Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron Letters 47 (2006) 3577–3581
Tetrahedron Letters

Fluorescence sensing of tartaric acid: a case of excimer emission caused by hydrogen bond-mediated complexation

Kumaresh Ghosh* and Suman Adhikari

Department of Chemistry, University of Kalyani, Kalyani, Nadia 741235, India

Received 10 December 2005; revised 3 March 2006; accepted 9 March 2006
Available online 5 April 2006

Abstract—A novel quinoline based receptor that shows monomer emission quenching followed by intramolecular excimer emission upon hydrogen bond mediated complexation of tartaric acid has been designed and synthesized. The excimer emission has been used to confirm the selective recognition of tartaric acid over its nonhydroxy analogue, succinic acid. Binding ability was studied by ^{1}H NMR, UV–vis and fluorescence spectroscopic methods.

Due to many applications in analytical chemistry and biomedical research, the development of receptors which have the ability selectively to bind and sense neutral molecules, anions and cations through an optical response has attracted much attention in recent years.[1] In this regard, one of the recent approaches to the design of fluorescent signalling systems relies on guest-induced folding of flexible receptors, which brings the fluorophores close enough as to function as an excimer.[2] This excimer emission formation is sometimes used to 'read out' the molecular recognition process more conveniently.

Given the importance of dicarboxylic acids due to their biological relevance,[3] the need for fluorescent receptors as sensors for carboxylic acids in different contexts of molecular recognition research[4] has recently been of paramount interest. In this respect, tartaric acid, a common natural product in wines and other grape derived beverages, has received attention due to its structural features possessing several hydrogen bond donors and acceptors. Many hydrogen bonding receptors for the binding of tartaric acid and its derivatives have been reported.[5]

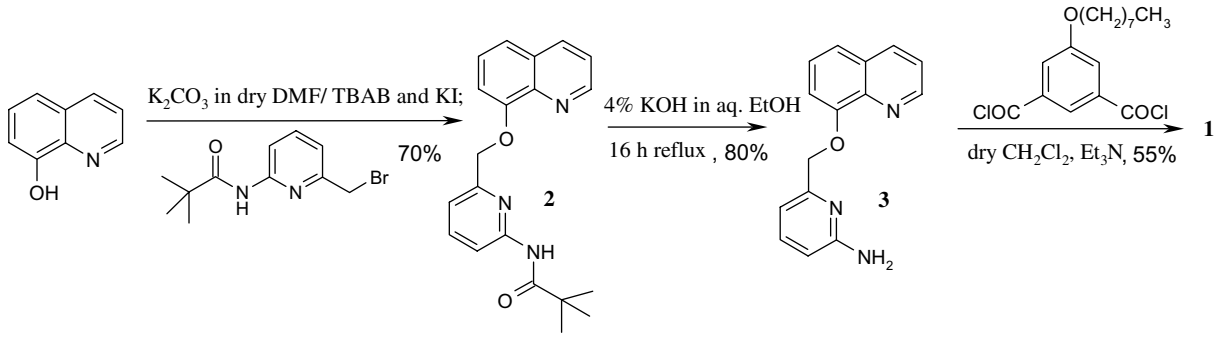
A binaphthol-based aminopyridyl group for enantioselective recognition of diacetyl tartaric acid derivatives,[6a] unique trench type binding on a porphyrin for tartaric acid derivatives,[6b] a colorimetric chemosensing ensemble for tartrate/malate in beverages developed by Anslyn and co-workers,[6c] are notable. Tryptophan-based chiral sensors[7a] for dibenzoyl tartrate and anthracene labelled fluorescent chiral sensors[7b] for enantiomeric discrimination of tartaric acid are also interesting. As a result of our research on molecular recognition,[8,4a] we herein report the design and synthesis of a quinoline-based sensor **1** which shows selective recognition of tartaric acid from its nonhydroxy analogue succinic acid by exhibiting selective excimer emission.

