Chemosensor for the optical detection of aliphatic amines and diamines†

Susanne Reinert* and Gerhard J. Mohr

Received (in Cambridge, UK) 19th November 2007, Accepted 25th February 2008
First published as an Advance Article on the web 13th March 2008
DOI: 10.1039/b717796h

Two new chemosensor dyes with either one or two trifluoroacetophenone recognition moieties have been investigated in terms of reversibly interacting with amines and diamines.

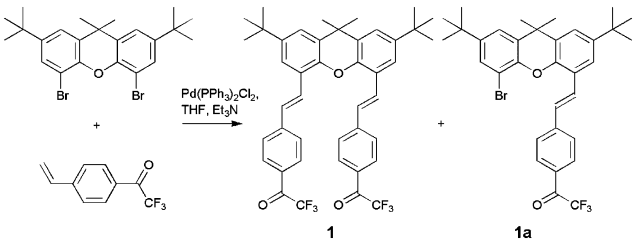
The determination of toxic compounds such as amines has become of large interest, since they are widespread pollutants in nature. Because of their extensive use in pharmaceutical industries and dye manufacturing it is necessary to develop new and effective sensors for aliphatic amines. Various biogenic amines such as cadaverine and putrescine are products of the enzymatical decarboxylation of amino acids. So the presence of these amines can serve as an indicator of food quality, *e.g.* for fish products.

Chromatographic and optical methods[1,2] are widely used for the detection of amines, but they are not feasible for online measurements. Other materials which are used range from crown and heterocrown ethers, recognising amines in their ammonium form[3] to indicators with aldehyde moieties as receptor units. Glass *et al.* described a fluorescent diamine sensor based on a quinoline chromophore with an aldehyde moiety as recognition unit.[4] Lavigne *et al.* reported on carboxylic acids as receptor units for diamines.[5]

It is known that the trifluoroacetyl group reversibly reacts with nucleophiles such as amines under the formation of hemiaminals.[6] Suzuki *et al.* developed a trifluoroacetophenone-based tripodal sensor molecule for the detection of amino acids.[7] The preparation of an amine-selective chemosensor with a (trifluoroacetyl)azobenzene reporter group incorporated into a dendrimer was reported by Beil and Zimmerman.[8]

Here we report on the synthesis and characterisation of a new optical sensor based on two chemosensor dyes and their use for the selective detection of aliphatic amines and diamines. The dyes are xanthen derivatives having either two (**1**) or one (**2**) trifluoroacetophenone moieties. Incorporated into polymer layers both are capable of reversibly binding amines from aqueous solutions.

Starting from 4,5-dibromo-2,7-di-*tert*-butyl-9,9-dimethylxanthene and 2,2,2-trifluoro-1-(4-vinylphenyl)-ethanone compound **1** was synthesised *via* Heck-reaction using a capped heavy-wall pyrex tube. Besides the disubstituted xanthen dye **1**, the monosubstituted compound **1a** was formed (Scheme 1).



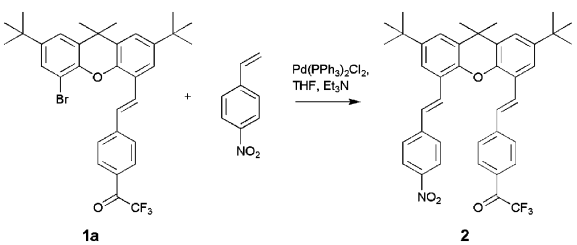
Scheme 1 Synthetic route for compound **1** and **1a**.

To distinguish between the selectivity of one and two trifluoroacetyl moieties towards mono- and diamines, compound **2** was synthesised. One nitro instead of one trifluoroacetyl group was used for **2**, because it has a similar acceptor strength (Hammett substitution constant) but no chemical reactivity towards amines. According to Scheme 2 compound **2** was synthesised *via* Heck-reaction from **1a** and 1-nitro-4-vinylbenzene.

Sensor layers S1 and S2 were prepared according to the literature.[9] Absorption measurements were performed by placing the sensor-layer-containing flow-cell in the spectrometer and pumping aqueous amine solutions through the cell. Additionally, the response of the dyes **1** and **2** to amines in homogenous solution (ethyl acetate) was investigated.

The acceptor capacity of the trifluoroacetyl groups in **1** and **2** is decreased when reacting with amines. Their conversion into a hemiaminal or a zwitterion leads to a change in the electron delocalisation within the dye molecule and subsequently to a shift in absorbance to shorter wavelengths.

