JOURNAL OF
Materials
CHEMISTRY

Reversible chemical reactions as the basis for optical sensors used to detect amines, alcohols and humidity

Gerhard J. Mohr,* Daniel Citterio, Caspar Demuth, Marc Fehlmann, Luzi Jenny, Christian Lohse, Allen Moradian, Tomas Nezel, Markus Rothmaier and Ursula E. Spichiger

Centre for Chemical Sensors, ETH Technopark, Technopark St. 1, CH-8005 Zurich, Switzerland; http://www.chemsens.ethz.ch

Received 12th March 1999, Accepted 9th April 1999

A new class of indicator dyes for use in analytical chemistry is presented. In contrast to most existing indicator dyes, which change colour upon complexation or protonation/deprotonation, the dyes presented here perform reversible chemical reactions with the analyte, resulting in changes in absorbance or fluorescence. Specifically, azo and stilbene dyes which exhibit a reactive trifluoroacetyl group, reversibly interact with alcohols, amines or water to give the respective diol, hemiaminal, hemiacetal or zwitterion.

Indicator dyes that combine the properties of a chemical reagent and a ligand molecule are termed 'chromo-' or 'fluororeactands'. They are embedded in various polymer materials and have been characterised for the optical sensing of aliphatic amines, alcohols and humidity. Furthermore, methacrylate derivatives of the dyes have been tested. They were prepared to link the dyes covalently to the polymer matrix. The optical and physical properties of the dye methacrylates make them promising candidates not only for optical sensing but also for applications in molecularly imprinted polymers and non-linear optics.

A wide range of optical sensors have been presented in recent years.[1,2] Most of these sensors make use of non-covalent interactions between the analyte and the ligand, which are then optically transduced by indicator dyes. The resulting physical interactions can be electrostatic, such as between ionic analytes and ionophores, and they can originate from hydrogen bonds or van der Waals forces between uncharged analytes and neutral ligands.[1] The number of ligands, ionophores and chromoionophores described to date runs into thousands. Despite this, there are hardly any molecules for the recognition of neutral analytes available so that few optical sensors based on these molecules exist.

Recently, two optical sensors for neutral analytes based on chemical reactions between the analyte and a dye have been presented. A sensor for the detection of hydrazine makes use of the reaction of hydrazine with *p*-(dimethylamino)benzaldehyde to form a coloured benzalazine.[3] The aldehyde is either physically entrapped or covalently immobilised in sol–gel glass. Regeneration is performed by heating the sensor to 50 °C in 1 M nitric acid. A sensor for glucose has been developed based on the well-known chemical reaction of boronic acid derivatives with glucose. It includes copolymerisation of (3-aminophenyl) boronic acid with aniline to form a polyaniline layer with analyte-dependent absorbance changes in the near infrared spectral range.[4,5] Its response to glucose is compromised by the layer's cross-sensitivity to pH, and the irreversibility of the reaction. A similar approach has been used to monitor the lifetime of fluorescence.[6]

The research group of Prof. Wilhelm Simon performed pioneering work on the use of chemical reactions to detect neutral analytes. They presented a reversible optical sensor for sulfur dioxide which is based on the bisulfite addition reaction of aldehydes with hydrogen sulfite.[7,8] The interaction is transduced optically *via* a pH indicator dye that is protonated during the chemical reaction. In a second approach, they used trifluoroacetophenone derivatives that are well-established in carbonate-sensitive ion-selective electrodes and applied them to measure humidity and ethanol.[9–12] The interaction of water and alcohols with these trifluoroacetophenone ligands causes a change in the absorbance at around 305 nm. Despite the novelty of this approach, the utility of these optical sensors is limited because they only absorb in the UV and are cross-sensitive to changes in pH.

In this article, we describe chromogenic and fluorogenic reactands that have been developed out of the innovative approach of Simon and his coworkers. The name 'reactand' was coined—analogous to the term 'ligand'—for this class of host compounds that perform a reversible chemical reaction with the analyte or target compound. We have improved the approach in that we have synthesised and investigated trifluoroacetophenone derivatives with higher extinction coefficients, and with absorbance and fluorescence in the visible spectral range.[13–19] Furthermore, these dyes exhibit two absorbing species corresponding to educt and product of the chemical reaction. This property enables us to measure signal ratios.

Synthesis and optical properties of the chromogenic and fluorogenic reactands

Two types of indicator dyes have been synthesised and investigated, namely azo and stilbene dyes. The syntheses of both are generic in that they allow modifications in order to tailor the physical properties of the compounds.[13,14,18,19] In the case of the azo dye, the synthon (trifluoroacetyl)aniline was diazo-coupled to dioctylaniline and hydroxy-substituted alkylanilines (Fig. 1).[13,18] Thus, the solubility of the dyes in polymer materials can be tailored by choosing the appropriate length and type of the alkyl chains. Furthermore, it is possible to obtain dyes that can be covalently immobilised to the polymer matrix. The optical properties can be tailored by choosing coupling components such as anilines, aminonaphthalenes, phenols, naphthols or CH-acids.

