

List of Patents where Wolfbeis is a named (co)inventor

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(2011) Dressing material for monitoring wound-healing

PCT Int. Appl. (2011), WO 2011098575 A2 20110818. Ger. Offen. (2011) DE 102010001855 A1 20110811. Published 18-Aug-2011. Assigned to Fraunhofer GmbH.

Inventors: Wolfbeis, O. S.; Mohr, G. J.; Szeimies, M.; Trupp, S.; Stich, M.

Abstract: A dressing material (a band aid) for monitoring a wound-healing comprises a binding base material and a control element. The control element is arranged in or on the binding base material, so that a check area of the control element is visible and a liquid or gaseous segregation of a wound is in contact with the control element, if the dressing material is applied on the wound. Furthermore, the control element is designed in order to cause a change of a characteristic of the wound based on a chemical indicator reaction producing a visible change of the check area, in order to make possible the monitoring of the wound-healing. Specifically, pH values of open wounds can be detected visually.



(2010) Irreversible coolness indicator with optical change of nanoparticle suspension

Inventor(s): Kagan, Michael; Mirsky, Vladimir; Wolfbeis, Otto

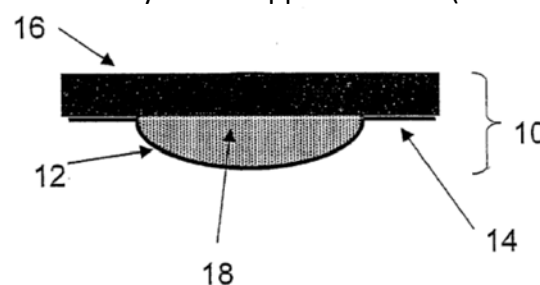
U.S. Patent Application 12/304,678, filed January 28, 2010.

Web: <https://patents.google.com/patent/US20100020846A1/en>

Abstract: The invention provides a temperature-threshold indicator device 10 comprising a sealed housing 12 having at least one surface 14 which is transparent and containing a suspension of inorganic nanoparticles 18 suspended in a liquid medium wherein the suspension undergoes an irreversible detectable change in optical characteristics upon freezing of the liquid medium due to aggregation of the nanoparticles, and wherein the device is provided with means for association thereof with a product whereby the temperature-threshold indicator device 10 serves to determine whether the product has been exposed to an environment of predetermined coldness.

Other: PCT Int. Appl. (2007), WO 2007148321 A2 20071227. Priority: Israel Appl. IL176396 (Jun. 19, 2006)

In a typical embodiment, a pad (18) is fixed on a sample. The pad is filled with D₂O which has a freezing point of 4 °C. It contains gold nanoparticles that give it a red coloration. On freezing, the nanoparticles aggregate and become colorless, this indicating that temperature has dropped to below freezing point. The process is irreversible.



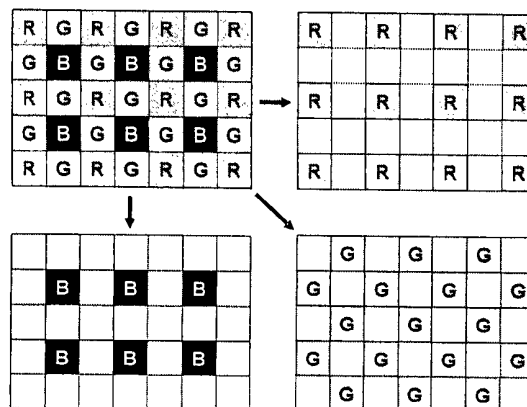
(2009) Procedure and measurement setup for seizing the distribution at least a variable of state in a measuring field with different probes [Machine Translation]

Ger. Offen. (2009), DE 102007054602 A1 20090528. Published 28-Jun-2009. Assigned to German Center for Space Res.

Inventor(s): Borisov, S.; Engler, R.; Henne, U.; Nagl, S.; Schaeferling, M.; Stich, M.; Wolfbeis, O.

Abstract: The method involves inserting different probes into a measuring field, and registering optical signals with different wavelengths from the probes by using a red-green-blue camera.

The optical signals from the probes are separately detected based on different RGB output signals of the camera, where camera is used as a charge coupled device camera and a complementary metal oxide semiconductor camera. Color channels of the camera are attached to the probes, where the camera is connected upstream of an extinction or edge filter. An independent claim is also included for a measuring system for detecting a distribution of a condition parameter in a measuring field.



(2007) **Sensor for measuring carbon dioxide levels in gases or liquids comprising a basic acceptor which is a polybasic inorganic anion or an organic anion.**

Swiss patent number CH 696675. Publ. 03-Jun-2004. Assigned to Bosch GmbH. Also published as DE10254841 (A1)

Web: <https://graz.pure.elsevier.com/en/publications/sensor-for-measuring-carbon-dioxide-levels-in-gases-or-liquids-co>

Inventors: Athanas Apostolidis, Thomas Brinz, Ingo Klimant, Mary Lewis, Otto Wolfbeis.

Abstract: Sensor for measuring carbon dioxide (CO₂) levels in gases or liquids comprises a basic CO₂ acceptor which is a **polybasic inorganic anion (such as phosphate) or an organic multianion**.

(2006) **Bioanalytical method for determining catalases and peroxidases, as well as conjugates, substrates, activators and inhibitors thereof**

US Patent 7,067,275; issued June 27, 2006. Assigned to Chromeon GmbH

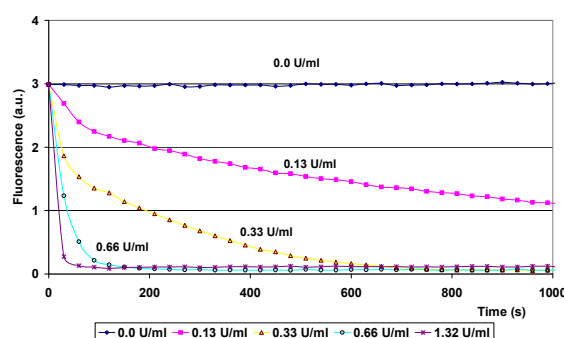
Inventor(s): Wolfbeis, Otto; Wu, Meng; Lin, Zhihong

Web: <https://patents.google.com/patent/US7067275B2/en>

Other: Ger. Offen. (2003), DE 10155160 A1 20030522;

Abstract: The invention concerns the determination of catalases and peroxidases as free enzymes or immobilized, and the determination of their conjugates, substrates, activators and inhibitors by (a) **using a reagent that contains europium(III) complexes with ligands and hydrogen peroxide** in solution or in solid form; (b) measuring the changes in fluorescence; (c) relating the signal to the quality or quantity of the analyte.

The enzymes change the local concentration of H₂O₂, and this is preferentially measured via measurement of luminescence decay time. Additional enzyme substrates can be added. Clinical, environmental samples, enzymes conjugated to nucleic acids, antibodies, antigens can be determined. The method can be used for screening drugs. Preferred ligand is tetracycline.



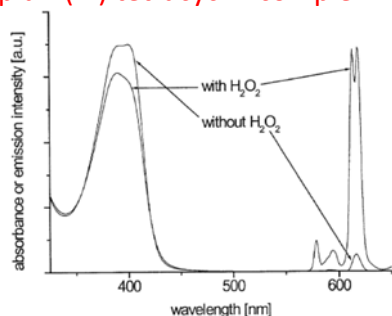
(2006) **Bioanalytical method using oxidases and lanthanoid-ligand complexes.**

U.S. Patent No. 7,052,864. Issued 30 May 2006. Assigned to Active Motif Chromeon GmbH.

Inventors: Durkop, Axel, Wolfbeis O. S.

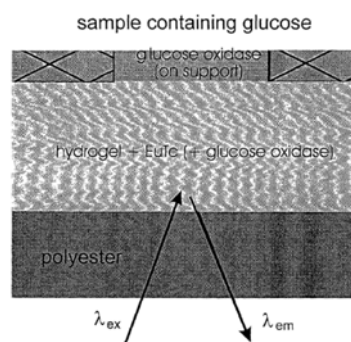
Web: <https://patents.google.com/patent/US7052864B2/en>

Abstract: The present invention concerns biological methods of determination using enzymes from the group of oxidases and using optical indicators from the group of lanthanoid-ligand complexes, specifically of **the europium(III) tetracyclin complex which is a fluorescent probe for enzymatically generated H_2O_2 .**



Above: Spectral changes (fluorescence) on addition of hydrogen peroxide.

Right: Sensor layer for continuous monitoring of glucose via glucose oxidase.



(2006) **Method for determination of acidic gases and sensor**

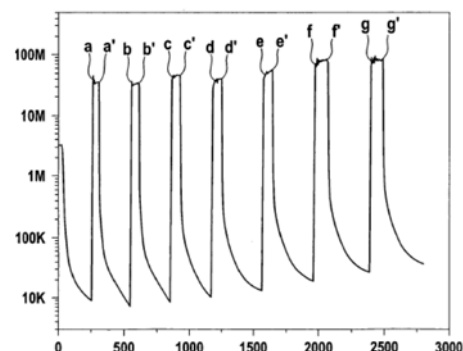
U.S. Patent Application 11/240,229, filed April 20, 2006. *Other:* Eur. Pat. Appl. (2006), EP 1643241 A2 20060405; Ger. Pat. Appl. 10 2004 047466. Assigned to Bosch GmbH.

Web: <https://patents.google.com/patent/US20060081032A1/en>

Inventor(s): Brinz, Thomas; Mirsky, Vladimir; Wolfbeis, Otto; Jockel, Joerg; Hao, Qingli

Abstract: A method and a **sensor for determination of acidic gases in gas mixtures, such as hydrogen chloride, sulfur dioxide, or nitrogen dioxide.**

A polymer layer whose electrical conductance changes under the effect of the gas to be determined is exposed to the gas mixture, and the **the electrical resistance, or the impedance of the polymer layer is determined. In order to desorb the gas from the sensor, the polymer layer is heated at certain time intervals to 60 - 400°** periodically to desorb the gases being analyzed. The sensor is equipped with a heating element for heating the polymer layer and a temperature sensor to det. the temperature of the polymer layer. The sensor can be used as a fire detector.



