Abel, F. G. A. Stone, G. Wilkinson), Pergamon, Oxford, **1995**, chap. 7.3, p. 741, and references therein.

[2] a) J. R. Berenguer, J. Forniés, E. Lalinde, F. Martínez, L. Sanchez, B. Serrano, *Organometallics* **1998**, *17*, 1640; b) F. Guerin, D. H. Conville, J. J. Vittal, G. A. P. Yap, *Organometallics* **1998**, *17*, 1290; c) A. Evenzahav, N. J. Turro, *J. Am. Chem. Soc.* **1998**, *120*, 10835; d) E. D. Jemmis, K. T. Gijn, *J. Am. Chem. Soc.* **1998**, *120*, 6952, and references therein; e) H.-F. Klein, M. Heiden, M. He, T. Jung, *Organometallics* **1997**, *16*, 2003; f) B. M. Trost, M. T. Sorvm, C. Chan, A. E. Harms, G. Rühter, *J. Am. Chem. Soc.* **1997**, *119*, 698, and references therein.

[3] a) A. J. Canty in *Comprehensive Organometallic Chemistry, Vol. 9* (Eds.: E. W. Abel, F. G. A. Stone, G. Wilkinson), Pergamon, Oxford, **1995**, chap. 5; b) P. M. Maitlis, P. Espinet, M. J. Russell in *Comprehensive Organometallic Chemistry, Vol. 6* (Eds.: E. W. Abel, F. G. A. Stone, G. Wilkinson), Pergamon, Oxford, **1982**, chap. 38.4; c) R. Usón, J. Forniés, *Adv. Organomet. Chem.* **1988**, *28*, 219; d) J. Browning, M. Green, J. L. Spencer, F. G. A. Stone, *J. Chem. Soc. Dalton Trans.* **1974**, 97.

[4] Reviews: a) M. J. Went, *Polyhedron* **1995**, *14*, 465, and references therein; b) A. J. Carty, *Pure Appl. Chem.* **1982**, *54*, 113; see also R. S. Dickson, T. Simone, R. J. Parker, G. D. Fallou, *Organometallics* **1997**, *16*, 1531; E. Lonattani, A. Lledós, J. Suades, A. Alvarez-Lorena, J. F. Piniella, *Organometallics* **1995**, *14*, 1053.

[5] a) E. Delgado, Y. Chi, W. Wang, G. Hogart, P. J. Low, G. D. Enright, S.-M. Peng, G.-H. Lee, A. J. Carty, *Organometallics* **1998**, *17*, 2936; b) P. Blenkiron, G. D. Enright, P. J. Low, J. F. Corrigan, N. J. Taylor, Y. Chi, J.-Y. Saillard, A. J. Carty, *Organometallics* **1998**, *17*, 2447; c) M. H. A. Benvenutti, M. D. Vargas, D. Braga, F. Grepioni, B. E. Mann, S. Naylor, *Organometallics* **1993**, *12*, 2947, and references therein.

[6] a) P. Rosa, P. Le Floch, L. Ricard, F. Mathey, *J. Am. Chem. Soc.* **1997**, *119*, 9417; b) Y. Miquel, A. Igau, B. Donnadieu, J. P. Majoral, L. Dupuis, N. Pirio, P. Meunier, *Chem. Commun.* **1997**, 279; *J. Am. Chem. Soc.* **1998**, *120*, 3504; c) W. Imhof, B. Eber, G. Huttner, C. Emmerich, *J. Organomet. Chem.* **1993**, *447*, 21; d) D. Montlo, J. Suades, F. Dahan, R. Matthieu, *Organometallics* **1990**, *9*, 2933; e) E. Sappa, G. Pasquinelli, A. Tiripicchio, M. Tiripicchio Camellini, *J. Chem. Soc. Dalton Trans.* **1989**, 601.

[7] a) M. A. Bennett, C. J. Cobley, E. Wenger, A. C. Willis, *Chem. Commun.* **1998**, 1307; b) A. Mahieu, Y. Miquel, A. Igau, B. Donnadieu, J. P. Majoral, *Organometallics* **1997**, *16*, 3086; c) D. K. Johnson, T. Rukachaisirikul, Y. Sun, N. J. Taylor, A. J. Canty, A. J. Carty, *Inorg. Chem.* **1993**, *32*, 5544.

