Molecular Recognition of Butylamines by a Binaphthyl-derived Chromogenic Calix[4]crown

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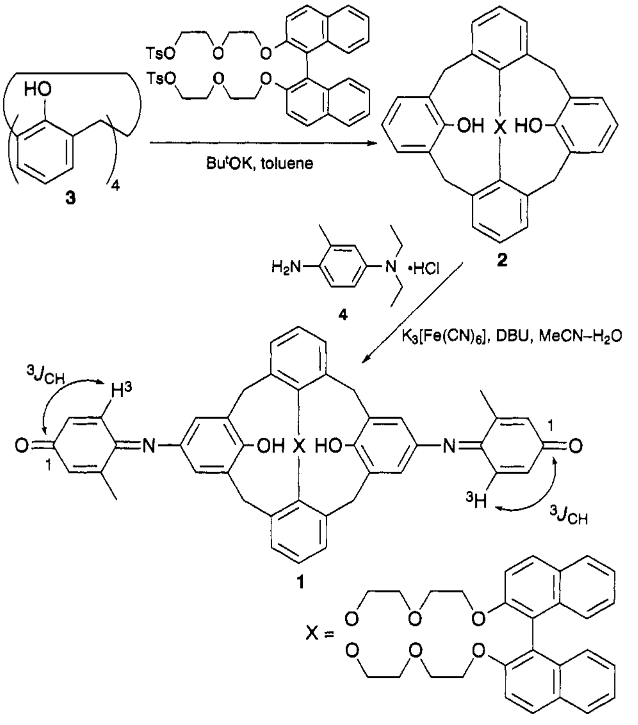
The synthesis of a new type of chromogenic calixarene, an indophenol- and binaphthylderived calix[4]crown **1**, and its novel sensory system for the shape of butylamines, are described.

Synthetic chromogenic receptors that give rise to a specific colour change on selective complexation with guest species have received much attention as efficient spectrophotometric analytical reagents for the detection of particular species[1] as well as the design of molecular devices having 'recognition and optical sensing functions'.[2] In the latter case, since the molecular recognition process could be efficiently amplified as an optical signal, a detailed understanding of receptor–substrate interactions in biological systems containing enzymes, the nervous system and so on becomes feasible using such a receptor. We are interested in the search for a molecular structure that can serve as an optical sensory system for selective recognition towards biologically and chemically important amines. To date, chromogenic crown ethers[3] and calixarenes[4] have been reported as optical receptors for amines. These compounds are useful for the detection of complementary interactions between host molecules and the shape of amines, which can be easily monitored by spectroscopy. However, no chromogenic receptor which can recognise the varying structures of butylamines has yet been prepared. Our interest in the development of such a chromogenic receptor led us to synthesize a chromogenic binaphthyl-derived calix[4]crown derivative in which the steric and/or electrostatic effects of the 1,1′-binaphthyl[5] unit could be useful for the molecular recognition of amines. Here we report the synthesis of calix[4]crown **1**, which has potential as a chromogenic receptor which can discriminate between butylamines.

Compound **2**, a 1,1′-binaphthyl-derived calix[4]crown, was synthesized by the condensing reaction between calix[4]arene **3**[6] and 2,2′-bis(2-toluene-*p*-sulfonylethoxyethoxy)-1,1′-binaphthalene in 52% yield. In order to introduce the chromogenic function into **2**, we condensed **2** with 4 equiv. of aniline derivative **4** in the presence of 8 equiv. of $K_3[Fe(CN)_6]$ as an oxidizing agent under alkaline conditions by the addition of 232 equiv. of DBU in MeCN–H_2O solution, so that a red–purple product **1**† was produced in 34% yield after column chromatography (Scheme 1), whereas the expected condensed product containing a diethylaminotoluidine unit was not detected. A possible reaction mechanism for the synthesis of **1** is as follows: (*a*) the phenolate of **2** was subjected to an electrophilic reaction with the semiquinone ion, formed by oxidation of **4**, to yield the corresponding leuco dye; (*b*) the hydrophobic effect of the binaphthyl unit protects the phenol segment of the leuco dye from oxidation by $K_3[Fe(CN)_6]$ and/or dissolved O_2, then allows the oxidation of the diethylaminotoluidine unit. Detailed discussions on the mechanism will be reported in a full paper. ^1H NMR shows that **1** possesses a 1,1′-binaphthyl-derived calixcrown unit: the conformation was assigned as a 'cone', *i.e.* the signals from the $ArCH_2Ar$ appear as two pairs of doublets [δ 3.37 and 4.38 (4 H, ABq, *J* 13.5 Hz); 3.37 and 4.43 (4 H, ABq, *J* 12.5 Hz)]. The fact that $\Delta\delta$ values between H_{exo} and H_{endo} are *ca.* 1 ppm supports a cone conformation.[7]