(2005) **Ozone detecting material and method for detecting ozone**

U.S. Patent 6,911,179. Issued June 28, 2005. Assigned to AIST; Tokyo.

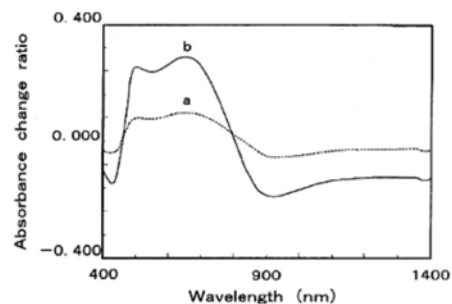
Web: <https://patents.google.com/patent/US6911179B2/en>

Other: Jpn. Kokai Tokkyo Koho (2003), JP 2003014723 A 2003011

Inventor(s): Ando, Masanori; Wolfbeis, Otto S.; Mirsky, Vladimir

Abstract: The present invention provides an ozone detecting material comprising a **polymer prepared by polymerization of at least one monomer selected from the group consisting of 2-, 3-, 4-halogen-substituted anilines or aniline substituted with C1-3-alkyl in N-position, and diphenylamine**, formed into a thin film coated on a transparent substrate, waveguide, or optical fiber, or additionally comprising a component selected from electro-conductive fine carbon powder, a semiconductive metal oxide,

or a semiconductive polymer material. It also includes a **method for detecting ozone** comprising the steps of contacting this ozone detecting material with an ozone-containing gas and determining the light absorption rate and/or electrical conductivity of the ozone detecting material at that time. The figure shows the ratio of the changes in the absorption spectrum of a polyaniline film on exposure to ozone.



(2005) Benz[cd]indole-fluorochromes for labelling biomolecules and polymer particles

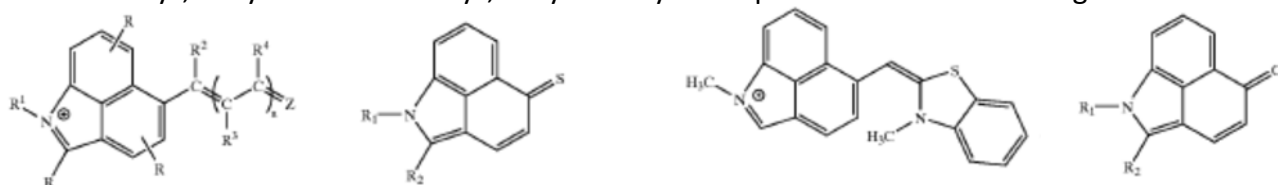
U.S. Patent 6,979,575 (*Fluorochromes for labelling biomolecules and polymer particles and bioanalytical and screening methods based thereon*). Issued December 27, 2005. Assigned to Chromeon GmbH.

Inventor(s): Romanov, N. N.; Wolfbeis, O. S.

Web: <https://patents.google.com/patent/US6979575B1/en>

Other: Eur. Pat. Appl. (2003), EP 1314981 A2 20030528.

Abstract: New **reactive benzoindolone dyes** are described which can be used to fluorescently label **bioorganic molecules such as amino acids, proteins, antibodies, nucleotides and also polymer particles**. The color of the new dyes and conjugates thereof can be varied over a wide range. In contrast to known symmetric cyanine dyes, the dyes of the invention contain only one reactive group. Hence the labelling takes place without the interfering cross-linking that occurs with bireactive dyes. Their fluorescence quantum yields are very high (especially in the conjugated form). Conjugates thereof with proteins, oligonucleotides or particles can be used in fluorescence-based analytical methods of determination e.g. in immunoassays, in hybridization assays, in cytometry or for pharmaceutical screening.



Other: Ger. Appl. 10157615.3 (26 Nov. 2001); Eur. Pat. Appl. 02026263.0.

(2005) Use of changes in electrocatalytic properties for electrochemical detection DNA hybridization without the use of electrochemical labels

Ger. Offen. (2005), DE 10242183 A1 20050224.

Inventor(s): Zhi, Zheng-Liang; Mirsky, Vladimir; Wolfbeis, Otto S.

Abstract: A method electrochemical detection of double-stranded DNA formation in a hybridization assay is described. **The assay is based on a new finding that single-stranded DNA can act electrocatalytically when immobilized on an electrode.** In contrast to this, double-stranded DNA does not show electrocatalytic activity. The various electrochemical characteristics of single and double-stranded DNA enable to identify a DNA with an array of a defined nucleotide sequence.

(2005) Solid support systems for the homogeneous fluorometric detection of biomolecule interactions without washing steps

PCT Int. Appl. (2005), WO 2005095982 A1 20051013. Published 13-Oct-2005. Assigned to Chromeon GmbH.

Inventor(s): Wolfbeis, O. S.; Bastian, P.; Gruber, M.; Wetzl, B. K.

Abstract: The invention relates to solid materials, e.g. glass or plastic plates, multiwell microtitration plates, microscopy supports, test strips and other items, which are covalently or noncovalently loaded with biomolecules while being, in particular, fluorescently labeled. These make it possible to directly detect at the interface, without washing steps, complementary biomolecules **by measuring the change in fluorescence intensity, in fluorescence decay time (lifetime or decay time), in an energy transfer or in an extinction of luminophores**. The invention also relates to a method, which is based on the use of solid materials, e.g. glass or plastic plates, celluloses or silicatic materials, multiwell microtitration plates, microscopy supports, test strips and other items that have been covalently or noncovalently loaded with biomolecules, and which indicates an interaction of biomolecules based on a change in fluorescence decay time and, eventually, on changes in fluorescence intensity.

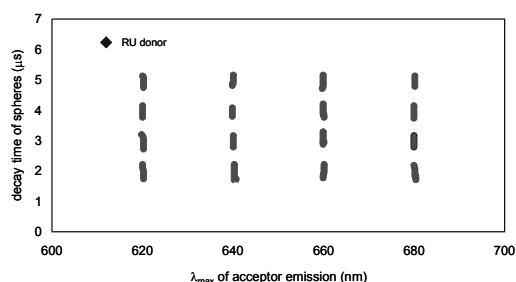
Other: Ger. Appl. 102 004 016 247.6 (01-Apr-2004).

(2005) Luminescence optical method for authenticating products

PCT Int. Appl. (2005), WO 2005095926 A2 20051013. Ger. Appl. 102 004 016 249.2 (01-Apr-2004).

Inventor(s): Wolfbeis, O. S.; Gruber, M.; Bastian, P.

Abstract: The invention relates to a **method for carrying out luminescence optical authentication during which a product is provided with at least one luminescent marker, and its authentication by determining the decay time of the luminescence of the marker at a specific emission wavelength**.



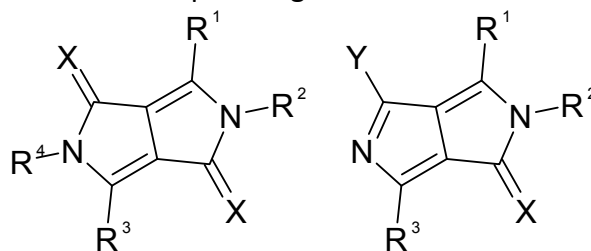
(2004) Pyrrolopyrroles for use as fluorescent labels for biomolecules and spherical particles

PCT Int. Appl. (2004), WO 2004092174 A1 20041028. Published 28-Oct-2004. Assigned to Chromeon GmbH.

Inventor(s): Wolfbeis, Otto S.;

Abstract: The invention relates to **pyrrolo(3,4-c)pyrroles** which absorption maxima between 400 and 650 nm and are suitable in reactive form for labeling of proteins, nucleic acids and biol. receptors, in addn. to polymer particles. Their fluorescent quantum yields are without exception higher than 0.5.

The invention also relates to corresponding fluorescently labeled proteins, oligonucleotides, and particles. The labeled materials may be used in analytical methods, e.g., in immunoassays, in hybridization assays, in cytometry, and in pharmaceutical screening.



Other: Ger. Appl. 10317817.1 (16-Apr-2003). PCT Appl. PCT/EP2004/03990

(2004) Bioanalytical method for the determination of molecular interactions by phosphorescence decay measurement

Ger. Offen. (2004), DE 10308814 A1 20040909. Published 09-Sep-2004. Assigned to Chromeon GmbH.

Inventor(s): Wolfbeis, Otto S.; Duerkop, Axel

Abstract: The invention concerns the detection of interactions between natural and synthetic mols., receptors and ligands, or receptors and drug candidates, prodrugs by **(a) labeling one of the interacting mols. with a phosphorescent marker with luminescence decay times of 50 nanosec - 1 s; (b) contacting the two components; (c) illuminating the system briefly with light between 300-1000 nm; (d) after switching off**

the light source up to 200 % of the natural decay time of the luminophor is allowed for the noise to decay; (e) the luminescence decay is measured with known methods; (f) the changes in the luminescence decay time are related to the concn. of the binding partner. Phosphorescent markers are metal-ligand complexes, general protein stains, DNA- and RNA-interchelators. Binding mols. are proteins, antibodies, antigens, protein receptors, nucleic acids, synthetic ligands, prodrugs.
Other: PCT/EP 2004/001972

(2004) Substrate for gas and liquid sensors

Ger. Offen. (2004), DE 10255463 A1 20040609. Publ. on 09-Jun-2004. Assigned to Bosch GmbH.

