SHORT PAPER

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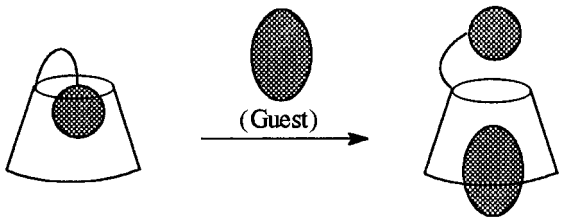
A new fluorescent chemosensor: synthesis and molecular recognition by sulfamidopyrrolidinylidene modified β-cyclodextrin†

L. Rajender Reddy, M. Arjun Reddy, N. Bhanumathi and K. Rama Rao*

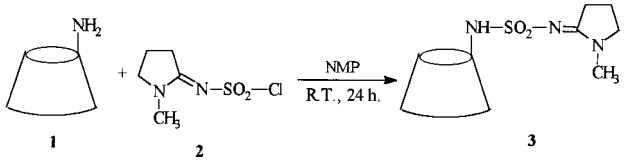
Organic Chemistry Division-I, Indian Institute of Chemical Technology, Hyderabad-500 007, India

Mono[6-deoxy-6-(1-methyl-2-pyrrolidinylidenesulfamido)-β-cyclodextrin synthesised as new artificial receptor has shown molecular recognition with remarkable sensitivity to various organic compounds with variation of fluorescence upon guest binding.

Signal transduction involving molecular recognition by artificial receptors is one of the frontier areas of supramolecular chemistry.[1,2] These artificial receptors will be having a chromophoric unit for spectral output which changes fluorescence upon guest binding. A variety of artificial receptors which function as chemosensors have been constructed.[3–10] The mechanism of signal transduction involves induced-fit changes in the conformation of the chemosensor receptors wherein the chemosensor changes fluorescence as it moves from inside to outside the cavity upon guest binding. Amongst various host–guest sensory systems studied so far, cyclodextrins (CDs) modified with a chromophore have acquired significance due to various studies that have been carried out, but most of the studies were directed towards dansyl substituted CDs.[11–20] In the course of our work on cyclodextrins,[21–23] we were in search of new fluorescence probes and have synthesised mono[6-deoxy-6-(1-methyl-2-pyrrolidinylidene sulfamido)]-β-cyclodextrin as a novel host–guest sensory system which shows remarkable molecular recognition in guest binding.



Mono[6-deoxy-6-(1-methyl-2-pyrrolidinylidenesulfamido)]-b-cyclodextrin (3) was prepared by the reaction of mono-6-deoxy-6-amino-b-cyclodextrin[24] (1) and 2-(chlorosulfonylimino)-1-methylpyrrolidine[25] (2) in 1-methyl-2-pyrrolidone (NMP) at room temperature for 24 hours.



Scheme 1

Fig. 1 shows the fluorescence spectra of **3** in 10% dimethyl sulfoxide aqueous solution in the presence and absence of 1-adamantanol (**8**). The compound **3** shows a fluorescence peak at 428 nm and the fluoresence intensity decreases with

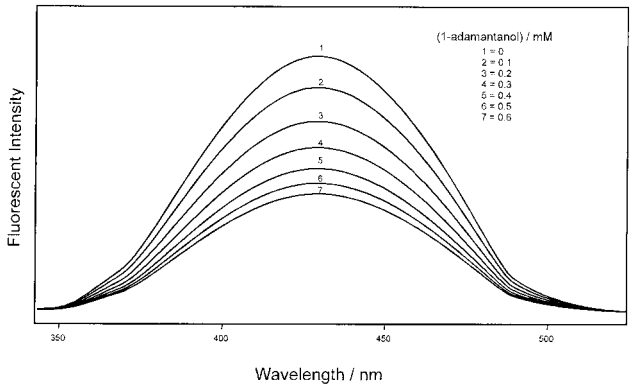


Fig. 1 Fluorescence spectra of 3 (2 x 10^{-6} M) in 10% DMSO aq solution in the presence of various concentrations of 1-adamantanol; excitation wavelength was 265 nm.

increasing concentration of 1-adamantanol. This guest-induced variation in the intensity of fluorescence suggests that the pyrrolidinyl moiety moves from the interior of the hydrophobic microenvironment of the cyclodextrin cavity towards the bulk water environment outside the cavity.

