Sensors

DOI: 10.1002/ange.200602045

New Methods for Anion Recognition and Signaling Using Nanoscopic Gatelike Scaffoldings**

Rosa Casasús, Elena Aznar, M. Dolores Marcos, Ramón Martínez-Máñez, Félix Sancenón, Juan Soto, and Pedro Amorós*

In the last ten years, interest in the molecular recognition of anions has grown.[1] The prominent roles that anions play in biological and environmental processes prompted researchers to investigate the design and synthesis of a number of receptors based on supramolecular concepts.[2] An emerging subdiscipline of the field of anion chemistry is the development of anion signaling protocols. Most of these systems are designed to observe tuned changes in color or fluorescence or both upon anion coordination.[3] Several approaches have been described in the design of anion chemosensors, but most of them are based on the use of suitable binding sites (or reactive sites) and signaling units (i.e., suitable dyes) that are usually covalently attached.[3] The signaling unit is a chromophore, whereas the binding site is designed to selectively coordinate a certain anion. This approach is widely used, but one that harbors certain limitations. For example, many anion-binding sites suffer competition from the strong hydrogen-bonding ability of water and many demand challenging synthetic routes, especially when the aim is the selective recognition of very similar guests.

In addition to this somewhat classical molecular approach, we are interested in seeking new methods for anion recognition and signaling. Some prominent examples involve the blending supramolecular chemistry with concepts derived from materials science.[4] For example, recently it was shown that cooperative signal amplification could be obtained by using functionalized silica nanoparticles with pre-organized fluorescent moieties at the surface.[5] In a different context, we

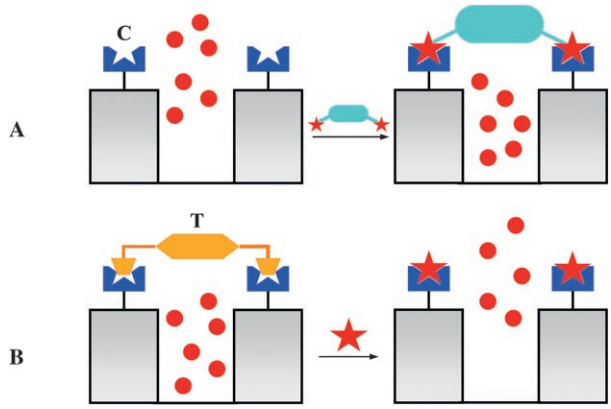
[*] R. Casasús, E. Aznar, Dr. M. D. Marcos, Prof. R. Martínez-Máñez, Dr. F. Sancenón, Dr. J. Soto
Instituto de Química Molecular Aplicada
Departamento de Química
Universidad Politécnica de Valencia
Camino de Vera s/n, 46022 València (Spain)
Fax: (+34) 963-879-349
E-mail: rmaez@qim.upv.es
Dr. P. Amorós
Institut de Ciència del Materials, ICMUV
Universitat de València
P.O. Box 2085, 46071 València (Spain)

[**] We thank the Ministerio de Ciencia y Tecnología (project MAT2003-08568-C03 and CTQ2006-15456-C04-01/BQU) for support F.S. also thanks the Ministerio de Educación y Ciencia for a Ramón y Cajal contract.

Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

believe that the use of hybrid mesoporous solids with nanoscopic cavities might be a promising approach towards the development of novel tunable sensory systems with enhanced recognition abilities. In fact, although mesoporous solids have received much attention because of their potential use in applications such as catalysis and optical devices, they are less-well studied in the context of molecular recognition based on supramolecular concepts.[6] In particular, we were interested in testing the potential use of molecular gatelike systems in hybrid scaffoldings as a new strategy for the chromofluorogenic signaling of target anions. A molecular gate is a device that modulates mass transport at the nanometric level and whose state (open or closed) can be controlled, for example, by the presence of certain chemical species. Several nanoscopic supramolecular gatelike systems, which are formed by coupling molecular systems and mesoporous materials, were reported.[7] These nanoscopic devices were designed as model systems for delivery purposes and use photochemical or electrochemical switching mechanisms. However, as far as we know, such functional gated nanoscaffolding has never been applied to the potential development of molecular-recognition and signaling methods.