Inventor(s): Brinz, Thomas; Lewis, Mary; Wolfbeis, Otto

Abstract: A substrate for an optical or electrical sensor for gases or vapors has a porous carrier layer to carry the sensitive layer. The porous layer is a sol-gel layer or a porous sintered layer which is applied into a sack hole, a through hole, or onto the surface of the substrate. The substrate can be used in the field of combinatorial chemistry.

(2004) Carbon dioxide sensor [Machine Translation].

From Ger. Offen. (2004), DE 10254841 A1 20040603. Publ. 03-Jun-2004. Assigned to Robert Bosch GmbH.

Inventor(s): Brinz, T.; Lewis, Mary; Wolfbeis, Otto; Apostolidis, A. ; Klimant, I.

Abstract: A sensor is introduced to the determination/regulation by carbon dioxide in gaseous or liquid media, with a sensor material, which contains a basic acceptor for the carbon dioxide. The basic acceptor is selected consisting of the group of inorganic or organic anions.

(2003) Synthesis of fluorophore pyrylium derivatives and use as label for amino group-containing biomolecules and polymer particles

U.S. Patent Application 10/287,450, filed September 18, 2003; and U.S. Patent Application 11/639,544, filed August 9, 2007. Assigned to Chromeon GmbH.

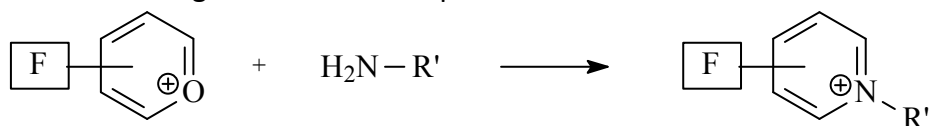
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<https://patents.google.com/patent/US20070184559A1/en>

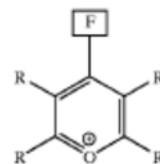
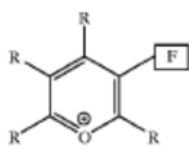
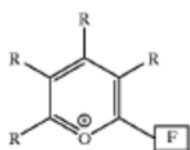
Other: DE 101 53 818.9 (Nov. 5, 2001); Eur. Pat. Appl. (2003) EP 1308728 A2 20030507

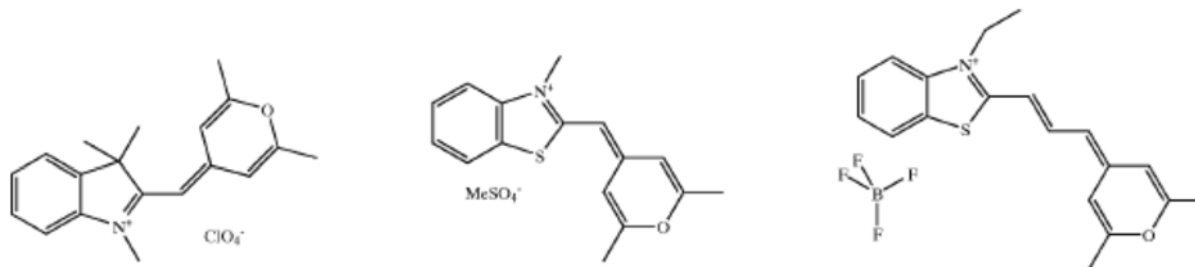
Inventor(s): Yarmoluk, S. M.; Kostenko, O. M.; Tolmachev, O. I.; Wolfbeis, O. S.

Abstract: The invention relates to a fluorescent label for bioorganic molecules carrying amino groups such as amino acids, proteins, pharmaceutical agents, antibodies, amino group-modified nucleotides and also polymers and polymer particles carrying amino groups by means of a chemical (covalent) binding. The method is based on the reaction of a pyrylium salt located on a fluorophore F with the amino group of a biomolecule or particle according to the reaction equation:



The method is selective, simple to carry out and results in high labelling yields. The spectral properties of the conjugates differ considerably from those of the starting compounds and their fluorescence quantum yields are often increased.





(2003) **Simultaneous optical determination of the pH-value and the dissolved oxygen content of a fluid**

PCT Int. Appl. (2003), WO 2003036293 A1 20030501. Publ. 01-May-2003. Assigned to Chromeon GmbH.

Inventor(s): Wolfbeis, Otto.

Abstract: The pH-value and the dissolved oxygen content of a soln. can be simultaneously detd. by optical methods, especially fluorometry. **A sensor matrix in the form of a film is used which consists of an org. polymer and contains at least two color indicators changing their color or their fluorescence properties depending on the pH or the concn. of dissolved oxygen of the solution.** The fluorometric methods can include the measurement of the fluorescence intensity, the time-resolved measurement of the fluorescence decay after pulsed excitation, measurement of the phase shift after frequency-modulated excitation, measurement of the efficiency of the radiative or non-radiative energy transfer from a donor dye to an acceptor dye, or gated fluorometry. The method can be used for the detn. of the pH-value and the dissolved oxygen concentration of serum or blood, in bioreactors, cell cultures, water, and wastewater.

(2003) **Optical-chemical sensor for chloride determination composed of luminescent indicator and polymer carrier**

U.S. Patent 6,613,282, issued September 2, 2003 and U.S. Patent 6,835,351, issued December 28, 2004.

Assigned to AVL List GmbH and F. Hoffmann La Roche AG.

Inventor(s): Huber, C.; Werner, T.; Wolfbeis, O. S.; Bell, D. E.; Young, C. H. S. T.

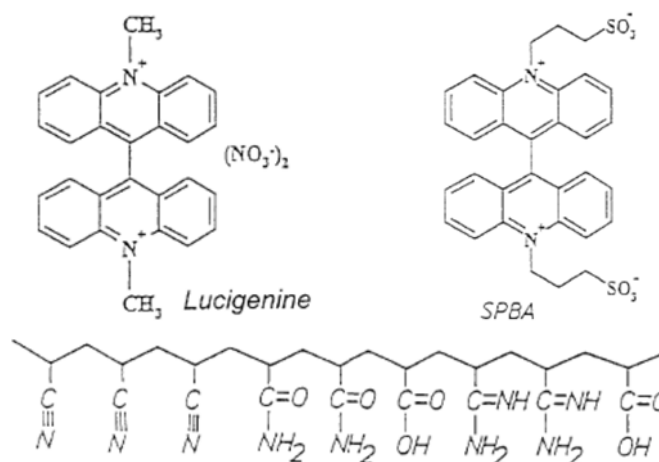
Web: <https://patents.google.com/patent/US6613282B2/en> and

<https://patents.google.com/patent/US6835351B2/en>

Other: PCT Int. Appl. (2000), WO 2000042438 A1 20000720.

Abstract: An optical-chemical sensor which is suitable for the continuous and discontinuous determination by luminescence optics of the **concentration of chloride** in an aqueous sample and which comprises a luminescence indicator (I) and a polymer (H) carrying the luminescence indicator (I) is characterized in that the **luminescence indicator (I) is a non-lipophilic acridine or bisacridine compound and the polymer (H) is a linear-chain hydrophilic polymer** soluble in an organic solvent.

It is possible to excite the sensor with commercially available LEDs, to manufacture very large numbers thereof at a moderate cost and in a reproducible way and, preferably, to use it for the determination of physiological chloride concentrations and the sensor furthermore has a wide dynamic analytical range for the determination of chloride; a high sensitivity, stability and reproducibility; a high selectivity for chloride; and a low pH cross-sensitivity.



(2002) Method for producing laterally organized structures on supporting surfaces

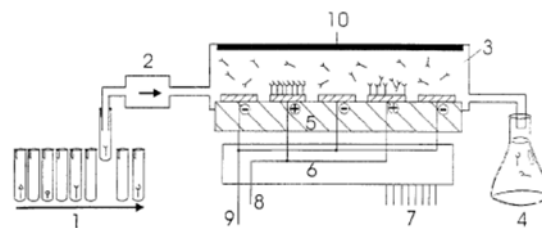
U.S. Patent 6,458,600. Issued 01-Oct-2002. Assigned to O. S. Wolfbeis

Web: <https://patents.google.com/patent/US6458600B1/en>

Inventors: Mirsky, V. M., Riepl M., Wolfbeis O. S.

Other: DE 1997151658

Abstract: The invention relates generally to (a) a structure on the surface of the support material of which structure molecular layers are immobilized so as to be electrically addressable, (b) **a method for the electrically addressable immobilization of molecules**, (c) a device for carrying out this method, and (d) the use of this structure as a chemo- and/or biosensor, in particular as a multisensor system for chemical, biological, and physical assays, and for applications in the **combinatorial synthesis** on the boundary surface.

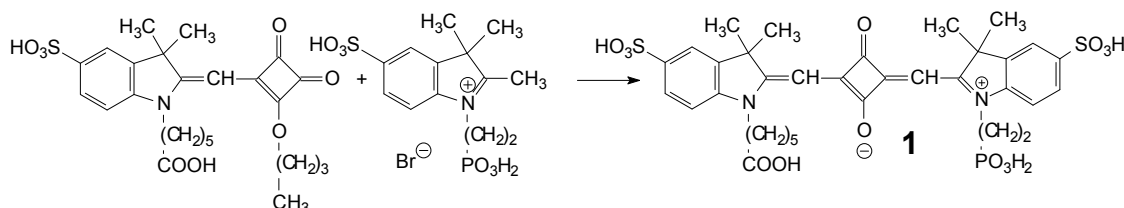


(2001) Methods for solubilizing optical markers

DE Appl. 19954934.6 (16-Nov-1999). WO 0136973 A2 (2001). Published 25-May-2001.

Inventors: Wolfbeis, O., Lehmann F., Arbter M.