The synthesis of the fluorogenic reactands based on the stilbene structure is performed either by synthesising bromostilbenes and subsequently introducing a trifluoroacetyl group[14] or *via* alkylated 4-vinylaniline, which is coupled to 4-bromo-α,α,α-trifluoroacetophenone by a palladium catalysed Heck reaction (Fig. 2).[19] Again, by alkylating the educts with appropriate alkyl halogenides, the physical properties of the resulting reactands can be tailored accordingly.

The reactands resulting from both synthetic procedures consist of an azo or stilbene chromophore and terminal

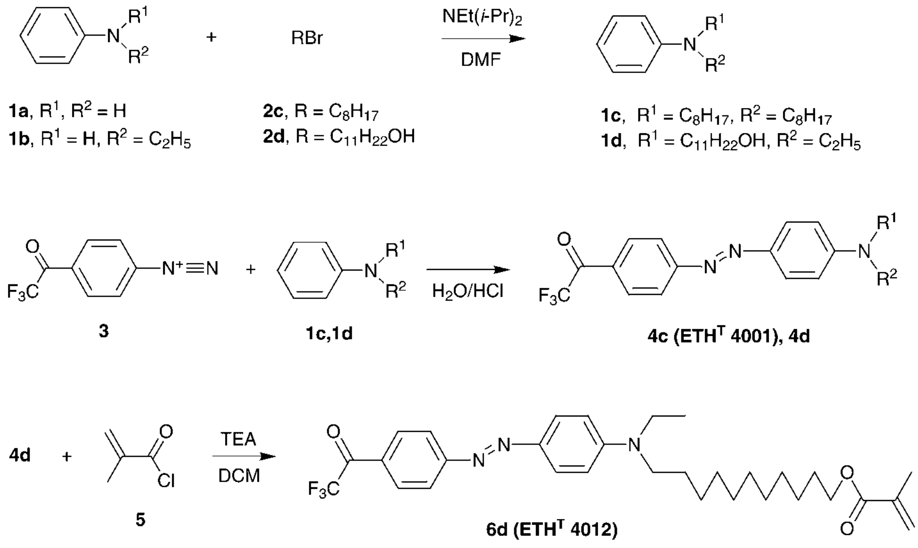

Fig. 1 Synthesis of chromoreactands ETH^T **4001** and ETH^T **4012**.