Fig. 2 shows the $\Delta I / I_o$ values (where I_o is the fluorescence intensity for **3** alone, I for a mixture of **3** and the guest and ΔI stands for I_o-I) obtained with various guests and reflects the sensitivity of the system to various guests. Fig. 2 shows that ursodeoxycholic acid (**4**) chenodeoxycholic acid (**5**) and 2-adamantanol (**9**) were detected with remarkably high sensitivities, exhibiting 0.59, 0.57 and 0.53 for ΔI/Io respectively. Ursodeoxycholic acid (**4**) has highest sensitivity amongst the steroids studied and cholic acid (**7**) has the lowest sensitivity. These steroids differ in the position of the hydroxyl groups. Among the other guests studied, 2-adamantanol (**9**) has the highest selectivity followed by *l*-borneol (**10**), 1-adamantanol

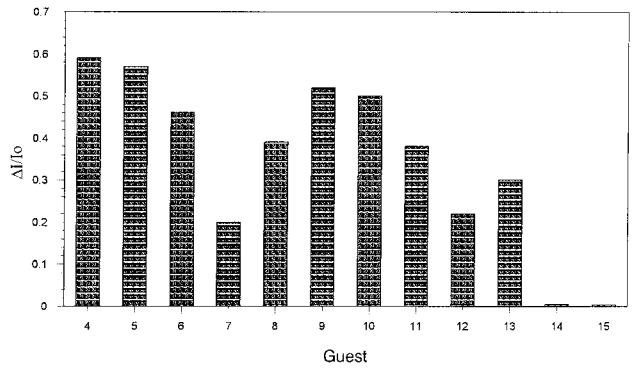


Fig. 2 The sensitivity factor DI/I_o of 3 (2 x 10-6 M) for various guests (0.1 mM)

* To receive any correspondence. E-mail: ramaraok@iict.ap.nic.in

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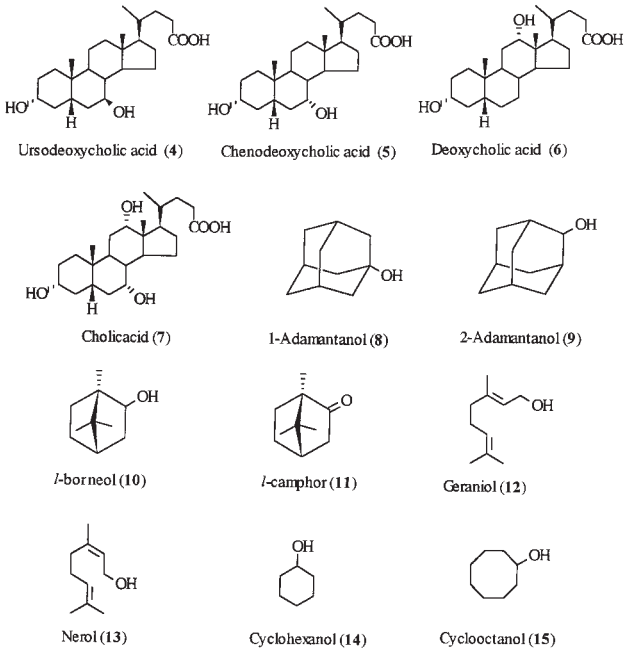
(**8**), geraniol (**12**) and camphor (**11**). The sensitivity of nerol (**13**) is comparatively less whereas that of cyclohexanol (**14**) and cyclooctanol (**15**) are almost negligible. 2-Adamantanol (**9**) is detected with higher sensitivity than the steroids deoxycholic acid (**6**) and cholic acid (**7**).



Thus in conclusion, the artificial receptor of **3** exhibits remarkable molecular ability in detecting different organic compounds by variation in fluoresence. This system has high sensitivity for ursodeoxycholic acid (**4**) chenodeoxycholic acid (**5**) and 2-adamantanol (**9**). It requires further studies to establish the relationship between the guest structure and sensitivity of this system.

Experimental

Melting points were recorded on a Büchi capillary melting point apparatus. The ^{1}H NMR spectra were recorded on a Gemini 200 MHz spectrometer, mass spectra were observed on V.G. Autospect M and optical rotations were measured on a JASCO DIP-360 polarimeter.

Synthesis of mono[6-deoxy-6(1-methyl-2-pyrrolidinylidenesulfamido)]-β-cyclodextrin (**3**): Mono(6-deoxy-6-amino)-β-cyclodextrin (1 mmol) and 2-(chlorosulfonylimino)-1-methylpyrrolidine (1.5 mmol) were dissolved in 20 ml of 1-methyl-2-pyrrolidone and the mixture was stirred at room temperature for 24 hours. Then the reaction mixture was poured into excess acetone (250 ml) and the product was filtered and washed with acetone. It was purified by dissolving in water, filtering and lyophilising, to get the desired product as white powder. Yield 1.2 g (92%), $[\alpha]_D^{25}$: +26° (c = 0.5, H_2O), ^{1}H NMR (D_2O) : δ 2.14 (m, 2H, >NCH$_2$CH_2), 2.91 (t, 2H, >NCH_2), 3.05 (s, 3H, >N-CH_3), 3.65 (m, 16H, H-2, H-4 of CD and CH_2-C(CH$_2$)=N-SO$_2$-), 3.95 (m, 28H, H-6, H-3, H-5 of CD), 5.12 (s, 7H, H-1 of CD). Mass (Maldi spectrum) : 1294 (M^+), 1316 [M^+ -1 + Na]. Analysis calcd. For $C_{47}H_{79}N_3O_{36}S$: (acc. mass 1293.4): C, 43.62; H, 6.15; N, 3.25; S, 2.48; Found : C, 43.44; H, 5.99; N, 3.05; S, 2.36%.