The receptor **1** was synthesized according to Scheme 1 and was isolated in 55% yield.[9] The lumophore, 8-hydroxyquinoline was first coupled with 2-*N*-pivaloylamino-6-bromomethylpyridine (obtained from 2-*N*-pivaloylamino-6-methylpyridine by reaction with NBS in dry CCl_4) to give compound **2**. Amide hydrolysis of **2** then afforded compound **3** in 80% yield. On coupling **3** with 5-octyloxy-1,3-benzenedicarbonyl chloride (prepared by etherification of diethyl 5-hydroxyisophthalate with octyl bromide in dry acetone using K_2CO_3 and hydrolysis of the esters followed by reaction with oxalyl chloride) yielded the desired receptor **1**.

The quinoline moiety has been coupled with a pyridyl unit to serve as a fluorophore as well as to involve the quinoline nitrogens as hydrogen bond acceptors. Energy minimization[10] of **1** ($E_{min} = 19.92$ kcal/mol) shows the nearly parallel arrangement of the pendent quinolines

Keywords: Molecular recognition; Excimer emission; Selective binding; Tartaric acid; Neutral molecule binding.
* Corresponding author. Tel.: +91 33 25828282x306; fax: +91 33 25828282; e-mail: ghosh_k2003@yahoo.co.in

0040-4039/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2006.03.044



Scheme 1. The synthesis of receptor **1**.

with a separation of distance of 4.01 Å and the open binding cleft assumes a nonplanar shape (Fig. 1). The hydrogen bonding groups in the cavity are well arranged for complexation of hydroxydicarboxylic acids.

The sensitivity and the selectivity of receptor **1** were evaluated by observing the change in ^{1}H NMR, UV–vis and fluorescence emission in $CHCl_3$.

^{1}H NMR of the receptor **1** in $CDCl_3$ (5.83×10^{-3} M) revealed the position of the amide protons at δ 8.96 ppm. The addition of powdered D-(−)-tartaric acid to this solution showed clear dissolution after sonication. This was evident from the downfield shift of the amide protons (δ 8.96–9.90 ppm = $\Delta\delta$ 0.94 ppm) of **1** as well as from the appearance of a new peak at δ 4.97 ppm due to methine protons in the 1:1 complex (Fig. 2). The integration ratio of tartaric acid methine protons to the receptor amide protons in the NMR spectrum of the complex (Fig. 2; top) clearly revealed the formation of a 1:1 complex. On dilution of the 1:1 complex, there was practically no shift of the receptor amide protons. This suggests strong complexation of tartaric acid into the open cleft of the receptor **1** as in the mode shown in complex **A** (Fig. 1).

Determination of the association constants was, however impossible because of the negligible change in the position of the amide protons after forming the 1:1 complex.

The absorption spectra of **1** and its 1:1 complexes with D-(−)-tartaric, *rac*-malic, and succinic acids in $CHCl_3$ were recorded to investigate the interactions in the ground state. Chloroform solutions of the 1:1 complexes were diluted gradually with chloroform and the change in intensity, as a function of the concentration was linear in each case. Figure 3 shows the effect of dilution on the UV spectra of the tartaric acid 1:1 complex with **1**. This change in the UV–vis spectra was used conveniently to study the binding since the lower concentration used led to a more accurate determination of the values of the association constants[11] for the acids (Table 1). The hydroxy analogues of succinic acid show higher binding constants due to the greater number of hydrogen bonds. Interestingly, the binding values were reduced 10-fold as the number of –OH groups decreases. The binding constant values in our case, however, are greater in magnitude than the previously reported naphthyridine-based receptors.[5b]

The fluorescence spectra of the receptor **1** were simultaneously recorded in $CHCl_3$ both in the presence and

