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Datasheet for the decision of 29 June 2011

Case Number: T 0497/08 - 3.3.01

Application Number: 01956112.5

Publication Number: 1307464

IPC: C07F 5/02

Language of the proceedings: EN

Title of invention:
Detection of analytes in aqueous environments

Applicant:
Sensors for Medicine and Science, Inc.

Headword:
Boron-containing compounds for detection of vicinal diols/SENSORS FOR MEDICINE AND SCIENCE, INC

Relevant legal provisions:
EPC Art. 123(2), 84, 83, 56, 54

Relevant legal provisions (EPC 1973):
-

Keyword:
"Novelty (yes)"
"Inventive step - (yes) - non obvious alternative"

Decisions cited:
-

Catchword:
-

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Case Number: T 0497/08 **-** 3.3.01

D E C I S I O N
of the Technical Board of Appeal 3.3.01
of 29 June 2011

Appellant: Sensors for Medicine and Science, Inc.
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Decision under appeal: **Decision of the Examining Division of the European Patent Office posted 5 May 2007 refusing European patent application No. 01956112.5 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman: P. Ranguis
Members: J.-B. Ousset
C.-P. Brandt

Summary of Facts and Submissions

I. An appeal was lodged against the decision of the examining division to reject European patent application 01 956 112.5.

II. In its decision, the examining division found the then pending main request as well as the two auxiliary requests to be neither novel nor inventive.

Among the prior-art documents cited by the examining division in its decision, the following are of particular relevance:

(1) EP-A-0 430 510
(2) US-A-5 661 040
(4) WO-A-9946600
(5) Nezu and Winnik, Biomaterials, 2000, vol. 21(4), pages 415-419
(10) US-A-6 002 954.

III. Claim 1 of the main and sole request before the board reads as follows:

1. A method for the production of an indicator macromolecule comprising a copolymer of:

a) one or more indicator component monomers; and

b) one or more hydrophilic monomers:

The molar ratio of monomer (b) to monomer (a) being from 2:1 to 1000:1, wherein one or more hydrophilic monomers are selected from methacrylamides, methacrylates, methacrylic acid, dimethylacrylamide, TMAMA or vinyls, and wherein the indicator component monomer comprises an N-(o-

boronobenzyl)aminomethylanthracene derivative, characterized in that the indicator macromolecule is obtained by the copolymerisation of monomers (a) and (b) and in that the indicator component monomers individually are not sufficiently water soluble to permit their use in an aqueous environment for detecting the presence or concentration of the analyte, wherein the analyte comprises a vicinal diol, and the indicator macromolecule has a detectable quality that changes in a concentration-dependent manner when said macromolecule is exposed to said analyte and is capable of detecting the concentration of the analyte in an aqueous environment, which comprises copolymerizing monomers (a) and (b)."

Claim 10 of the main request reads as follows:

"10. An indicator macromolecule comprising a copolymer of:

a) one or more indicator component monomers; and

b) one or more hydrophilic monomers:

the molar ratio of monomer (b) to monomer (a) being from 2:1 to 1000:1, wherein the one or more hydrophilic monomers are selected from methacrylamides, methacrylates, methacrylic acid, dimethylacrylamide, TMAMA or vinyls, characterized in that the indicator macromolecule is obtained by the copolymerisation of monomers (a) and (b) and in that the indicator component monomers individually are not sufficiently water soluble to permit their use in an aqueous environment for detecting the presence or concentration of the analyte, wherein the analyte is a vicinal diol, and the indicator macromolecule has a detectable quality that changes in concentration-dependent manner

when said macromolecule is exposed to said analyte and is capable of detecting the concentration of the analyte in an aqueous environment, wherein the indicator component monomer (a) is selected from the group consisting of:

9-[[N-methacryloylaminopropyl-N-(o-boronobenzyl) amino]methyl]anthracene;
9-[N-[2-(5,5-dimethyl-[1,3,2]dioxaborinan-2-yl)benzyl]-N-[3-(methacrylamido)propylamino]methyl]-10-[N-[2-(5,5-dimethyl-[1,3,2]dioxaborinan-2-yl)benzyl]-N-[2-(2-hydroxyethoxy)-ethylamino]methyl]anthracene;
9-[N-(2-boronobenzyl)-N-[3-(methacrylamido)propylamino]methyl]-10-[N-(2-boronobenzyl)-N-[2-(2-hydroxyethoxy)ethylamino]methyl] anthracene;
9,10-bis[N-(2-boronobenzyl)-N-[3-(methacrylamido)-propylamino]methyl]anthracene ;
9-[N-[2-(5,5-dimethyl-[1,3,2]dioxaborinan-2-yl)benzyl]-N-[2-(2-methacroyloxyethoxy)ethylamino]methyl]-10-[N-[2-(5,5-dimethyl-[1,3,2]dioxaborinan-2-yl)benzyl]-N-[2-(2-hydroxyethoxy)-ethylamino]methyl]anthracene ;
9-[N-(2-boronobenzyl)-N-[2-(2-methacroyloxyethoxy)-ethylamino]methyl]-10-[N-[2-boronobenzyl)]-N-[2-(2-hydroxyethoxy)ethylamino]methyl]anthracene ;
9,10-bis[N-[2-(5,5-dimethyl-[1,3,2]dioxaborinan-2-yl)benzyl]-N-[2- (2-methacroyloxyethoxy)ethylamino]methyl]anthracene;
9,10-bis[N-(2-boronobenzyl)-N-[2-(2-methacroyloxyethoxy)ethylamino]methyl]anthracene;
N-[3-(methacrylamido)propyl]-3,4-dihydroxy-9,10-dioxo-2-anthracenesulfonamide ;