[8] a) R. Usón, J. Forniés, M. Tomás, B. Menjón, C. Fortuño, A. J. Welch, D. E. Smith, *J. Chem. Soc. Dalton Trans.* **1993**, 275; b) J. Forniés, M. A. Gómez-Saso, E. Lalinde, F. Martínez, M. T. Moreno, *Organometallics* **1992**, *11*, 2873; c) I. Ara, J. R. Berenguer, E. Eguizabal, J. Forniés, E. Lalinde, A. Martín, F. Martínez, *Organometallics* **1998**, *17*, 4578; d) J. R. Berenguer, L. R. Falvello, J. Forniés, E. Lalinde, M. Tomás, *Organometallics* **1993**, *12*, 6; e) J. Forniés, E. Lalinde, A. Martín, M. T. Moreno, A. J. Welch, *J. Chem. Soc. Dalton Trans.* **1995**, 1333; f) I. Ara, L. R. Falvello, S. Fernández, J. Forniés, E. Lalinde, A. Martín, M. T. Moreno, *Organometallics* **1997**, *16*, 5923.

[9] I. Ara, Universidad de Zaragoza, personal communication.

[10] a) M. I. Bruce, A. Catlow, M. G. Humphrey, G. A. Koutsantonis, M. R. Snow, E. R. T. Tiekink, *J. Organomet. Chem.* **1988**, *338*, 59, and references therein; b) P. M. Maitlis, *J. Organomet. Chem.* **1980**, *200*, 161; c) E. A. Kelley, P. M. Maitlis, *J. Chem. Soc. Dalton Trans.* **1979**, 167.

[11] a) J. Albert, J. Granell, J. Sales, J. Xolans, *J. Organomet. Chem.* **1989**, *379*, 177; b) A. D. Ryabov, R. van Eldik, G. Le Borgne, M. Pfeffer, *Organometallics* **1993**, *12*, 1386; c) J. P. Sutter, M. Pfeffer, A. De Cian, J. Fisher, *J. Organomet. Chem.* **1992**, *11*, 386; d) G. Zhao, Q.-G. Wang, T. C. W. Mak, *Tetrahedron: Asymmetry* **1998**, *9*, 2253; e) J. Vicente, I. Saura-Llamas, J. Turpin, M. C. Ramirez de Arellano, P. G. Jones, *Organometallics* **1999**, *18*, 2689.

[12] a) C. Slugove, K. Mereiter, R. Schmid, K. Kirchner, *J. Am. Chem. Soc.* **1998**, *120*, 6175; b) C. P. Casey, S. Chung, Y. Ha, D. R. Powell, *Inorg. Chim. Acta* **1997**, *265*, 127; c) D. Huang, M. Olivan, J. C. Huffman, O. Eisenstein, K. G. Caulton, *Organometallics* **1998**, *17*, 4700; d) Ch. S. Yi, N. Liu, A. L. Rheingold, L. M. Liable-Sands, *Organometallics* **1997**, *16*, 3910; e) H. Werner, R. Wiedemann, P. Steiner, J. Wolf, *Chem. Eur. J.* **1997**, *3*, 127; f) A. C. Dema, C. M. Lukehart, *Inorg. Chim. Acta* **1997**, *264*, 193; g) S. A. Benyunes, L. Brandt, A. Fries, M. Green, M. F. Mahon, T. M. Papworth, *J. Chem. Soc. Dalton Trans.* **1993**, 3785; h) A. C. Dema, C. M. Lukehart, A. T. McPhail, D. R. McPhail, *J. Am. Chem. Soc.* **1990**, *112*, 7229; i) A. Furlani, M. V. Russo, A. C. Villa, A. G. Manfredoti, C. Guastini, *J. Chem. Soc. Dalton Trans.* **1977**, 2154.

[13] a) A. J. Carty, S. E. Jacobson, R. T. Simpson, N. J. Taylor, *J. Am. Chem. Soc.* **1975**, *97*, 7254; b) A. J. Carty, D. K. Johnson, S. E. Jacobson, *J. Am. Chem. Soc.* **1979**, *101*, 5612; c) N. J. Taylor, S. E. Jacobson, A. J. Carty, *Inorg. Chem.* **1975**, *11*, 2648; see also d) A. J. Carty, G. Hogarth, G. Enright, G. Frapper, *Chem. Commun.* **1997**, 1883.

