

A Supramolecular Chemosensor for Aromatic Hydrocarbons

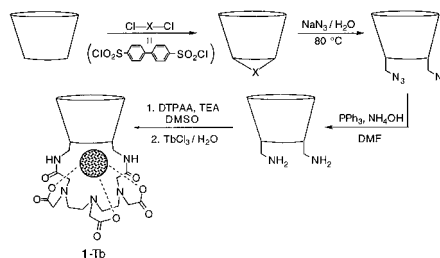
Mark A. Mortellaro and Daniel G. Nocera*

Department of Chemistry, Michigan State University
East Lansing, Michigan 48824

Received April 22, 1996

Molecular architectures composed of macropolycyclic structures of complementary function provide the underpinning of supramolecular chemistry.¹ When the supramolecular structure juxtaposes light-absorbing and -emitting centers, a variety of processes may take place that are modulated by the organization of the photoactive subunits.^{2–8} We have been interested in designing supramolecules that feature a binding site for substrate and a photoactive center capable of emitting visible light.⁹ By manipulating the fundamental parameters governing energy flow within the supramolecule, we can trigger bright luminescence from the photoactive center upon the molecular recognition of substrate at the binding site. In our efforts to design supramolecular assemblies capable of optically detecting aromatics and polycyclic aromatics, we have synthesized a cyclodextrin (CD) derivatized with a europium aza crown (1,4,10,13-tetraoxa-7,16-diazacyclooctadecane) at the primary side of the CD cavity.¹⁰ Red emission from the Eu³⁺ center occurs when an absorption-energy transfer–emission (AETE) process is established by inclusion of a light-harvesting substrate in the CD cup. Tethered at only one nitrogen, the aza crown prefers to assume a conformation that is swung away from the hydrophobic cup, and therefore the triggered luminescence response is weak owing to the long distance for energy transfer.¹¹ Because a shorter distance is imposed when the lanthanide ion binding site is cradled under the CD, we suspected that the aza crown tethered to the CD cup via its two nitrogens would show a significantly larger triggered luminescent response.¹² Surprisingly, the triggered luminescence from this supramolecular architecture is actually very weak as compared to the swing CD.^{9c,13} Although the intrinsic energy transfer process is more efficient in the cradle CD, the overall optical response is limited by the association of the benzene to the CD cup. Apparently the 3+ charge of the appended europium cradle at the bottom of the cup makes the interior of the CD less hydrophobic and hence decreases the association of benzene in the cup. We now report the synthesis of a CD supramolecule appended with a diethylenetriaminepentaacetic acid (DTPA) binding site that neutralizes

Scheme 1



the charge of the lanthanide ion in a cradle geometry. The supramolecular active site detects mono- and bicyclic aromatics with a visible luminescence response at high sensitivity, thereby providing a powerful new approach in the design of BTEX (benzene, toluene, ethylbenzene, xylene) and PAH (polycyclic aromatic hydrocarbon) chemosensing schemes.

The lanthanide ion binding site was attached to the A,D-positions^{14,15} of the primary side of the β -CD cup according to Scheme 1. The synthetic procedure was centered on the reaction of A,D-diamino- β -cyclodextrin with DTPA dianhydride and excess triethylamine (TEA) in DMSO. The A,D-diamino- β -cyclodextrin was prepared by modifying Tabushi's method¹⁶ using biphenyl-4,4'-disulfonyl-A,D-capped β -cyclodextrin¹⁷ to direct the A,D-regiochemistry. The product was purified by reversed phase liquid chromatography and characterized by ¹H NMR, ¹³C NMR, and elemental analysis.¹⁸ Aqueous solutions of the 1-Tb complex were prepared *in situ* from the reaction of 1 and TbCl₃·5H₂O.

Very weak emission is observed from aqueous solutions of 1-Tb when the metal ion is directly excited owing to the low absorbance of the ⁵D₁ emitting state manifold.¹⁹ The luminescence spectrum is characteristic of transitions between the lowest energy ⁵D₄ excited state to the ⁷F_J spin-orbit manifold of the Tb³⁺ ion. The lifetime of 1-Tb in H₂O is 1.7 ms as compared to 2.7 ms for D₂O solutions of the complex. The difference arises from the presence of water in the primary coordination sphere of the lanthanide ion. Indeed, the nonradiative decay rate of lanthanide ions correlates directly to the number of coordinated O–H oscillators;²⁰ a comparison of the H₂O and D₂O lifetime data reveals a single water molecule bound to the lanthanide ion. This result is consistent with the formulation of 1-Tb, where eight of the nine lanthanide coordination sites are filled by the DTPA, leaving one site available for coordination to a water molecule.