The general idea of using molecular gatelike hybrid ensembles for guest-sensing purposes is outlined in Scheme 1 and involves molecular-recognition events coupled with the



Scheme 1. Anion recognition and signaling by using nanoscopic gatelike scaffoldings through: A) opened-to-closed; B) closed-to-opened anion-induced protocols; see text for full description.

control of dye transport; it entails the use of solids with nanoscopic 3D organized surfaces (e.g., MCM-41-type mesoporous materials) that have been functionalized at the outer surface with certain binding sites (labeled C in Scheme 1). Additionally, the pores have been loaded with a suitable dye (depicted as a red dot in Scheme 1). From this functionalized hybrid system, two basic approaches can be considered: In the first case (Scheme 1 A) there is an open gatelike system that is able to deliver the enclosed dye to the solution. The addition of a target anionic guest capable of forming a suitable complex with the binding site, C, might "close the gate", which would lead to recognition and signaling of the target anion by the inhibition of the mass-delivery process. In the second case, the binding sites are blocked with a large polydentate molecule (T). The interaction of T with C has to be strong enough to avoid liberation of the dye but not be very selective. The addition of a suitable anion able to form strong complexes with C will lead to the displacement of T, the delivery of the dye to the bulk solution, and the signaling of the anion. These two situations (Scheme 1 A and B), based on nanoscopic mass control, are reminiscent of the fluorescence enhancement/quenching or color development/bleaching observed in classical fluorogenic or chromogenic sensors.

In the development of new methods for guest sensing by nanoscopic hybrid supramolecular concepts based on gatelike ensembles and as a proof of the concept, we report herein an example based on Scheme 1 A that involves the use of an MCM-41 mesoporous solid support functionalized on the external surface with polyamines (C in Scheme 1 A) which are suitable receptors for anions. For this purpose the MCM-41 mesoporous solid was prepared from tetraethylorthosilicate (TEOS) as the hydrolytic inorganic precursor and the surfactant hexadecyl trimethylammonium bromide (CTAB) as the porogen species. After removal of the surfactant by calcination, solid MCM-41 (pore diameter 2.5 nm; 1.0 g) was suspended in anhydrous acetonitrile (50 mL) and heated at 110 °C in a Dean–Stark apparatus to remove adsorbed water by azeotropic distillation. The dye tris(2,2′-bipyridyl)ruthenium(II) chloride (0.6 g, 0.8 mmol) was added to the suspension and stirred for 24 h with the aim of loading the pores of the MCM-41 scaffolding to the maximum. Excess 3-[2-(2-aminoethylamino)ethylamino]propyl trimethoxysilane (4.3 mL, 15.0 mmol) was then added and the suspension was stirred for 5.5 h. The final orange solid (S1) was collected by filtration, washed with acetonitrile, and dried at 70 °C for 12 h. After this grafting procedure, the polyamines are preferentially attached to the pore outlets rather than inside the pore walls, which are full of the $[Ru(bipy)_3]^{2+}$ dye.

Figure 1 shows the powder X-ray pattern of solid S1. The expected features of the MCM-41 phase are evident, which

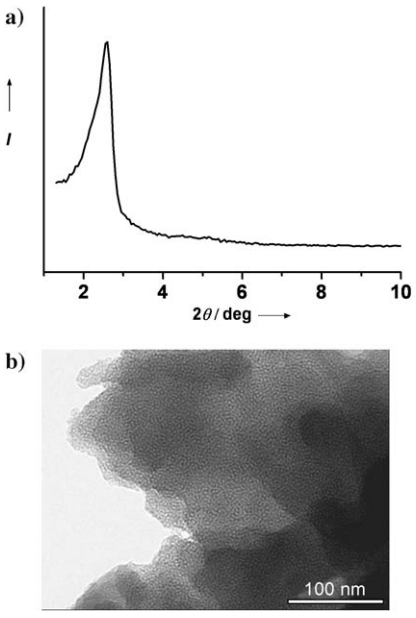


Figure 1. a) X-ray pattern, and b) TEM image of the hybrid solid, S1.

indicates that filling the pores with $[Ru(bipy)_3]^{2+}$ and anchoring the polyamine at the pore outlets do not change the mesoporous structure. Figure 1 also shows a representative TEM image of S1. The final solid contained 7.0 wt% polyamine substituent and the amount of $[Ru(bipy)_3]^{2+}$ in the pores was 10 wt% (both values are derived from elemental analysis and X-ray microanalysis).