[14] a) A. Dormond, A. Dahchour, *J. Organomet. Chem.* **1980**, *193*, 321; b) R. Usón, J. Forniés, P. Espinet, E. Lalinde, P. G. Jones, G. M. Sheldrick, *J. Organomet. Chem.* **1985**, *288*, 249, and references therein.

[15] A. C. Albeniz, P. Espinet, Y.-S. Lin, *J. Am. Chem. Soc.* **1996**, *118*, 7145, and references therein.

[16] Crystal data for **8** ($C_{74}F_{20}H_{36}P_3Pt_2$): orthorhombic, space group $Pca2_1$, $a = 23.197(2)$, $b = 14.068(2)$, $c = 23.264(2)$ Å, $V = 7591.8(11)$ Å^3, $Z = 4$, $\mu = 3.83$ mm^{-1}, $T = 173(2)$ K. A total of 47379 reflections were collected, of which 17225 were unique ($R(\text{int}) = 0.0534$). The refinement converged to $R1 = 0.048$, $wR2 = 0.116$, and $S = 0.999$. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-115339 and 115340. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

Exploiting the Self-Assembly Strategy for the Design of Selective Cu^{II} Ion Chemosensors[**]

Patrizia Grandini, Fabrizio Mancin, Paolo Tecilla,[*]
Paolo Scrimin, and Umberto Tonellato[*]

Chemosensors, small abiotic molecules that signal the presence of analytes, typically combine two components: a recognition site that binds the target substrate and a readout system that signals binding.[1] In the case of metal ion sensors the recognition site is a metal-chelating molecule designed to bind the target ion selectively and the readout system is very often a fluorophore. The two components are usually covalently linked through a spacer and the complexation of the metal ion results in a variation of the position and/or intensity of the emission band of the fluorophore. With this set-up a large number of molecular sensors has been devised for the detection of alkali and transition metal ions in solution.[1] Among the latter group, Cu^{II} has attracted

---

[*] Prof. P. Tecilla,[+] Prof. U. Tonellato, Dr. P. Grandini,
Dr. F. Mancin, Prof. P. Scrimin
Dipartimento di Chimica Organica e Centro
CNR Meccanismi di Reazioni Organiche
Università di Padova
Via Marzolo 1, I-35131 Padova (Italy)
Fax: (+390) 49-8275239
E-mail: tecilla@mail.chor.unipd.it
tonum@mail.chor.unipd.it

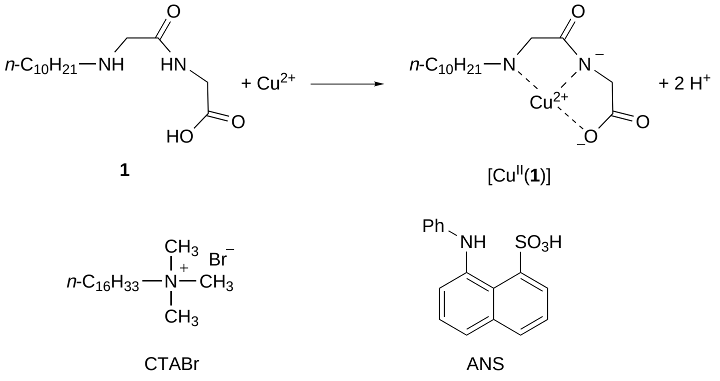
[+] New address:
Dipartimento di Scienze Chimiche, Università di Trieste
Via L. Giorgieri 1, I-34127 Trieste (Italy)

[**] This work was supported by funds from the Italian Ministry of the University, MURST, under the framework of the "Supramolecular Devices" project.

particular attention.[2] For instance, Fabbrizzi et al.,[3] Czarnik et al.,[4] Imperiali et al.,[5] and Marchelli et al.[6] have connected fluorescent probes to different types of selective Cu^{II} ligand subunits. The binding of the metal ion causes a quenching of the fluorescence emission of the probe and allows its detection in the micro- or submicromolar range. In these systems the quenching is ascribed to a photoinduced metal-to-fluorophore electron-transfer mechanism.[3] However, sensors in which the binding of a Cu^{II} ion causes an increase in the fluorescence emission or in which the fluorophore and the metal ion do not interact directly have been reported by the groups of Bharadwaj[7] and Arnold,[8] respectively.

