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Synthesis of the Tripodal-Amine Capped Benzo Crown *p-tert*-Butylcalix[4]arene and Its Host-Guest Chemistry

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Abstract: The tripodal-amine capped benzo crown *p-tert*-butylcalix[4]arene (**6**) was synthesised. The basicity of the nitrogen donors in **6** based on the protonation constants was measured by potentiometric titration. The complexation studies of **6** with Zn(II) ions were also carried out by ^{1}H NMR spectroscopy.
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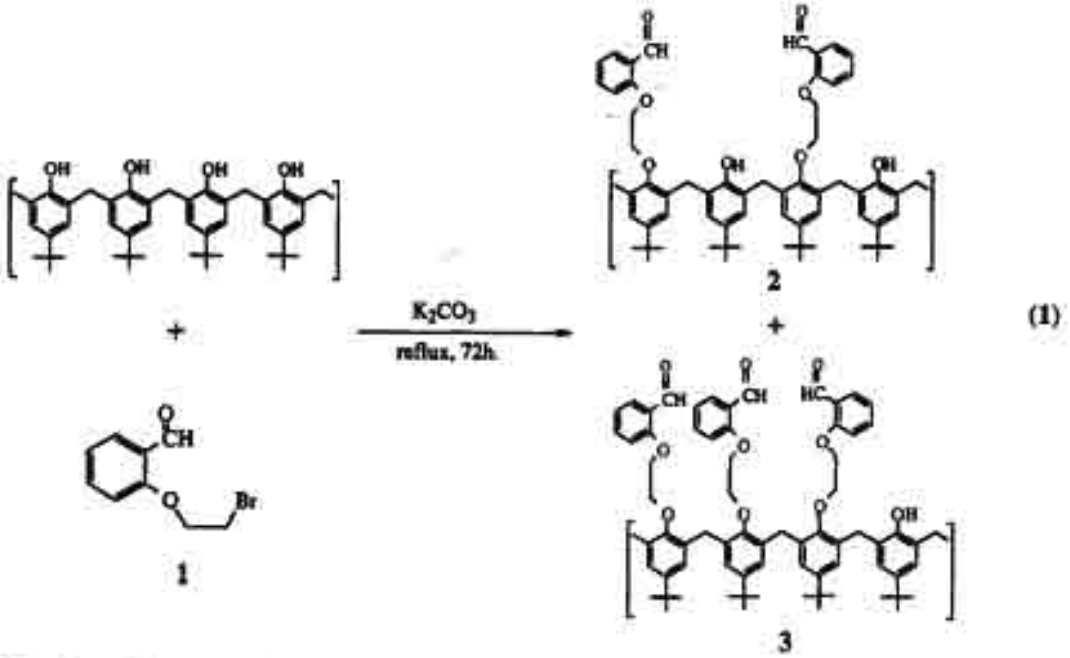
One of the most important types of macrocyclic compounds that plays a very important role in host-guest chemistry is the cage molecules such as cryptands.[1] They possess three dimensional structures which enhance the ability to encapsulate metal ions and anions.[2-4] *p-tert*-Butylcalix[4]arene has been shown to be an important starting building block for host-guest chemistry because it can be chemically modified at the phenolic oxygens (lower rim) and at the para-positions (upper rim). The chemical modifications associated with the conformational properties lead to a large variety of fascinating receptors.[5-7] It is of interest to combine the calix[4]arene framework with the cage constructing unit such as tris(2-amino)ethylamine, **tren**, to synthesise a compound that has great potential to bind metal ions and anions. We report herein the preparation of the tripodal-amine capped benzo crown *p-tert*-butylcalix[4]arene (**6**). To our knowledge, this is the first **tren** capped benzo crown *p-tert*-butylcalix[4]arene that has been synthesised. The compound **6** is a heterotopic receptor containing both the N_4 cage and the crown ether like units. It can, therefore, possibly exhibit appealing host-guest chemistry with metal ions and anions. The preliminary complexation studies of **6** with Zn(II) salts are also described.

The compound **6** can be prepared from the substitution reaction of calix[4]arene with 2.7 equiv. of 2[(1-formyl-2-phenyl)oxy]ethylbromide,[8] **1**, in the presence of K_2CO_3 in acetonitrile. The reaction under the condition shown in eq. 1 yielded dialdehyde calix[4]arene, **2** (50%) and trialdehyde calix[4]arene, **3** (6%). The compounds **2** and **3** were separated by silica gel chromatography using CH_2Cl_2 as an eluent. The compound **3** was characterised by spectroscopy and elemental analysis.[9] ^{1}H NMR spectrum of **2** shows (C=O)-*H* signals at 9.75 and 10.41 ppm in 1:2 integral ratio. Interestingly, signals in the methyl region corresponding to methyl protons on *tert*-butyl groups exhibit complicated patterns suggesting that the calix[4]arene framework is not rigid in the solution. Condensation reaction of **3** with 1.1 equiv. of tris(2-amino)ethylamine in acetronitrile precipitated an imine or Schiff base product, **4** (46%) which was characterised by spectroscopy.[10] The signals due to (C=O)-*H* protons disappear, and the signals due to RN=C*H* protons display at 8.82 and 8.92 ppm in the

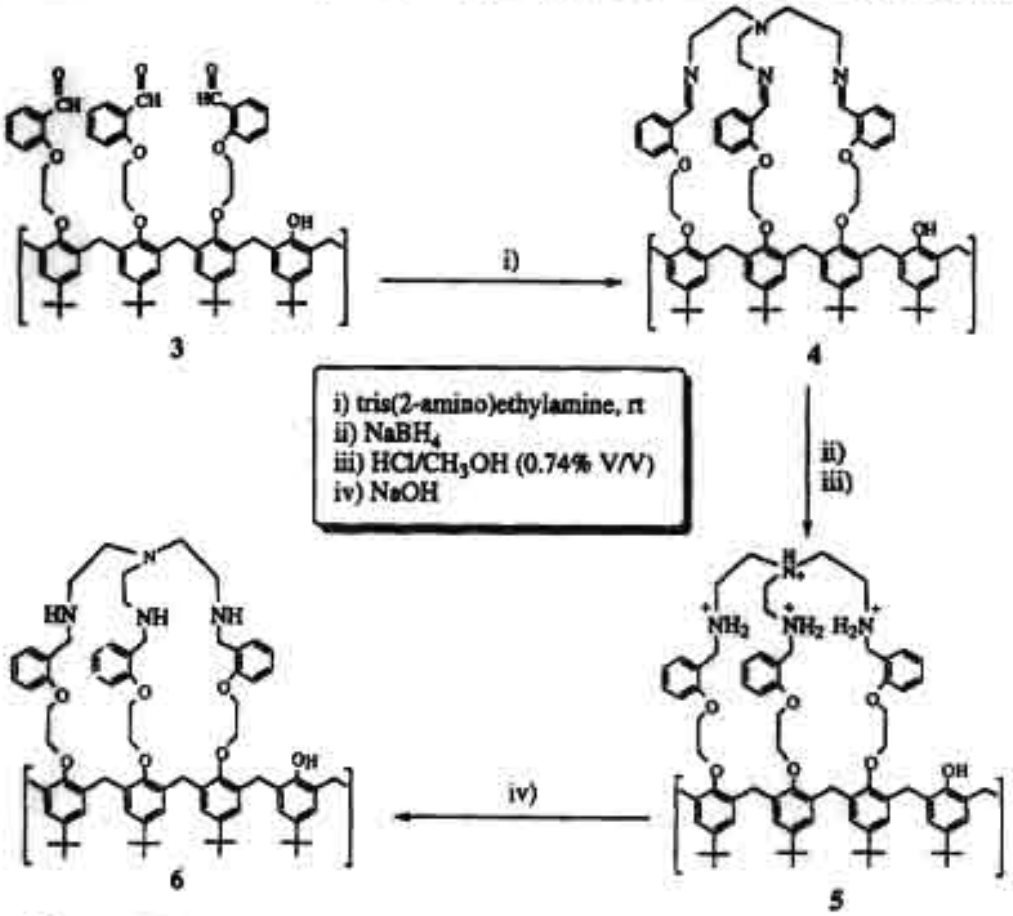
^{1}H NMR spectrum of **4**. The methyl proton signals exhibits only three singlet lines at 1.35, 1.22 and 0.73 ppm in 1:1:2 ratio, respectively indicating that the molecule possesses the cone conformation. It also implies that the structure of **4** is more rigid than that of **3** when capped with the tren unit. Hydrogenation of **4** by 20 equiv. of $NaBH_4$ and subsequently acidifying with HCl/CH_3OH (0.74% v/v) yielded an ammonium derivative, **5** (86%) which shows very broad signals in ^{1}H NMR spectrum due to the effect of positive charges. There are signals due to R-NH_2^+-R and R_3NH^+ appear at 8.55, 9.55 and 10.02 ppm; however, the integral ratio cannot be estimated. Due to the mechanism of FAB MS, the mass spectrum of **5** shows a strong signal at m/z 1191.7 corresponding to molecular weight of the neutralised species **6**. Nevertheless, elemental analysis suggests the existence of **5**.[11] Neutralisation of **5** with NaOH in methanol provided the neutral tripodal-amine capped benzo crown calix[4]arene, **6** (46%). ^{1}H NMR spectrum (400 MHz) of **6** suggests a rigid cone conformation of the calix[4]arene unit observed from 3 singlet signals due to *t*-butyl protons at 0.86, 1.39 and 1.41 ppm and 4 doublet signals (J = 13 Hz) due to the bridging methylene protons on the calix[4]arene unit identified by a COSY experiment at 3.23, 3.37, 4.45 and 4.85 ppm.[12]