The performance of the amine-functionalized dye-containing S1 material as a nanoscopic molecular gatelike system was tested in water. In a typical experiment, solid S1 (10 mg) was suspended in water (25 mL) and the pH value adjusted. The suspension was stirred at 40 °C and the solid isolated by filtration with teflon filters. The delivery of the dye into aqueous solution was easily detected by monitoring the spin-allowed d–π metal-to-ligand charge-transfer (MLCT) transition band of the $[Ru(bipy)_3]^{2+}$ complex centered at 454 nm. A complete description of the dye delivery as a function of pH value in aqueous solution will be described in due course. It is important to state that at acidic pH (acidified with sulfuric acid) the amines are fully protonated, the gate in S1 is closed, and no $[Ru(bipy)_3]^{2+}$ is released. This functional nanoscopic pore blockage is related to the repulsion between protonated polyamines—which are pushed away from each other towards the pore openings—and the cationic $[Ru(bipy)_3]^{2+}$ dye. Furthermore, the interaction of the polyamines with a large number of sulfate counterions at the pore outlet might help to close the path of the dye from the pore voids to the bulk aqueous solution. In contrast, at neutral and slightly basic pH, the attached polyamines are only partially protonated, the effects contributing to pore blockage are much less pronounced, and there is a massive delivery of the $[Ru(bipy)_3]^{2+}$ dye from the pores to the solution.

Solid S1 at neutral pH was used as the starting open-gate system (see Scheme 1), which contains binding sites at the pore openings (amines) and a dye in the pore voids. These partially protonated polyamines in S1 at neutral pH form complexes with anions through hydrogen-bonding interactions and electrostatic attractive forces.[8] Therefore, the ability of solid S1 to deliver the ruthenium(II) dye at neutral pH (pH 7.8, tris(hydroxymethyl)aminomethane (Tris) 10^{-3} mol dm^{-3}) was studied in the presence of the anions fluoride, chloride, bromide, iodide, nitrate, phosphate, sulfate, acetate, and carbonate without noteworthy differences in the delivery process. Even at concentrations up to 0.01 mol dm^{-3} of anions, there was no significant influence in the dye-delivery process and in all cases, virtually identical dye-release kinetics were found. This fact could be ascribed to the relatively poor coordination of the anions tested with the polyamines in the pore openings. Pore blockage was also not observed with larger anions, such as guanosine monophosphate (GMP; see Figure 2).

In contrast, upon adding S1 to neutral aqueous solutions of adenosine triphosphate (ATP) and adenosine diphosphate (ADP; concentration of anions: 1×10^{-4} mol dm^{-3}), the solutions remained essentially colorless, which indicates that the pores of the solid were blocked (Figure 2). A schematic representation is shown in Scheme 2. This selective response—the inhibition of the release of the $[Ru(bipy)_3]^{2+}$ complex—in the presence of these two nucleotides clearly