By making use of the cavity constructed by the binaphthyl-derived crown ether unit, **1** could be a chromogenic receptor for molecular recognition of amines; we investigated to see if **1** would act such a function. Compound **1** in 99% EtOH is red, with an absorption band at 512.5 nm (ε_{max} 12250 $dm^3 mol^{-1} cm^{-1}$). The addition of Bu^tNH_2 turned the solution blue with a large bathochromic shift of 148 nm: a new band at 660.5 nm was observed at 25 °C as shown in Fig. 1. Use of a continuous variaton method[8] indicated the formation of a 1 : 1 complex between **3** and Bu^tNH_2, the colour change in **1** probably being due to the ionization of the



Scheme 1

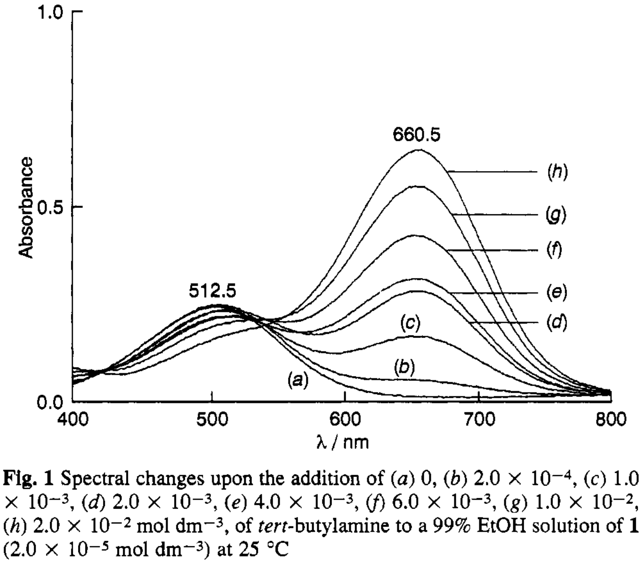


Fig. 1 Spectral changes upon the addition of (*a*) 0, (*b*) 2.0 × 10^{-4}, (*c*) 1.0 × 10^{-3}, (*d*) 2.0 × 10^{-3}, (*e*) 4.0 × 10^{-3}, (*f*) 6.0 × 10^{-3}, (*g*) 1.0 × 10^{-2}, (*h*) 2.0 × 10^{-2} mol dm^{-3}, of *tert*-butylamine to a 99% EtOH solution of **1** (2.0 × 10^{-5} mol dm^{-3}) at 25 °C

phenol unit of the indophenol chromophore. Fig. 2 shows a Benesi–Hildebrand plot[9] for a mixture of **1** and Bu^tNH_2 in 99% EtOH at 25 °C: the plot is linear, supporting the 1 : 1 stoichiometry of the complex. The apparent association constant K calculated from the slope was established to be (1090 ± 135) $dm^3\ mol^{-1}$. Similar measurements for other butylamines have been carried out, and the apparent association constants K are summarized in Table 1. A marked difference between the K values was found, which was attributable to the shape of the butyl substituents: **1** interacts with butylamines in the following order: $Bu^t \gg Bu^s > Bu^i > Bu^n$. Note that the complexation ability increases markedly in going from Bu^s to Bu^t. Consequently, **1** showed that the ratio of K_{Bu^t}/K_{Bu^n} is as high as 11. The results are quite interesting because no calixarene derivative exhibiting a significant preference for binding Bu^tNH_2 over other butylamines has been reported so far, in spite of the fact that some calixarene-type host molecules for amine recognition have been synthesized.[10]

^{13}C NMR spectra (100.7 MHz) were used to investigate the coordination structure. Compound **1** in CD_3OD–$CDCl_3$ (9 : 1 *v*/*v*) at 27 °C displays a broad signal in the range δ 70.61–75.45 which is attributable to the carbons of the crown ether unit of **1**, and indicates that conformational interconversion is rather slow on the NMR timescale at 27 °C. However, upon interaction with an excess of Bu^tNH_2, the spectral pattern was found to change to four signals (δ 71.00, 71.30, 71.75 and 74.735) for the methylene carbons of the crown ether unit. From these results, the complexation is presumed to involve the crown oxygens and phenolate group. Although the cause of the selectivity for Bu^tNH_2 in **1** is not clear, the inspection using CPK models has suggested that the Me unit of the Bu^t substituent would be very close to the binaphthyl unit of **1**. Full NMR studies of the complex, as well as an attempt to obtain an X-ray structure are now underway.