Abstract: A method is described for **making labels better water-soluble by introducing phosphate groups into the label molecule**. An example is given here:

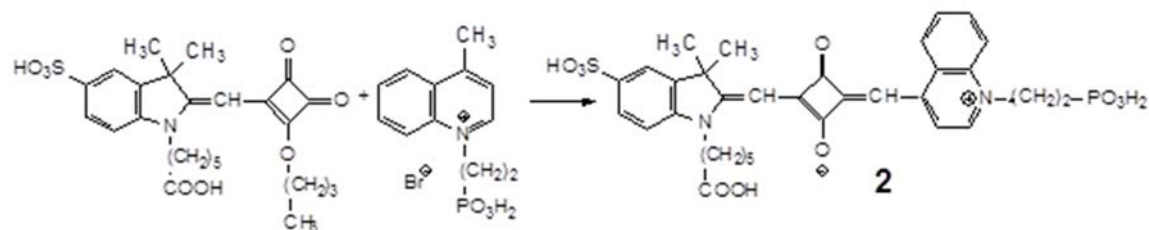


(2000) Pyridine dyes and quinoline polymethine dyes used as markers for biomolecules, polymers, medicinals, and particles

PCT Int. Appl. WO 2000034394 A2 20000615; and Ger. Offen. (2000), DE 19856152 A1 20000608. Publ. 15-Jun-2000. Assigned to Chromeon GmbH.

Inventor(s): Wolfbeis, O. S.; Probst, M.; Lehmann, F.

Abstract: **Pyridinium and quinolinium dyes of specified structure are useful in the title applications** and lack the drawbacks of known markers. **Water-soluble fluorescent markers are prepared from quaternized pyridine and quinoline derivatives**. Typical assay procedures are based on the reaction of marked antigens, antibodies or DNA segments with their resp. complementary species. Thus, I was prepd. in multiple steps from 4-methylquinoline, 6-bromohexanoic acid, 2-methylbenzothiazole, butane sultone, and diphenyl-formamidine, converted to its N-hydroxysuccinimide ester, and used in marking antibodies. An example is given below:



(2000) **Optical ion-sensor based on the coextraction of the analyte with a dye by an ionophore**

Eur. Pat. Appl. (2000), EP 973033 A1 20000119. Publ. 28-Aug-2002. Assigned to AVL Medical Instrum.

Inventor(s): Krause, C.; Huber, C.; Leiner, M. J. P.; Werner, T.; Wolfbeis, O. S.

Abstract: The invention concerns an **optical sensor for the detection of ions** that is composed of a hydrophilic surface with hydrophobic islets; ionophores are embedded in the hydrophobic islets; **dyes with opposite charge to the analyte are immobilized onto the hydrophilic surface; upon contacting the hydrophilic surface, the analyte ions are coextracted with the dye-counterions by the ionophore into the hydrophobic islets**; the fluorescence of the dye undergoes changes, thus forming a signal. Alkali metals, alkaline earth metals and chloride can be detected using the sensor. Hydrophobic islets are formed from plasticizers, high boiling-point org. solvents, and stabilized with a detergent. Multi-block copolymers are also used. These are composed of hydrophilic and lipophilic segments.

(2000) **Sensor membrane of an optical sensor**

U.S. Patent 6,139,798, issued October 31, 2000. Assigned to AVL Medical Instrum. AG and Roche Diagnostics.

Web: <https://patents.google.com/patent/US6139798A/en>

Inventors: Klimant, I., Karpf H., Wolfbeis O. S.

Other: Eur. Pat. Appl. (1994) EP 585212 A2; issued on 02.03.1994.

Abstract: The sensor membrane of an optical sensor for detection of oxygen, H₂O₂, SO₂ or halogenated hydrocarbons in a sample contains an indicator substance that is homogeneously immobilized in the polymer matrix of the sensor membrane and is, at least indirectly, in contact with the sample, changing at least one of its optical properties upon a change of the parameter to be measured. **The indicator substance contains an inorganic salt of a transition metal complex with α -diimine ligands. Metal complexes include those of Ru, OS, Ir, Rh, Pd, Pt and Re.** The indicator substance is homogeneously distributed in the polymer matrix, which essentially consists of at least one substance belonging to the group of cellulose derivatives, polystyrenes, polytetrahydrofuranes, or their respective derivatives.

(1999) **Luminescence indicator including ionophoric moiety**

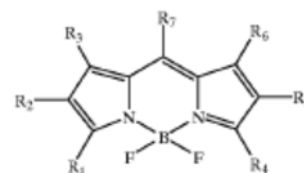
U.S. Patent Application US5981746A and US Patent 6,001,999, issued December 14, 1999. Assigned to Roche Diagnostics Corp.

Inventors: Wolfbeis, O. S.; Daub, J.; Gareis, T.; Kollmannsberger, M.; Heinel, S.; Werner, T.; Huber, C.; Boila-Gockel, A.; Leiner, M. J.-P.

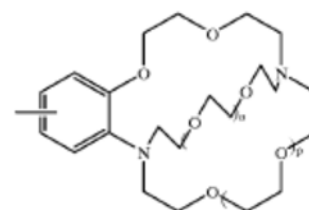
Web: <https://patents.google.com/patent/US5981746A/en> and <https://patents.google.com/patent/US6001999A/en>

Other: Eur. Pat. Appl. (1998), EP 881225 A2 19981202.

Abstract: **Indicators** are claimed which are described by the general formula I (**where one of R₁₋₇ is an ionophore** while the others are independently selected from H, lipophilic groups, hydrophilic groups, or reactive groups for coupling to a polymer or a biomolecule, or R₂ and R₃ can couple together to form an aromatic ring system and R₅ and R₆ can also form an aromatic ring system). The ionophore is preferably a diaza cryptand (see formula). Use as indicators, especially for the determination of pH values and alkali metal cations in aqueous solution, is indicated.



I



(1999) **Luminescence optical method and sensor layer for the quantitative determination of at least one chemical component of a gaseous or liquid sample**

U.S. Patent 5,942,189, issued August 24, 1999 and U.S. Patent No. 6,046,055. Issued 4 Apr. 2000. Assigned to AVL Medical Instruments AG.

Web: <https://patents.google.com/patent/US5942189A/en> and

<https://patents.google.com/patent/US6046055A/en>

Inventor(s): Wolfbeis, O. S.; Werner, T.; Klimant, I.; Kosch, U.; Leiner, M. J.-P.

Other: Eur. Pat. Appl. (1998), EP 837327 A1 19980422.

Abstract: In a sensor layer for quantitative determination of at least one chemical component in a gaseous or liquid sample medium containing (a) a chromophore which is directly or indirectly responsive to the component being determined by changing its absorption spectrum, and (b) a luminophore which is not responsive to the component being determined, where there is an at least partial overlap between the emission spectrum of the luminophore and the absorption spectrum of the chromophore, and where the energy transfer between luminophore and chromophore produces a measurable change in at least one luminescence characteristic of the luminophore. The luminophore L and the chromophore Γ are ionic substances with differing electrical charges, which are incorporated in a matrix material that is permeable to the chemical component being determined. Examples are given for sensor layers sensitive to the determination of pH, CO₂ partial pressure, Cl⁻, and K⁺.

pH-sensitive Chromophores

Chromophore	Absorption wavelength [nm] protonated/deprotonated	pKa
<u>Triphenylmethane dyes</u>		
Bromophenol blue	430/617	3.8
Bromothymol blue	430–435/615–618	6.7
Dibromoxylene blue	420/614	7.6
<u>Azo dyes</u>		
Calmagite	530/605	8.0
Nitrazine yellow	460/590	6.5
<u>Others</u>		
o-chlorophenol-indophenol	555/625	7.1
Naphthol-phthalein	428/661	6.7, 7.9

Inert luminophores that undergo energy transfer:

Cationic Luminophores

Luminophore (L)	Abbrev.	Absorption maximum (nm)	Luminescence maximum (nm)
[(Ru(II)-tris-(2,2'-bipyridyl)] ²⁺	Ru(bpy) ₃ ²⁺	452	628
[(Ru(II)-tris-(4,4'-diphenyl-2,2'-bipyridyl)] ²⁺	Ru(dph-bpy) ₃ ²⁺	474	632
[(Ru(II)-tris-(1,10-phenanthroline)] ²⁺	Ru(phen) ₃ ²⁺	447	604
[(Os(II)-bis-(terpyridine)] ²⁺		510	729
[(Os(II)-tris-(1,10-phenanthroline)] ²⁺		650	690

(1998) **Sensor membrane for indicating the pH of a sample, the fabrication and use thereof.**

U.S. Patent 5,853,669, issued December 29, 1998. Assigned to Joanneum Research and Merck Patent GmbH.

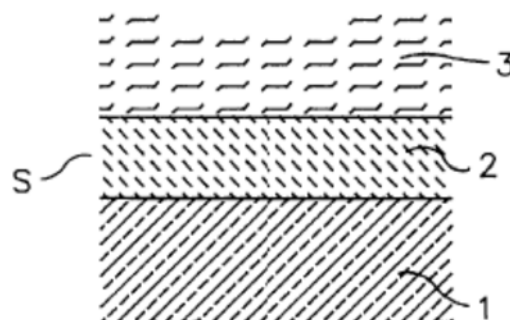
Web: <https://patents.google.com/patent/US5853669A/en>

Inventor: Wolfbeis, O. S.

Other: WO1993007483A1; PCT/EP1992/002245, Eur. Pat. EP9202245W; WO9307483A1. Web:

<https://patents.google.com/patent/WO1993007483A1/en%20US4325121.pdf>. The USP is a continuation of the application Ser. No. 08/211,272, filed Mar. 29, 1994.

Abstract: For the purpose of reversible optical indication of the pH value of a sample, a hydrophilic accommodating layer is disposed on a hydrophobic mechanically stable support element, which layer contains the indicator dye proper in an immobilized form. This provides a sensor membrane which can be fabricated in a simple manner and is cost-effective, which has a rapid response time and can also be fabricated as a mass product to be used only once.