The ligand **6** possesses both nitrogen donors and oxygen donors. It can possibly accommodate metal ions and anions in the cavity of amine nitrogen donors or phenolic oxygen donors. We have examined the basicity of the nitrogen donors by determining protonation constants of **6** in 0.01 M methanolic solution of tetramethylammonium chloride at 25 °C with potentiometric titration. The titrations were carried out four times at the pH range of 2.968-12.030. The first, second, third and fourth protonation constants of **6** obtained from computer evaluation of the potentiometric titration data are log K_1 = 11.80±0.05, log K_2 = 10.88±0.09, log K_3 = 7.75±0.10 and log K_4 = 4.97±0.12, respectively.[13] The first two values are higher than the protonation constants of tren and bis-tren reported by Martell and Lehn by approximately an order of magnitude.[14]

The ligand **6** shows selectivity towards metal ions and anions. Complexation of Zn(II) ions with the ligand **6** can be studied by ^{1}H NMR titration experiments.[15] The possible structures of Zn(II)-**6** complexes, deduced from the NMR data and the previous studies on similar calix[4]arene derivatives, are illustrated in Scheme 2.[16,17] Although the signals due to the RNCH_2CH_2NR are broad when **6** forms complex with Zn(II)

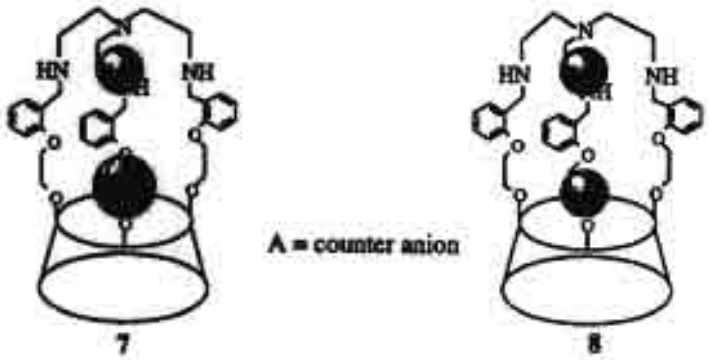
ions, we can observe the displacement of signals due to Ar-*t*-C(CH_3)$_3$ (a) and *t*-C(CH_3)$_3$Ar-*H* (b) on the calix[4]arene framework. In the $ZnBr_2$ case, signals (a) and (b) shift downfield (2-10 Hz) with respect to the free



Scheme 1. Preparation method for the compound **6**.

ligand **6** upon increasing mole ratio of $ZnBr_2$. The plot between mole ratio of $ZnBr_2$:**6** and the magnitude of displacement reveals a 1:1 complex formation. One Zn(II) ion may reside in the cavity of the amine nitrogen donors while one of Br^- ions may be induced into the cavity of phenolic oxygen, Scheme 2 (**7**). The calix[4]arene framework must adjust the cavity to enclathrate a Br^- ion. This results in the displacement of protons (a) and (b). Curve fitting by iteration technique has been applied to calculate the stability constant for $ZnBr_2$-**6**: log K = 2.58.[16] In addition, we have isolated the $ZnBr_2$-**6** complex and characterised it by elemental analysis: anal. calcd. (found) for $C_{77}H_{98}N_4O_7ZnBr_2$: C, 65.28 (65.44); H, 6.97 (6.60); N, 3.95 (3.68).[18] The result thus agrees with the proposed 1:1 structure. ^1H NMR titration of **6** with $Zn(NO_3)_2$ also gives the displacement of protons (a) and (b); however, the displacement does not proceed in the same direction. In addition, we observe that the methyl protons signals of *tert*-butyl groups are very complicated suggesting the existence of more than one species in the NMR solution.[19] Another possible species is the 2:1 complex in which two Zn(II) ions reside in **6**; one Zn(II) ion must reside in the amine nitrogen cavity while the other is in the phenolic oxygen cavity, Scheme 2 (**8**).[17]

This preliminary study, therefore, indicates the selectivity of the ligand **6** towards a metal and anions. Further studies of the complexation of **6** with other zinc salts by NMR spectroscopy are currently under investigation. Future work will also be focused on elucidation of the structures of Zn(II)-**6** complexes by X-ray crystallography.



7 8

Scheme 2. Possible structures of Zn(II)-6 complexes.

Acknowledgements

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9. Anal. Cald. for **3** ($C_{71}H_{80}O_{10}$): C, 77.99; H, 7.37. Found: C, 78.11; H, 7.17. ^{1}H NMR (δ ppm, $CDCl_3$, 200 MHz): 0.8-1.5 (36H, m, -ArC(CH_3)$_3$); 3.25 and 4.22 (4H each, m, ArCH_AH_BAr); 4.16, 4.42 and 4.92 (12H, m, -OCH_2CH_2O-); 5.20 (1H, s, ArO*H*); 6.32-7.85 (20H, m, aromatic protons); 9.75 and 10.41 (1H and 2H, s each, -Ar(C=O)*H*). FAB MS (m/z): 1092.5.
10. Anal. Cald. for **4**•H_2O ($C_{77}H_{94}N_4O_8$): C, 76.84; H, 7.87; N, 4.65. Found: C, 76.70; H, 7.61; N, 4.24. ^{1}H NMR (δ ppm, $CDCl_3$, 200 MHz): 0.73, 1.22 and 1.35 (18H, 9H, 9H, s each, ROArC(CH_3)$_3$ and HOArC(CH_3)$_3$); 3.32, 3.53, 4.32 and 4.35 (2H each, d (J = 13 Hz), ArCH_AH_BAr); 2.85 (12H, b, m, -NCH_2CH_2N-); 4.03, 4.50 and 5.15 (12H, m, -OCH_2CH_2O); 5.30 (1H, s, -ArO*H*); 6.42-7.90 (20H, m, aromatic protons); 8.82 and 8.92 (1H and 2H, s each, -C*H*=N-). FAB MS (m/z): 1185.7.
11. Anal. Cald. for **5**•$4H_2O$($C_{77}H_{110}N_4Cl_4O_{11}$): C, 65.69; H, 8.44; N, 3.78. Found: C, 65.61; H, 7.87; N, 3.97. FAB MS (m/z): 1191.7.
12. Anal. Cald. for **6** ($C_{77}H_{98}N_4O_7$): C, 77.61; H, 8.29; N, 4.70. Found: C, 77.57; H, 7.85; N, 4.32. ^{1}H NMR (δ ppm, $CDCl_3$, 400 MHz): 0.86, 1.39 and 1.41 (18H, 9H, 9H, s each, ROArC(CH_3)$_3$ and HOArC(CH_3)$_3$); 1.99-2.66 (12H, b, m, RNCH_2CH_2NR); 3.23, 3.37, 4.45 and 4.85 (2H each, d (J = 13 Hz), ArCH_AH_BAr); 3.75 and 4.18 (4H and 2H, d (J = 14 Hz), ArCH_2NR); 3.86, 4.03, 4.32 and 4.98 (12H, m, -OCH_2CH_2O-); 5.20 (1H, s, -ArO*H*); 6.25, 6.93, 7.15 and 7.47 (12H, m, -Ar*H*OCH_2-); 6.56 and 7.20 (4H, each, s, *t*-C(CH_3)$_2$Ar*H*CH_2-). FAB MS (m/z): 1191.7.
13. The protonation constants of **6** were estimated by the Superquad computer program: Gans, P.; Sabatini, A.; Vacca, A. *J. Chem. Soc., Dalton Trans.* **1985**, 1195. The deprotonation constant of methanol at 25 °C was calculated to be log K = -16.7.
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15. Typically, the ligand **6** (0.036 g, 0.030 mmol) was dissolved in $CDCl_3$ (2.40 mL) and placed into 6 NMR tubes (0.40 mL each). Zinc salts (0.053 mmol) in CD_3OD (1 mL) were then added to the ligand solution in each tube by varying the ratio of Zn(II):**6** from 0.5:1 to 3:1.
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18. A methanolic solution (5 mL) of $ZnBr_2$ (0.020 g, 0.088 mmol) was added into a stirred CH_2Cl_2 solution (5 mL) of **6** (0.100g, 0.084 mmol). The reaction was allowed to stir at room temperature for 48 h. White solids precipitated from the reaction. The solvent volume was subsequently reduced, and white solids were separated by filtration and washed with diethylether. (0.061 g, 51%).
19. The proton signals due to *tert*-butyl groups appear at 0.53, 0.60, 0.65, 0.67, 1.03, 1.13, 1.17 and 1.19 ppm.

