's general knowledge to identify such mixtures and to separate them, in the Examining Division's view the claimed enantiomer was known, according to the principle laid down in G 1/92 (OJ EPO, 1993, 277).

IV. The Appellant filed with the statement of grounds of appeal of 1 October 1997 (received 2 October 1997) a set of claims headed "Auxiliary Request" and with telefax of 23 November 1999 four sets of claims as second-, third-, fourth- and fifth auxiliary request.

V. Oral proceedings before the Board of Appeal took place on 2 December 1999.

VI. The Appellant contested that the principle laid down in G 1/92 was applicable in assessing whether an enantiomer is novel over a known mixture of (+) and (-) enantiomers and he submitted that document (B) neither specifically described the enantiomer of formula ((+)-I) nor provided an enabling disclosure

how to obtain it.

The Appellant also submitted that Claim 2 was novel over the teaching of any of documents (B) and (C), WO 88/05048, since these documents were silent about the optically active forms of the presently claimed compounds.

VII. The Appellant requested that the decision under appeal be set aside and that a patent be granted as main request on the basis of the claims and description as listed in the decision under appeal or as auxiliary requests on the basis of the set of claims headed auxiliary request accompanying the statement of grounds of appeal filed 1 October 1997 or the sets of claims headed second, third, fourth or fifth auxiliary request filed 23 November 1999.

Reasons for the Decision

1. The appeal is admissible.

2. *Novelty*

The only issue to be dealt with is whether the claimed subject-matter is novel in view of document (B) or (C).

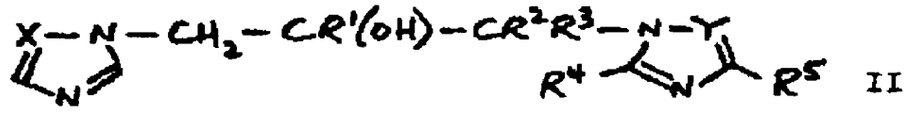
2.1 *Main request*

2.1.1 Claim 1

2.1.1.1 Claim 1 is a product claim directed to the specific enantiomer of formula ((+)-I), which the Board interprets as the pure (+)-enantiomer.

Thus, in assessing novelty, the only question to be decided is whether the enantiomer of formula ((+)-I) has been made available to the public by the disclosure of document (B).

2.1.1.2 Document (B), which is acknowledged as prior art on page 2, line 44 of the published application in suit, relates to a generically defined class of azoles of formula (II)



II

(page 1, line 23 to page 3, line 26). On page 8, lines 2 to 11 of this document, it is taught that in such azoles at least the carbon atom bearing R^1 and hydroxy is asymmetrically substituted and, consequently, that the azoles exist in racemic, meso or **optically-active forms** (emphasis added).

Furthermore, example 11 discloses 2-(2,4-difluorophenyl)-1-[3-[(E)-4-(2,2,3,3-tetrafluoropropoxy)styryl]-1H-1,2,4-triazol-1-yl]-3-(1H-1,2,4-triazol-1-yl)propan-2-ol obtained according to the method described in example 4, without giving any further information about the stereochemical configuration thereof.

2.1.1.3 Since the technical teaching of an example may be combined with general technical teaching disclosed elsewhere in the same document, in the absence of reasons to the contrary (see, for example, T 990/96 OJ EPO, 1998, 489, point 9.2 of the reasons), the Board has no reason to believe that a skilled person would not combine the disclosure of example 11 with the reference to the racemic, meso and optically-active forms.

2.1.1.4 It is, however, consistent jurisprudence of the Boards of Appeal that the novelty of an individual chemical compound can only be denied if there is a direct and unambiguous disclosure of this very compound in the form of a technical teaching (see T 181/82, OJ EPO 1984, 401, No. 8 of the reasons, and T 296/87, OJ EPO 1990, 195, Nos. 6 and 7 of the reasons). It is thus not sufficient for denying novelty in the present case that the claimed enantiomer of formula ((+)-I) belongs conceptually to the group of possible optically-active forms mentioned in document (B) unless there is a pointer to the individual member of the group at stake, ie the specific (+)-enantiomer.

2.1.1.5 The claimed enantiomer being incontestably neither a racemate nor a meso form, the assessment of novelty over document (B), consequently, crystallises on the question, whether the claimed enantiomer of formula ((+)-I) is directly and unambiguously derivable from the teaching of example 11 when combined with the reference to the optically active forms.