The dyes embedded in thin layers of plasticised PVC as well as in homogenous solution showed changes in absorbance on exposure to aliphatic amines. To study the hemiaminal formation with monoamines, 1-propylamine (PA), diethylamine and triethylamine were used. The main focus, however, was on the interaction with aliphatic diamines of different chain length, *i.e.* diaminomethane up to 1,6-diaminohexane.



Scheme 2 Synthesis of compound **2**.

Institute of Physical Chemistry, Friedrich-Schiller University Jena, Lessingstr. 10, D-07743 Jena, Germany. E-mail: susanne.reinert@uni-jena.de; Fax: +49 3641 948302; Tel: +49 3641 948379

† Electronic supplementary information (ESI) available: Experimental and spectroscopic data of **1** and **2**, preparation of sensor layers S1 and S2, absorption spectra of S1 and S2 with PA, mass spectra of the bridged hemiaminal. See DOI: 10.1039/b717796h

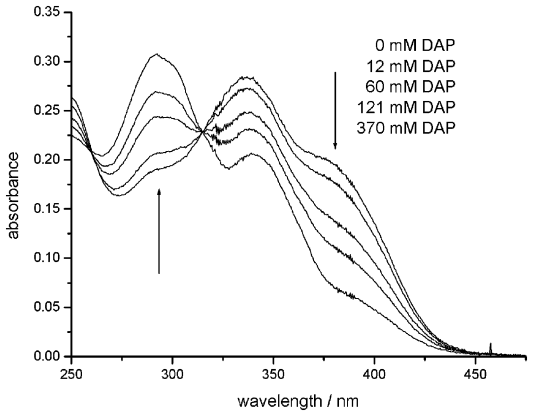


Fig. 1 The absorption spectra of sensor membrane S1 upon exposure to increasing concentrations of 1,3-diaminopropane (DAP). A decrease in absorbance at 380 nm and an increase at 290 nm is observed.

The sensor layer S1 has its absorbance maximum at around 335 nm and exhibits the largest signal changes upon addition of different aqueous amine solutions at 380 nm and at 290 nm, respectively. All amines reacted within 5 minutes to form the hemiaminal or zwitterion (in the case of triethylamine). Kinetic studies with analogous compounds were performed by Zimmerman *et al.*[11] Fig. 1 shows the absorption spectra of membrane S1 upon addition of different concentrations of 1,3-diaminopropane (DAP) solutions.

The sensitivity of S1 towards diamine DAP is comparable to monoamine PA (see ESI†).

In contrast to sensor layer S1, sensor layer S2 showed no change in absorption upon exposure to aqueous solutions containing DAP (Fig. 2). Obviously, no reaction took place, indicating the high selectivity of S1 over S2. The same behaviour was observed for diaminomethane and 1,2-diaminoethane. Considering S2, marginal sensitivity was found for 1,4-diaminobutane, 1,5-diaminopentane and 1,6-diaminohexane (Table 1).

The response and sensitivity of S1 and S2 towards monoamines is comparable, only the magnitude in signal changes is smaller for S2 because only one functional group in **2** can react

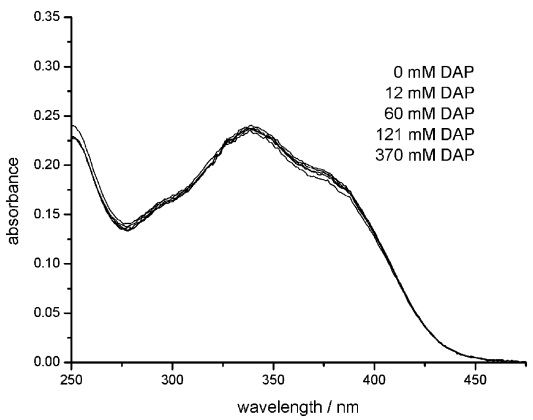


Fig. 2 Absorption spectra of sensor membrane S2 upon addition of increasing concentrations of 1,3-diaminpropane (DAP). No change in absorbance is observed.

Table 1 Equilibrium constants K_{eq} for the formation of hemiaminals from compound **1** and **2** with different amines measured in plasticized PVC layers (layer thickness 3–5 μm). Additionally, octanol–water partition coefficients (Log *P*)[10] are given

Amine	K_{eq}/M^{-1} (S1)	K_{eq}/M^{-1} (S2)	Log *P*
Diaminomethane	1	nd[a]	−2.17
1,2-Diaminoethane	4	nd[a]	−2.04
1,3-Diaminopropane	8	nd[a]	−1.43
1,4-Diaminobutane	4	1	−0.7
1,5-Diaminopentane	8	2	−0.26
1,6-Diaminohexane	11	4	+0.28
1-Propylamine	15	12.5	+0.48
Diethylamine	2	1	+0.58
Triethylamine	5.5	5	+1.45

[a] Not determined because of negligible changes in absorbance.

with amines (Table 1). To illustrate the sensitivity of S1 to primary amines the calibration functions are given in Fig. 3.