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RESEARCH ARTICLE

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Synthesis of Tetraalkylated Calix(4)arenes and Studies of Their Conformational Behaviors

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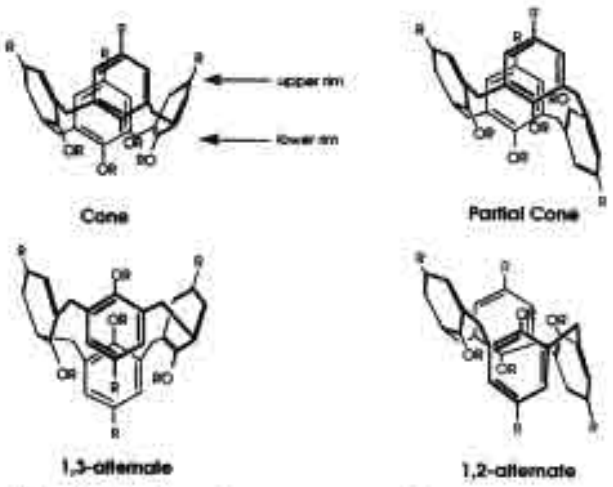
ABSTRACT Three new tetraalkylated calix[4]arenes, 25,27-[*N,N'*-di-((2-ethoxy)benzyl)propylene diamine]-26,28-dimethoxy-*p*-*tert*-butylcalix[4]arene dihydrochloride, **7**, 25,27-[di(2-ethoxy) nitrobenzene]-26,28-dimethoxy-*p*-*tert*-butylcalix[4]arene, **10**, and 25,27-[di(2-ethoxy)azobenzene]-26,28-dimethoxy-*p*-*tert*-butylcalix[4]arene, **11**, have been synthesized. These compounds underwent the conformational interconversion of the calix[4]arene unit which could be studied by variable temperature ^{1}H NMR experiments. Rates of conformational interconversion of **7** were determined to be 111.0 s^{-1} and 94.6 s^{-1} in DMSO-d_6 at 50°C and CD_3OD at 27°C, respectively. In $CDCl_3$ at - 30°C, compound **10** was found to exist in both cone and partial cone conformations with the ratio of 43:57. Cyclization of **10** by reductive coupling to **11** confined the calix[4]arene unit in cone conformation. The compound **11** in $CDCl_3$ then underwent conformational interconversion upon isomerization of the azobenzene unit leading to mixed conformations of calix[4]arene.

KEYWORDS: calixarene, conformation, interconversion, isomerization, azobenzene.

INTRODUCTION

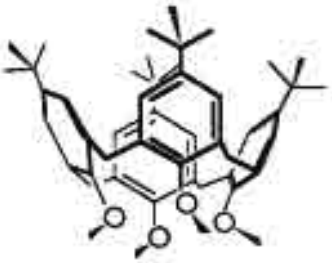
Calix[4]arene is a versatile supramolecular building block.[1-3] The molecule possesses a well preorganized cavity for accommodating guests such as metal ions. Both lower rim and upper rim of the calix[4]arene unit, in particular, can be modified to have useful moieties for complexing cations, anions and organic molecules. Besides these attractive properties, calix[4]arene also has an interesting conformational interconversion which occurred by rotation of the aryl rings through the methylene bridges. The possible conformations of calix[4]arene are cone, partial cone, 1,2-alternate and 1,3-alternate (Scheme 1). The cone conformation is the most favored among these 4 conformations due to the very strong intramolecular hydrogen bonding between the 4 OH groups at the lower rim of the calix.

Conformational analysis of tetramethylated calix[4]rene, **1**, is one of the most interesting aspects of these supramolecular building blocks. All possible conformations of compound **1** are found by theoretical calculations and NMR studies.[4-7] Shinkai and coworkers reported that upon increasing solvent polarity the concentration of the cone conformation of the calix[4]arene unit in **1** increased.[8] Later Reinhoudt and coworkers have reported the mechanism of conformational interconversion of a series of calix[4]arene derivatives, **2**, containing 4 methoxy groups at the lower rim and a bridging group at the upper rim.[9] They found that the conformation of these compounds are confined to cone and partial cone and the movement of the aryl rings depends on the lengths of the bridging groups. Böhmer and colleagues demonstrated that the calix[4]arene unit in a calix[4]arene derivative, **3**, tended to be in 1,3-alternate conformation for a shorter bridging chain.[10]



Scheme 1. Possible conformations of calix[4]arene.

Our group has been working on the synthesis and complexation studies of di- and trisubstituted calix[4]arenes by ^{1}H NMR analysis for a number of years.[11-13] Understanding of the conformational



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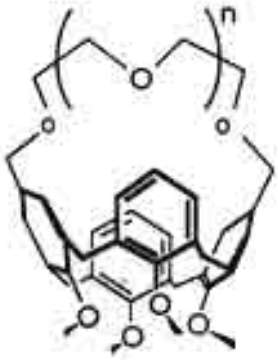

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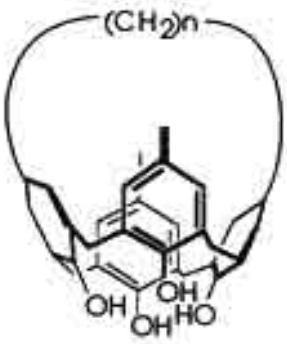

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interconversion of the calix[4]arene conformation is thus an important subject to pursue for better knowledge to control the complexation ability of this superb supramolecular building block. This article describes the synthesis and characterization of 25,27-*N,N'*-di((ethoxy)benzyl)propylenediamine-26,28-dimethoxy-*p-tert*-butylcalix[4]arene dihydrochloride, 7, 25,27-[di(2-ethoxy) nitrobenzene]-26,28-dimethoxy -*p-tert*-butylcalix[4]arene, 10, and 25,27-[di(2-ethoxy)azobenzene]-26,28-dimethoxy-*p-tert*-butylcalix[4]arene, 11. Both 7 and 11 contain two methoxy groups and bridging groups with different lengths and rigidity at the lower rim. We have studied effects of solvents and bridging groups towards the conformational interconversion of the calix[4]arene unit in these compounds.

Experimental Section

Materials

All materials were standard analytical grade, purchased from Fluka, JT Baker or Merck, and used without further purification. Commercial grade solvents such as acetone, dichloromethane and methanol were distilled and stored over 4 Å molecular sieves. Acetonitrile was dried according to the standard techniques.[14] Chromatographic separations were performed on silica gel columns (kieselgel 60, 0.063-0.200 mm, Merck). Thin layer chromatography (TLC) was carried out using silica gel plates (kieselgel 60 F_{254}, 1 mm, Merck). 25,27-Di-(2-ethoxy)benzaldehyde-*p-tert*-butylcalix[4] arene, 4,[15] and 26,28-dimethoxy-*p-tert*-butylcalix[4] arene, 9,[6] were prepared according to methods described in the literature. Unless otherwise noted, all reactions were carried out under nitrogen.