A common feature of all the sensors described so far is a covalent linkage between the two components. While this ensures their proximity, it requires a proper design and synthetic efforts. Our goal was to realize a system in which the active components assemble spontaneously to give a sensor, without the need for any covalent link between them.[9] We reasoned that a lipophilic ligand, a fluorophore, and a surfactant would self-assemble in water to give a comicellar aggregate.[10] The proximity between the ligand and the fluorophore inside this aggregate should ensure contact between the complexed metal ion and the dye. Herein we present a sensor for Cu^{II} ions that is able to compete in selectivity and sensitivity with other more sophisticated systems. This is realized by simply mixing, under suitable conditions, commercially available surfactants and fluorophores with a dipeptide-based ligand. We have also applied a combinatorial approach to emphasize the versatility of this self-assembly strategy.

To achieve strong and highly specific binding of Cu^{II} ions in neutral water we selected the glycylglycine dipeptide **1**, bearing a C_{10} linear alkyl chain at the N-terminus, as the ligand. The dipeptide is known[11] to coordinate Cu^{II} ions by means of its amino group, the deprotonated amido nitrogen atom, and the carboxylate group as shown in Scheme 1. The key feature for the selective formation of a strong complex is the deprotonation of the amido nitrogen atom, which occurs under slightly acidic or neutral pH exclusively with Cu^{II} ions, and not with other metal ions such as Zn^{II}, Ni^{II}, or Co^{II}. While ligand **1** dissolves in water up to millimolar concentrations in the pH range 2–9, the neutral complex $[Cu^{II}(\mathbf{1})]$ is only slightly soluble above pH 5. Clear and stable solutions of the complex can be obtained by addition of a surfactant such as CTABr when $[CTABr]/[Cu^{II}(\mathbf{1})] \geq 2/1$. The uncomplexed ligand also partitions in CTABr and the resulting comicelles have a critical micellar concentration (cmc) of 2.6×10^{-4} M (CTABr). The commercial fluorophore 8-anilino-1-naphthalenesulfonic acid (ANS) strongly binds to the above aggregates as highlighted by the strong increase in the fluorescence associated with its transfer from the aqueous solution to the less polar micellar environment.[1b] The binding is very effective and ultrafiltration experiments show that, even at a concentration of CTABr as low as the cmc, the fluorophore is fully bound to the aggregate. Thus, the ligand and the fluorophore spontaneously self-assemble in water containing CTABr aggregates. Titration of such assemblies at pH 7 with $Cu(NO_3)_2$ results in the almost total quenching of the fluorescence emission of ANS, which reaches a plateau at about 5% of its initial intensity (Figure 1). Formation of the complex $[Cu^{II}(\mathbf{1})]$ is the essential prerequisite to observe the fluorescence quenching. No effect is observed in the absence of the ligand, or in the presence of an excess of the hydrophilic ligand ethylenediaminetetraacetic acid (EDTA), or at a pH value below 5 where the complex is not formed. The system is rather stable and reproducible: titrations made with different micellar preparations or measurement of the fluorescence emission of the same solution at different times give identical results within experimental error (<2%). Only in the case of the more diluted comicelles (● of Figure 1) has a relatively higher (<5%) variation of the fluorescence data been observed.



Scheme 1.

