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Recognition of the chain length of α,ω-diamines by a *meso*-ternaphthalene derivative with two crown ethers

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Abstract

A new ditopic receptor **2** consisting of a *meso*-ternaphthalene backbone and two crown rings has been shown to selectively complex and transfer dipicrate of 1,9-diaminononane and 1,10-diaminodecane from aqueous solution into the organic phase.

Keywords: crown ethers; molecular recognition; diamines.

Over the past two decades, many synthetic receptors have been constructed based on the fact that some of their properties, such as shape, size and functional groups, complement those of a guest molecule. Several ditopic receptors have been reported to recognize the length of α,ω-diamines. They have carboxylic acids[1] or crown ethers[2] to bind to amines using specific hydrogen-bonding interactions. Recently, we reported the preparation of chiral ter- and quaternaphthalene derivatives.[3] These compounds are expected to be backbones for host molecules for recognizing the length of α,ω-diamines due to their upright nature. In this paper, we report new ditopic receptors **1** and **2** consisting of a *meso*-ternaphthalene backbone and two crown rings, the latter of which showed sharp recognition of the length of α,ω-diamines **3**.

The synthetic route to the host molecules **1** and **2** is outlined in Scheme 1. Racemic ternaphthalene **4**[3] was methylated and then subjected to deacetylation followed by reductive removal of the benzyl group to give *meso*-ternaphthalene **5**, which was then converted to ditriflate **6** in 74% overall yield from **4**. The coupling partner **7** was prepared from the corresponding bromide[4] in 50% yield. The reaction of triflate **6** with boric acid **7** under modified Suzuki coupling conditions[5] gave the desired host **1** in 80% yield. Simultaneous deprotection of an allylic group took place under these reaction conditions. Methylation of **1** gave **2** in 65% yield.

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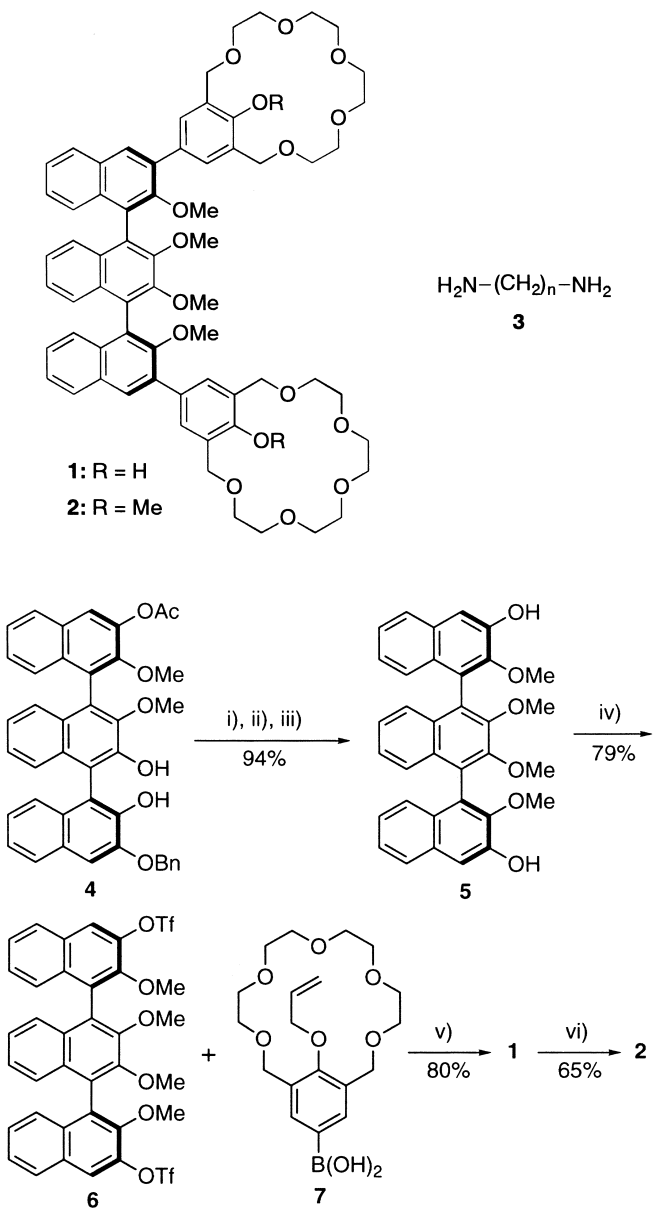