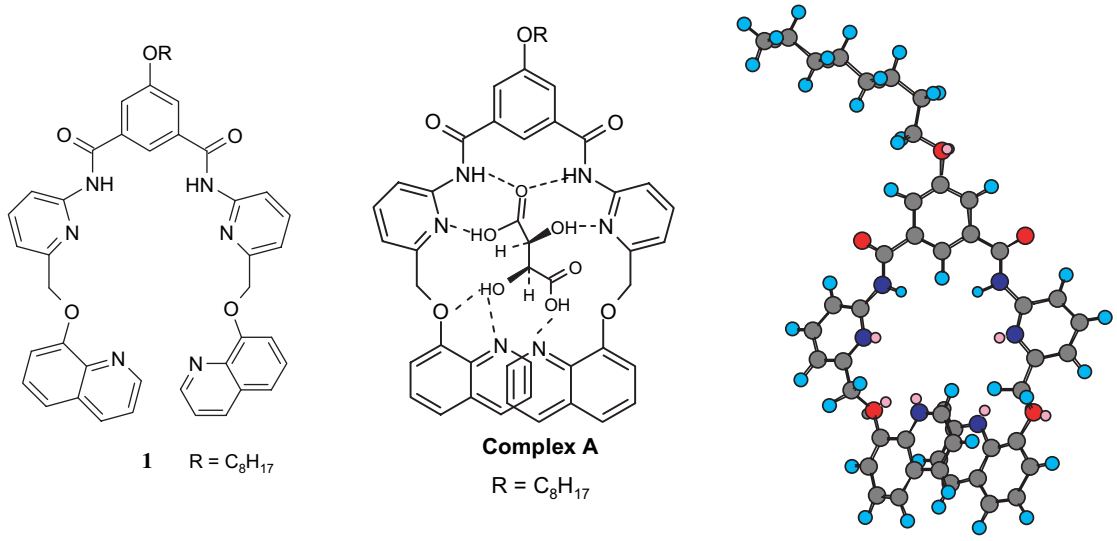


Figure 1. Energy minimized structure of **1**.

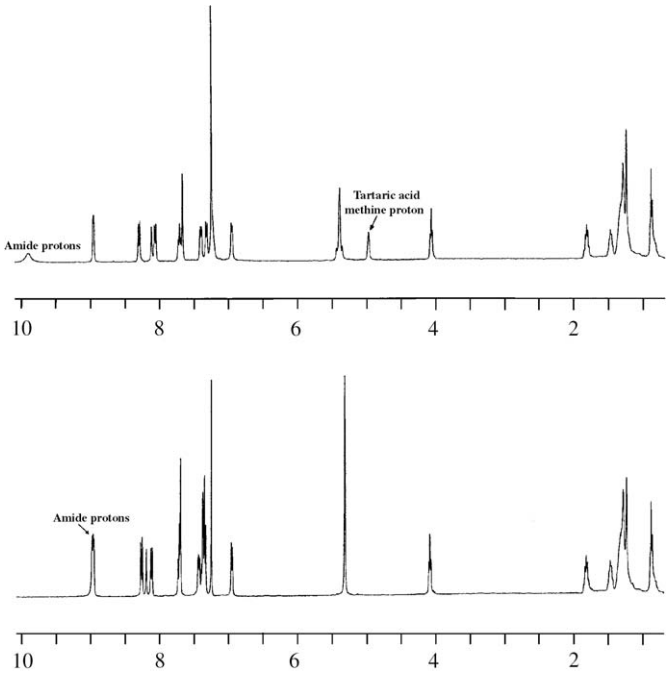


Figure 2. ^{1}H NMR (in $CDCl_3$) spectra of receptor **1** (bottom) and the 1:1 complex with tartaric acid (top).

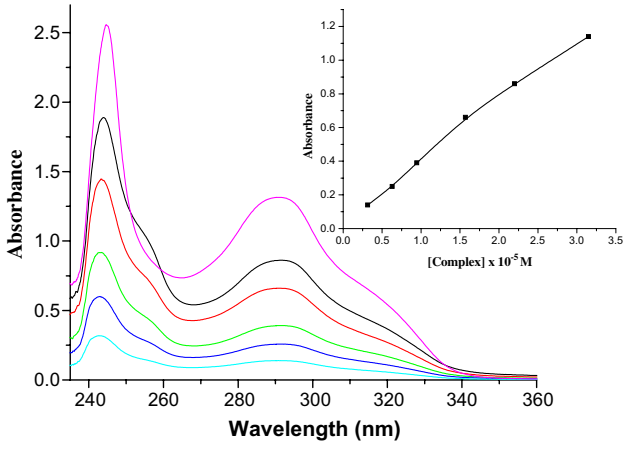


Figure 3. UV spectra of complex **A** and its change of absorbance on dilution; (inset) plot of absorbance versus concentration of the complex of tartaric acid with **1**.