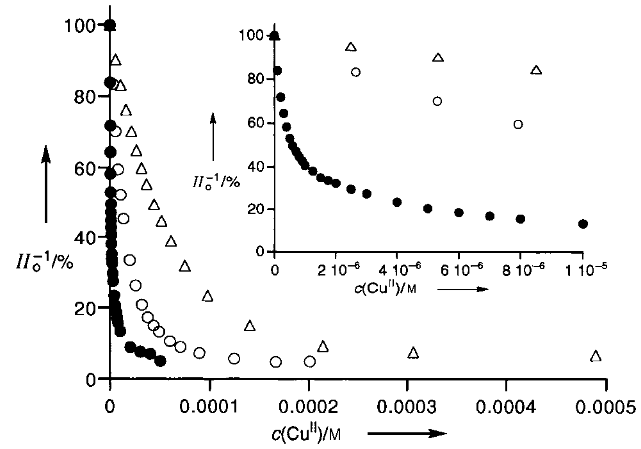


Figure 1. Spectrofluorimetric titrations of CTABr/**1**/ANS comicelles with $Cu(NO_3)_2$ in HEPES buffer 0.01 M, pH 7. Conditions: $[ANS] = 5.0 \times 10^{-7}$ M; $[CTABr]/[\mathbf{1}] = 2$; $[CTABr] = 9.4 \times 10^{-4}$ M (△); 4.7×10^{-4} M (○); 2.4×10^{-4} M (●). Inset: enlargement of the first part of the titrations. $I I_0^{-1}$ = ratio of fluorescence intensity and original fluorescence intensity.

The sensitivity of the system strongly depends on the ratio [CTABr]/[ANS] reaching the micromolar range while the concentration of the surfactant is close to the cmc (Figure 1). At high surfactant concentration, when the number of micelles exceeds the number of dye molecules, it is reasonable to assume that some micelles do not contain ANS. As a consequence, binding of Cu^{II} ions to the empty aggregates is ineffective relative to the quenching process. Hence, the dependence of the quenching efficacy on the total concentration of surfactant allows one to tune the sensitivity of the system. For example, the amount of $\mathrm{Cu^{II}}$ ions that reduces the initial fluorescence intensity to 50% ($[\mathrm{Cu^{II}}]_{50\%}$) decreases from 4×10^{-5} to 1×10^{-6} M on changing the concentration of CTABr (and **1**, the ratio being 2/1) from 9.45×10^{-4} to 2.34×10^{-4} M. The ratio [CTABr]/[ligand] is another important factor that determines the sensitivity. By keeping the concentration of ANS (5×10^{-7} M) and **1** (2.3×10^{-4} M) constant and increasing the ratio [CTABr]/[**1**] from 2/1 to 5/1 and 10/1, $[\mathrm{Cu^{II}}]_{50\%}$ increases from 1×10^{-5}, to 5×10^{-5}, and 1.5×10^{-4} M, respectively. Thus, dilution of the ligand in the aggregate inhibits the quenching process, making the contact between the fluorophore and the $\mathrm{Cu^{II}}$ complex less favorable.

Selectivity is of paramount importance for a chemosensor and to prove it for the present system we have titrated (Figure 2) comicelles made from CTABr, **1**, and ANS with other divalent metal ions, mainly belonging to the 3d series. No effect was observed with all cations investigated, except $\mathrm{Fe^{II}}$.[12] With this latter metal ion the $[\mathrm{Fe^{II}}]_{50\%}$ is 2.0×10^{-4} M from which a $\mathrm{Cu^{II}/Fe^{II}}$ selectivity of 20 may be determined. More importantly a titration of $\mathrm{Cu^{II}}$ in the presence of all cations listed in Figure 2 (each 1.0×10^{-4} M) gives a curve superimposable to the one obtained exclusively in the presence of $\mathrm{Cu^{II}}$ ions. Therefore, the sensor not only does not respond to other metal ions but is also selective towards $\mathrm{Cu^{II}}$ ions in their presence.

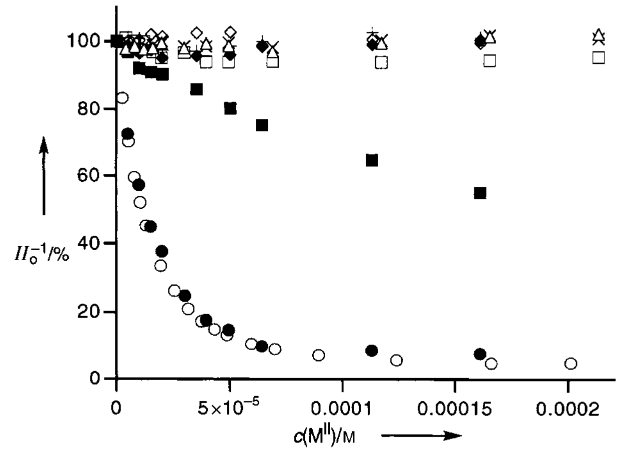
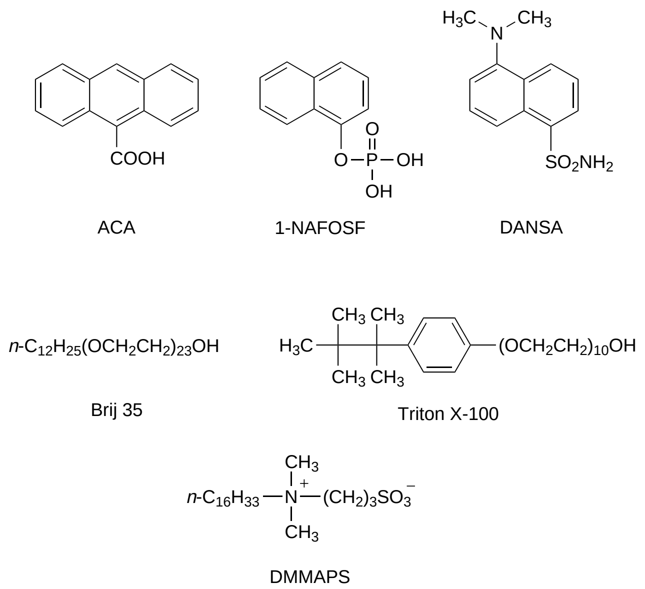