α,α'-bis[N-[2-(5,5-dimethylborinan-2-yl)benzyl]-N-[3-(methacrylamido)propylamino]-1,4-xylene; and salts or derivatives thereof."

Claim 11 relates to a method for detecting the concentration of an analyte, which is a vicinal diol using an indicator macromolecule according to claim 10.

IV. The appellant argued as follows:

- The amendments made to the claims were based on the description as originally filed.

- The terms used in the claims were clear.

- The person skilled in the art could reproduce the claimed invention in its whole scope without undue burden.

- The claimed matter was novel over the cited prior art, because the copolymerisation process of claim 1 was not described in the cited prior art.

- The claimed subject-matter was inventive, because the prior art did not relate to the same matter as that claimed in the present application.

V. During oral proceedings, the appellant withdrew the main request as well as auxiliary requests 1 to 3, all filed with his letter of 1 June 2011, and filed a new main request on which the present decision is based (see point III).

VI. The appellant requested that the decision under appeal be set aside and that a patent be granted on the basis

of the main request, dated of 29 June 2011, filed during oral proceedings.

VII. At the end of the oral proceedings, the decision of the board was announced.

Reasons for the Decision

1. The appeal is admissible.

2. Amendments

2.1 Claim 1

The introduction into claim 1 of the ratio of the hydrophilic monomer to the indicator component monomer ranging from 2:1 to 1000:1 is based on page 9, lines 26 to 28 of the description as originally filed.

The limitation of the type of hydrophilic monomer to be used in the process of claim 1 to methacrylamides, methacrylates, methacrylic acid, dimethylacrylamide, TMAMA or vinyls is based on page 9, lines 5 to 9 of the description as originally filed.

The limitation to a vicinal diol of the nature of the analyte to be detected is justified by the passage on page 6, line 18 of the description as originally filed.

That the hydrophilic monomer and the indicator component monomer are copolymerized is based on page 9, lines 29 to 32 of the description as originally filed.

Lastly, the limitation of the nature of the indicator component monomer to an N-(o-boronobenzyl)aminomethylanthracene derivative is based on claim 3 as originally filed.

The board thus concludes that claim 1 fulfils the requirements of Article 123(2) EPC.

2.2 Claim 10

Claim 10 contains the same limitations as those mentioned for claim 1 (see above). However, the nature of the indicator component monomer has been further limited to a list of ten specific N-(o-boronobenzyl)aminomethylanthracene derivatives. These specific compounds were disclosed in claim 4 in these of claims as originally filed.

Consequently, claim 10 also fulfils Article 123(2) EPC.

2.3 Claim 11 finds support in claims 27 and 28 as originally filed and the other parts of the application cited above. The main request fulfils the requirements of Article 123(2) EPC.

3. Clarity

3.1 The introduction into independent claims 1 and 10 of the hydrophilic monomers, namely methacrylamides, methacrylates, methacrylic acid dimethylacrylamide, TMAMA and vinyls, does not render the wording of these claims unclear, since these terms represent groups of compounds whose meanings are well known in the art.

The term "vicinal diol" introduced into claims 1 and 10 is also clear and non-ambiguous.

The expression "N-(o-boronobenzyl)aminomethylanthracene derivative", which characterizes the indicator component monomer, has been added to claim 1. This expression is clear for the person skilled in the art, since it embraces any compound having this specific moiety in its chemical structure.

Furthermore, this expression is no longer present in claim 10, where it has been replaced by specific N-(o-boronobenzyl)aminomethylanthracene derivatives. These specific organic compounds are also clear.

3.2 In view thereof, the board concludes that the main request fulfils the requirements of Article 84 EPC.

4. Reproducibility

4.1 In view of the limitations carried out in the wordings of claims 1 and 10, the board is convinced that the claimed invention is reproducible by the person skilled in the art without undue burden using the description and his common knowledge for the following reasons:

Example 1 of the description (see page 17, line 9 to page 21, line 8) describes the preparation of a "N-(o-boronobenzyl)aminomethylanthracene derivative" and also the preparation of the indicator containing macromolecule. Moreover, an example of coupling reaction between the said indicator containing macromolecule with glucose (a vicinal diol) is also given in this example. Moreover, further examples show

the preparation of different N-(o-boronobenzyl)aminomethylanthracene derivatives as well as the use of different hydrophilic monomers for the preparation of the indicator macromolecule (see examples 4 to 7).