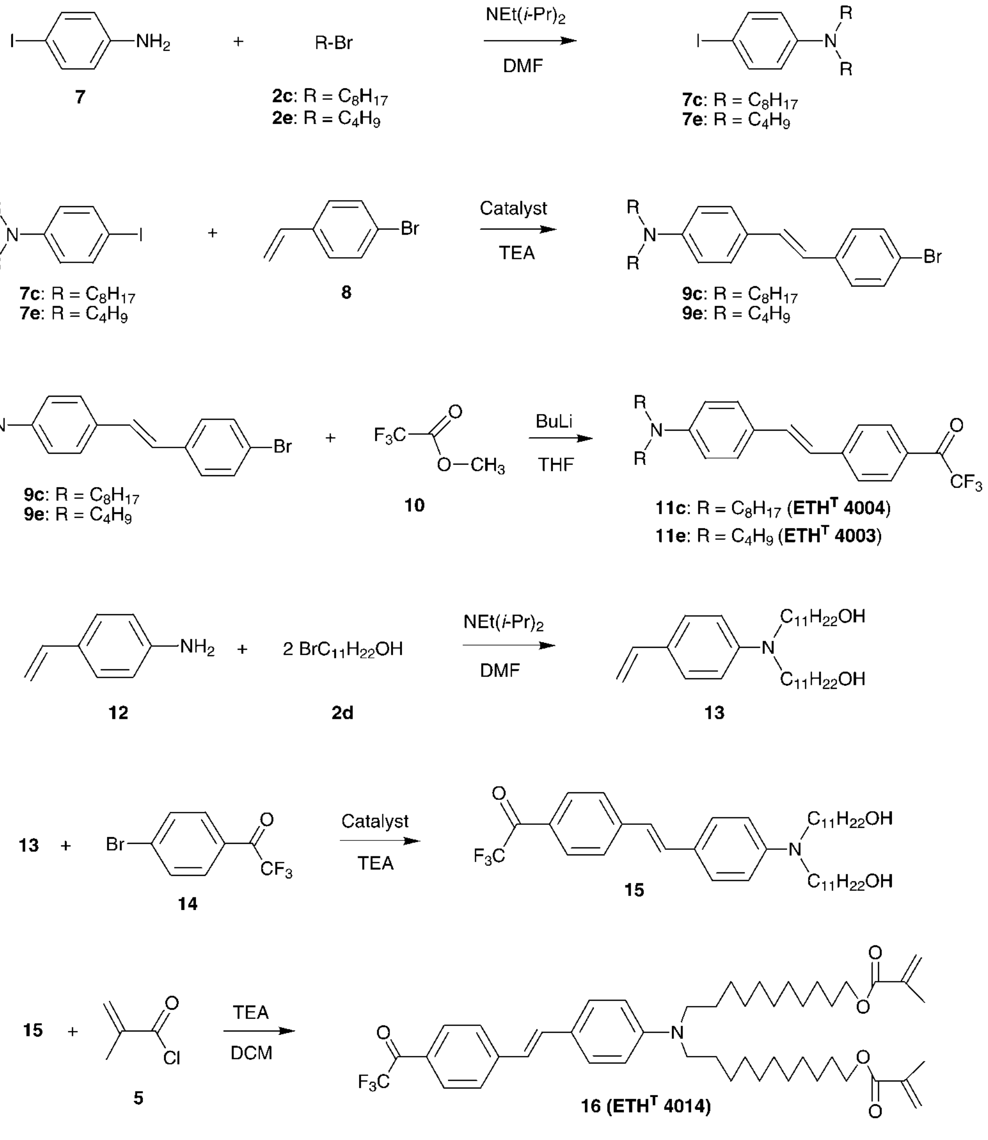

Fig. 2 Synthesis of fluororeactands ETH^T **4003**, ETH^T **4004** and ETH^T **4014**.

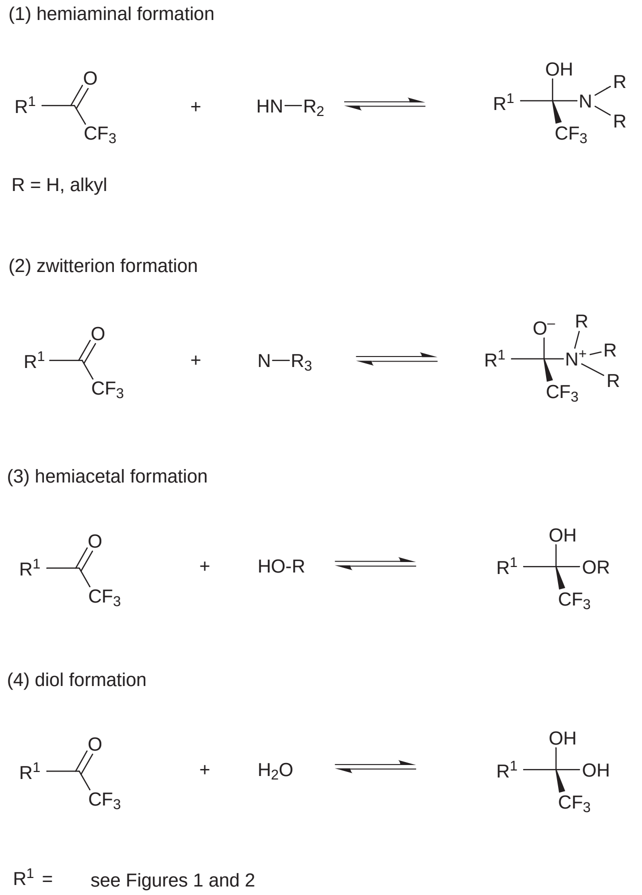

Fig. 3 Reaction of the trifluoroacetyl group with amines, alcohols and water.

donor–acceptor substituents. The alkylamino group serves as an electron donor and the long alkyl chains attached to the nitrogen atom are used for tailoring the solubility in polymer materials or for introducing the polymerisable methacrylate groups. The acceptor part of the fluorescent reactand is the trifluoroacetyl group, where the C-nucleus is attacked by nucleophilic reagents, such as alcohols and amines (Fig. 3).[20] The conversion of the trifluoroacetyl group into a hemiacetal, hemiaminal, zwitterion or diol brings about a change in the degree of electron delocalisation and, therefore, results in a blue-shift in the absorbance or fluorescence spectrum.

Both **ETH^T 4001** and **ETH^T 4003** or **4004** are solvatochromic. For **ETH^T 4001** a shift in the absorbance maximum from 467 to 497 nm is observed in going from cyclohexane to acetonitrile (Table 1). However, the wavelength shift caused by different solvents is small compared to the spectral changes induced by the chemical conversion of the trifluoroacetyl group caused by reaction with alcohols and amines. As a result, the absorbance maxima of **ETH^T 4001** in primary amines and alcohols such as ethanol or prop-1-ylamine are found in the range 420 to 430 nm (Table 1). For **ETH^T 4003**, a pronounced solvatochromism is observed for the fluorescence emission, with the emission maxima shifting from 476 nm in cyclohexane to 674 nm in acetonitrile (Table 1), whereas the shift in the absorbance maxima from 431 to 449 nm is rather small. The absorbance and fluorescence emission maxima in alcohols and amines are around 360 and 440 nm, respectively. Both dyes do not significantly react with propan-2-ol or *tert*-butyl alcohol which is probably due to the fact that bulky alcohols are hindered to interact with the trifluoroacetyl group of the reactand (Table 1).