Figure 2. Spectrofluorimetric titrations of CTABr/**1**/ANS comicelles (4.7×10^{-4} M/2.3×10^{-4} M/5.0×10^{-7} M) in HEPES buffer 0.01 M, pH 7 with different metal ions: $\mathrm{Mn^{II}}$ (+); $\mathrm{Fe^{II}}$ (■); $\mathrm{Co^{II}}$ (◇); $\mathrm{Ni^{II}}$ (◆); $\mathrm{Zn^{II}}$ (x); $\mathrm{Cd^{II}}$ (□); $\mathrm{Pb^{II}}$ (△); $\mathrm{Cu^{II}}$ (○); $\mathrm{Cu^{II}}$ in the presence of all the other metal ions each 1×10^{-4} M (●).

A major advantage in using the self-assembling strategy is the easy interchange of the different components to achieve the desired properties and the facile set up of a combinatorial approach for the selection of the most effective system. To investigate this aspect we performed a series of experiments checking all combinations of **1**, surfactants, and dyes. The results are summarized in Figure 3 as the percentage of residual fluorescence in the presence of $\mathrm{Cu^{II}}$ ions (5×10^{-5} M), fluorophore (5.0×10^{-7} M), **1** (2.3×10^{-4} M), and the minimum amount of surfactant needed to solubilize the complex (see caption of Figure 3 for details). Of the systems investigated that made up of CTABr and 1-naphthylphosphate (1-NAFOSF) proved to be the most effective. This result is probably related to: a) the low [surfactant]/[ligand] ratio attainable with CTABr and b) a possible weak interaction of the phosphate group with the $\mathrm{Cu^{II}}$ complex. A more detailed investigation is under way to assess the role played by other factors, such as the charge of the surfactant and the structure of the dye.



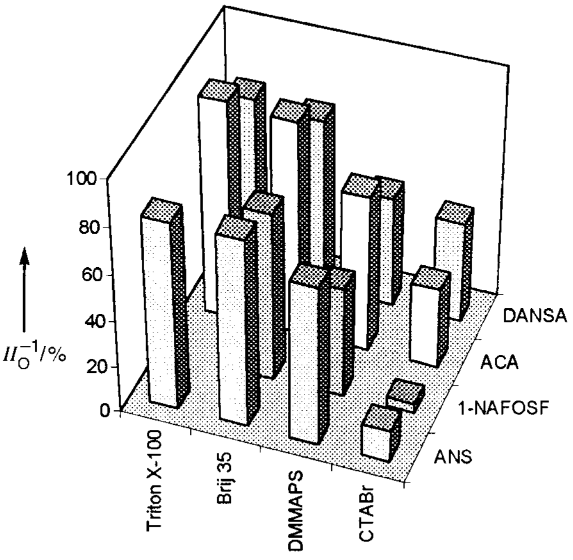


Figure 3. Percentage of residual fluorescence in the presence of 5.0×10^{-5} M $\mathrm{Cu^{II}}$ measured for the different comicellar systems. Conditions: HEPES buffer 0.01 M, pH 7; [fluorophore] = 5.0×10^{-7} M; [**1**] = 2.3×10^{-4} M; [surfactant]/[**1**] = 2 (CTABr); 6 (DMMAPS); 10 (Brij 35); 10 (Triton X-100). The couple Triton X-100/1-NAFOSF was not investigated because of the high background level of fluorescence emitted by the surfactant when irradiated at 286 nm.