Scheme 1. Reactions and conditions: (i) MeI, K_2CO_3, acetone, reflux; (ii) NaOH, H_2O–THF, rt; (iii) Pd/C, HCO_2NH_4, THF–MeOH, 60°C, 1 h; (iv) Tf_2O, *i*-Pr_2NEt, CH_2Cl_2, rt; (v) $Pd(PPh_3)_4$, Na_2CO_3, toluene–MeOH–H_2O, 80°C, 26 h; (vi) MeI, NaH, DMF, 0°C–rt

Interaction between host **1** and α,ω-diamines **3** was examined by the UV–vis spectroscopic method. Absorption at 375 nm increased upon addition of these diamines to the host **1** in THF:H_2O (4:1). Job plots suggested that the host:guest ratio in complexes was 1:1 at 25°C. The association constants (K_a) were determined by titration, and analyzed by the Rose–Drago method.[6] The results are summarized in Table 1. No relationship was observed between the association constants and the length of α,ω-diamines (entries 1–5). The behavior of **1** and nonylamine indicated 1:1 complexation, and its *K*a of 139±13 (entry 6) was almost the same as those

of **1** and diamines. These results indicate that complexation is based on acid-base interaction between only one of the phenol crown rings of **1** and one of the amino groups of α,ω-diamines **3**.[7]

Table 1
The association constant (K_a) of the complexes of the hosts **1** and **2** with diamines **3**

entry	diamine **3** (n =)	host[a]	*K*a (M^{-1})	method[b]
1	4	**1**	326 ± 23	a
2	8	**1**	281 ± 11	a
3	10	**1**	219 ± 7	a
4	12	**1**	246 ± 17	a
5	14	**1**	168 ± 6	a
6	nonylamine	**1**	139 ± 13	a
7	6	**2**	(6.88 ± 0.50) x 10^3	b
8	8	**2**	(4.05 ± 0.27) x 10^5	b
9	9	**2**	(6.87 ± 0.21) x 10^6	b
10	10	**2**	(6.92 ± 0.28) x 10^6	b
11	11	**2**	(1.22 ± 0.18) x 10^6	b
12	12	**2**	(2.96 ± 0.10) x 10^5	b
13	14	**2**	(3.44 ± 0.24) x 10^5	b

[a] [Host] = 1.23 x 10^{-3} M for entries 1-6 and $[Host]_{org}$ = 1.10 x 10^{-3} M for entries 7-13. [b] a) Determined by the titration. See the text. b) Determined by diammonium picrate liquid-liquid extraction from H_2O to $CHCl_3$. The *K*a values are given by $[\mathbf{2}\bullet\mathbf{3}^{2+}\bullet Pic_2^{2-}]_{org}/[\mathbf{2}]_{org}[\mathbf{3}^{2+}\bullet Pic_2^{2-}]_{org}$, where $[\ ]_{org}$ indicates the concentration in $CHCl_3$. See ref. 2i.

The ability of the ditopic receptor **2** to recognize dipicrates of α,ω-diamines **3** was investigated by the method based on picrate liquid–liquid extraction from H_2O to $CHCl_3$ at 25°C.[2i,8] The K_a values were calculated, assuming that a 1:1 complex was formed. The K_a values clearly depend on the chain length of the guests (entries 7–13). It was shown that the host **2** specifically bind diamines **3** ($n = 9$ and 10). The K_a values clearly decreased for complexes of **2** with 1,11-diaminoundecane or the longer and with 1,8-diaminooctane or the shorter, due to the rigid nature of the framework of the host **2**. In general, ditopic receptors sharply distinguish the amine with optimal length from those of a shorter length, while the recognition of the length is rather loose for diamines longer than that of optimal length. As can be seen from Table 1, the K_a value for 1,11-diaminoundecane is approximately six times less than that of 1,10-diaminodecane (see entries 11 and 10). The only example showing sharp discrimination of the length of guest includes a bisanthracenyl macrotricyclic receptor reported by Lehn et al.[2]

The structures of **1** and **2** were determined by an X-ray crystallographic analysis.[9] Host **1** cocrystallized with two disordered toluene molecules. The central naphthyl ring was also disordered in the opposite sense in a ratio of about 1:1 in the crystalline state (Fig. 1a,b). The crystals of host **2** obtained from acetonitrile contain two molecules of the solvent. No disorder of the central naphthyl ring was observed, although an oxygen atom in the crown ring was disordered (Fig. 1c).[10] A marked difference between the crystal structures of **1** and **2** was found in the

conformation of the crown rings. Two rings of **2** were bent over to create a cavity, while those of **1** were spread out, which may explain the selective complexation of **2** with diamines.