Analytical Instruments

Elemental analyses were carried out on a Perkin Elmer CHON/S analyser (PE2400 series II). Melting points were taken on an Electrothermal 9100 apparatus. UV-visible spectra were recorded on a Spectronic 3000 array spectrophotometer. The ^{1}H-NMR spectra were recorded either on a Bruker ACF 200 MHz or a Bruker AM 400 MHz nuclear magnetic resonance spectrometer. Variable temperature NMR experiments were carried out on a JEOL 500 MHz NMR spectrometer at the Scientific and Technological Research Equipment Center of Chulalongkorn University. Temperatures employed are 120, 100, 50, 27, 0, -15, -25, -35 and -40°C depending on the solvents. In most cases, samples were dissolved in deuterated chloroform and chemical shifts were recorded using a residual chloroform signal as internal reference.

Preparation of 25,27-di-((2-ethoxy)benzaldehyde) -26,28-dimethoxy-p-tert-butylcalix[4]arene, 5. Compound 4 (1.12 g, 1.19 mmol), BaO (0.19 g, 1.21 mmol) and dry THF (80 mL) were placed in a 250 mL two-necked round bottom flask and stirred for 1.5 hours. Then, *t*-BuOK (0.41 g, 3.63 mmol) and CH_3I (0.39 mL, 6.24 mmol) were added to the mixture. The reaction was heated at reflux for 1 hour. After the reaction was cooled to room temperature, THF was evaporated by reduced pressure to dryness. The residue was dissolved in CH_2Cl_2 and washed with 1 M HCl. The organic layer was subsequently separated, dried over anhydrous Na_2SO_4 and evaporated to dryness. The residue was chromatographed on a silica gel column using 10% EtOAc in hexane as eluant to separate a crude product of 5 which was further purified by column chromatography using 1% CH_3OH in CH_2Cl_2 as eluent (0.33 g, 28%).

δ_H (200 MHz; $CDCl_3$) 0.79 and 1.04 (9H each, br s, CH_3OAr-t-C_4H_9), 1.27 (18H, br s, ROAr-t-C_4H_9), 3.14 (4H, br s, $ArCH_2Ar$), 3.82 (6H, s, OCH_3), 4.03-4.50 (12H, m, OCH_2CH_2O- and $ArCH_2Ar$), 6.50 (4H,

br s, CH_3OArH), 6.98-7.05 (8H, m, aromatic and ROAr*H*), 7.52 (2H, t, *J* 8.3, aromatic), 7.82 (2H, d, *J* 7.7, aromatic), 10.44 (2H, br s, C*H*O); Anal. Calc. for $C_{64}H_{76}O_8$: C, 78.98; H, 7.87. Found C, 78.97; H, 7.77.

Preparation of 25,27-[N,N'-di-((2-ethoxy) benzyl)propylenediimine]-26,28-dimethoxy-p-tert-butylcalix[4]arene, 6. Into a stirred solution of compound 5 (0.56 g, 0.58 mmol) in CH_3CN (60 mL) was added dropwise a solution (CH_3OH, 12 mL) of 1,3-diaminopropane (0.08 mL, 0.96 mmol). The reaction was heated at reflux for 24 hours. White solid of 6 precipitated after the reaction mixture was cooled to room temperature. It was isolated by filtration, washed with cold CH_3OH and dried (0.32 g, 55%).

δ_H (200 MHz; $CDCl_3$) 0.79 and 1.03 (9H each, br s, CH_3OAr-*t*-C_4H_9), 1.27 and 1.32 (9H each, br s, ROAr-*t*-C_4H_9), 1.52-1.70 (1H, m, $NCH_2CH_2CH_2N$), 1.85-2.05 (1H, m, $NCH_2CH_2CH_2N$), 2.80-3.32 (8H, m, NCH_2CH_2 and $ArCH_2Ar$), 3.32-3.61 (3H, br m, OCH_3), 3.74 (3H, br s, OCH_3), 3.90-4.50 (12H, m, OCH_2CH_2O- and $ArCH_2Ar$), 6.43 and 6.50 (4H, br s, CH_3OArH), 6.70-7.10 (8H, m, aromatic and ROAr*H*), 7.27-7.32 (2H, m, aromatic), 7.90 (2H, d, *J* 7.2, aromatic), 8.65 (2H, br s, *H*C=N); Anal. Calc. for $C_{67}H_{82}N_2O_6$: C, 79.57; H, 8.17; N, 2.77. Found C, 79.49; H, 8.03; N, 2.62.

Preparation of 25,27-[N,N'-di-((2-ethoxy) benzyl)propylenediamine]-26,28-dimethoxy-p-tert-butylcalix[4]arene dihydrochloride, 7. Compound 6 (0.47 g, 0.46 mmol) was stirred with suspended $NaBH_4$ (0.48 g, 12.64 mmol) in CH_2Cl_2 (100 mL) for 2 days. Excess $NaBH_4$ was then destroyed by adding a copious amount of water. The organic layer was separated, dried over anhydrous Na_2SO_4 and evaporated to dryness to give a white residue. The residue was added 2% HCl in CH_3OH until pH of the solution became 1. Upon removal of CH_3OH, white solid of 7 precipitated (0.39 g, 77%).

δ_H (500 MHz at 100 °C; DMSO-d_6) 0.95 (18H, s, CH_3OAr-*t*-C_4H_9), 1.30 (18H, br s, ROAr-*t*-C_4H_9), 2.03 (2H, br m, $NCH_2CH_2CH_2N$), 2.84 (4H, br m, $NCH_2CH_2CH_2N$), 3.28 (4H, br m, $ArCH_2Ar$), 3.54 (4H, br s, $ArCH_2N$), 4.11 (6H, br s, OCH_3), 4.16-4.18 (8H, br m, $ArCH_2Ar$ and OCH_2CH_2O), 4.38 (4H, br m, OCH_2CH_2O), 6.65 (4H, br s, CH_3OArH), 7.02 (2H, t, *J* 8.3, aromatic), 7.12 (2H, d, *J* 7.2, aromatic), 7.16 (4H, s, ROAr*H*), 7.38 (2H, t, *J* 8.3, aromatic), 7.59 (2H, d, *J* 7.2, aromatic); MALDI-TOF MS for [M$^+$]; 1014.2 m/z.

Preparation of 2-(2'-bromoethoxy)nitrobenzene, 8. In a 500 mL two-necked flask equipped with a magnetic bar and a reflux condenser, *o*-nitrophenol (4.45 g, 32.0 mmol), 1,2-dibromoethane (60.11 g, 320.0 mmol) and K_2CO_3 (8.85 g, 64.0 mmol) were mixed in CH_3CN (150 mL). The mixture was refluxed for 24 hours and then allowed to cool to room temperature. The solid was separated by filtration and washed with CH_2Cl_2. The combined solution was then evaporated to dryness to obtain a yellow residue. Methanol was subsequently added to dissolve this residue, and the solution was chilled in an ice bath to precipitate white solid identified as dinitrophenoxy ethylene. The white precipitate was filtered and washed with cold methanol (0.55 g, 7%). The supernatant was evaporated to dryness. The residue was then dissolved in diethyl ether. The desired product, 8, crystallized as a bright yellow solid by adding hexane (5.80 g, 74%).

Melting point: 164-165°C; δ_H (200 MHz; $CDCl_3$) 3.65 (2 H, t, *J* 6.0, -OCH_2CH_2Br), 4.40 (2 H, t, *J* 6.0, -OCH_2CH_2Br), 7.02-7.10 (2 H, m, aromatic), 7.52 (1 H, t, *J* 8.0, aromatic), 7.81 (1 H, d, *J* 8.0, aromatic); Anal. Calc. for $C_8H_8BrNO_3$: C, 39.05; H, 3.28; N, 5.69. Found C, 39.07; H, 3.21; N, 5.65.