Comparing sensor membranes S1 and S2 two main results are obtained. First, S1 shows higher sensitivity to diamines than S2. Almost no change in absorbance was detected for the reaction of S2 with diamines. Within the diamines, the K_{eq} values demonstrate the higher sensitivity of S1 towards more lipophilic 1,6-diaminohexane than for diaminomethane. This observed tendency corresponds to the Log *P* value of the respective diamine. Increasing chain length of the amine increases its lipophilicity, which, in turn affects its extraction into the lipophilic polymer layer (described by the 1-octanol/water partition coefficient Log *P*). With respect to monoamines, S1 and S2 show comparable sensitivity for 1-propylamine, diethylamine and triethylamine, with highest sensitivity for the primary and less sensitivity for the secondary and tertiary amine. The response of S1 and S2 to secondary and tertiary amines is smaller although they have much higher Log *P* values. A reason for this is the steric hindrance of the amine. Bulky chains lessen the interaction with the trifluoroacetyl group and therefore decrease its response to the sensor.[9] The equilibrium constants of S1 and S2 in the polymer sensor layer are a combination of both, the extraction of the amine from the aqueous phase into the polymer layer (dependent on the

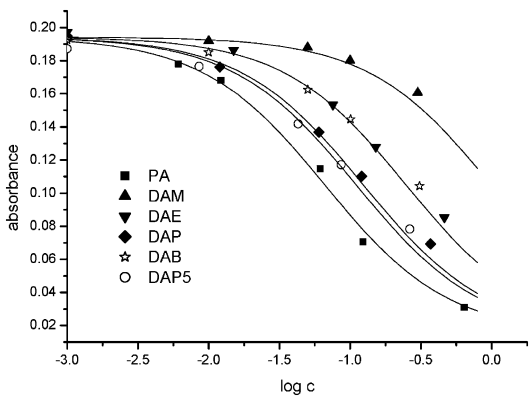


Fig. 3 Response function of S1 on exposure to aqueous amines measured at pH 13.0 and at 350 nm (PA, 1-propylamine; DAM, diaminomethane; DAE, 1,2-diaminoethane; DAP, 1,3-diaminopropane; DAB, 1,4-diaminobutane; DAP5, 1,5-diaminopentane). The solid lines are the calculated values for K_{eq}.

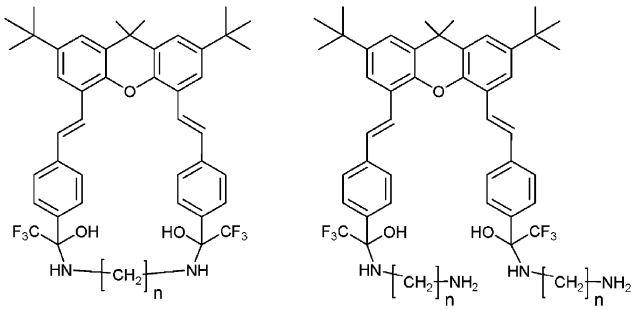


Fig. 4 Structures of the bridged (left) and unbridged (right) hemiaminals after reaction of **1** with diamines.

log *P* value of the amine) and the chemical reaction of the amine with **1** or **2**.

The reason for the difference in selectivity of S1 and S2 is based on the different chemical structures of **1** and **2**. In the case of the reaction of compound **1** and **2** with monoamines there is only one possible way to form the hemiaminal. Each trifluoroacetyl function reacts with one amino group. In the case of the reaction of **1** with diamines there are two possible reacting pathways. First, it is possible that one diamine reacts *via* its two amino groups to form a bridge between the two binding sites of **1**. Second, it is also possible that two diamines each bind *via* one amino group to the trifluoroacetyl moieties, forming hemiaminals. The second amino group allows the formation of hydrogen bonds which stabilises the hemiaminal structure.[11] The structures of the resulting hemiaminals are given in Fig. 4.