4.2 In view of the different exemplified variations, the general description and the breadth of claims 1, 10 and 11, the board concludes that the person skilled in the art can reproduce the claimed invention in its whole scope without undue burden (Article 83 EPC).

5. Novelty

5.1 Claim 10

None of the cited documents discloses an indicator macromolecule comprising a copolymer of one of the specific ten indicator component monomers listed in claim 10 for the preparation of a polymeric indicator macromolecule and an hydrophilic (meth)acrylic monomer. Therefore, novelty of the subject-matter of claim 10 is acknowledged vis-à-vis documents (1), (2), (4), (5) and (10).

5.2 Claim 1

None of the documents (1), (2) or (5) mentions the use of a component monomer containing the moiety N-(o-boronobenzyl)aminomethylanthracenyl for the preparation of an indicator macromolecule. Thus, novelty of the process of claim 1 is acknowledged vis-à-vis these documents.

Document (4) does not describe any process for the preparation of a copolymeric entity containing an indicator moiety. The process claimed in claim 1 is therefore novel over document (4).

Document (10) describes the preparation of a biocompatible material in which amplification components have been immobilized (see column 10, lines 22 to 30). Moreover, the said matrix should be permeable to the analyte and more particularly glucose (a vicinal diol) (see column 10, lines 53 to 54). Furthermore, the amplification components used in this document can also be N-(o-boronobenzyl)aminomethylanthracenyl derivatives (see compound 7 on Fig. 12 and compound 11 in Fig. 13). Additionally, document (10) discloses that the matrix with the immobilized amplification component can be made by incorporation of the components into the polymerisation mixture in such a manner that the components will be covalently bonded to the polymer during formation (see column 15, lines 3 to 10). However, the polymers used in document (10) for the making of the matrix are different from those obtained in the process of claim 1 of the present application, since the polymer matrix used in document (10) can be a silicon-containing polymer, a polyurethane or a polyurea (see column 10, lines 39 to 45). Furthermore, with the exception of the examples, no ratio of hydrophilic monomer to the indicator component monomer is given in document (10).

The board thus concludes that the subject-matter of claim 1 is novel over document (10). This finding also applies to claim 11.

5.3 The main request is thus novel over the cited documents, since all remaining claims of this request are dependent on claim 1, claim 10 or claim 11 (Article 54 EPC).

6. Inventive step

6.1 Claim 1

6.1.1 Document (10) represents the closest prior art, since it discloses a process to immobilize the amplification system into a polymer matrix (see column 15, lines 3 to 10). Furthermore, this system aims at determining the levels of polyhydroxylated compounds like glucose (a vicinal diol (see column 3, lines 17 to 19) and the detection of the signal can determine the quantity of the polyhydroxylated compound (see column 3, lines 28 to 30). As detailed in point 5.2, the subject-matter of claim 1 differs from that of the present application in the nature of the polymeric matrix in the macromolecular product used to detect glucose.

6.1.2 In the absence of any comparative data with the closest prior art, any problem formulation based on a better aqueous solubility of the macromolecular indicator (see page 2, lines 12 to 17) cannot be considered as credibly solved.

Therefore, the problem underlying the current application can be seen in the provision of a process to make available an alternative macromolecule indicator.

6.1.3 In view of the examples given in the description, the board is convinced that this problem has been solved.

Starting from document (10), the person skilled in the art would not find any information in document (1) or (2) or (5), since none of these documents mentions the use of N-(o-boronobenzyl)aminomethylanthracene derivatives in a process to make available indicator macromolecules, or in document (4), which although describing the preparation of indicator molecules for detecting the presence or concentration of cis-diols like glucose (see page 1, lines 25 to 28) does not disclose the attachment of the said indicator molecules to any kind of polymers and even less to polymers obtained by polymerisation of the hydrophobic monomers listed in claim 1 of the present application.

6.2 The board concludes therefore that the subject-matter of claim 1 is inventive (Article 56 EPC).

6.3 Claim 10

6.3.1 Starting from the closest prior-art document (10), the problem to be solved can be seen in the provision of alternative indicator macromolecules useful to detect analytes comprising a vicinal diol.

6.3.2 The examples given in the description show that this problem has been solved.

Starting from the disclosure of document (10), the person skilled in the art would not arrive at the claimed invention. Document (10) discloses neither the polymer matrix having the type of hydrophilic monomers

listed in claim 10 or one of the specific indicator monomers listed in claim 10, nor the claimed indicator macromolecule. Nor would the person skilled in the art find this information in any of the documents (1), (2), (4) or (5).

Claim 11 is based on the same inventive concept and derives its patentability from the same basis as claims 1 and 10.

Since the remaining claims are dependent on claim 1, claim 10 or claim 11, they are also considered inventive over the cited prior art.

6.4 It is thus concluded that the subject-matter of the request is based on an inventive step (Article 56 EPC).

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the first instance with the order to grant a patent on the basis of the main request (claims 1-12), dated 29 June 2011 and filed during the oral proceedings, and after any necessary consequential amendment of the description.

The Registrar The Chairman

M. Schalow P. Ranguis