One promising feature arising from the pronounced solvatochromism of both dyes should also be considered, namely that the solvatochromism of the azo- and stilbene-based reactands means it is possible to characterise polymer materials in terms of the polarity of the material. The solvatochromism of the reactands constitutes a more comprehensive measure of polymer polarity than parameters such as the relative permittivity, lipophilicity or viscosity of the single components (plasticizers, polymers) since it reflects the complete picture of all intermolecular forces acting on the dye and the polymer matrix.[19] This information can help in describing the interaction of the polymer matrix with the analyte, *i.e.* in predicting such parameters as the sensor's selectivity or sensitivity.

Applications

Optical amine sensor

Sensor layers composed of 33 wt% poly(vinyl chloride) (PVC), 66 wt% bis(2-ethylhexyl) sebacate (DOS) and 1 wt% of **ETH^T 4001** react with aqueous amine solutions by showing a decrease in absorbance of the trifluoroacetyl form of the reactand at around 490 nm. At the same time, a new maximum is formed at around 420 nm, which corresponds to the hemiaminal form of the dye (Fig. 4). This chemical reaction corresponds to changes in the IR spectrum showing the disappearance of the carbonyl function on exposure to gaseous amine (Fig. 5). Fig. 4 also shows the spectral change caused by diol formation, which occurs when the dry sensor membrane is exposed to 0.1 M sodium hydroxide solution. Both reactions, namely the diol formation and the hemiaminal formation, are fully reversible.

The sensor layer exhibits sensitivity to aqueous but-1-ylamine with a sensitivity range of 1–100 mM and a detection

Table 1 Absorbance maxima of **ETH^T 4001**, and fluorescence excitation and emission maxima of **ETH^T 4003** in different solvents

Reactand	**ETH^T 4001**	**ETH^T 4003**	Reactand	**ETH^T 4001**	**ETH^T 4003**
Solvent	$\lambda_{max.}$/nm	$\lambda_{max.,em.}$/nm	Solvent	$\lambda_{max.}$/nm	$\lambda_{max.,em.}$/nm
Cyclohexane	467	431/476	Butan-2-ol	422	361/436
Diethyl ether	476	440/554	*tert*-Butanol	484	445/612
Ethyl acetate	489	446/596	Prop-1-ylamine	422	N.d.[a]
Dichloromethane	501	449/635	But-1-ylamine	422	362/440
Acetone	497	447/650	Iso-butylamine	420	342/422
Acetonitrile	497	449/674	*tert*-Butylamine	416	382/439[b]
Methanol	430	362/454	Diethylamine	418	363/411
Ethanol	425	362/442	Triethylamine	415	361/413[b]
Propan-1-ol	424	362/441	Pyrrolidine	426	362/432[b]
Propan-2-ol	468	444/605	Aniline	459	N.d.[a]
Butan-1-ol	425	362/438	Pyridine	464	386/447[b]

[a] Not determined. [b] Fluorescence maxima with highest emission intensity. A significant emission of the trifluoroacetyl form is still observable, albeit with lower emission intensity.

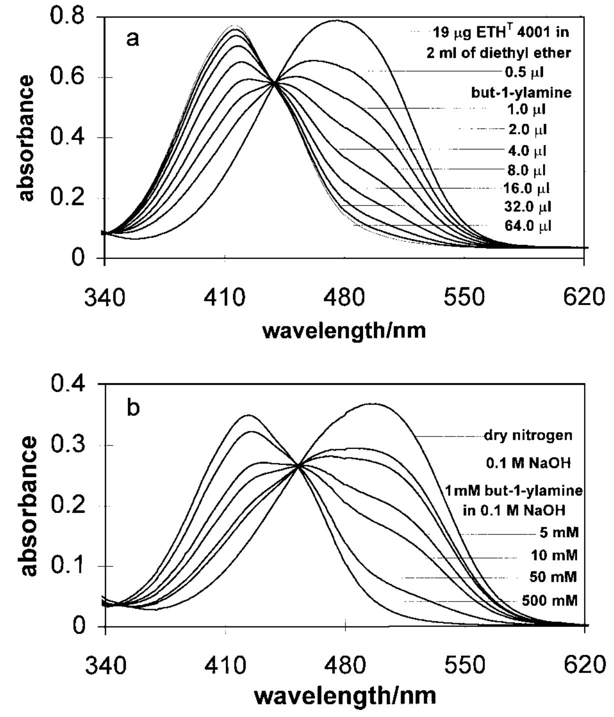

Fig. 4 (a) Absorbance spectra of **ETH^T 4001** in diethyl ether upon exposure to different concentrations of but-1-ylamine showing the formation of the hemiaminal; (b) absorbance spectra of a sensor layer composed of **ETH^T 4001**, PVC and DOS in contact with dry nitrogen and different concentrations of aqueous but-1-ylamine at pH 13.0. When changing from nitrogen to 0.1 M sodium hydroxide solution, the diol is formed, whereas, when changing from plain buffer to aqueous but-1-ylamine, the hemiaminal form occurs. Both types of reactions are fully reversible.