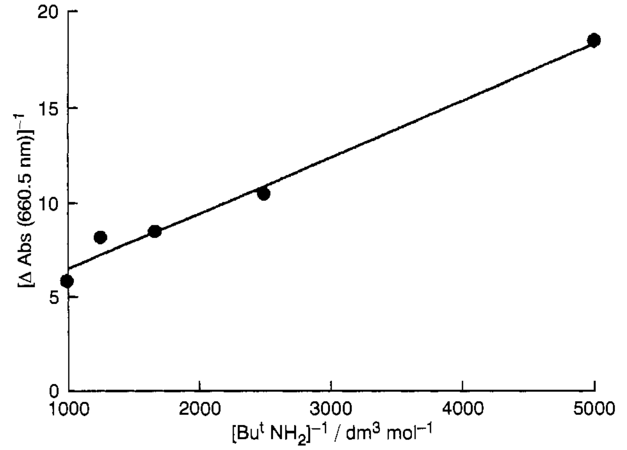


Fig. 2 Benesi–Hildebrand plot for a mixture of **1** and *tert*-butylamine in 99% EtOH at 25 °C; [**1**] = 2.0×10^{-5} mol dm^{-3}

Table 1 Association constants K of **1**[a] with several butylamines

Amine	λ_{max}[b]/nm	K[c]/$dm^3\ mol^{-1}$
Bu^nNH_2	653	95.9 ± 23.5
Bu^iNH_2	657	350 ± 40.0
Bu^sNH_2	658	656 ± 68.0
Bu^tNH_2	660.5	1090 ± 135

[a] [**1**] = 2.0×10^{-5} mol dm^{-3}. [b] Absorption maximum for **1**–butylamine complex. [c] Benesi–Hildebrand equation was used: the errors reported are based upon the standard deviations of three independent measurements.

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Footnote

† Compound **1** was identified by NMR and MS, and elemental analyses. *Selected data*: ^1H NMR (400 MHz, $CDCl_3$), δ 2.28 (6 H, s), 3.15–3.24 (2 H, m), 3.37 and 4.38 (4 H, ABq, *J* 13.5 Hz), 3.37 and 4.43 (4 H, ABq, *J* 12.5 Hz), 3.63 (2 H, t), 3.72–3.90 (8 H, m), 4.22–4.27 (2 H, m), 4.44–4.49 (2 H, m), 6.43 (2 H, dd, *J* 1.9, 10.2 Hz), 6.54 (2 H, s), 6.66 (2 H, d, *J* 2.1 Hz), 6.77 (2 H, d, *J* 2.1 Hz), 6.81 (2 H, t), 6.92 (2 H, d, *J* 7.2 Hz), 7.00 (2 H, d, *J* 7.4 Hz), 7.07 (2 H, d, *J* 10.2 Hz), 7.21 (2 H, d, *J* 8.3 Hz), 7.25 (2 H, t), 7.34 (2 H, t), 7.47 (2 H, d, *J* 9.0 Hz), 7.86 (2 H, d, *J* 8.1 Hz), 7.96 (2 H, d, *J* 9.0 Hz), 8.31 (2 H, s); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 18.20, 30.64, 31.43, 70.09, 70.16, 70.38, 76.19, 115.10, 120.64, 122.59, 122.66, 123.84, 125.49, 125.53, 126.54, 127.81, 127.95, 128.03, 128.79, 129.15, 129.37, 129.41, 130.23, 131.74, 132.87, 133.65, 134.26, 141.57, 149.93, 151.94, 152.76, 152.88, 154.15, 156.45, 188.22; *m*/*z* 1090 ($M^+ + 2$). Satisfactory elemental analysis (C, H, N) was obtained. To determine the structure of **1** in the ground state, a 2D ^{13}C–^1H COLOC NMR experiment was performed, so that the cross section by $^3J_{CH}$ coupling between C(1) and H(3) was observed.

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