Preparation of 25,27-[di(2-ethoxy)nitrobenzene]-26,28-dimethoxy-p-tert-butylcalix[4]arene, 10. In a 250 mL two-necked flask equipped with a magnetic bar and a condenser, 9 (1.37 g, 2.03 mmol), K_2CO_3 (1.12 g, 8.11 mmol), KOH (3-5 pellets) were mixed in CH_3CN (50 mL). After stirring at 35-40°C for 4 hours, 8 (1.00 g, 4.06 mmol) in CH_3CN (40 mL) was then slowly added . The mixture was refluxed for 48 hours and allowed to cool to room temperature. The mixture was filtered and the solid residue was washed with CH_2Cl_2. The filtrate was combined and the solvent was removed to give a brown viscous residue. The residue was dissolved in CH_2Cl_2, washed with saturated NH_4Cl solution and extracted with H_2O (2 x 20 mL). The organic phase was subsequently separated and dried over anhydrous Na_2SO_4. After separation of Na_2SO_4, the solvent was removed to give a dark brown residue. The residue was redissolved in a minimum amount of CH_2Cl_2 and chromatographed on a silica gel column with 10% ethyl acetate in hexane as eluent. The desired product, 10, was crystallized in methanol to give orange needles (0.41 g, 20%).

Melting point: 189-191°C; δ_H (200 MHz; $CDCl_3$) 0.84 and 1.05 (9 H each, br s, CH_3OArt-*Bu*), 1.28 (18 H each, br s, ROAr*t*-*Bu*), 3.00-3.40 (4 H, br, $ArCH_2Ar$), 3.47 (6 H, s, -OCH_3), 3.60-4.60 (12 H, br, $ArCH_2Ar$ and -OCH_2CH_2O-), 6.40-6.69 (4 H, br, CH_3OArH), 6.92-7.30 (8 H, br, nitrobenzene and ROAr*H*), 7.51 (2 H, t, *J* 7.0, nitrobenzene), 7.81 (2 H, d, *J* 8.0,

nitrobenzene); Anal. Calc. for $C_{82}H_{74}N_2O_{10}$: C, 73.93; H, 7.40; N, 2.78. Found C, 73.92; H, 7.46; N, 2.76.

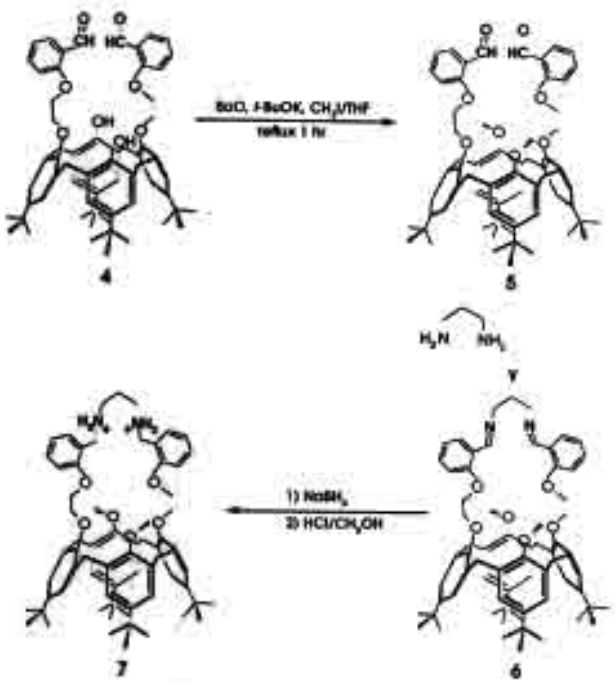
Preparation of 25,27-[di(2-ethoxy)azobenzene]-26,28-dimethoxy-p-tert-butylcalix[4]arene, 11. Compound 10 (0.51 g, 0.50 mmol) in isopropanol (10.0 mL), NaOH (0.20 g, 5.00 mmol) in H_2O (2 mL) and zinc (0.13 g, 2.00 mol) were placed in a 50 mL round-bottom flask. The mixture was refluxed for 2 days and allowed to cool to room temperature. The mixture was filtered and the residue was washed with CH_2Cl_2. The combined filtrate was evaporated to obtain an orange residue. The residue was dissolved in CH_2Cl_2, washed with NH_4Cl and extracted with H_2O (2 x 20 mL). The organic phase was separated and dried over anhydrous Na_2SO_4. The product was then filtered and purified by silica gel column with 5% ethyl acetate in hexane as eluent. It was crystallized in methanol and ethyl acetate to give orange crystals (0.06 g, 12 %).

Melting point: 228-230°C; δ_H (400 MHz; $CDCl_3$) 0.82 and 1.28 (18 H each, s, *t*-Bu protons), 3.10 and 4.23 (4 H each, d, J_{AB} 12.0, ArCH_2Ar), 3.44 (6 H, s, -OCH_3), 4.34 and 4.63 (8 H, m, -OCH_2CH_2O-), 6.42 (4 H, s, CH_3OAr*H*), 6.94 (2 H, m, azobenzene), 7.01 (4 H, s, ROAr*H*), 7.08 (4 H, m, azobenzene), 7.41 (2 H, m, azobenzene); Anal. Calc. for $C_{82}H_{74}N_2O_8$: C, 78.95; H, 7.91; N, 2.97. Found C, 79.06; H, 7.91; N, 2.97; UV/vis [l (nm), e ($dm^3 \cdot mol^{-1} \cdot cm^{-1}$)]: 334, 19385; 440, 7714.

Results and Discussion

Synthesis and Characterization

We have synthesized 25,27-*N,N'*-di((ethoxy) benzyl) propylenediamine-26,28-dimethoxy-*p*-tert-butylcalix[4]arene dihydrochloride, 7, according to the procedure shown in Scheme 2. The preparation of 7 started from methylation of 4 with 2 equiv. of CH_3I in the presence of BaO and *t*-BuOK in THF to obtain the methylated product, 5, in 28%. The product 5 was further reacted with propylene diamine (1:1 stoichiometry) in acetonitrile to precipitate a Schiff base, 6, in 55%. The Schiff base was subsequently reduced with $NaBH_4$ in CH_2Cl_2 and then protonated with 2% v/v HCl/CH_3OH to give the desired product 7 in 76%. ^1H NMR spectra of 5, 6 and 7 in $CDCl_3$ at

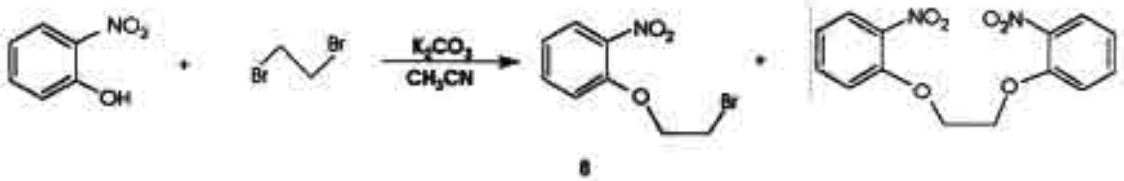


Scheme 2. Synthetic procedure for preparation of 7.

room temperature showed broad signals indicating the conformational interconversion of the calix[4]arene framework due to lack of intramolecular hydrogen bonding. However, elemental analysis results of compounds 5-7 agree with the proposed structures.

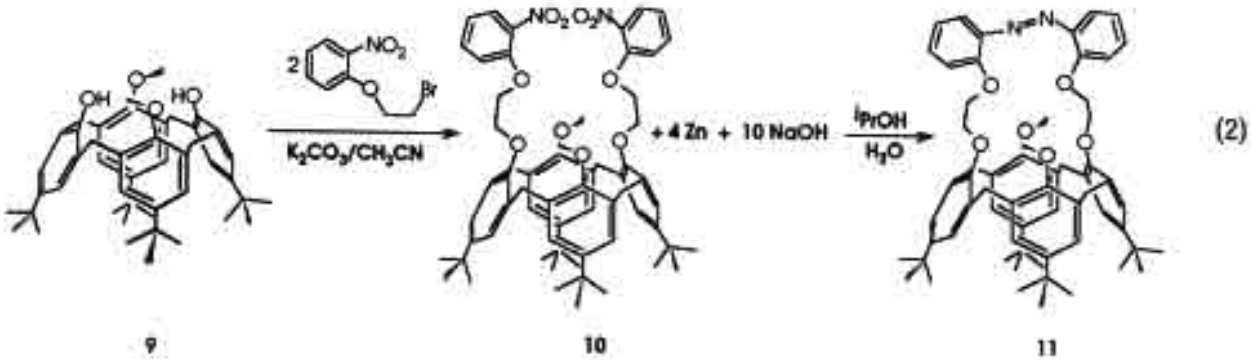
We have synthesized other tetrasubstituted calix[4]arenes by attaching two ethoxy nitrobenzene groups into the dimethoxy calix[4]arene (9) framework. Reductive coupling of nitrobenzene groups was then employed to afford the azobenzene crown ether calix[4]arenes. This synthetic procedure started from a nucleophilic substitution reaction between *o*-nitrophenol and excess 1,2-dibromoethane resulting in the isolation of the monosubstituted compound 8 (74%) and disubstituted compound (7%), eq 1. Excess 1,2-dibromoethane was needed in order to produce the monosubstituted product. If the equimolar amount of 1,2-dibromoethane was used, the major product was found to be the disubstituted compound.