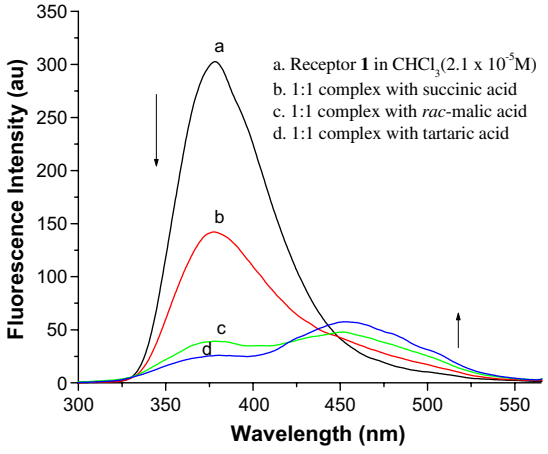


Figure 4. Fluorescence change of **1** in $CHCl_3$ in the presence of dicarboxylic acids ($\lambda_{ex} = 290$ nm).

Table 1. Association constants determined by UV ($CHCl_3$)

Guest	Association constant K_a (M^{-1})
D-(−)-Tartaric acid	9.81×10^5
rac-Malic acid	4.96×10^4
Succinic acid	9.38×10^3

absence of dicarboxylic acid guests. Figure 4 shows the fluorescence spectra of **1** and its 1:1 complexes with D-(−)-tartaric, *rac*-malic and succinic acids in $CHCl_3$. On complexation with these acids significant fluorescence quenching takes place.

However, the degree of quenching is dependent on the nature of the acid. The magnitude of the quenching

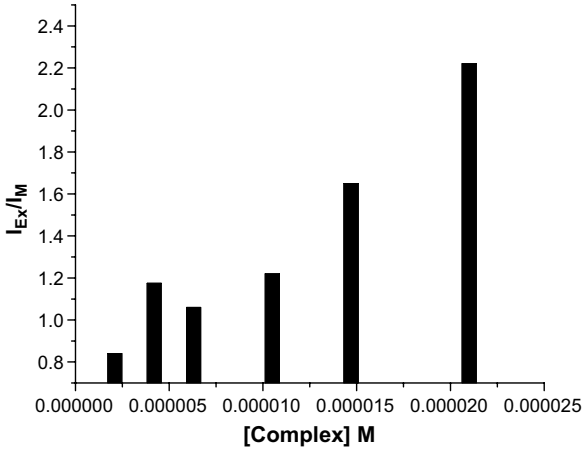


Figure 5. Plot of the ratio of excimer to monomer emission versus concentration of the complex of **1** with tartaric acid.