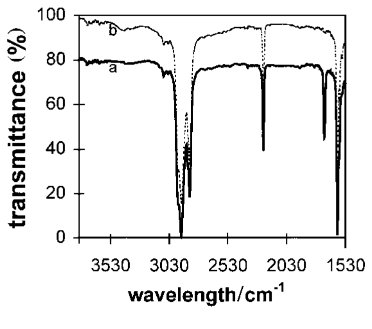

Fig. 5 Infrared spectra of the amine sensor membrane (composed of 16% **ETH^T 4001**, 28% PVC and 56% 2-octyloxybenzonitrile) upon exposure to air (a) and gaseous hex-1-ylamine (b). The carbonyl band of the trifluoroacetyl form of the reactand at 1709 cm^{-1} disappears upon conversion to the hemiaminal. Also shown are the nitrile group of the plasticizer at 2227 cm^{-1} and the CH-vibrations of PVC and the plasticizer at 2856 and 2927 cm^{-1}.

limit of 0.3 mM. The forward response time for a ten-fold increase in concentration, t_{95} (time needed for 95% of the total signal change to occur), of a bulk membrane of 3–5 μm thickness is in the range of 6 min, whereas the reverse response for a ten-fold decrease in concentration is in the range of 5 min. The response of the sensor layer to secondary, tertiary and aromatic amines is governed by three parameters, namely their lipophilicity, nucleophilicity and the bulkiness. As shown in Table 2, the sensors exhibit high sensitivity to primary amines with long unbranched alkyl chains. Although the lipophilicities of the branched and unbranched amines lie within the same range, the response to the branched amines is significantly lower than that to the unbranched amines.[21] We attribute this difference to the fact that the branched amines have a sterically demanding structure, and are consequently repulsed by the trifluoroacetyl group. A similar effect is observed for secondary and tertiary amines, as well as for the aromatic amines. These species are hindered in approaching the trifluoroacetyl group by the bulky groups near the amino moiety. In the case of aniline, the lower nucleophilicity has to be considered as well.

Table 2 Selectivity coefficients (log K^{opt})[a] of the amine sensor membranes based on **ETH^T 4001** for aliphatic and aromatic amines in comparison to but-1-ylamine, and log K_{OW}[b] values of amines and alcohols

Amine	log K_{OW}	log K^{opt}	Amine	log K_{OW}	log K^{opt}
Ammonia	—	−2.3	But-1-ylamine	0.86	0.0
Methylamine	−0.57	−1.3	*tert*-Butylamine	0.40	−1.8
Ethylamine	−0.13	−1.2	Hex-1-ylamine	—	0.9
Diethylamine	0.58	−1.6	Pyridine	0.65	−1.7
Triethylamine	1.45	−1.1	Aniline	0.90	−1.5
Prop-1-ylamine	0.48	−0.5	Ethanol	−0.30	−2.8
Isopropylamine	—	−1.8	Propan-1-ol	0.25	−2.3

[a]log K^{opt} values represent the logarithm of the relative selectivities between the interfering analytes, see ref. 16. [b]log K_{OW} values represent the logarithm of the partition coefficients of organic substances between octan-1-ol and water.

The behaviour of sensor layers based on the stilbene dye is very similar to the azo dye in terms of selectivity, whereas the sensitivity is lower by a factor of ten. This is caused by the different reactivity of **ETH^T 4003** and **4004** compared to **ETH^T 4001**. The azo group *para* to the trifluoroacetyl group is a strong electron acceptor (Hammett constant $\sigma_p = 0.39$), whereas the stilbene moiety exhibits no significant electron acceptor strength (Hammett constant $\sigma_p = -0.07$). Consequently, the trifluoroacetyl group is activated by the presence of the electron acceptor and reacts more easily with nucleophilic analytes.

The fluorescence excitation maxima of **ETH^T 4004** in plasticized PVC are located at 453 and 468 nm, and the emission maximum at 576 nm. Exposure to amines causes a decrease in fluorescence intensity at 576 nm. At the same time, the conversion of the reactand results in an increase in the fluorescence of the hemiaminal form with an excitation maximum at 384 nm and an emission maximum at 426 nm. The selectivity pattern for amines is nearly identical to the amine sensor based on **ETH^T 4001**. However, the response to aniline, *i.e.* the decrease in fluorescence intensity at 576 nm, is higher than expected. In this specific case, fluorescence quenching is attributed to the signal decrease of the sensor layer caused by the conversion of the trifluoroacetyl group.[16]

In order to investigate polymers with enhanced shelf and operational lifetimes, copolymers from **ETH^T 4012** and from different ratios of methyl methacrylate and butyl acrylate were prepared.[18] The resulting copolymer layers exhibit similar sensitivity to that of sensors based on plasticized PVC but are more stable operationally. Thus, the relative standard deviations for 12.1 and 120.5 mM aqueous prop-1-ylamine ($n = 20$) over a period of two weeks are found to be 1.57 and 1.96%, respectively. Unfortunately, higher ratios of methyl methacrylate result in longer response times (up to 30 min). Additionally, the polymerisation reactivities of methacrylates and acrylates differ, producing copolymers whose composition may be different from the composition of the monomer feed. Consequently, new copolymers were prepared composed of **ETH^T 4014** and hexyl methacrylate only.[19] These layers appear to be mechanically very flexible and respond much more quickly than layers based on methyl methacrylate and butyl acrylate. They are also easier to prepare and characterise because they are made of just two components. The operational lifetime of copolymers made from **ETH^T 4014** and hexyl methacrylate is similar to that of copolymers composed of methyl methacrylate, butyl acrylate and **ETH^T 4012**.