Nitrobenzene calix[4]arenes, 10, was synthesized by a nucleophilic substitution reaction between 8 and 9 in the presence of K_2CO_3. Sugar-like crystals



(1)

8



(2)

9 10 11

of 10 was obtained in 20% after separation and purification. Reductive coupling of 10 using zinc metal in propanol/water gave the azobenzene, 11, which was crystallized from hot methanol to give orange crystals (12%), eq 2. ^{1}H NMR spectra and microanalysis results of 8, 10 and 11 agree well with the proposed structures.

Effects of Solvents and Temperatures towards Conformational Interconversion of 7

Due to the bridge between 2 opposite phenoxy oxygens at the lower rim, the possible conformation of the calix[4] arene framework of 7 are cone, partial cone and 1,3-alternate. We thus studied the conformational behaviors of 7 by ^{1}H NMR spectroscopy. ^{1}H-NMR spectra of 7 in $CDCl_3$, DMSO-d_6 and CD_3OD at room temperature were recorded. The ^{1}H-NMR spectrum in $CDCl_3$, an aprotic solvent, showed complicated lines of *t*-butyl signals and broad lines in the aromatic region. In DMSO-d_6 (Figure 1c), there are three broad singlets appear at 0.81, 0.98 and 1.27 ppm due to CH_3OAr-*t*-C_4H_9 and ROAr-*t*-C_4H_9. The signals in the aromatic region are also complicated and broad. The results show that the conformational interconversion of the calix[4]arene framework occurs in $CDCl_3$ and DMSO-d_6. Interestingly, the ^{1}H NMR spectrum of 7 in CD_3OD (Fig 1b), a polar protic solvent, shows two sharp singlets of *t*-butyl protons at 0.99 and 1.34 ppm and also two broad singlets at 7.21 and 6.71 ppm due to ROAr*H* and CH_3OArH. This signifies the effect of solvents on the rate of the aryl ring interconversion in the calix[4]arene unit.

The temperature dependence of the conformational interconversion in $CDCl_3$, DMSO-d_6 and CD_3OD were then investigated by variable temperature NMR spectroscopy. Unfortunately, the spectra of 7 in $CDCl_3$ showed complicated signals in all regions and the coalescence point cannot be observed. However, upon increasing temperature, the ^{1}H NMR spectra of 7 in DMSO-d_6 became sharper. We have noticed that the singlet at 1.30 ppm was always sharp at various temperatures while the singlet at 0.95 ppm was broad and became more resolved at higher temperature. The signal at 1.30 ppm must belong to $R_{ind}OArC(CH_3)_3$ and the latter is assigned to $CH_3OArC(CH_3)_3$ because the aryl rings of $R_{ind}OArC(CH_3)_3$ cannot move as freely as the rings containing CH_3O- groups. The spectrum recorded at 100 °C is illustrated in Figure 1d. The singlets for CH_3OArH and ROAr*H* appear at 6.65 and 7.16 ppm, respectively. The four aromatic protons of the bridging group become distinct from each other and appear at 7.02, 7.12, 7.38 and 7.59 ppm. The - OCH_3 signal appears at 4.11 ppm. We have found that the coalescence temperature was at 50 °C with the line width (at 6.65 ppm) of 50 Hz. The rate of the conformational interconversion was then calculated to be 111.0 s^{-1}.[16]

In addition, studies of the conformational interchange of 7 at lower temperature have been performed in CD_3OD. The spectrum at -40°C (Fig 1a) shows several singlet peaks in the *t*-butyl region and a very complicated signals due to methylene bridge protons suggesting a mixed conformation of the calix[4]arene framework upto 2 conformations in the solution (possibly cone and partial cone). Unfortunately, the spectrum is too complicated to identify the ratio of each conformation. The coalescence temperature was found at 27°C with the line width (at 6.72 ppm) of 43 Hz. The rate of conformational interconversion was calculated to be 94.6 s^{-1} in CD_3OD. However, judging from the coalescence temperature which is lower in CD_3OD, the rate of interconversion seems to be faster in CD_3OD than in DMSO-d_6 or $CDCl_3$ at the same temperature. The presence of the hydrogen bonding in CD_3OD may thus be responsible for increasing the interconversion rate of the aryl rings of calix[4]arene.

In order to examine the effect of conformational interconversion on the complexation ability of 7, the

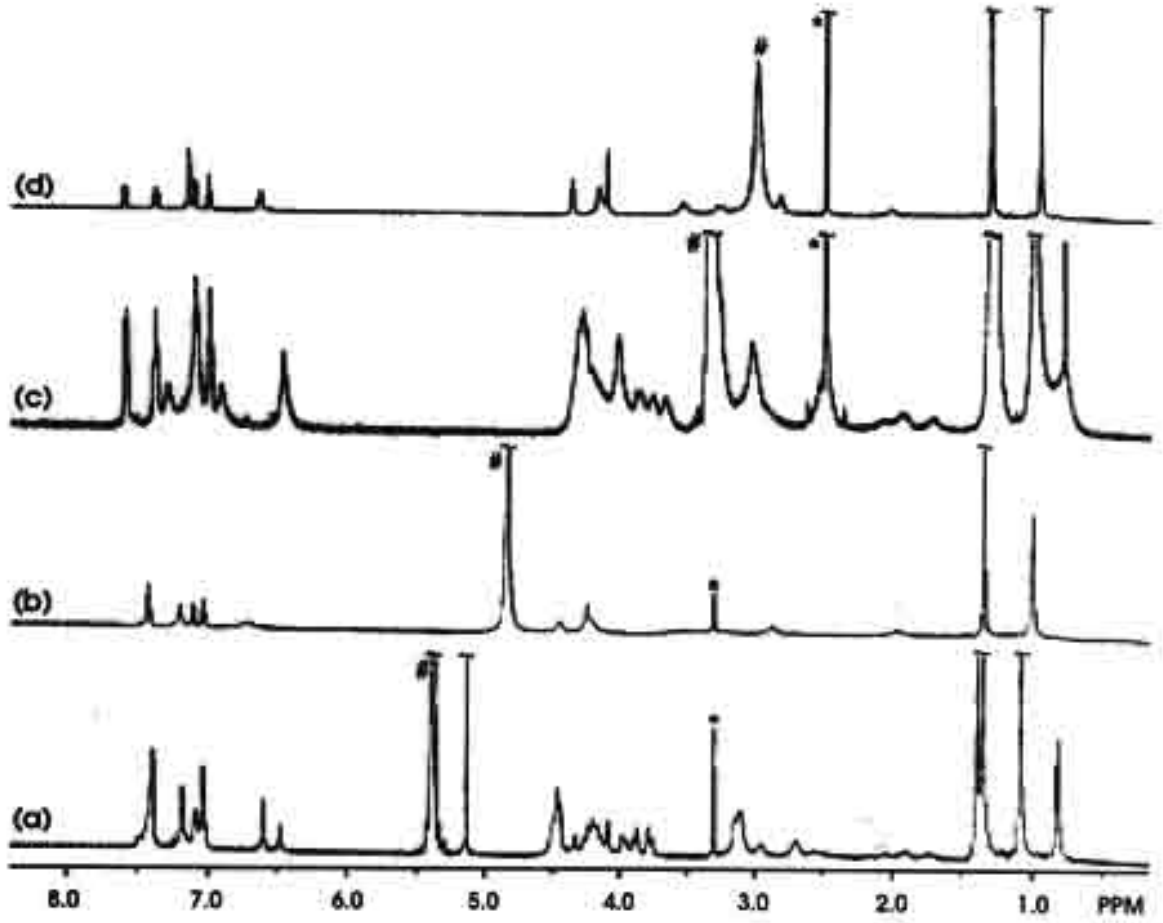


Fig 1. ^{1}H NMR spectra of 7 (a) in CD_3OD at -40°C (b) in CD_3OD at 27°C (c) in DMSO-d_6 at 27°C (d) in DMSO-d_6 at 100°C. * and # denote the trace of water in the solvent and the solvent signal, respectively.

complexation studies of 7 with Zn^{2+} was performed by potentiometric titration.[17] The result showed that 7 did not form a complex with Zn^{2+} as its analogous compound, 25,27-[*N,N'*-di-((2-ethoxy)benzyl) propylenediamine]-26,28-dihydroxy-*p*-*tert*-butylcalix[4]arene, did.[12] The conformational interconversion may, therefore, prohibit 7 to form a complex with Zn^{2+}.