The emission from 1-Tb is markedly enhanced in the presence of aromatic and bicyclic aromatic hydrocarbons. The

- (1) Lehn, J.-M. *Supramolecular Chemistry*; VCH: Weinheim, 1995.
- (2) *Supramolecular Photochemistry*; Balzani, V., Scandola, F., Eds.; Ellis Horwood: West Sussex, England, 1991.
- (3) Steemers, F. J.; Verboom, W.; Reinhoudt, D. N.; van der Tol, E. B.; Verhoeven, J. W. *J. Am. Chem. Soc.* **1995**, *117*, 9408.
- (4) (a) Sabbatini, N.; Guardigli, M.; Lehn, J.-M. *Coord. Chem. Rev.* **1993**, *123*, 201. (b) Sabbatini, N.; Guardigli, M.; Manet, I.; Ungaro, R.; Casnati, A.; Fischer, C.; Ziessel, R.; Ulrich, G. *New J. Chem.* **1995**, *19*, 137.
- (5) Deschenaux, R.; Ruch, T.; Deschenaux, P.-F.; Juris, A.; Ziessel, R. *Helv. Chim. Acta* **1995**, *78*, 619.
- (6) Matsumoto, H.; Shinkai, S. *Chem. Lett.* **1994**, 901.
- (7) Georgiev, E. M.; Clymire, J.; McPherson, G. L.; Roundhill, D. M. *Inorg. Chem.* **1994**, *227*, 293.
- (8) Slone, R. V.; Yoon, D. I.; Calhoun, R. M.; Hupp, J. T. *J. Am. Chem. Soc.* **1995**, *117*, 11813.
- (9) (a) Mortellaro, M. A.; Nocera, D. G. *ChemTech* **1996**, *26*, 17. (b) Nocera, D. G. *New Sci.* **1996**, *149*, 24. (c) Pikramenou, Z.; Yu, J.-A.; Lessard, R. B.; Ponce, A.; Wong, P. A.; Nocera, D. G. *Coord. Chem. Rev.* **1994**, *132*, 181. (d) Hartmann, W. K.; Gray, M. H. B.; Ponce, A.; Nocera, D. G.; Wong, P. A. *Inorg. Chim. Acta* **1996**, *243*, 239. (e) Ponce, A.; Wong, P. A.; Way, J. J.; Nocera, D. G. *J. Phys. Chem.* **1993**, *97*, 11137.
- (10) Pikramenou, Z.; Nocera, D. G. *Inorg. Chem.* **1992**, *31*, 532.
- (11) The rate constant for energy transfer exhibits a 1/*r*⁶ (Förster) or e^{- αr} (Dexter) distance dependence (*Modern Molecular Photochemistry*; Turro, N. J., Ed.; Benjamin/Cummings: Menlo Park, CA, 1978; p 305).
- (12) Pikramenou, Z.; Johnson, K. M.; Nocera, D. G. *Tetrahedron Lett.* **1993**, *34*, 3531.
- (13) Pikramenou, Z.; Hartmann, W. K.; Mortellaro, M. A.; Nocera, D. G. To be published.

- (14) Tabushi, I. *Acc. Chem. Res.* **1982**, *15*, 66.
- (15) Breslow, R. *Acc. Chem. Res.* **1995**, *28*, 146.
- (16) Tabushi, I.; Shimokawa, K.; Fujita, K. *Tetrahedron Lett.* **1977**, 1527.
- (17) Tabushi, I.; Yamamura, K.; Nabeshima, T. *J. Am. Chem. Soc.* **1984**, *106*, 5267.
- (18) A solution of A,D-diamino- β -cyclodextrin (231 mg, 0.204 mmol), diethylenetriaminepentaacetic acid dianhydride (72.7 mg, 0.204 mmol, 1 equiv) and triethylamine (1 drop) was stirred in anhydrous DMSO (2 mL) for 8 h. This solution was added dropwise into acetone (60 mL) with stirring and the resulting white powder collected by vacuum filtration. The powder was dissolved in a minimal amount of water and loaded onto octadecyl-functionalized silica gel. The column was eluted with water (150 mL) by using a multistaltic pump and a flow rate of 1 mL/min, during which an unidentified cyclodextrin was isolated. Elution was then continued with 20% CH₃CN; 1 (127 mg, 42%) was isolated as a white powder upon the removal of solvent: *R*_f = 0 (5:3:3:1 1-propanol/ethyl acetate/water/ammonia); ¹H NMR (300 MHz, D₂O) δ 4.90 (s, 7H), 3.97–3.45 (m, 49H), 3.42 (t), 3.35–3.10 (m, 8H); ¹³C NMR (500 MHz, D₂O) δ 172.1, 171.6, 168.8, 101.0, 82.1, 80.6, 72.5, 72.2, 71.5, 71.3, 69.3, 59.7, 56.9, 56.3, 54.4, 51.0, 50.8, 39.3. Anal. Calcd for C₅₆H₉₁O₄₁N₅·5H₂O: C, 42.56; H, 6.44; N, 4.43. Found: C, 42.83; H, 6.28; N, 4.59.
- (19) *Systematics and the Properties of the Lanthanides*; Sinha, S. P., Ed.; NATO ASI Series 109; Reidel: Dordrecht, The Netherlands, 1983.
- (20) Horrocks, W. D., Jr. In *Progress in Inorganic Chemistry*; Lippard, S. J., Ed.; Wiley: New York, 1984; Vol. 30, p 1.