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References

1 A.W. Czarnik. *Fluorescent Chemosensors for Ion and Molecule Recognition*; ACS Symposium Series 538; American Chemical Society; Washington, DC, 1993.
2 A.W. Czarnik, Chemosensors of Ion and Molecule Recognition; Desvergne, J.-P., Ed.; *NATO Symposium Series*; Kluwer Academic Publishers, Dordrecht, 1997.
3 F. Fages, R.-P. Desvergne, K. Kampke, H. Bouas-Laurent, J.-M. Lehn, M. Meyer, and A.-M. Albrecht-Gary, *J. Am. Chem. Soc.*, 1993, **115**, 3658.
4 Y. Kubo, S. Maeda, S. Tokita and M. Kubo, *Nature*, 1996, **382**, 522.
5 M. Takeshita and S. Shinkai, *Chem. Lett.*, 1994, 125.
6 S. Shinkai, *J. Chem. Soc., Chem. Commun.*, 1992, 730.
7 A. Ueno, *Supramol. Sci.*, 1996, **3**, 31.
8 K. Hamasaki, H. Ikeda, A. Nakamura, A. Ueno, F. Toda, I. Suzuki and T. Osa, *J. Am. Chem. Soc.*, 1993, **115**, 5035.
9 I. Aoki, Y. Kawahara, T. Sasaki, T. Harada and S. Shinkai, *Bull. Chem. Soc. Jpn.*, 1993, **66**, 927.
10 G.K. Walkup and B. Imperiali, *J. Am. Chem. Soc.*, 1997, **119**, 3443.
11 A. Ueno, S. Minato, I. Suzuki, M. Fukushima, M. Ohkubo, T. Osa, F. Hamada and K. Murai, *Chem. Lett.*, 1990, 605.
12 H.Ikeda, M. Nakamura, N. Ise, N. Oguma, A. Nakamura, T. Ikeda, F. Toda and A. Ueno. *J. Am. Chem. Soc.*, 1996, **118**, 10980.
13 K. Hamasaki, S. Usui, H. Ikeda, T. Ikeda and A. Ueno, *Supramol. Chem.*, 1997, **8**, 125.
14 H. Ikeda, M. Nakamura, N. Ise, F. Toda and A. Ueno, *J. Org. Chem.*, 1997, **62**, 1411.
15 F. Hamada, Y. Kondo, R. Ito, I. Suzuki, T. Osa and A. Ueno, *J. Inclusion Phenom. Mol. Recognit. Chem.*, 1993, **15**, 273.
16 Y. Wang, T. Ikeda, H. Ikeda, A. Ueno and F. Toda, *Bull. Chem. Soc. Jpn.*, 1994, **67**, 1598.
17 Y. Wang, T. Ikeda, A. Ueno and F. Toda, *Chem. Lett.*, 1992, 863.
18 M. Saviano, A. Lombardi and V. Pavone, *Chem. Eur. J.*, 1996, **2**, 373.
19 R. Corradini, A. Dossena, G. Galaverna, R. Marchelli, A. Panagia and G. Sartor, *J. Org. Chem.*, 1997, **62**, 6283.
20 F. Hamada, S. Minato, T. Osa and A. Ueno, *Bull. Chem. Soc, Jpn.*, 1997, **70**, 1339.
21 K. Rama Rao and P.B. Sattur, *J. Chem. Soc., Chem. Commun.*, 1989, 342.
22 L. Rajender Reddy, M. Arjun Reddy, N. Bhanumathi and K. Rama Rao, *Synlett.*, 2000, **3**, 339.
23 K. Rama Rao, N. Bhanumathi and L. Rajender Reddy, *Synth. Commun.*, 1999, **29**, 1703.
24 S. Hanessian, A. Benalil and C. Laferrire, *J. Org. Chem.*, 1995, **60**, 4786.
25 K. Rama Rao, Y.V.D. Nageswar, T.N. Srinivasan and P.B. Sattur, *Synth. Commun.*, 1988, **18**, 877.