2.1.1.6 Since optical activity is the property displayed by chemical compounds having an asymmetrically

substituted carbon atom to rotate the plane of polarisation of plane-polarised light when passing through them, the term "optically-active forms" in document (B) is to be interpreted as embracing any stereochemical form of the disclosed 1,3-di-azolyl-2-propanoles having such property, independently of whether such property is obtained by a pure stereochemical isomer or by any mixture of such isomers. This interpretation concurs with the common general knowledge, as disclosed in Enantiomers, Racemates, and Resolutions (1981), John Wiley and Sons, J. Jacques and A. Collet, page 4, third full paragraph, that the "expression *optically active substance* may signify a pure enantiomer or a mixture containing an excess of one of the two."

In document (B) the term "optically-active forms" provides thus no information about any specific stereochemical form(s) of the chemical compound disclosed in example 11. In other words, from a stereochemical point of view, the disclosure in document (B) must be regarded as undifferentiated, with the effect that the said term cannot be equated to an individualised disclosure of a specific enantiomer.

Therefore, in the Board's judgement, the specific configuration of the ((+)-I) enantiomer of Claim 1 is not directly and unambiguously derivable from the teaching of document (B) and the novelty of the claimed ((+)-I) enantiomer is not destroyed by this disclosure.

2.1.1.7 In the Examining Division's view the claimed

enantiomer of formula ((+)-I) should be considered to be disclosed in document (B) according to the opinion G 1/92.

However, that opinion of the Enlarged Board of Appeal rules that a chemical composition of a product is state of the art when the product as such is available to the public and can be analysed and reproduced by the skilled person, irrespective of whether or not particular reasons can be identified for analysing the composition. It deals with the point of law concerning the interpretation of the requirement "made available to the public" in relation to the prior use of a product (see point 1.1 of the reasons) and relates only to the composition as such being made available to the public. This opinion cannot be extended to a further principle that the public prior use of a composition is to be construed as a public disclosure of each component of that composition in its pure form. Thus opinion G 1/92 is not relevant to the present case.

2.1.2 Claim 2

2.1.2.1 The Board interprets Claim 2 as being related to the pure (+)-enantiomer or the pure (-)-enantiomer of formula (II), by analogy with the claim directed to the enantiomer of formula ((+)-I) (see point 2.1.1.8).

In assessing novelty, it is to be decided whether any of the enantiomers according to Claim 2 has been made available to the public by any of the disclosures of documents (B) and (C).

2.1.2.2 The only disclosure in document (B) of a compound having a chemical formula as defined in Claim 2 can be found in example 4, describing the use of 2-(2,4-difluorophenyl)-2,3-epoxy-1-(1,2,4-triazol-1-yl)propane as intermediate. Since this example is completely silent about the stereochemical configuration of this intermediate and according to the jurisprudence of the Boards of Appeal of the EPO the novelty of any of the enantiomers is not destroyed by the description of a racemate (T 296/87, point 6.2 of the reasons), the disclosure of this compound does not destroy the novelty of Claim 2.

2.1.2.3 The only mentioning of compounds having a chemical formula as defined in present Claim 2 in document (C) can be found in preparative example 6 thereof, describing the conversion of 1-[[(2,4-difluorophenyl)-oxiranyl]methyl]-1H-1,2,4-triazole into 2-(2,4-difluorophenyl)-3-(1H-1,2,4-triazol-1-yl)-1,2-propanediol.

Since this example is completely silent about the stereochemical configuration of the compounds involved, also for the reason given in point 2.1.2.2 such disclosure does not destroy the novelty of the subject-matter of present Claim 2.

This finding is not affected by the statement on page 27, third full paragraph, that the stereochemical configuration is already fixed in the intermediates (II) and that it is possible to separate cis and trans forms at this **or even an earlier stage**. Since the two enantiomers according to present Claim 2 contain only **one** asymmetrically substituted carbon atom whereas the

above disclosure concerns the cis and trans forms of compounds, having **at least two** asymmetrically substituted carbon-atoms, the said statement cannot concern the compounds described in preparative example 6.

2.1.3 It follows from the above that the remaining Claims 3 to 17 are necessarily also novel over the disclosure of documents (B) and (C) for the same reasons as Claims 1 and 2.

2.2 *Auxiliary requests*

In the light of the above findings, there is no need to consider the auxiliary requests.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The matter is remitted to the first instance for further prosecution on the basis of Claims 1 to 17 as listed in the decision under appeal.

The Registrar: The Chairman:

E. Görgmaier A. Nuss