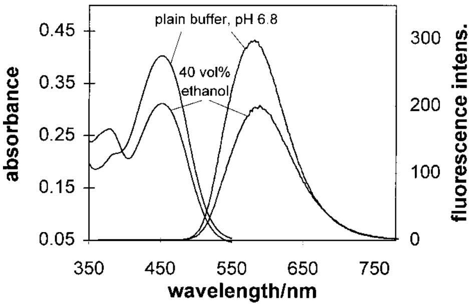

Fig. 6 Absorbance and fluorescence spectra of the ethanol sensor layer (**ETH^T 4004**, 20 mol% tridodecylammonium chloride (TDMACl) relative to the reactand, PVC, DOS) in contact with a plain buffer and 40 vol% of ethanol, showing the decrease in absorbance and fluorescence emission of the trifluoroacetyl form and the increase in absorbance of the hemiacetal.

Optical alcohol sensor

The reactands **ETH^T 4001** and **4004** have been successfully used to measure highly nucleophilic amines in aqueous solution. Although the nucleophilicity of alcohols is lower than that of amines it should be possible to use the same reactands to measure alcohols as well. Indeed, when using **ETH^T 4001** in plasticized PVC, the response to ethanol appears to be optically similar in behaviour to amines.[13] As with the amine sensor layers, a decrease in absorbance of the trifluoroacetyl group at around 490 nm is observed upon exposure to ethanol, with an increase in absorbance at 430 nm. However, the response times of membranes identical to the ones used for amine-sensing are in the range of several hours rather than minutes. Consequently, a catalyst (tridodecylmethylammonium chloride, (TDMACl) 20 mol% relative to the reactand) has to be used. It promotes the interaction of alcohols with the trifluoroacetyl group, thus reducing the response time to a matter of minutes.

Although the sensor has been used to measure the ethanol content in beverages, it turns out not to be so suitable for monitoring ethanol on-line in beverages because the sensor is cross-sensitive to pH changes.[13] This limitation can be overcome by using the fluorescent reactand **ETH^T 4004**, together with a perm-selective coating. This microporous PTFE coating is placed on top of the sensor layer and usually serves as a protective coating for ambient interfering light. More important in this case, however, is the fact that the layer is impermeable to ionic species, so that the sensor's cross-sensitivity to pH is no longer a problem.[15]

The fluorescence excitation maxima of the fluorogenic ligand, **ETH^T 4004**, in plasticized PVC are located at 452 and 468 nm, and the emission maximum at 576 nm (Fig. 6). Exposure to alcohol results in a decrease in fluorescence intensity at 576 nm, which correlates with the decrease in absorbance of the sensor layer at 453 nm. At the same time the conversion of the ligand results in an increase in the fluorescence of the hemiacetal form at 420 nm, which correlates with the increase in absorbance at 373 nm (see Fig. 6). The fluorescence intensity of the hemiacetal is approximately 10 times lower than the fluorescence of the trifluoroacetyl form and is at a shorter wavelength.

The relative decrease in fluorescence in going from 0 to 40 vol% ethanol is as high as -35%. The limit of detection for ethanol is 0.8 vol% ethanol and the dynamic range is within 0.7 to 7.0 M ethanol. This sensitivity is lower by a factor of 10–100 than it is for amine sensors, due to the lower nucleophilicity of alcohols *versus* amines. The forward response time for a decade change in concentration, t_{95}, is in the range 3–4 min, whereas the time for the reverse response is in the range 5–10 min (Fig. 7).

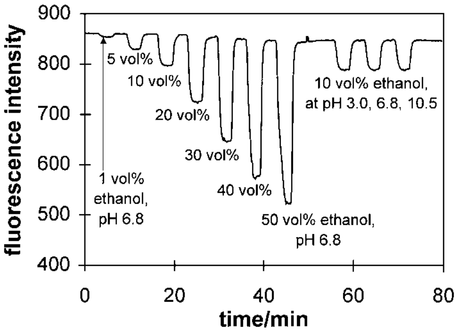

Fig. 7 Response curve of the ethanol sensor layer (**ETH^T 4004**, 20 mol% TDMACl relative to the reactand, PVC, DOS) on exposure to aqueous ethanol solutions. The excitation and emission wavelengths were set to 450 and 560 nm, respectively.

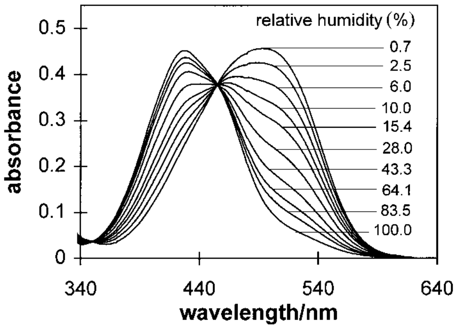

Fig. 8 Absorbance spectra of the humidity-sensitive layer (**ETH^T 4001**, 20 mol% TDMACl relative to the reactand, polyurethane Tecoflex) in contact with different concentrations of humid air. When changing from dry to humid air, the trifluoroacetyl group of the reactand **ETH^T 4001** is converted into a diol. The chemical reaction is fully reversible.