To evaluate whether the formation of bridged hemiaminals takes place, we had to isolate the respective hemiaminal and to analyse its structure. Since the chemical reaction is reversible, the equilibrium had to be shifted towards the hemiaminal form by adding *N*-trimethylsilylimidazole (TSIM) to a solution of **1** and DAP. TSIM is a powerful silylating agent, particularly for alcohols. So the hemiaminal OH-group is locked and the reverse reaction to form the trifluoroacetyl group is impeded. Hence, it became possible to isolate and to analyse the structure of the hemiaminal. The presence of a bridged structure for the reaction of **1** with DAP was shown by mass spectroscopy (see ESI†). The spectra gave a clear signal for the bridged and no signal for the unbridged structure. Hence, we conclude that the short-chained diamines are bridge-like bound when reacting with **1**, thus causing the difference in selectivity of **1** over **2**.

Comparing the interaction of **1** and **2** with amines in homogenous solution (Table 2), several results are found. First, **1** and **2** show similar K_{eq} values for the reaction with 1-propylamine (monoamine). Second, for the reaction of **1** and **2** with diamines the K_{eq} values are significantly increased, when compared with the results for the monoamine. They are highest for 1,2-diaminoethane and lowest for 1,4-diaminobutane. These results lead to the conclusion that an increasing chain length of the diamine lessens the equilibrium constant. This tendency is consistent with the results found by Mertz *et al.*[12] Comparing the reaction of **1** and **2** with diamines, a significantly higher selectivity in the case of **1** compared to **2** is observed. This is similar to the results for the sensor layers, attributed to the possibility of macrocycle formation between dye **1** and the diamines.

Table 2 Equilibrium constants K_{eq} for the formation of hemiaminals from compound **1** and **2** with different amines measured in ethyl acetate

Amine	K_{eq}/M^{-1} (**1**)	K_{eq}/M^{-1} (**2**)
1-Propylamine	195	210
1,2-Diaminoethane	30 000	5000
1,3-Diaminopropane	26 000	3500
1,4-Diaminobutane	13 000	700

This work was supported by the project No. MO 1062/3-1 of Deutsche Forschungsgemeinschaft. This support is gratefully acknowledged.

Notes and references

1 J. B. Noffsinger and N. D. Danielson, *J. Chromatogr.*, 1987, **387**, 520.
2 W. H. Chan, K. K. Shiu and X. H. Gu, *Analyst*, 1994, **119**, 2809; B. García-Acosta, M. Comes, J. L. Bricks, M. A. Kudinova, V. V. Kurdyukov, A. I. Tolmachev, A. B. Descalzo, M. D. Marcos, R. Martínez-Máñez, A. Moreno, F. Sancenón, J. Soto, L. A. Villaescusa, K. Rurack, J. M. Barat, I. Escriche and P. Amorós, *Chem. Commun.*, 2006, 2239.
3 K. Fuji, K. Tsubaki, K. Tanaka, N. Hayashi, T. Otsubo and T. Kinoshita, *J. Am. Chem. Soc.*, 1999, **121**, 3807; I. O. Sutherland, *Pure Appl. Chem.*, 1989, **61**(9), 1547.
4 K. Secor, J. Plante, C. Avetta and T. Glass, *J. Mater. Chem.*, 2005, **15**, 4073.
5 T. L. Nelson, C. O'Sullivan, N. T. Greene, M. S. Maynor and J. J. Lavigne, *J. Am. Chem. Soc.*, 2006, **128**, 5640.
6 G. J. Mohr, C. Demuth and U. E. Spichiger-Keller, *Anal. Chem.*, 1998, **70**, 3868; G. J. Mohr, *Chem. Eur. J.*, 2004, **10**, 1082.
7 S. Sasaki, A. Hashizume, D. Citterio, E. Fujii and K. Suzuki, *Angew. Chem.*, 2002, **114**(16), 3131; S. Sasaki, G. Monma, D. Citterio, K. Yamada and K. Suzuki, *Chimia*, 2005, **59**(5), 204.
8 J. B. Beil and S. C. Zimmerman, *Chem. Commun.*, 2004, 488.
9 G. J. Mohr, *Sens Actuators B*, 2005, **107**, 2; G. J. Mohr, *Anal. Chim. Acta*, 2004, **508**, 233.
10 J. Sangster, *Octanol–Water Partition Coefficients*, Wiley-VCH, West Sussex, 1997.
11 E. Mertz, J. B. Beil and S. C. Zimmerman, *Org. Lett.*, 2003, **5**(17), 3127; G. Lu, J. E. Grossman and J. B. Lambert, *J. Org. Chem.*, 2006, **71**, 1769.
12 E. Mertz, S. L. Elmer, A. M. Balija and S. C. Zimmerman, *Tetrahedron*, 2004, **60**, 11191.