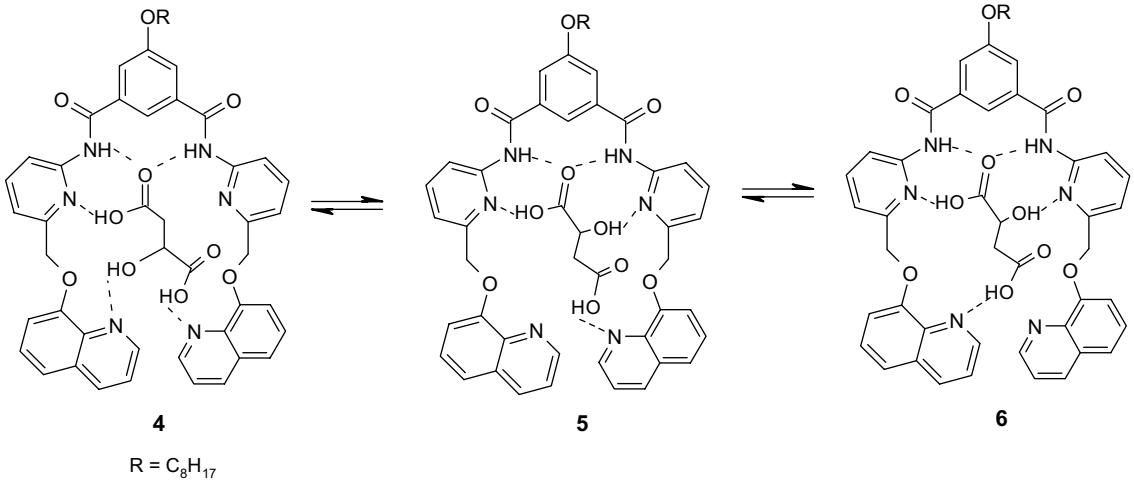


Figure 6. Possible hydrogen bonding structures of **1** with *rac*-malic acid.

efficiency (ϕ_Q)[12] follows the order of D-(−)-tartaric acid (0.92) > *rac*-malic acid (0.87) > succinic acid (0.53), reflecting the stabilities of the complexes (see the binding constant values in Table 1). In the case of D-(−)-tartaric acid, an additional peak at 453 nm along with monomer emission at 377 nm was noticed due to excimer formation. The excimer emission resulted from the intramolecular excimer, rather than intermolecularly, as indicated by the dilution experiments at different concentrations in which the intensities of the ratio of excimer to monomer emission changed gradually (Fig. 5). The formation of this excimer in the presence of D-(−)-tartaric acid could be attributed to the tartaric acid templated hydrogen bond induced organization of the quinoline moieties. Such excimer formation was not observed in the case of succinic acid due to the lack of –OH groups which are necessary to bring closer together the pendant quinoline groups of the binding arms via hydrogen bond formation. This was confirmed using *rac*-malic acid where the excimer emission was observed (Fig. 4) due to the possibility of hydrogen bonding structure **4** which may remain in equilibrium with **5** and **6** (Fig. 6). It is, therefore, worth noting that the conformation of **1** was changed substantially only on binding with hydroxydicarboxylic acids rather than with a dicarboxylic acid of the same chain length.

In pursuit of a fluorescent sensor we have demonstrated that hydrogen bond-mediated complexation of tartaric acid with **1** results in monomer emission quenching followed by intramolecular excimer emission. This excimer emission is moderate and convenient for practical use to distinguish tartaric acid from its nonhydroxy analogue succinic acid. Further study on this subject is underway in our laboratory.

Acknowledgements

We thank CSIR [01(1922)/04/EMR-II], New Delhi, India, for financial support and DST-FIST, for providing the facilities in the Department.