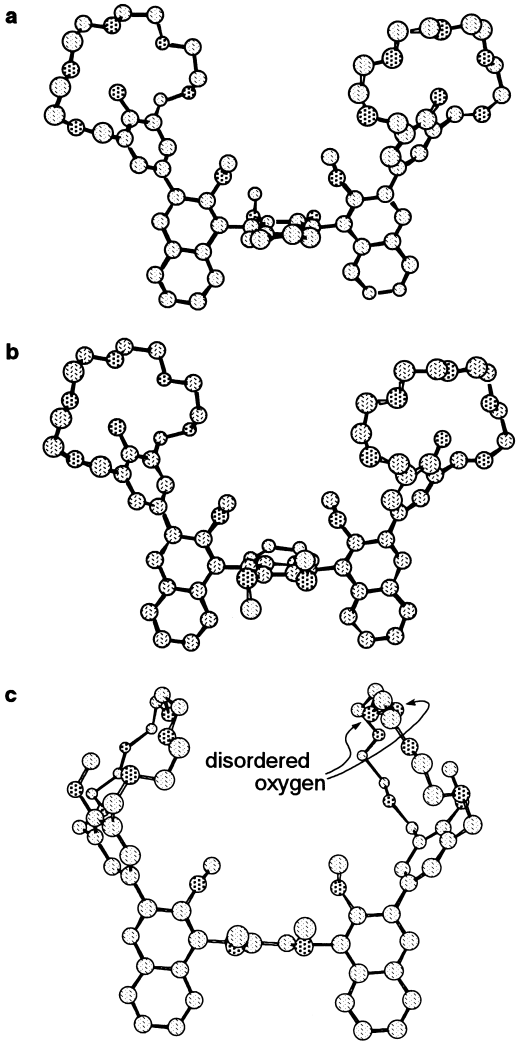

Figure 1. X-Ray crystal structures of **1** (a) and (b), and **2** (c). Hydrogen atoms and solvent molecules have been omitted for clarity

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References

1. Li, C.; Medina, J. C.; Maguire, G. E. M.; Abel, E.; Atwood, J. L.; Gokel, G. W. *J. Am. Chem. Soc.* **1997**, *119*, 1609–1618.