In conclusion, we have demonstrated that the self-assembly strategy can be conveniently used for the construction of a $\mathrm{Cu^{II}}$ sensor. The components of the system employed in this study are commercially available or can be easily synthesized. They spontaneously self-assemble in neutral water giving rise to an assembly that displays some of the most important features of a sensor, such as sensitivity and selectivity. This modular approach allows for the easy variation of the components, which makes the process of system optimization very simple. Work is in progress to extend such a concept to ligands selective towards other metal ions and to widen its scope to the sensing of neutral molecules.

Experimental Section

N-Decylglycylglycine (**1**) was synthesized following a reported procedure[13] and was isolated as the CF_3COOH salt. All spectral and analytical data were in agreement with the proposed structure. Representative data for **1**: m.p. 109–110 °C; elemental analysis calcd for $C_{16}H_{29}N_2O_5F_3$: C 49.7, H 7.56, N 7.25; found: C 50.1, H 7.51, N 7.27; ^1H NMR (250 MHz, CD_3OD, 25 °C, TMS): $\delta = 0.94$ (t, $J = 6.5$ Hz, 3H), 1.38 (m, 14H), 1.74 (m, 2H), 3.07 (t, $J = 6.7$ Hz, 2H), 3.88 (s, 2H), 4.03 (s, 2H).

Critical micellar concentrations were obtained from surface tension measurements using a Krüss K6 apparatus. Ultrafiltrations were performed with a 8010 Amicon cell equipped with a regenerated cellulose Millipore filter with a cut-off of 10^4 Daltons. Emission spectra were recorded on a Perkin–Elmer LS-50B spectrofluorimeter. Titrations were performed in a 4-(2-hydroxyethyl)piperazine-1-ethanesulfonic acid (HEPES) buffer 0.01 M, pH 7, and 25 °C. Excitation and emission wavelengths (nm) were, respectively: 375 and 500 for ANS; 286 and 360 for 1-NAFOSF; 362 and 415 for 9-anthracenecarboxylic acid (ACA); 325 and 530 for dansylamide (DANSA).

Received: May 10, 1999 [Z13396IE]
German version: *Angew. Chem.* **1999**, *111*, 3247–3250

Keywords: copper · fluorescent sensor · micelles · self assembly · supramolecular chemistry

[1] a) "Fluorescent Chemosensors for Ion and Molecule Recognition": *ACS Symp. Ser.* **1993**, *538*; b) A. P. de Silva, H. Q. N. Gunaratne, T. Gunnlaugsson, A. J. M. Huxley, C. P. McCoy, J. T. Rademacher, T. E. Rice, *Chem. Rev.* **1997**, *97*, 1515–1566.

[2] R. Krämer, *Angew. Chem.* **1998**, *110*, 804–806; *Angew. Chem. Int. Ed.* **1998**, *37*, 772–773.

[3] G. De Santis, L. Fabbrizzi, M. Lichelli, C. Mangano, D. Sacchi, N. Sardone, *Inorg. Chim. Acta* **1997**, *257*, 69–76.

[4] J. Yoon, N. E. Ohler, D. H. Vance, W. D. Aumiller, A. W. Czarnik, *Tetrahedron Lett.* **1997**, *38*, 3845–3848.

[5] A. Torrado, G. K. Walkup, B. Imperiali, *J. Am. Chem. Soc.* **1998**, *120*, 609–610.

[6] R. Corradini, A. Dossena, G. Galaverna, R. Marchelli, A. Panagia, G. Sartori, *J. Org. Chem.* **1997**, *62*, 6283–6289.

[7] P. Ghosh, P. K. Bharadwaj, S. Mandal, S. Ghosh, *J. Am. Chem. Soc.* **1996**, *118*, 1553–1554.

[8] D. Y. Sasaki, D. R. Shnek, D. W. Pack, F. H. Arnold, *Angew. Chem.* **1995**, *107*, 994–996; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 905–907.