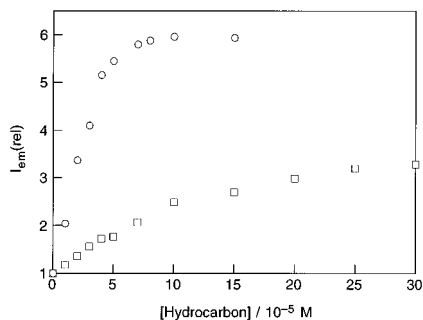


Figure 1. Relative emission intensity from an aqueous solution of **1**-Tb (2.5×10^{-4} M) as a function of naphthalene (○) and 1,2,4,5-tetramethylbenzene (□) concentrations. The luminescence of the Tb³⁺ ion was detected at 544 nm with excitation wavelengths of 275 and 278 nm for naphthalene and 1,2,4,5-tetramethylbenzene, respectively.

emission intensities of the $^5D_4 \rightarrow ^7F_J$ transitions increase monotonically with increasing aromatic hydrocarbon concentration to an asymptotic limit, which differs for each of the substrates. The energy and lifetime of Tb³⁺ luminescence is invariant with sensitizer concentration, as has been observed for other DTPA-Tb³⁺-sensitizer complexes.²¹ Figure 1 shows the titration profile of the luminescence intensity of the $^5D_4 \rightarrow ^7F_5$ transition at 544 nm as a function of the concentration of substrate. The differences in the limiting luminescence intensity between the two titrations reflect dissimilar molar absorptivity coefficients of the substrates ($\epsilon_{275} = 5530 \text{ M}^{-1} \text{ cm}^{-1}$ for naphthalene and $\epsilon_{278} = 692 \text{ M}^{-1} \text{ cm}^{-1}$ for durene), which is a result of the AETE process (vide infra), and different association constants of substrate to the CD cup ($K_{\text{assoc}} = 18\,000$ and $4\,000 \text{ M}^{-1}$ for naphthalene and durene,²² respectively). The association constant of naphthalene to **1**-Tb is ~ 25 -fold greater than its binding to β -CD ($K_{\text{assoc}} = 760 \text{ M}^{-1}$), which is consistent with the enhanced binding of hydrophobic guests to CDs spanned by flexible and rigid caps.^{14,23-25} Although we are not aware of any reports in which binding constants for substrates bound to a cyclodextrin capped with a neutral metal complex have been measured, the increased affinity of aromatic substrates to **1**-Tb is typical (up to 10^2) for capped β -CDs.

The increase in emission intensity with added substrate is accompanied by the appearance of bands in the excitation spectra that are energetically coincident with the absorption maxima of the aromatics. As shown in Figure 2 for the naphthalene titration, a profile that is identical to the absorption profile of naphthalene is obtained when the intensity of the Tb³⁺ emission at 544 nm is recorded as the excitation wavelength is scanned from 240 to 320 nm. When durene is the titrant, the excitation profile precisely matches the absorption spectra of durene. The naphthalene and durene $^1\pi\pi^*$ excited states are too short lived to participate in a bimolecular energy transfer reaction with the aromatic substrate. Consistent with this contention is the insensitivity of Tb³⁺ luminescence intensity and the absence of the aromatic $^1\pi\pi^*$ transitions in the excitation

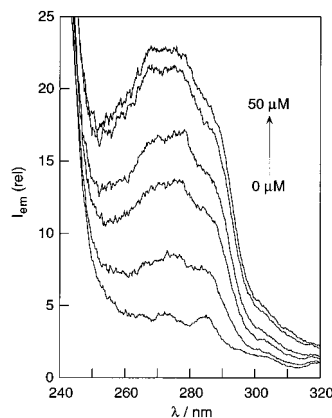


Figure 2. Excitation spectra ($\lambda_{\text{ex}} = 275 \text{ nm}$, $\lambda_{\text{det}} = 544 \text{ nm}$) for a 2.5×10^{-4} M aqueous solution of **1**-Tb with increasing concentrations of naphthalene (0, 10, 20, 30, 40, and $50 \mu\text{M}$).

spectrum of the DTPA complex of Tb³⁺ when titrated with substrate. The congruence between the excitation and aromatic absorption profiles and the enhancement of the Tb³⁺ emission intensity with substrate cannot be ascribed to intermolecular energy transfer. Instead these results are consistent with the indirect excitation of the 7F_J excited state manifold of the lanthanide ion by a unimolecular AETE process²⁶ from the aromatic residing in the CD cup to the Tb³⁺ ion cradled within the appended DTPA binding site at the bottom of the CD cup.