(1995) Optical chemical sensors based on enzyme inhibition

PCT Int. Appl. (1995), WO 9520051 A1 19950727.

Inventor(s): Wolfbeis, Otto S.; Klainer, Stanley M.

Abstract: An optical sensor for detecting a first species, comprises an optical sensor which produces and optical signal which varies as a function of concentration of a second species, a chem. substrate, and an enzyme which acts on the chem. substrate to produce the 2nd species and which is inhibited by the 1st species acting on the substrate to produce the 2nd species. Further, a method for detecting a 1st species, comprises exposing a chem. substrate to an agent which acts on the substrate to produce a 2nd species and which is inhibited by the 1st species from acting on the substrate to produce the 2nd species, optically detecting changes in concn. of the 2nd species, and detg. changes in the 1st species from detected changes in the 2nd species.

(1995) Microbial optical sensors and methods

PCT Int. Appl. (1995), WO 9516052 A1 19950615. Publ. 27-Jul-1995. Assigned to FiberChem Inc. (Las Vegas).

Inventor(s): Wolfbeis, O. S.; Klainer, S. M.

Abstract: A method and app. for measuring a variety of analytes is based on a biological cell culture, e.g., yeast, bacteria or combinations thereof, and an optical chemical sensor with a species-sensitive indicator. Oxygen and carbon dioxide chemical sensors using yeast and *Methylomonas flagellata*, resp., are examples of sensors for measuring biochemical oxygen demand and methane. The yeast metabolizes org. matter in a sample and consumes oxygen. The decrease in oxygen produces a measurable increase in signal from the oxygen detector by suppression of quenching of fluorescence of the oxygen sensitive indicator. The signal from the oxygen sensor can be used for quantifying BOD. The *M. flagellata* reacts with methane to yield CO₂ which is measured by the carbon dioxide sensor. The signal from the carbon dioxide sensor can be related to methane concentration.

(1995) Method for quality control of packaged organic substances and packaging material for use with this method

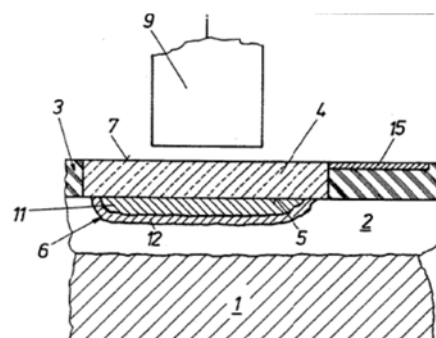
U.S. Patent 5407829, issued April 18, 1995. Assigned to AVL Medical Instruments AG.

Web: <https://patents.google.com/patent/US5407829A/en>

Inventor(s): Wolfbeis, O. S.; List, H.

Other: Eur. Pat. EP 449798 A2 19911002. Jap. Pat. JP 04215929

Abstract: For quality control of packaged org. substances, preferably packaged foods and drugs, the materials to be examined are brought into contact with a planar optical sensor element which is applied on the inside of the wrapping and responds to a change in the gas compound in the gas space above the sample by a change in color or fluorescence. The change of one of the optical properties of the sensor element is detected visually or opto-electronically.



(1994) Ion-selective fluorosensor based on the inner filter effect

PCT Int. Appl. (1994), WO 9417388 A1 19940804. Publ. 04-Aug-1994. Assigned to FiberChem. Inc. (Las Vegas).

Inventor(s): Wolfbeis, Otto S.

Abstract: An ion selective optical chemical sensor makes use of a primary absorber dye whose color changes with the analyte concn., and a fluorophore whose excitation and/or emission is modulated by the

changing absorption of the dye. In a membrane an ion carrier captures target ions from a soln. Through charge exchange or co-extraction the absorber changes its absorption characteristics and acts as an inner filter. The sensing scheme provides high flexibility in the selection of dyes and results in detection limits of around 1 μmol . The preferred absorber dye is 4-(2',4'-dinitrobenzeneazo)-2-octadecylaminocarbonyl-1-naphthol.

(1994) Sensor membrane of an optical sensor for the determination of a physical or chemical parameter of a sample

Eur. Pat. Appl. (1994), EP 578630 A1 19940112. Issued 21-Feb-1996. Assigned to AVL Medical Instrum. AG. .
Inventor(s): Klimant, I.; Wolfbeis, O. S.; Leiner, M. J.-P.; Karpf, H. ; Kovacs, B.

Abstract: In a sensor membrane containing an **indicator homogeneously immobilized in a polymer matrix, comprising a cationic or anionic dye mol. and >1 counter ion, the counter ion is derived from a compd. which contains an ionic group and (a) an oligomeric residue of the monomer forming the polymer matrix; (b) long-chain alkyl or alkylene groups; or (c) silyl groups;** the counter ion has phys.-chem. properties matching those of the polymer matrix, and the dye mol. is coupled to the polymer matrix by the counter ion.

(1994) Method for the determination of the concentration of an enzyme substrate and a sensor for carrying out the method

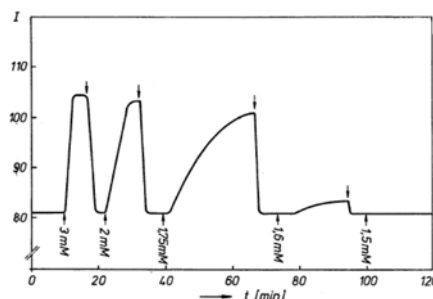
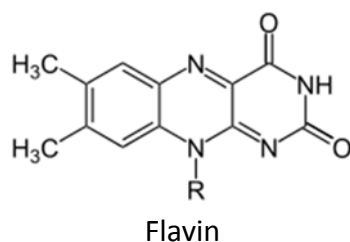
U.S. Patent No. 5,340,722. Issued 23 Aug. 1994. Assigned to AVL Medical Instruments AG.

Web: <https://patents.google.com/patent/US5340722A/en>

Inventor(s): Wolfbeis, Otto S.; Trettnak, Wolfgang

Other: Eur. Pat. Appl. (1990), EP 356418 A2 19900228.

Abstract: An **enzyme substrate is determined by reaction with an oxidase or oxygenase having a bound flavin coenzyme (FAD; FMN)** which is reduced by the substrate and reoxidized by dissolved O_2 , and measurement of the **change in fluorescence of the flavin**. The enzyme may be immobilized in a membrane-covered gel or on the surface of a transport optical sensor, e.g. a plastic fiber-optic device for in vivo monitoring. Preferred embodiments of the apparatus are described with schematic diagrams. Thus, a carrier with a cavity containing flavin-dependent glucose oxidase solution was covered with an enzyme-impermeable membrane for detn. of glucose in an O_2 -saturated solution.



(1993) Method for optical determination of the catalytic enzyme activity and arrangement for implementing this method (chromogenic enzyme substrate placed at the tip of an optical fiber)

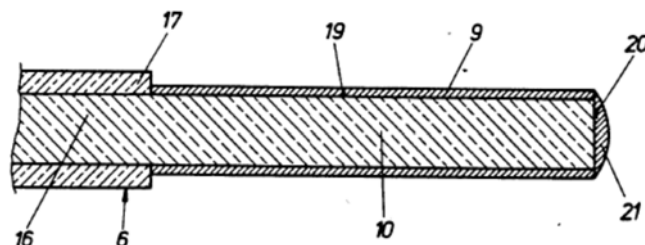
U.S. Patent 5,238,809, issued August 24, 1993. Assigned to AVL Medical Instruments (Switzerland).

Web: <https://patents.google.com/patent/US5238809A/en>

Inventor: Wolfbeis, O. S.

Abstract: For optical **determination of the catalytic enzyme activity** of a sample by means of enzyme reactants which are split under the influence of the enzyme to be measured, the enzyme reactant (**an enzyme substrate**) is placed at the end of an **optical fiber** and brought into contact with the sample to be determined.

The measurements are carried out by **observing the rate of change in spectral characteristics of the enzyme substrate**, or its reaction products, resulting from the enzyme reaction. The method permits measurements of undiluted blood and in-vivo determinations of enzyme activities.



(1993) **Method for quantitative determination of at least one chemical parameter of a sample medium**

(luminescence energy transfer and lifetime method)

U.S. Patent 5,232,858, issued August 3, 1993. Assigned to AVL Medical Instruments AG.

Web: <https://patents.google.com/patent/US5232858A/en>

Inventors: Wolfbeis, O. S., Leiner, M. J. P.

Abstract: A method for the quantitative determination of one or more chemical parameters of a sample medium employs a fluorescent agent which is not responsive to the parameter to be determined and which has an excitation spectrum and an emission spectrum, and a closely adjacent chromogenic agent which responds to the parameter of the sample medium to be determined by a change in its absorption spectrum the emission spectrum of the fluorescent agent at least partially overlapping the absorption spectrum of the chromogenic agent.

Fluorescent substance (donor)	Chromogenic substance (receptor)	Measuring wavelength (nm)	Chemical parameter
7-diethylamino-coumarin-3-carboxylic acid	methyl orange	480	H ⁺
8-aminopyrene-1,3,6-trisulphonate	phenol red	490	H ⁺
rhodamine 101	alizarin complexon	590	Ba ²⁺
rhodamine 6G	beryllone	570	Mg ²⁺
2,7-dichloro-fluorescein	catechol violet	540	Cd ²⁺
fluorescein	chrome azurol S	520	Al ³⁺
coumarin 7	eriochrome black T	485	Ca ²⁺ , Pb ²⁺
coumarin 343	murexide	450	Cu ²⁺
coumarin 334	zincone	440	Zn ²⁺

The absorption maximum of chromogenic agent is shifted in accordance with the parameter to be determined, causing a reduction of fluorescence decay time in the fluorescent agent, thereby enabling quantitative determination of the chemical parameter with improved long-term stability and infrequent calibrations.