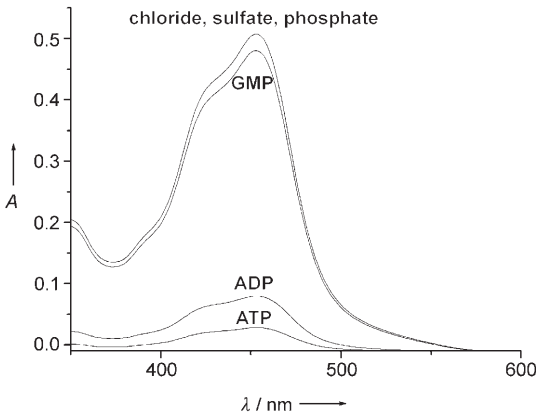
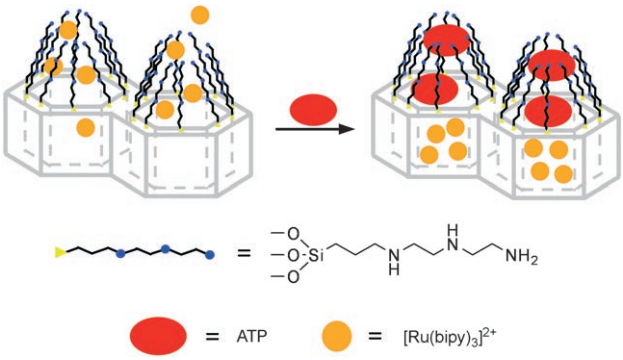


Figure 2. Absorbance of solutions containing solid S1 (10 mg) and different anions in water at pH 7.8 (Tris 10^{-3} mol dm^{-3}). The band centered at 454 nm is due to the delivery of the $[Ru(bipy)_3]^{2+}$ dye from the pores to the aqueous solution. The anions were tested at a concentration of 10^{-4} mol dm^{-3}.



Scheme 2. ATP recognition and signaling by inhibiting dye release with nanoscopic supramolecular gatelike systems on mesoporous MCM-41 supports.

indicates the relevance of this gated solid system in the context of molecular recognition and sensing.

The chromogenic response of S1 is related to the ability of the protonated polyamines to strongly coordinate nucleotides.[9] The extent of this coordination is good enough at neutral pH to block the pores and the strength of the interaction is enhanced by the preorganization effect that arises from grafting the polyamine moieties onto the inorganic supports. As can be seen in Figure 2, this blockage is not dependent on size, as the GMP anion has a similar volume to that of ADP and yet is not able to close the gate of S1. In fact, pore blockage is observed for anions that form strong complexes with polyamines (ATP > ADP > GMP). This colorimetric recognition of ATP and ADP with respect to GMP, based on the switching of a supramolecular functionality (mass transport control), is not unusual and would have been hard to achieve using classical chemosensors.[10]

Coordination in relation to dye transport in mesoporous hybrid solids has been used as a signaling method for anions. This approach has not been used previously and displays potential that cannot be considered for classical receptors. For example, the modulation of the pore size, the nature of the

appended molecular gate by using some other anion binding sites, and the properties of the loaded signaling dye can be easily modified.

In summary, we have shown herein—for the first time and as a proof of the concept—how nanoscopic molecular gatelike systems (i.e., functionalized mesoporous materials that contain polyamines) can be used for the design and development of new anion-recognition and signaling systems. These findings, along with others recently reported,[11] offer new perspectives in the use of 3D functionalized solid hosts for innovative advanced functional "hetero-supramolecular" methods.

Received: May 23, 2006
Published online: September 20, 2006

Keywords: host–guest systems · mesoporous materials · molecular devices · molecular recognition · sensors

[1] *Supramolecular Chemistry of Anions* (Eds.: E. Bianchi, K. Bowman-James, E. García-España), Wiley-VCH, New-York, **1997**.

[2] P. D. Beer, P. A. Gale, *Angew. Chem.* **2001**, *113*, 502 – 532; *Angew. Chem. Int. Ed.* **2001**, *40*, 486 – 516; ; F. P. Schmidtchen, M. Berger, *Chem. Rev.* **1997**, *97*, 1609 – 1646; C. R. Bondy, S. J. Loeb, *Coord. Chem. Rev.* **2003**, *240*, 77 – 99; J. L. Sessler, S. Camiolo, P. A. Gale, *Coord. Chem. Rev.* **2003**, *240*, 17 – 55.

[3] R. Martínez-Máñez, F. Sancenón, *Chem. Rev.* **2003**, *103*, 4419 – 4476; R. Martínez-Máñez, F. Sancenón, *J. Fluoresc.* **2005**, *15*, 267 – 285.