The results reported here present a novel method for detecting aromatic substrates by triggering a visible light response against a dark background. To date most optical detection methods of aromatics and polyaromatics rely on measuring the blue fluorescence produced upon direct excitation of the substrate.²⁷ Practically, laser-induced fluorescence approaches are problematic because the blue fluorescence of the aromatic or polycyclic aromatic substrates must be deconvoluted from the blue fluorescence of other organic interferences. Recently, a triggered luminescence response has been observed when PAHs displace fluorophores from DNA.²⁸ But the low affinity of small cyclic aromatics for DNA has prevented their detection by this method. The success of **1**-Tb in producing bright luminescence upon the molecular recognition of aromatic substrates in the CD cup arises as a result of the supramolecule's design. First, the short distance needed for efficient energy transfer in the AETE process is imposed by attaching the DTPA at the A,D-glucose sites of a β -cyclodextrin. Second, the three carboxylates of the DTPA cradle neutralize terbium's positive charge, which otherwise interferes with the association of a neutral, apolar guest into the hydrophobic CD cavity. Finally, the dimension of the β -CD cup is commensurate with that of mono- and bicyclic aromatics. Larger aromatics may in principle be detected by strapping the DTPA ligand to γ -CD. Conversely, applications desiring the exclusive detection of monocyclic aromatics can be realized with a DTPA-modified α -CD.

Acknowledgment. We thank Wanda K. Hartmann for helpful discussions and lifetime measurements. Financial support for this work was provided by the Air Force Office of Scientific Research (Grant F49620-94-0170) and the Center for Sensor Materials, a Materials Research Science and Engineering Center sponsored by the National Science Foundation (Grant DMR-9400417).

JA961323R

(21) Li, M.; Selvin, P. R. *J. Am. Chem. Soc.* **1995**, *117*, 8132.

(22) Equilibrium constants were determined by two independent methods based on absorption and fluorescence. For the former, the increase of the absorbance of naphthalene at 275 nm and of durene at 278 nm as a function of the **1**-Tb concentration in aerated aqueous solutions was measured. The reference cell contained an aqueous solution that was saturated in an aromatic; therefore, the increase in absorbance was a direct measure of the binding of the aromatic to **1**-Tb. Association constants were verified by employing standard Benesi-Hildebrand analysis of the change in luminescence of **1**-Tb upon substrate addition. Association constants measured by the two methods were within 10% of each other for a given substrate.

(23) (a) Breslow, R.; Czarniecki, M. F.; Emert, J.; Hamaguchi, H. *J. Am. Chem. Soc.* **1980**, *102*, 762. (b) Emert, J.; Breslow, R. *J. Am. Chem. Soc.* **1975**, *97*, 670.

(24) (a) Fujita, K.; Shinoda, A.; Imoto, T. *J. Am. Chem. Soc.* **1980**, *102*, 1161. (b) Fujita, K.; Ejima, S.; Ueda, T.; Imoto, T.; Schulten, H.-R. *Tetrahedron Lett.* **1984**, *25*, 3711.

(25) Tabushi, I.; Shimokawa, K.; Shimizu, N.; Shirakata, H.; Fujita, K. *J. Am. Chem. Soc.* **1976**, *98*, 7855.

(26) A carboxylate ligand-to-metal charge transfer excited state interferes with the AETE process when the metal ion is Eu³⁺. Therefore, in contrast to our previous work (refs 10 and 12), we chose the nonreducible Tb³⁺ as the lanthanide ion for supramolecule **1**. Spectroscopic details of the **1**-Tb and **1**-Eu complexes will be presented in ref 13.

(27) Kumke, M. U.; Lohmannsroben, H.-G.; Roch, T. *J. Fluoresc.* **1995**, *5*, 139.

(28) Harvath, J. J.; Gueguetkeri, M.; Gupta, A.; Penumatchu, D.; Weetall, H. H. In *Biosensor and Chemical Sensor Technology*; Rogers, K. R., Mulchandani, A., Zhou, W., Eds.; ACS Symposium Series 613; American Chemical Society: Washington, DC, 1995; Chapter 5.