[9] A different approach to a self-assembling sensor is based on the competition between the target substrate and the dye for the receptor. For a recent example, see A. Metzger, E. V. Anslyn, *Angew. Chem.* **1998**, *110*, 682–684; *Angew. Chem. Int. Ed.* **1998**, *37*, 649–651.

[10] For a different strategy to self-assembling systems, see J. W. Canary, B. C. Gibb, *Prog. Inorg. Chem.* **1997**, *45*, 1.

[11] H. Siegel, R. B. Martin, *Chem. Rev.* **1982**, *82*, 385–426.

[12] The observed quenching is at least partly due to the absorbance of the $Fe(NO_3)_2$ solution at the wavelength used for the excitation of ANS ($\varepsilon \approx 1000\,M^{-1}cm^{-1}$ at 375 nm). Experiments performed in the presence of excess EDTA show that at least 30% of the quenching observed is a result of the absorbtion of the exciting light.

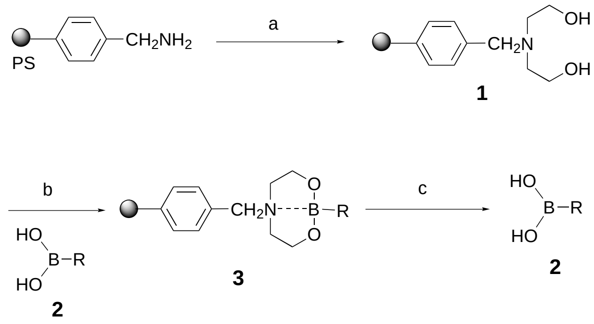
[13] M. C. Cleij, P. Scrimin, P. Tecilla, U. Tonellato, *J. Org. Chem.* **1997**, *62*, 5592–5599.

N,N-Diethanolaminomethyl Polystyrene: An Efficient Solid Support to Immobilize Boronic Acids[**]

Dennis G. Hall,[*] Jyoti Tailor, and Michel Gravel

Insoluble resins that selectively couple to a functional group are vital in combinatorial chemistry to immobilize substrates to be derivatized by solid-phase synthesis.[1] They are also employed as scavenger or "fishing out" resins in the solution-phase parallel synthesis of small molecule libraries.[2] Despite the use of boronic acids as intermediates in reactions such as the Suzuki cross-coupling[3] and in biological applications including sugar recognition[4] and inhibition of serine proteases,[5] there are currently no solid supports available that couple to the boronic acid functionality. Herein we report on the preparation of *N,N*-diethanolaminomethyl polystyrene (DEAM-PS), the first resin capable of immobilizing boronic acids, along with a preliminary assessment of its usefulness toward combinatorial chemistry applications. DEAM-PS resin can immobilize aryl, alkenyl, and alkyl boronic acids almost quantitatively in a wide range of organic solvents. Moreover, it is easily synthesized at low cost and can be recycled.

Diethanolamine boronate adducts have long been employed to stabilize, purify, and characterize boronic acids.[6] We looked at several ways to derivatize polystyrene resin to include such a diethanolamine anchor. We have best achieved this goal through the reaction of aminomethylated polystyrene (AM-PS) with excess ethylene oxide at 50 °C in a THF/water solvent mixture in a sealed, pressure-resistant tube (Scheme 1). Under these conditions, quaternization to give the triethanolalkylammonium hydroxide salt and oxirane



Scheme 1. Synthesis of DEAM-PS resin **1**. Immobilization and subsequent release of boronic acids **2**. a) Ethylene oxide (excess), THF/H_2O 9/1 (sealed tube), 50 °C, 24 h; b) boronic acid **2** (see Table 1), solvent, RT, 15 min; c) $THF/H_2O/AcOH$ 90/5/5, RT, 1 h; or THF/H_2O 9/1, RT, 2 h.

---

[*] Prof. D. G. Hall, J. Tailor, M. Gravel
Department of Chemistry, University of Alberta
Edmonton, AB, T6G 2G2 (Canada)
Fax: (+1) 780-492-8231
E-mail: dennis.hall@ualberta.ca

[**] Financial support for this research by the Natural Sciences and Engineering Research Council (NSERC) of Canada and by the University of Alberta is gratefully acknowledged. D.G.H. also acknowledges receipt of a Research Innovation Award from the Research Corporation. M.G. thanks NSERC for a Postgraduate Scholarship.