Effects of the length and rigidity of the bridging group

In the same manner as 7, the ^{1}H NMR spectrum of 10 in $CDCl_3$ at room temperature (Figure 2a) shows complicated broad signals which indicate the existence of conformation interconversion leading to a mixed conformation of the calix[4]arene framework. However, the ^{1}H NMR spectrum of 10 is more resolved than that of 7 in $CDCl_3$ suggesting the increasing rigidity of calix[4]arene in 10. Upon decreasing temperature, the broad signals became sharper. However, signals due to protons on nitrobenzene rings do not change much when compared to other signals. This implies that the movement of the calix[4]arene unit occurs on the aryl ring containing OCH_3 group. The 500 MHz ^{1}H NMR spectrum of 10 at -30°C (Figure 2b) reveals that in solution ($CDCl_3$) 10 exists as a mixture of two conformers: partial cone and cone conformations. The cone conformation possesses two planes of symmetry. The *t*-butyl protons appear as two singlets at 0.78 and 1.29 ppm. The methoxy protons appear as a singlet at 3.81 ppm. On the other hand, the partial cone conformation has only one plane of symmetry. The *t*-butyl protons appear as three singlets at 1.04, 1.18 and 1.28 ppm (ratio 2:1:1). The methoxy protons appear as two singlets at 3.01 and 3.18 ppm (ratio 1:1). There should be 3 pairs of signals due to methylene bridge protons in the spectrum; however, the signals are superimposed on the glycolic proton signals which appear as 4 sets of multiplets between 4.00-4.50 ppm. The ratio of cone:partial cone can be calculated from the integration ratio of the methyl protons of each conformation to be 43:57.

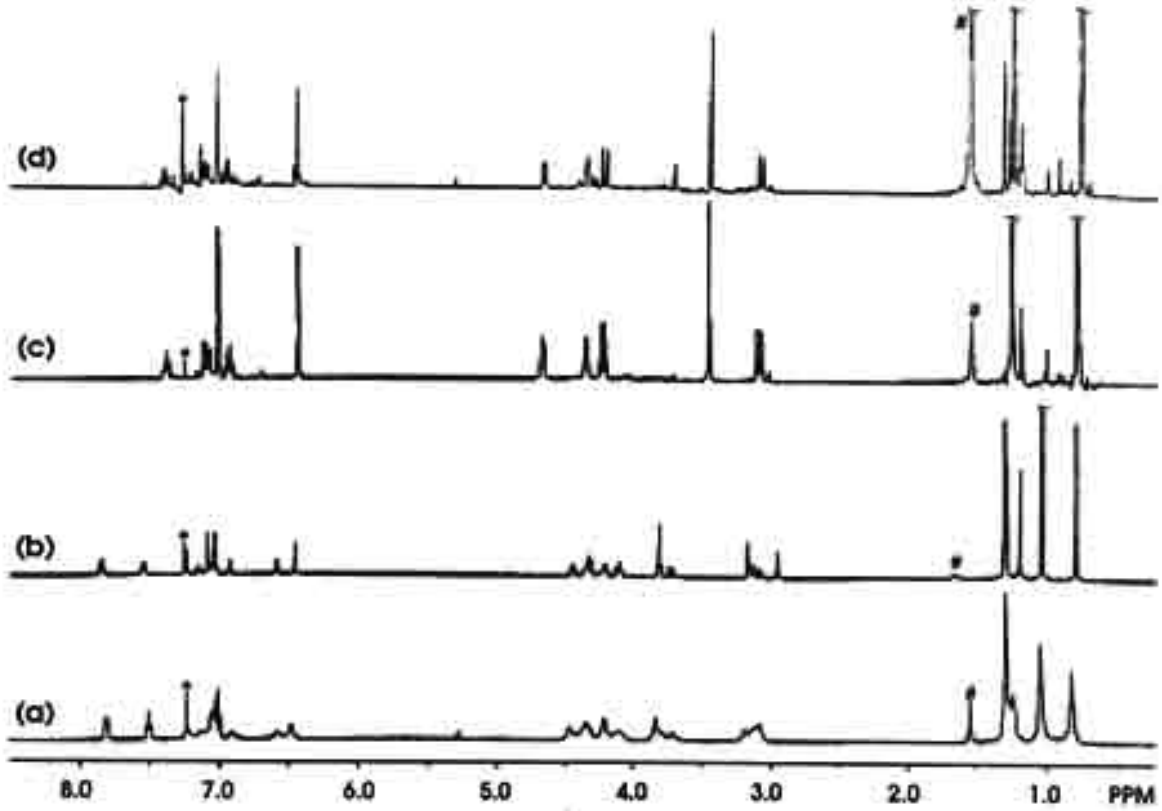


Fig 2. ^{1}H NMR spectra ($CDCl_3$) of (a) 10 at 27°C (b) 10 at -30°C (c) 11 at 25°C (d) 11 at 25°C after isomerization. * and # denote the trace of water in the solvent and the solvent signal, respectively.

The ^{1}H NMR spectrum of the coupling product ($CDCl_3$, room temperature), 11, is quite well resolved (Figure 2c), compared to that of 10. The spectrum suggests that 11 exists in a cone conformation which represents by one pair (AB system) of methylene bridge protons at 3.10 and 4.23 ppm (J = 12 Hz) and two singlets at 6.24 and 7.01 ppm corresponding to the *meta*-protons on the phenyl rings of calix[4]arene. The *t*-butyl protons appear as two sharp singlets at 0.82 and 1.28 ppm. The result shows that the bridging group of 11 (ethoxyazobenzene) can enhance the rigidity of the calix[4]arene framework probably by squeezing the two connected aryl rings together, which makes it harder for the methoxy groups to swing through the calixarene annulas.

It is well known that azobenzene exists in two isomers: *cis* and *trans*.[18] These two isomers can be switched by light. Upon standing in the day light for several hours, the ^{1}H NMR spectrum of 11 changed dramatically. In Fig 2d, there are many singlets due to *t*-butyl protons between 0.7-1.4 ppm. The region of the methylene and aromatic protons becomes very complicated. Another singlet probably due to methoxy protons appears at 3.72 ppm. The results suggest the occurrence of mixed conformations in the NMR time scale and also show that the conformational interconversion of the calix[4]arene unit takes place upon isomerization of the azobenzene unit which acts as a bridging group. Compared to the results obtained by Reinhoudt et al,[9] compound 2 containing shortest glycolic chain (n = 1) still showed conformational interconversion. The length of the bridging chains may not be the only one factor in controlling the conformational interconversion. The rigidity or inflexibility of the bridging group must also be accounted for governing the conformational behavior of calix[4]arene. Recently, Okada and colleagues have discovered that using the proper bridging groups between aryl rings at the *ortho* and para positions (with respect to the hydroxy groups) resulted in rigid calix[4]arene frameworks.[19,20]

Conclusion

The calix[4]arene unit in 7 containing a benzo propylenediamine bridging group was found to undergo conformational interconversion at different rates depending on solvents. In a protic solvent like

CD_3OD, the conformational interconversion seemed to be faster than in aprotic solvents such as $CDCl_3$ and DMSO-d_6 at the same temperature. Changing two substituents to ethoxy nitrobenzene in 10 increased the rigidity of calix[4]arene. Compound 10 existed in both cone and partial cone conformation (43:57) in $CDCl_3$ at - 30 °C. Reductive coupling of nitrobenzene to azobenzene in 11 allowed the calix[4]arene unit to exist in cone conformation. Reducing rigidity upon isomerization of the azobenzene group caused the conformational interconversion to occur and resulted in mixed conformations of calix[4]arene. We have thus demonstrated that temperature, solvent, length and rigidity of bridging groups have strong effects on conformational behaviors of the calix[4]arene unit.