(1993) **Method for detection and determination of human serum albumin**

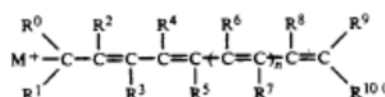
U.S. Patent 5,182,214, issued January 26, 1993. Assigned to Inventors.

Web: <https://patents.google.com/patent/US5182214/en>

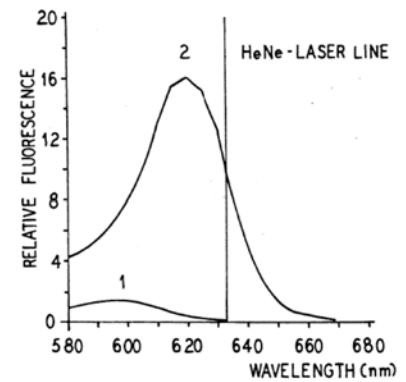
Inventor(s): Kessler, M.; Wolfbeis, O. S.

Other: Eur. Pat. Appl. (1991), EP 413678 A2 19910220.

Abstract: An optical method for quantitative determination of human serum albumin (HSA) in biological liquids such as urine is based on the observation that the absorption and fluorescence of certain anionic cyanine dyes possessing a terminal cyano group and having the general formula



are strongly affected by HSA. This approach is distinctly more sensitive than existing techniques, allowing the detection and quantization of micro-albuminuria (i.e. detection of HSA in the 1-10 mg per liter concentration range) at costs which are distinctly lower than those for existing immunological assays. It is also much more specific for HSA than existing assays based on dye binding. Because the dyes has long wave absorptions and emissions, use can be made of electro-optical components based on semiconductor technology.



(1992) **One-way measuring element** (microfluidic disposable device with integrated sensors)

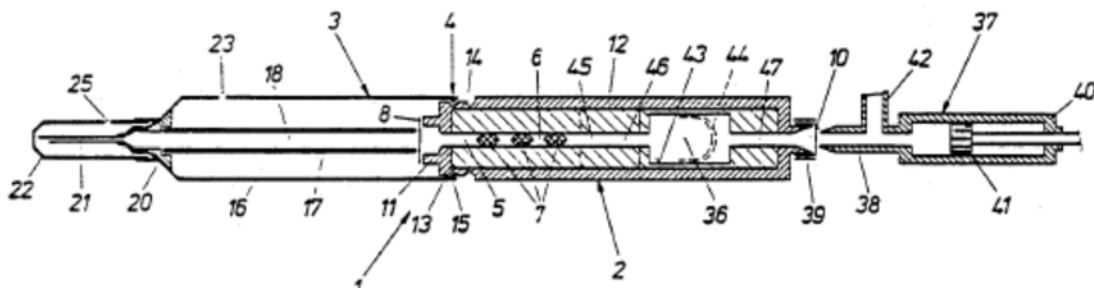
U.S. Patent 5,080,865. Issued January 14, 1992. Assigned to AVL AG.

Web: <https://patents.google.com/patent/US5080865A/en>.

Inventors: Leiner, M. J.-P.; Harnoncourt, K.; Kirchmayer, G.; Kleinhapfl, E.; List, H.; Marsoner, H.; Wolfbeis, O. S.; Ziegler, W. E.;

Other: Eur. Pat. Appl. (1990), EP 354895 A2 19900214.

Abstract: In order to improve a one-way sensing element, which may be inserted into an analyzer for analyzing gaseous or liquid samples and which comprises a measuring channel with a measuring zone and one or more sensors located therein, the proposal is put forward that the one-way measuring element be provided with a sensor part whose measuring channel has seals on both ends, and with a sample-taking part, and that a coupling element be placed at the inlet end of the measuring channel for direct coupling of the sample-taking part containing the gaseous or liquid sample, and that the measuring channel be filled with a calibrating and storage medium prior to the measuring process, and that the calibrating and storage medium contained in the measuring channel be displaced by the sample flowing in after the sample-taking part has been coupled to the sensor part. The one-way measuring elements obtained in this way are characterized by great simplicity of design and ease of handling.



(1992) **Optical sensor for determining at least one parameter in a liquid or gaseous sample with an immobilized fluorescence indicator, and process for its production** (sensor using microparticles as carriers for indicators)

U.S. Patent 5,114,676, issued May 19, 1992. Assigned to AVL AG.

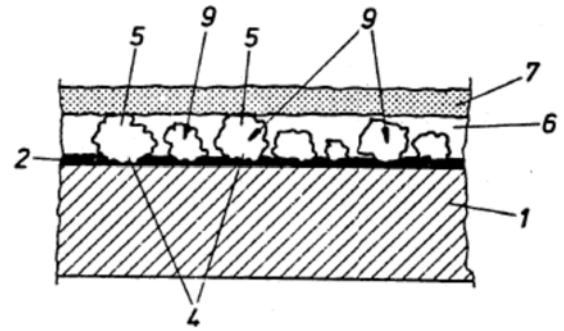
Web: <https://patents.google.com/patent/US5114676A/en>

Inventor(s): Leiner, M. J. P.; Weis, L.; Wolfbeis, O. S.

Other: Eur. Pat. Appl. (1990), EP 354204 A2 19900207.

Abstract: In order to improve the response behavior of an optical sensor for determining at least one parameter in a liquid or gaseous sample, the sensor including a substrate which is provided with carrier particles and a fluorescent indicator immobilized thereon, the substrate is configured as a polymer film transparent to both excitation and emission radiation, and the individual carrier particles carrying the fluorescent indicator in immobilized form are bonded with only part of their surface to a thin layer of

a thermoplastic material adhering to the polymer film and assume thermosetting properties after the carrier particles have been pressed in, whereas the other part of the surface of the carrier particles extend into an optically transparent hydrogel layer which covers the thermoplastic layer and in which the carrier particles are anchored mechanically. Such sensors may easily be attached to the end of an optical waveguide and may be made in any size by a simple punching operation.



(1992) Sensor element for optical determination of substances in gaseous or liquid samples

U.S. Patent 5,039,490 and US Patent 5,157,262, issued October 20, 1992. Assigned to AVL Medical Instrum.

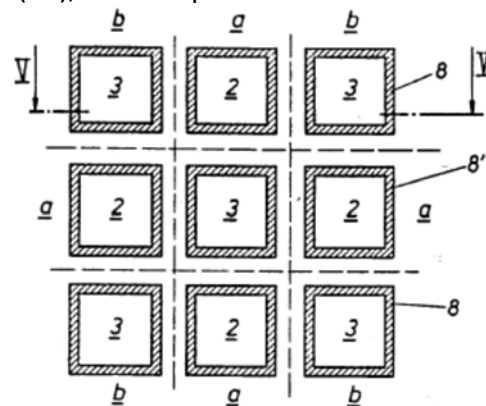
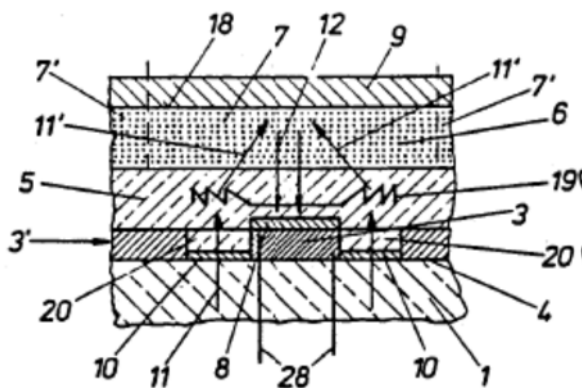
Web: <https://patents.google.com/patent/US5157262A/en> and

<https://patents.google.com/patent/US5039490A/en>

Inventor(s): Marsoner, H.; Kroneis, H.; Karpf, H.; Wolfbeis, O.; List, H.; Leitner, A.

Other: DE4A1094/86 and AT0109486A; Eur. Pat. Appl. (1987), EP 244394 A2 19871104,

Abstract: Due to the size of the devices used for the excitation and measuring of light, conventional sensor elements for optically determining the concentrations of substances contained in gaseous and liquid samples, featuring an indicator layer with one or more indicator substances, are not well suited for use with microanalysis equipment, nor are they easy to mass-produce. These disadvantages are eliminated by integrating on the carrier layer (1) at least one photosensitive element (3) and its electric contact leads in planar arrangement, and by establishing optical contact between the indicator substance (7, 7') of the indicator layer (6) stimulated by the excitation radiation (11), and the photosensitive elements (3).



(1992) Process for the quantitative determination of at least one parameter of a liquid or gaseous sample

U.S. Patent 5,108,932, issued April 28, 1992 to AVL AG.

Web: <https://patents.google.com/patent/US5108932A/en>

Inventor: Wolfbeis, Otto S.

Other: Eur. Pat. Appl. (1990), EP 357586 A2 19900307

Abstract: For the simultaneous **measurement of two parameters** of a liquid or gaseous sample, in a fluorescence measuring device in which the influence of the aging processes of the indicator substance and the fluctuations in the light intensity of the excitation light source are to be avoided, it is proposed that the change in the **first parameter** to be measured is obtained from the change in the ratio of two intensity values, determined for different wavelengths of the excitation and emission spectrum of the indicator substance, and the change of a **second parameter** is obtained from the change in the decay time t of the fluorescence radiation of the same indicator substance from the group of aromatic hydrocarbons, the aromatic heterocycles and the metal organic complexes.

(1990) Sensor for the determination of electrolyte concentrations

U.S. Patent 4,892,640, issued January 9, 1990 to AVL AG.