[4] G. Cooke, *Angew. Chem.* **2003**, *115*, 5008 – 5018; *Angew. Chem. Int. Ed.* **2003**, *42*, 4860 – 4870; ; Y. Umezawa, H. Aoki, *Anal. Chem.* **2004**, *76*, 321A – 326A; E. Katz, I. Willner, *Angew. Chem.* **2004**, *116*, 6166 – 6235; *Angew. Chem. Int. Ed.* **2004**, *43*, 6042 – 6108.

[5] M. Montalti, L. Prodi, N. Zacheronni, G. Falini, *J. Am. Chem. Soc.* **2002**, *124*, 13540 – 13546; M. Montalti, L. Prodi, N. Zaccheroni, *J. Mater. Chem.* **2005**, *15*, 2810 – 2814; E. Brasola, F. Mancin, E. Rampazzo, P. Tecilla, U. Tonellato, *Chem. Commun.* **2003**, 3026 – 3027; E. Rampazzo, E. Brasola, S. Marcuz, F. Mancin, P. Tecilla, U. Tonellato, *J. Mater. Chem.* **2005**, *15*, 2687 – 2696; L. Basabe-Desmonts, J. Beld, R. S. Zimmerman, J. Hernando, P. Mela, M. F. García Parajó, N. F. van Hulst, A. van den Berg, D. N. Reinhoudt, M. Crego-Calama, *J. Am. Chem. Soc.* **2004**, *126*, 7293 – 7299; M. Crego-Calama, D. N. Reinhoudt, *Adv. Mater.* **2001**, *13*, 1171 – 1174.

[6] V. S.-Y. Lin, C.-Y. Lai, J. Huang, S.-A Song, S. Xu, *J. Am. Chem. Soc.* **2001**, *123*, 11510 – 11511; D. R. Radu, C.-Y. Lai, J. W. Wiench, M. Pruski, V. S.-Y. Lin, *J. Am. Chem. Soc.* **2004**, *126*, 1640 – 1641; A. B. Descalzo, K. Rurack, H. Weisshoff, R. Martínez-Máñez, M. D. Marcos, P. Amorós, K. Hoffmann, J. Soto, *J. Am. Chem. Soc.* **2005**, *127*, 184 – 200; M. Comes, M. D. Marcos, R. Martínez-Máñez, F. Sancenón, J. Soto, L. A. Villaescusa, P. Amorós, D. Beltrán, *Adv. Mater.* **2004**, *16*, 1783 – 1786; K. Inumaru, Y. Inoue, S. Kakii, T. Nakano, S. Yamanaka, *Chem. Lett.* **2003**, *32*, 1110 – 1111; K. Inumaru, Y. Inoue, S. Kakii, T. Nakano, S. Yamanaka, *Phys. Chem. Chem. Phys.* **2004**, *6*, 3133 – 3139; M. Comes, G. Rodríguez-López, M. D. Marcos, R. Martínez-Máñez, F. Sancenón, J. Soto, L. A. Villaescusa, P. Amorós, D. Beltrán, *Angew. Chem.* **2005**, *117*, 2978 – 2982; *Angew. Chem. Int. Ed.* **2005**, *44*, 2918 – 2922; A. B. Descalzo, D. Jiménez, M. D. Marcos, R. Martínez-Máñez, J. Soto, J. El Haskouri, C. Guillem, D. Beltrán, P. Amorós, M. V. Borrachero, *Adv. Mater.* **2002**, *14*, 966 – 969; A. B. Descalzo, M. D. Marcos, R. Martínez-Máñez, J. Soto, D. Beltrán, P. Amorós, *J. Mater. Chem.* **2005**, *15*, 2721 – 2731.