Optical humidity probe

If the reactand **ETH^T 4001** is embedded in aliphatic polyurethane rather than in plasticized PVC as the polymer matrix, a significant increase in sensitivity to humidity is observed.[17] A reaction to humidity (diol formation) has already been noted in amine and ethanol sensors, albeit much smaller (see also Fig. 4b). The hydrophilic polyurethane provides a hydrophilic microenvironment for the reactand. As a consequence, exposure to water causes the trifluoroacetyl group in the reactand to undergo full conversion into the diol, with no further reactions with alcohols or amines (Fig. 8). Apparently, the use of the hydrophilic polyurethane favours the extraction of water, and thus provides an appropriate matrix for a humidity sensor.

The forward and reverse response times of the sensor layer are very slow (3–4 h), which means that is it clearly not suitable for humidity sensing. The slow response is due to the fact that the reactivity of water is significantly lower than the reactivity of amines and alcohols. However, the layer sensitive to humidity could be used as an indicator test strip in order to evaluate the exposure of water-sensitive goods to humidity.

Selectivity

The selectivity of optical sensors based on trifluoroacetophenone derivatives within one chemical class of analytes (amines or alcohols) is mainly governed by the latter's lipophilicity and chemical structure. This means that the sensors are highly sensitive to lipophilic primary amines and only slightly sensitive to secondary and tertiary amines. A similar selectivity pattern is encountered for the alcohol sensor layers which show a preference for lipophilic primary alcohols. The selectivity between the different chemical species, however, can be affected by additional parameters, such as the sample pH, the choice of polymer matrix, the addition of a catalyst, and the use of perm-selective coatings. Thus, sensors for aqueous amines have to operate at high pH because the reactands do not respond to alkylammonium ions. Furthermore, sensors for amines do not require any catalyst and since they are not very reactive with water and alcohols, they are less sensitive to these analytes (Table 2). Whereas the sensor membranes used for ethanol measurements respond to ethanol in the molar range, the response of alcohol sensor layers to amines is in the mM range. Furthermore, the sensor membranes for ethanol only show sufficient response in the presence of a catalyst.[13–15] Nevertheless, sensor membranes composed of tridodecylmethylammonium chloride, **ETH^T 4001** and **ETH^T 4004** are useful in alcohol sensing because, in beverages and in bioreactor broth (the target samples for alcohol sensors), amines are found in the μM range only.[13,14] Furthermore, the pH in beverages and in bioreactor broth is neutral or acidic. Therefore, any interfering amine would be present in the ammonium form, which does not interact with the reactands.

Both the sensors for amines and alcohols respond to humidity, albeit with relatively small signal changes. By changing the polymer matrix to a more hydrophilic one, the response to humidity can be increased while the response to lipophilic alcohols remains relatively small. As with all these types of sensor membranes, ionic analytes do not interfere. In the case of the amine sensor no ionic additives are present so that ionic analytes can not be extracted into the sensor layer. In the case of the ethanol sensor, where cationic additives improve the response behaviour, the sensor layers are coated with ion-impermeable microporous PTFE coatings. Thus, the presented sensor layers respond to neither hydronium ions nor carbonate which are well-known to interact with trifluoroacetophenone derivatives.[22]

Outlook: what other applications are possible?

The new reactands are interesting synthons for non-linear optical (NLO) structures that exhibit a chemical functionality. Dyes based on the azobenzene or stilbene structure comparable to the dyes presented here have been extensively studied since the early 90s.[23–25] In order to show a non-vanishing first-order hyperpolarisability and a second-order non-linear susceptibility (χ^2), the material must exhibit an asymmetric electronic distribution at a molecular and a macroscopic level. Consequently, isotropic solids, such as, *e.g.*, amorphous NLO-polymers, require an orientation process (poling) to avoid the overall centrosymmetry of the dipoles in the material. This means that the covalent link of the dye to the polymer, *e.g.* by methacrylate groups, is very important in obtaining a stable orientation of the dye in the matrix. Both requirements, namely having a high dipole moment and allowing polymerization, are met by the dye monomers, **ETH^T 4012** and **4014**. They could be especially interesting for use in NLO since their optical properties can be 'switched on and off' by specific chemical reactions.

For molecularly imprinted polymers (MIPs), the new reactands could provide a means of combining the recognition of the analyte by the imprint matrix with the optical transduction by the indicator dye. So far, optical signal changes have usually been obtained by using labelled analytes or non-specific indicator dyes. In the first case, an imprint matrix for a specific analyte is saturated with a dye-labelled analyte. Upon exposure to the sample solution containing the analyte, the labelled analyte is competitively exchanged with the analyte and detected by its absorbance or fluorescence.[26] This approach cannot be used in all cases because labelled analytes do not necessarily fit into the imprint.