Web: <https://patents.google.com/patent/US4892640A/en>

Inventors: Wolfbeis, O. S., Braun P. (= Hochmuth, Petra)

Other: Eur. Pat. Appl. (1986), EP 198815 A2 19861022,

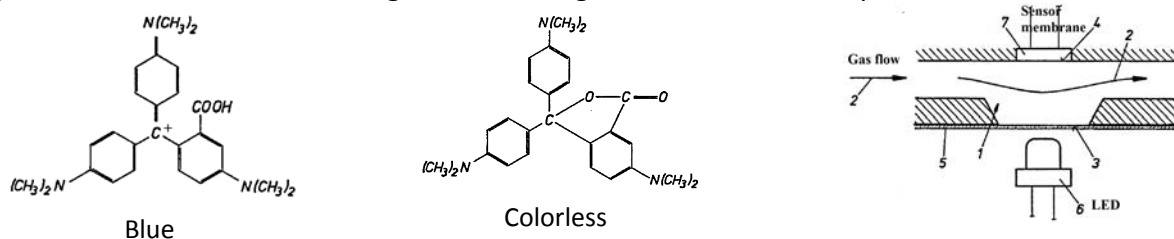
Abstract: An ion-selective sensor for determining an electrolyte concentration in an aqueous solution includes an ion-selective layer and a **potential-sensitive fluorescent indicator** in the ion-selective layer, the fluorescence intensity of the potential-sensitive fluorescent indicator being measured to provide an indication of the electrolyte concentration.

(1990) Method for determination of solvent vapor using an o-carboxytriphenylmethane color-forming agent

Austrian Patent AT 391759 B 19901126. Issued 1990. Assigned to inventors.

Inventor(s): Wolfbeis, O. S.; Koller, E.

Abstract: **Vapors of polar solvents** (such as of Et₂O, THF, AcOEt, etc.) in a carrier gas (e.g., air) can be continuously and reversibly detected by contacting the gas sample with the color-forming agent. The device consists of a thin optically transparent **test strip coated with the color-forming agent** (for formulas see below) for a color reaction, an LED light source, a light detector, and an opto-electronic unit.



(1990) Fluorophore-chromophore spectrochemical method for determining a chemical parameter of a sample

Eur. Pat. Appl. (1990), EP 397641 A2 19901114. Publ. 14-Nov-1990. Assigned to AVL Med. Instrum. GmbH.

Inventor(s): Leiner, Marco Jean Pierre; Wolfbeis, Otto S.;

Abstract: A method is described, where 2 substances in close contact are used, the 1st substance a fluorophore not responding to the analyte parameter with an excitation and emission spectra and the 2nd substance a material reacting to the analyte parameter of the sample medium by changing its absorption spectrum. **The emission spectrum of the fluorophore overlaps with the absorption spectrum of the 2nd substance.** To improve the long-term stability and to avoid frequent calibrations, the absorption max. is shifted relative to the analyte parameter and by the **energy transfer (FRET) between the chromophore and fluorophore**, a **decrease is produced in the fluorescence decay time** in the determination of the chemical parameter of interest.

(1990) Sensor element with enlarged surface for fluorescence-optical analysis

U.S. Patent 4,965,087, issued October 23, 1990. Assigned to AVL AG, Schaffhausen (CH).

Web: <https://patents.google.com/patent/US4965087A/en>

Inventor(s): Kroneis, H.; Offenbacher, H.; Wolfbeis, O. S.

Other: Ger. Offen. (1984), DE 3343636 A1 19840607

Abstract: A sensor element useful in making measurements of pH or oxygen and other analytes includes a **substrate having a carrier surface, particles having a large specific surface area which are glued, melted or**

sintered onto the carrier surface so as to provide small elevations of a regular distribution on the carrier surface, and an indicator substance immobilized on the particles. Additional substances can be applied to the particles to reduce undesirable influences of properties of the sample on the indicator substance.

(1989) Method for continuous quantitative detection of sulfur dioxide and an arrangement for implementing this method

U.S. Patent 4,857,472. Issued August 15, 1989. Assigned to AVL AG (Schaffhausen, Switzerland).

Web: <https://patents.google.com/patent/US4857472A/en>

Inventor: Wolfbeis, Otto S.

Abstract: In order to obtain a higher measuring accuracy and better selectivity in the optical quantitative analysis of sulphur dioxide in gaseous or liquid media, it is proposed that the medium to be analyzed be brought into contact with a fluorescent indicator which emits fluorescent light upon excitation and which is from the group of **triphenylmethane dyes, and that the extent to which fluorescence is quenched by the SO₂ quencher** be used as a measurable variable for quantitative determination of the content of sulfur dioxide in the medium.

(1989) Pyrenesulfonic acids useful in fluorescent lipid probes

U.S. Patent 4,844,841, issued July 4, 1989. Assigned to *Inventors*.

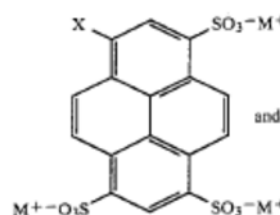
Web: <https://patents.google.com/patent/US4844841A/en>

Inventor(s): Koller, Ernst; Wolfbeis, Otto S.

Abstract: Compounds of the formula on the right wherein

- X is long-chain alkyloxy, long-chain alkylamino or long-chain dialkylamino,
- M is alkali metal, pyridinium or ammonium.

They are especially useful in photometric and fluorimetric investigations of lipids and lipid-water interactions and of cationic biomolecules such as nicotine adenine dinucleotide.

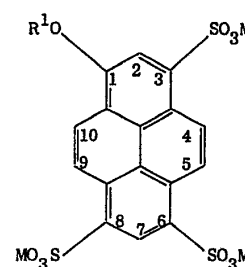


(1988) Preparation of pyrenesulfonic acid derivatives for photometric determination of enzyme activity

Austrian Pat. AT 385755 B 19880510. Publ. 10-May-1988. Assigned to inventors.

Inventors: E. Koller O. S. Wolfbeis

Abstract: Title compounds (where M = alkali or alk. earth metal or pyridinium; R¹ = acyl) are prep'd. for use in **photometric determination of esterase enzyme activity**. In a typical method for preparing a butyryl ester, a mixture of 5.2 g I (R¹ = H, M = Na) in DMSO solution is treated with 4.7 g butyric anhydride over 10 h at room temp. to give 89% I (R¹ = CH₃-CH₂-CH₂-CO-). Lipase activity was measured photometrically using I (R¹ = n-C₁₅H₃₁CO; M = Na).



(1988) Instrument for determining halides and pseudohalides using a fluorescent indicator, and a method for producing the sensor element for this arrangement

Austrian Pat. AT 384891 B 19880125 (1988). Publ. 25-Jan-1988. Assigned to AVL Medical Instrum.

Other: Later to become U.S. Patent 6,613,282.

Inventor(s): Urbano, Edmund; Wolfbeis, Otto S.; Offenbacher, Helmut

Abstract: A fluorescence-optical indicator is brought into contact with the sample, the indicator fluoresces after stimulation by an excitation light source in relation to the halide concn., and the arrangement

measures and evaluates the fluorescent light. This indicator, contained in a superficial sensor element brought into contact with the sample, is selected from a group of (hetero)arom., polycyclic compds. and polyene dyes specifically in cationic form, where the **indicator is covalently bonded onto the surface of a solid support** in thin layers, and spacer groups are positioned between the support and the indicator mols. **The fluorescence of the indicator is quenched by halides. The indicator may be quinine, 6-methoxyquinoline, acridine, quinazoline, acridizine, and harman**, while the support material may be an org. polymer such as poly(meth)acrylate, poly(meth)acrylamide, polyacrylonitrile, polystyrene, cellulose, or glass.

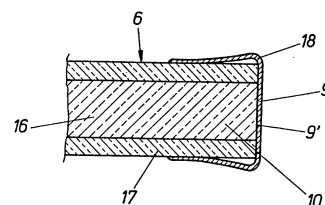
(1987) Optical determination of enzyme activity: use of fiber optic-immobilized substrate

Ger. Offen. (1987), DE 3701833 A1 19870806.

Inventor(s): Wolfbeis, Otto S.

Abstract: A method for optical determination of enzyme activity comprises localization of the enzyme substrate at the end of a fiber optic cable, e.g. by immobilization on a membrane covering the end of the cable, and measuring spectral changes which occur when the cable-substrate device is brought into contact with the (enzyme-containing) sample to be analyzed.

A carboxylate group-containing coumarin derivative which is a substrate for butyryl cholinesterase was immobilized in the form of a film (9) on the surface of aminopropyl triethoxysilane-treated fiber optic (10, 16). When this end of the fiber was brought into contact with a sample contg. the enzyme, an increase in light absorption of 410-430 nm and an increase in fluorescence intensity at 460-470 nm occurred.



(1987) Determination of a material, specifically oxygen, contained in substance by using a luminescence indicator

Ger. Offen. (1987), DE 3702210 A1 19870730. Publ. 30-Jul-1987. Assigned to AVL AG. (Switz.)

Inventor(s): Wolfbeis, Otto S.

Abstract: A method is described where the luminescence intensity of the analyte is diminished or quenched and, to avoid problems with photodecomposition and fluctuation of indicator concentration, **the decay time t of the luminescence is measured using a luminescence indicator coming in contact with the analyte**, and the concn. of the analyte is detd. from the known or, esp. determined decay time t_0 of the unquenched luminescence indicator. Therefore, the measurement of indicator concn. and the measurement of false light components are unrelated.

(1987) Method for determining ionic strength of a sample

U.S. Patent 4,716,118, issued December 29, 1987. Assigned to AVL AG, Schaffhausen (CH).

Web: <https://patents.google.com/patent/US4716118A/en>

Inventors: Wolfbeis, Otto S.; Offenbacher, Helmut

Other: Ger. Offen. (1985), DE 3430935 A1 19850314.