2. (a) Kotzyba-Hibert, F.; Lehn, J.-M.; Vierling, P. *Tetrahedron Lett*. **1980**, *21*, 941–944. (b) Kotzyba-Hibert, F.; Lehn, J.-M.; Saigo, K. *J. Am. Chem. Soc*. **1981**, *103*, 4266–4268. (c) Kintzinger, J.-P.; Kotzyba-Hibert, F.; Lehn, J.-M.; Pagelot, A.; Saigo, K. *J. Chem. Soc., Chem. Commun*. **1981**, 833–836. (d) Pascard, C.; Riche, C.; Cesario, M.; Kotzyba-Hilbert, F.; Lehn, J.-M. *J. Chem. Soc., Chem. Commun*. **1982**, 557–560. (e) Shinkai, S.; Honda, Y.; Kusano, Y.; Manabe, O. *J. Chem. Soc., Chem. Commun*. **1982**, 848–850. (f) Shinkai, S.; Honda, Y.; Minami, T.; Ueda, K.; Manabe, O.; Tashiro, M. *Bull. Chem. Soc. Jpn*. **1983**, *56*, 1700–1704. (g) Hamilton, A. D.; Lehn, J.-M.; Sessler, J. L. *J. Chem. Soc., Chem. Commun*. **1984**, 311–313. (h) Smeets, J. W. H.; Sijbesma, R. P.; van Dalen, L.; Spek, A. L.; Smeets, W. J. J.; Nolte, R. J. M. *J. Org. Chem*. **1989**, *54*, 3710–3713. (i) Smeets, J. W. H.; Visser, H. C.; Kaats-Richters, V. E. M.; Nolte, R. J. M. *Rec. Trav. Chim. Pays-Bas*, **1990**, *109*, 147–153. (j) Misumi, S. *Pure Appl. Chem*. **1990**, *62*, 493–498. (k) Sutherland, I. O. *Pure Appl. Chem*. **1990**, *62*, 499–504. (l) de Silva, A. P.; Sandanayake, K. R. A. S. *Angew. Chem., Int. Ed. Engl*. **1990**, *29*, 1173–1175. (m) Voyer, N.; Deschênse, D.; Bernier, J.; Roby, J. *J. Chem. Soc., Chem. Commun*. **1992**, 134–136. (n) Fages, F.; Desvergne, J.-P.; Bouas-Laurent, H.; Lehn, J.-M.; Konopelski, J. P.; Marsau, P.; Barrans, Y. *J. Chem. Soc., Chem. Commun*. **1990**, 655–658. (o) Fages, F.; Desvergne, J.-P.; Kampke, K.; Bouas-Laurent, H.; Lehn, J.-M.; Meyer, M.; Albrecht-Gary, A.-M. *J. Am. Chem. Soc*. **1993**, *115*, 3658–3664. (p) Jeong, K.-S.; Park, J. W.; Cho, Y. L. *Tetrahedron Lett*. **1996**, *37*, 2795–2798. (q) Hayashi, T.; Nonoguchi, M.; Aya, T.; Ogoshi, H. *Tetrahedron Lett*. **1997**, *38*, 1603–1606. (r) Fuji, K.; Tsubaki, K.; Tanaka, K.; Hayashi, N.; Otsubo, T.; Kinoshita, T. *J. Am. Chem. Soc*. **1999**, *121*, 3807–3808. (s) Kubo, Y.; Murai, Y.; Yamanaka, J.; Tokita, S.; Ishimaru, Y. *Tetrahedron Lett*. **1999**, *40*, 6019–6023.
3. Tanaka, K.; Furuta, T.; Fuji, K.; Miwa, Y.; Taga, T. *Tetrahedron: Asymmetry* **1996**, *7*, 2199–2202.
4. von Gent, J.; Sudhölter, E. J. R.; Lambeck, P. V.; Popma, T. J. A.; Gerritsma, G. J.; Reinhoudt, D. N. *J. Chem. Soc., Chem. Commun*. **1988**, 893–895.
5. Thompson, W. J.; Gaudino, J. *J. Org. Chem*. **1984**, *49*, 5237–5243.
6. Rose, N. J.; Drago, R. S. *J. Am. Chem. Soc*. **1959**, *81*, 6138–6145.
7. Browne, C. M.; Ferguson, G.; McKervey, M. A.; Mulholland, D. L.; O'Connor, T.; Parvez, M. *J. Am. Chem. Soc*. **1985**, *107*, 2703–2712.
8. Koenig, K. E.; Lein, G. M.; Stuckler, P.; Kaneda, T.; Cram, D. J. *J. Am. Chem. Soc*. **1979**, *101*, 3553–3566.
9. Crystal data for **1**·(toluene)$_2$: $C_{80}H_{88}O_{16}$, $M = 1305.55$, triclinic, $a = 10.334(3)$ Å, $b = 33.582(5)$ Å, $c = 10.303(2)$ Å, $\alpha = 94.77(2)^\circ$, $\beta = 95.61(2)^\circ$, $\gamma = 94.31(2)^\circ$, $V = 3533(1)$ Å^3, space group P-1(#2), $z = 2$, $D = 1.227$ g cm^{-1}, μ(Cu-Kα) = 6.87 cm–1, Rigaku AFC7R diffractormeter with graphite-monochlomated Cu-Kα ($\lambda = 1.54178$ Å, $T = 293$ K). No. of measured reflections: 12422. Structure solution by direct method (SHELX-86), refinement by full-matrix least-squares using all reflections, $R = 0.083$ ($|F_0| > 4\ \sigma(F0)$), $Rw = 0.101$ (all reflections), GOF = 2.79, Occ. = 0.5 for **1a** and 0.5 for **1b**. Crystal data for **2**·$(CH_3CN)_2$·$(H_2O)_2$: $C_{72}H_{86}N_2O_{18}$, $M = 1267.47$, triclinic, $a = 15.172(1)$ Å, $b = 17.771(2)$ Å, $c = 14.481(2)$ Å, $\alpha = 106.29(1)^\circ$, $\beta = 109.718(9)^\circ$, $\gamma = 67.694(7)^\circ$, $V = 3348.0(7)$ Å^3, space group P-1(#2), $z = 2$, $D = 1.257$ g cm^{-1}, μ(Cu-Kα) = 7.39 cm^{-1}, Rigaku AFC7R diffractormeter with graphite-monochlomated Cu-Kα ($\lambda = 1.54178$ Å, $T = 293$ K). No. of measured reflections: 11844. Structure solution by direct method (SHELX-97), refinement by full-matrix least-squares using all reflections, $R = 0.089$ ($|F_0| > 5\ \sigma(F_0)$), $Rw = 0.129$ (all reflections), GOF = 3.45.
10. Disorder of the central naphthyl ring similar to that of **1** was found in the crystals obtained from acetone.