[7] R. Casasús, M. D. Marcos, R. Martínez-Máñez, J. V. Ros-Lis, J. Soto, L. A. Villaescusa, P. Amorós, D. Beltrán, C. Guillem, J. Latorre, *J. Am. Chem. Soc.* **2004**, *126*, 8612 – 8613; N. K. Mal, M. Fujiwara, Y. Tanaka, *Nature* **2003**, *421*, 350 – 353; N. K. Mal, M. Fujiwara, Y. Tanaka, T. Taguchi, M. Matsukata, *Chem. Mater.* **2003**, *15*, 3385 – 3394; Q. Yang, S. Wang, P. Fan, L. Wang, Y. Di, K. Lin, F.-S. Xiao, *Chem. Mater.* **2005**, *17*, 5999 – 6003; R. Hernandez, H.-R. Tseng, J. W. Wong, J. F. Stoddart, J. I. Zink, *J. Am. Chem. Soc.* **2004**, *126*, 3370 – 3371; T. D. Nguyen, H. R. Tseng, P. C. Celestre, A. H. Flood, Y. Liu, J. F. Stoddart, J. I. Zink, *Proc. Natl. Acad. Sci. USA* **2005**, *102*, 10029 – 10034; C.-Y. Lai, B. G. Trewyn, D. M. Jeftinija, K. Jeftinija, S. Xu, S. Jeftinija, V. S.-Y. Lin, *J. Am. Chem. Soc.* **2003**, *125*, 4451 – 4459; J. A. Gruenhagen, C. Y. Lai, D. R. Radu, V. S.-Y. Lin, E. S. Yeung, *Appl. Spectrosc.* **2005**, *59*, 424 – 431; S. Giri, B. G. Trewyn, M. P. Stellmaker, V. S.-Y. Lin, *Angew. Chem.* **2005**, *117*, 5166 – 5172; *Angew. Chem. Int. Ed.* **2005**, *44*, 5038 – 5044.

[8] F. Sancenón, A. Benito, J. M. Lloris, R. Martínez-Máñez, T. Pardo, J. Soto, *Helv. Chim. Acta* **2002**, *85*, 1505 – 1516; M. M. G. Antonisse, D. N. Reinhoudt, *Chem. Commun.* **1998**, 443 – 444; M. E. Huston, E. U. Akkaya, A. W. Czarnik, *J. Am. Chem. Soc.* **1989**, *111*, 8735 – 8737; S. Y. Hong, A. W. Czarnik, *J. Am. Chem. Soc.* **1993**, *115*, 3330 – 3331; D. H. Vance, A. W. Czarnik, *J. Am. Chem. Soc.* **1994**, *116*, 9397 – 9398.

[9] M. W. Hosseini, A. J. Blacker, J.-M. Lehn, *J. Chem. Soc. Chem. Commun.* **1988**, 596 – 597; H. Fenniri, M. W. Hosseini, J.-M. Lehn, *Helv. Chim. Acta* **1997**, *80*, 786 – 803; M. T. Albelda, M. A. Bernardo, E. García-España, M. L. Godino-Salido, S. V. Luis, M. J. Melo, F. Pina, C. Soriano, *J. Chem. Soc. Perkin Trans. 2* **1999**, 2545 – 2549; M. T. Albelda, J. Aguilar, S. Alves, R. Aucejo, P. Díaz, C. Lodeiro, J. C. Lima, E. García-España, F. Pina, C. Soriano, *Helv. Chim. Acta* **2003**, *86*, 3118 – 3134.

[10] Selective chemosensors for chromogenic ATP sensing: F. Sancenón, A. B. Descalzo, R. Martínez-Máñez, M. A. Miranda, J. Soto, *Angew. Chem.* **2001**, *113*, 2710 – 2713; *Angew. Chem. Int. Ed.* **2001**, *40*, 2640 – 2643; S. C. McCleskey, M. J. Griffin, S. E. Schneider, J. T. McDevitt, E. V. Anslyn, *J. Am. Chem. Soc.* **2003**, *125*, 1114 – 1115; C. Yin, F. Gao, F. Huo, P. Yang, *Chem. Commun.* **2004**, 934 – 935; C. Li, M. Numata, M. Takeuchi, S. Shinkai, *Angew. Chem.* **2005**, *117*, 6529 – 6532; *Angew. Chem. Int. Ed.* **2005**, *44*, 6371 – 6374.

[11] A. B. Descalzo, R. Martínez-Máñez, F. Sancenón, K. Hoffmann, K. Rurack, *Angew. Chem.* **2006**, *118*, 6068 – 6093; *Angew. Chem. Int. Ed.* **2006**, *45*, 5924 – 5948.