Abstract: A method and apparatus are described for detg. the ionic strength of an electrolyte soln. by measuring the pH of the soln. **The apparatus contains 2 optical pH sensors having the same indicator material but different surface modification so that they respond in a different way to the ionic strength of the electrolyte.** An empirical value relating to the ionic strength is obtained from the difference of the responses of the 2 sensors. The pH sensors are prepd. by immobilization of a fluorescence indicator substance on the surface of a glass substrate. The pH value obtained is related to the ionic strength of the soln. The technique was illustrated on a pH fluorescence sensor based on 7-hydroxycoumarin-3-carboxylic acid.

(1987) Chromogenic and fluorogenic esters for photometric or fluorimetric determination of phosphatases or sulfatases

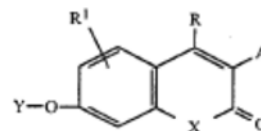
U.S. Patent 4,659,657. Issued April 21, 1987. Assigned to Bayer AG.

Web: <https://patents.google.com/patent/US4659657A/en>

Inventors: Harnisch, H., Wolfbeis O. S.,

Other: Ger. Offen. (1984), DE 3248043 A1; UK Pat. Appl. (1984), GB 2133007 A 19840718.

Abstract: The present invention relates to new **chromogenic and fluorogenic phosphoric acid esters and sulphuric acid esters of the formula shown (Y = phosphate or sulfate)**. These are colorless but form highly fluorescent colored anions under the influence of phosphatases or, respectively, sulphatases and can be used for an improved photometric or fluorimetric determination of phosphatases and sulfatases.



(1987) Sensor element for determining the oxygen content and a method of preparing the same

U.S. Patent 4,657,736, issued April 14, 1987. Assigned to AVL AG.

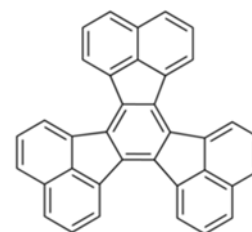
Web: <https://patents.google.com/patent/US4657736A/en>

Inventor(s): Marsoner, Hermann; Kroneis, Herbert; Wolfbeis, Otto

Abstract: In an oxygen sensor element which contains a fluorescent indicator substance, a polymerized silicone polymer is used as a carrier material in which the indicator substance is incorporated in solubilized form and in an at least approximately homogeneous distribution. **Solubilization of the indicator substance may essentially be performed in analogy to Friedel-Crafts alkylation of aromatics, which will increase solubility of the indicator substance in the polymer carrier without affecting quenching behavior. The introduction of tertiary butyl groups into aromatic compounds such as decacylene (see formula) is a preferred method. The resulting decacylene carries up to 6 tertiary butyl groups.**

To make a sensor layer, 0.2 g solubilized decacylene is dissolved in 10 g silicone rubber, the soln. is spread to a thickness of ~20 µm. Then another soln. of decacylene and silicone rubber, this time contg. Fe oxide, is spread over the hardened layer to a thickness of 20 µm. After vulcanization, the sensor is ready for use.

Other: Eur. Pat. Appl. (1984), EP 109959 A2 19840530.



(1986) Method for fluorometric determination of the concentrations of substances in a sample and arrangement for implementing this method

U.S. Patent 4,580,059. Issued April 1, 1986. Assigned to AVL AG.

Web: <https://patents.google.com/patent/US4580059A/en>

Web: <https://patents.google.com/patent/AT390840B/en-20US4325121.pdf>

Inventor(s): Wolfbeis, O.; Urbano, E.

Abstract: For the simultaneous measurement of the concentrations of several substances a number of fluorescence measurements corresponding to the number of substances to be tested are performed using at least one fluorescent indicator which is non-specific relative to at least one of the substances to be tested, **each fluorescent indicator having different quenching constants with regard to the individual substances quenching its intensities.** From the known unquenched fluorescence intensities of the fluorescent indicators employed, the quenched fluorescence intensities obtained by measuring, and from the quenching constants that are known, or rather, have been determined beforehand by graphical methods or calculation, the concentrations and/or concentration ratios of the individual substances are

obtained. The technique was illustrated by the simultaneous detn. of Cl-, Br-, and I- by using quinine, acridine, and harman as the fluorescent indicators, resp.; and by the simultaneous determination of oxygen and halothane in anesthesia gas.

Other: Ger. Offen. (1984), DE 3420947 A1 19841213. Priority: Austria AT390840B

(1986) Sensor element for fluorescence-optical measurement using an interpenetrating network

U.S. Patent 4,568,518. Issued February 4, 1986. Assigned to AVL AG.

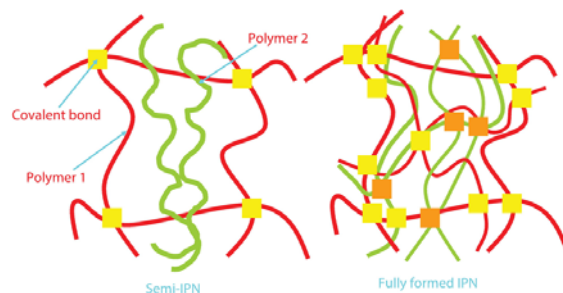
Web: <https://patents.google.com/patent/US4568518A/en>

Inventor(s): Wolfbeis, O.; Kroneis, H.; Offenbacher, H.

Abstract: Fluorescence-optical **indicator material is chemically bonded in a network structure permeating a carrier membrane** of the sensor element.

As this network structure is independent of the membrane and not chemically bonded thereto, the properties of the membrane and the indicator are not affected by the immobilization. In one example, acetoxypyrene-trisulfochloride is immobilized on a membrane with hexamethyldiamine or polyethylenimine as crosslinkable material.

Other: Ger. Offen. (1984), DE 3343637 A1 19840607.



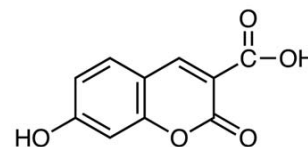
(1985) Chromogenic and fluorogenic glycosides for photometric and fluorimetric determination of glycosidases

Ger. Pat. Appl. DE 3540917.7. Publ. 19. Nov. 1985. Assigned to Bayer AG.

Inventor(s): E. Koller, O. S. Wolfbeis, H. Harnisch

Abstract: New glycosides of **7-hydroxycoumarins (see formula) and hydroxyquinolinones** are described that are almost colorless and have no fluorescence, but if hydrolyzed by enzymes out of the group of glycosidases become colored and strongly fluorescent. This enables kinetic assays of glycosidase enzymatic activities.

Other: Appl. in US, CDN, Eur. Pat.



(1985) Chromogenic and fluorogenic carboxylic esters as agents for detecting and determining hydrolases

DE 3329394 A1 19850228. Eur. Pat. EP0137177A1. Jap. Pat. JPS6058980A.

Inventor(s): Wolfbeis, Otto S.; Harnisch, Horst. Assigned to Bayer AG.

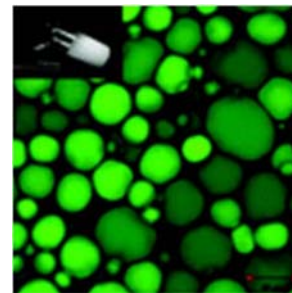
Abstract: New **esters of 7-hydroxycoumarin and 7-hydroxyquinolinone with carboxy acids** were prepared that are almost colorless and have no fluorescence, but if hydrolyzed by enzymes out of the group of esterases become colored and fluorescent. Thus, 3-(2-benzoxazolyl)-7-hydroxycoumarin was acetylated by treatment with acetic anhydride in DMF to give 3-(2-benzoxazolyl)-7-acetoxycoumarin in 85% yield.

(1984) Measurement device for determining the carbon dioxide content of a sample

From Eur. Pat. Appl. (1984), EP 105870 A2 19840418

Inventor(s): Marsoner, Hermann; Kroneis, Herbert; Wolfbeis, Otto

Abstract: A pH-dependent fluorescent dye is evenly distributed in a gas-permeable polymer membrane as aq. drops of diameter 0.1-100 μm . The fluorescence intensity is a function of the pH of the reaction chamber, which in turn depends on the CO_2 content. Suitable polymers are SLM 40060, SLM 40061 or SLM 40062 or polyacrylamide. Suitable dyes are pyranine for sensing CO_2 , and benzo(ghi)perylene for sensing oxygen via quenching of fluorescence. The picture shows a water/buffer-in-silicone emulsion with the fluorescent dye pyranine in the aqueous phase.

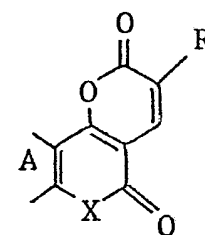


(1977) Pyranopyrandiones and pyranopyridinediones as optical brighteners

Ger. Offen. (1976), DE 2649457 A1 19770505. Publ. 05-May-1977. Assigned to CIBA Geigy AG (Switz.).

Inventor(s): Wolfbeis, Otto; Ziegler, Erich;

Abstract: New fluorophores were prepared by reaction of a 4-hydroxycoumarin with PhNH_2 and $\text{HC}(\text{OEt})_3$ and cyclocondensation of the resulting 3-[(phenylimino)methyl]coumarin with a cyanoacetic acid deriv. Thus, reaction of 4,7-dihydroxycoumarin with PhNH_2 and $\text{HC}(\text{OEt})_3$ in AcOH gives after 10 min reflux 84% 4,7-dihydroxy-3-[(phenylimino)methyl]coumarin which reacts with $\text{NCCH}_2\text{CO}_2\text{Et}$ in DMF in presence of EtOK at $80-90^\circ$ to give after 10 min 69% I.



The compounds are useful as fluorescent brighteners or laser dyes.

Other: Ger. Offen. DE 2649457.

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