References and notes

1. (a) *Chemosensors of ion and Molecule Recognition*; Desvergne, J. P., Czarnik, A. W., Eds.; NATO ASI Series; Kluwer Academic: Dordrecht, 1997; Vol. 492; (b) De Silva, A. P.; Gunaraine, H. Q. N.; Gunnlaugsson, T.; Huxley, A. J. M.; McCoy, C. P.; Rademacher, J. T.; Rice, T. E. *Chem. Rev.* **1997**, *97*, 1515; (c) Pfeffer, F. M.; Gunnlaugsson, T.; Jensen, P.; Kruger, P. E. *Org. Lett.* **2005**, *7*, 5357, and references cited therein.
2. (a) Aoki, I.; Harada, T.; Sakaki, T.; Kawahara, Y.; Shinkai, S. *J. Chem. Soc., Chem. Commun.* **1992**, 1341; (b) Liao, J.-H.; Chen, C.-T.; Fang, J.-M. *Org. Lett.* **2002**, *4*, 561; (c) Bai, Y.; Zhang, B.-G.; Xu, J.; Duan, C.-Y.; Dang, D.-B.; Liu, D.-J.; Meng, Q.-J. *New J. Chem.* **2005**, *29*, 777; (d) Nishizawa, S.; Kaned, H.; Uchida, T.; Teramae, N. *J. Chem. Soc., Perkin Trans. 2* **1998**, 2325.
3. Styrer, L. *Biochemistry*, 3rd ed.; Freeman: New York, 1988; p 188; pp 373–394; p 376; pp 575–625.
4. (a) Goswami, S.; Ghosh, K.; Dasgupta, S. *J. Org. Chem.* **2000**, *65*, 1907; (b) Yang, D.; Li, X.; Fan, Y.-F.; Zhang, D.-W. *J. Am. Chem. Soc.* **2005**, *127*, 7996, and references cited therein.
5. (a) Zhao, J.; Davidson, M. G.; Mahon, M. F.; Kociok-Kohn, G.; James, T. D. *J. Am. Chem. Soc.* **2004**, *126*, 16179; (b) Goswami, S.; Ghosh, K.; Mukherjee, R. *Tetrahedron* **2001**, *57*, 4987; (c) Hernandez, J. V.; Almaraz, M.; Raposo, C.; Martin, M.; Lithgow, A.; Crego, M.; Cabellero, C.; Moran, J. R. *Tetrahedron Lett.* **1998**, *39*, 7401.
6. (a) Garcia-Tellado, F.; Albert, J.; Hamilton, A. D. *J. Chem. Soc., Chem. Commun.* **1991**, 1761; (b) Kuroda, Y.; Kato, Y.; Ito, M.; Hasegawa, J.; Ogoshi, H. *J. Am. Chem. Soc.* **1994**, *116*, 10338; (c) Lavigne, J. J.; Anslyn, E. V. *Angew. Chem., Int. Ed.* **1999**, *38*, 3666.
7. (a) Xu, K.-X.; He, Y.-B.; Qin, H.-J.; Qing, G.-Y.; Liu, S.-Y. *Tetrahedron* **2005**, *16*, 3042; (b) Zhao, J.; James, T. D. *Chem. Commun.* **2005**, 1889.
8. (a) Ghosh, K.; Masanta, G. *Supramol. Chem.* **2005**, *17*, 331; (b) Goswami, S.; Ghosh, K.; Dasgupta, S. *J. Org. Chem.* **2000**, *65*, 1907–5504.
9. Receptor **1**: Mp 110–111 °C, ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.96 (s, 2H, –NHCO–), 8.95 (d, 2H, $J = 8$ Hz), 8.26 (d, 2H, $J = 8$ Hz), 8.19 (s, 1H), 8.12 (d, 2H, $J = 8$ Hz), 7.71 (t, 4H, $J = 8$ Hz), 7.42 (m, 2H), 7.37–7.33 (m, 6H),

6.95 (d, 2H, $J = 8$ Hz), 5.32 (s, 4H), 4.08 (t, 2H, $J = 8$ Hz), 1.85–1.80 (m, 2H), 1.46 (m, 2H), 1.33–1.15 (m, 8H), 0.86 (t, 3H, $J = 6$ Hz). ^{13}C ($CDCl_3$, 125 MHz): δ 165.2, 160.3, 155.4, 154.3, 151.6, 149.7, 140.7, 139.5, 136.4, 136.1, 129.8, 126.9, 122.1, 120.5, 118.1, 118.0, 117.9, 113.7, 109.9, 71.1, 69.1, 32.2, 29.7, 29.6, 29.5, 26.3, 23.4, 14.5. HRMS calcd for $C_{46}H_{44}N_6O_5$: 760.3363. Found: 760.3382. FTIR (KBr) ν_{max}: 3300, 2924, 2853, 1674, 1597, 1577, 1457, 1109 cm^{-1}.

10. MM2 calculations were performed using CS Chem 3D version 6.0.
11. Colquhoun, H. M.; Goodings, E. P.; Maud, J. M.; Stoddart, J. F.; Wolstenholme, J. B.; Williams, D. J. *J. Chem. Soc., Perkin Trans. 2* **1985**, 607.
12. The quenching efficiency was determined using the equation: $\phi_Q = (I_{host} - I_{complex})/I_{host}$, where I_{host} and $I_{complex}$ are the fluorescence intensities (377 nm) of **1** and its complex, respectively.