In the second case, the analyte interacts with a dye that is copolymerised with the imprint matrix.[27] The advantage of this approach is that, unlike with labelling, selectivity problems due to chemical modification (*via* labelling) of the analyte do not arise. However, a colour change due simply to the close proximity of the analyte and the dye cannot be guaranteed in all cases. The limitations of both approaches could be overcome by preparing molecular imprints with copolymerised reactands. Thus, the number of possible analytes capable of interacting with the reactand can be influenced by changing the shape of the molecular imprint, while optical recognition depends on the chemical reaction of the dye with the analyte.

The presented approach based on reactands is not limited to the chemical reactivity of trifluoroacetophenone derivatives. Conceivably, other chemical reactions can also be used as the basis for reversible optical sensors, such as the reaction of non-fluorescent hydrazine derivatives with aldehydes to form fluorescent hydrazones, the bisulfite addition reaction, Schiff base formation, or the Michael addition. We are currently exploring these reactions as the basis for novel optical sensors to detect neutral analytes.

References

1. O. S. Wolfbeis (ed.), *Fiber Optic Chemical Sensors and Biosensors*, CRC Press, Boca Raton, FL, 1991.
2. U. E. Spichiger-Keller, *Chemical Sensors and Biosensors for Medical and Biological Applications*, Wiley VCH, Weinheim, Germany, 1998.
3. C. Gojon, B. Dureault, N. Hovnanian and C. Guizard, *Sens. Actuators*, *B*, 1997, **38–39**, 154.
4. E. Pringsheim, E. Terpetschnig and O. S. Wolfbeis, *Proc. Europt(r)ode IV*, (Münster) 1998, 235.
5. E. Pringsheim, E. Terpetschnig and O. S. Wolfbeis, *Chimia*, 1998, **7–8**, 398.
6. O. S. Wolfbeis, I. Klimant, T. Werner, C. Huber, U. Kosch, C. Krause, G. Neurauter and A. Dürkop, *Sens. Actuators*, *B*, 1998, **51**, 17.
7. M. Kuratli, M. Badertscher, B. Rusterholz and W. Simon, *Anal. Chem.*, 1993, **65**, 3473.
8. M. Kuratli and E. Pretsch, *Anal. Chem.*, 1994, **66**, 85.
9. K. Wang, K. Seiler, J. P. Haug, B. Lehmann, S. West, K. Hartman and W. Simon, *Anal. Chem.*, 1991, **63**, 970.
10. K. Seiler, K. Wang, M. Kuratli and W. Simon, *Anal. Chim. Acta*, 1991, **244**, 151.
11. U. E. Spichiger, M. Kuratli and W. Simon, *Biosens. Bioelectron.*, 1992, **7**, 715.
12. R. Wild, D. Citterio, J. Spichiger and U. E. Spichiger, *J. Biotechn.*, 1996, **50**, 37.
13. G. J. Mohr, D. Citterio and U. E. Spichiger, *Sens. Actuators*, *B*, 1998, **49** 226.
14. G. J. Mohr and U. E. Spichiger, *Anal. Chim. Acta*, 1997, **344**, 215.
15. G. J. Mohr and U. E. Spichiger, *Anal. Chim. Acta*, 1997, **351**, 189.
16. G. J. Mohr, C. Demuth and U. E. Spichiger, *Anal. Chem.*, 1998, **70**, 3868.
17. G. J. Mohr and U. E. Spichiger, *Mikrochim. Acta*, 1998, **130**, 29.
18. G. J. Mohr, N. Tirelli C. Lohse and U. E. Spichiger, *Adv. Mater.*, 1998, **10**, 1353.
19. G. J. Mohr, N. Tirelli and U. E. Spichiger, *Anal. Chem.*, 1999, **71**, 1534.
20. M. L. M. Schilling, H. D. Roth and W. C. Herndon, *J. Am. Chem. Soc.*, 1980, **102**, 4271.
21. J. Sangster, *Octanol–Water Partition Coefficients: Fundamentals and Physical Chemistry*, Wiley, West Sussex, England, 1997.
22. C. Behringer, B. Lehmann, J. P. Haug, K. Seiler, W. E. Morf, K. Hartman and W. Simon, *Anal. Chim. Acta*, 1990, **233**, 41.
23. D. Brown, A. Natansohn and P. Rochon, *Macromolecules*, 1995, **28**, 6116.
24. M. Zhao, M. Bautista and W. T. Ford, *Macromolecules*, 1991, **24**, 844.
25. G. S'Heeren, A. Persoons, P. Rondou, M. Van Beylen and C. Samyn, *Eur. Polym. J.*, 1993, **29**, 975.
26. R. Levi, S. McNiven, S. A. Piletsky, S.-H. Cheong, K. Yano and I. Karube, *Anal. Chem.*, 1997, **69**, 2017.
27. P. Turkewitsch, B. Wandelt, G. D. Darling and W. S. Powell, *Anal. Chem.*, 1998, **70**, 2025.

Paper 9/01961H