Acknowledgements

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Recognition Studies of a Pyridine-Pendant Calix[4]arene with Neutral Molecules: Effects of Non-covalent Interactions on Supramolecular Structures and Stabilities

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Key words: pyridine-pendant, *p-tert*-butylcalix[4]arene, neutral molecule recognition, NMR titrations, NOESY, supramolecular framework

Abstract

A new calix[4]arene derivative containing hydrogen bond acceptors, 5,11,17,23-tetra-*tert*-butyl-25,27-bis[(4-pyridylmethyl)oxy]-26,28-dihydroxycalix[4]arene (**L**), has been synthesized. ^{1}H-NMR titrations in chloroform-*d* were carried out to investigate the host–guest chemistry of **L** towards neutral molecules containing a wide variety of hydrogen bond donor groups such as aldehyde derivatives of *p-tert*-butylcalix[4]arenes (compounds **3** and **4**), acetylacetone, 1,2-diaminoethane, 2,6-diaminopyridine, catechol, resorcinol, hydroquinone, phthalic acid, isophthalic acid and terephthalic acid. **L** can form complexes with resorcinol, phthalic acid and catechol in 1 : 1 (log K = 3.13), 1 : 1 (log K = 5.41) and polymeric fashions, respectively. In addition, the solution structures of these complexes have been revealed by NOESY experiments. **L** forms a 1 : 1 complex with resorcinol by hydrogen bonding and van der Waals interactions resulting in a supramolecular framework. The phthalic acid molecule interacts with **L** via hydrogen bonding and is included into the lower rim cavity of **L**.

Introduction

The assembly of organic supramolecular species incorporates non-covalent interactions such as van der Waals effects and hydrogen bonding to produce specific structural and functional properties [1]. Examples are liquid crystals [2] and molecular devices such as molecular cages and capsules [3, 4]. Calix[4]arenes, one of the most versatile building blocks in supramolecular chemistry, were derivatized and their self-assembly interactions investigated. Shimizu *et al.* have demonstrated the use of self-complementary hydrogen bonding to construct molecular capsules from calix[4]arene derivatives containing urea moieties at the upper rim [5]. This type of molecule can bind several polycyclic compounds such as nopinone, myrtenal, camphor and tricyclene to a different extent depending on the orientation of the guest molecules [6]. Böhmer and coworkers have also demonstrated the use of ^{1}H NMR spectroscopy to unambiguously determine the structures of tetraurea calix[4]arenes and also the exchange rates for four sets of protons by NOESY experiments [7]. Scheerder *et al.* [8] showed that the bis(ureido)calix[4]arenes gave a hydrogen-bonded dimer in a pinched cone conformation.

Several assemblies of calix[4]arene derivatives towards neutral molecules were also investigated [9–11]. Calix[4]arenes containing pyridone moieties at the upper rim can bind urea derivatives such as imidazolidone in a 1 : 1 fashion [9]. A calix[4]arene substituted with four carboxylic groups at the upper rim interacted with a calix[4]arene containing pyridine moieties at the lower rim to form a 1 : 1 complex, **1**, via hydrogen bonding interactions [10]. Corazza *et al.* have synthesized an interesting oxo-molybdenum calix[4]arene in which oxo-molybdenum binds four oxygen atoms from the phenolic O-atoms of a calix[4]arene [11]. The oxo-molybdenum calix[4]arene reacted with calix[4]arene to give a product, **2**, which could be crystallized in nitrobenzene. The crystal structure of the product shows that nitrobenzene is probably stabilized in the structure by both hydrogen bonding with a H_2O molecule and van der Waals interactions of the arene rings. Thus far, the understanding of how interactions between hosts and guests affected the structures of the assembled molecules is still unclear and, thus, should be a subject to pursue.

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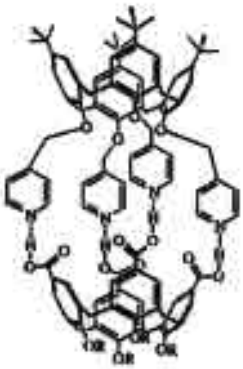

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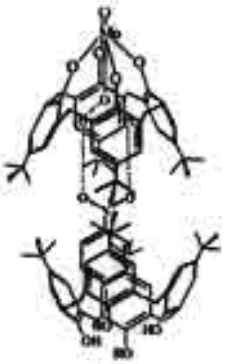

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Besides the work of van Loon *et al.* [9], other pyridinocalixarenes have been reported in the literature [12–14]. Shinkai and colleagues synthesized (2-pyridylmethoxy)calix[n]arenes (n = 6 and 8) and found that they were efficient extractants for UO_2 at 100 °C [12]. Pappalardo *et al.* [13] synthesized nine conformers of [2-pyridylmethyl)oxy]calix[4]arenes by alkylation of calix[4]arenes with 2-(chloromethyl)pyridine in the presence of various bases. Later, they studied the extractive ability of tetrapyridinocalix[4]arene towards alkali cations and found that the selectivity followed the order $Na^+ > K^+ > Rb^+ > Cs^+ > Li^+$ [14].

Due to the versatile donor abilities of pyridinocalix[4]-arenes, we are interested in synthesizing a pyridinocalix[4]arene and studying its interactions with neutral molecules containing hydrogen bond donor groups such as aldehydes, ketones, amines, alcohols and carboxylic acids. The complexation studies are carried out by ^{1}H-NMR titrations, and the solution structures of the complexes are determined by 2D-NMR spectroscopy. The results lead to the understanding of the relationship between size, shape, interactions between host/guest and structures of aggregated molecules.

Experimental

Materials

Unless otherwise stated, all materials and solvents were standard analytical grade, purchased from Fluka, J. T. Baker or Merck, and used without further purification. Commercial grade solvents such as acetone, dichloromethane and methanol were distilled and stored over 4 Å molecular sieves. Chromatographic separations were performed on silica gel columns (kieselgel 60, 0.063–0.200 mm, Merck). Deuterated solvents (chloroform-*d*, methanol-d_4 and DMSO-d_6) were stored over 3 Å molecular sieves. *p-tert*-Butylcalix[4]arene [15] and its derivatives, **3** [16] and **4** [17], were prepared as previously described. 1,2-Dihydroxybenzene (catechol), 1,3-dihydroxybenzene (resorcinol) and 1,4-dihydroxybenzene (hydroquinone) were purified by standard procedures [18]. Benzene-1,3-dicarboxylic acid (isophthalic acid) was synthesized according to the procedure described in the literature [19].

Analytical procedures

Elemental analysis was performed on a Perkin Elmer CHON/S analyzer (PE2400 series II). MALDI-TOF mass spectra were recorded on a Bruker MALDI-TOF mass spectrometer (BIFEX) using α-cyanocinnamic acid as matrix. The melting point measurement was carried out on an Electrothermal 9100 apparatus. ^{1}H NMR titration and ^{13}C NMR experiments were conducted on a Bruker ACF 200 MHz nuclear magnetic resonance spectrometer. Two dimentional NMR spectra were recorded on a Jeol 500 MHz nuclear magnetic resonance spectrometer. Typically, samples were dissolved in deuterated chloroform and chemical shifts were recorded using a residual chloroform signal as internal reference. All NMR experiments were carried out at room temperature (25 °C).

Synthetic procedures

Preparation of 5,11,17,23-tetra-tert-butyl-25,27-bis[(4-pyridylmethyl)oxy]-26,28-dihydroxycalix[4]arene (**L**)

The following procedure was adapted from the method used for synthesizing 5,11,17,23-tetra-*tert*-butyl-25,27-bis[(2-pyridylmethyl)oxy]-26,28-dihydroxycalix[4]arene [13]. A suspension of calix[4]arene (2.00 g, 3.08 mmol) and potassium carbonate (4.25 g, 30.8 mmol) in the presence of NaI (2.30 g, 15.3 mmol) in acetonitrile (200 mL) was heated to reflux under nitrogen for 30 minutes. The methanolic solution (50 mL) of 4-(chloromethyl)pyridine hydrochloride (1.05 g, 6.40 mmol) was subsequently added dropwise to the reaction mixture over a 15 minute period. The dark brown slurry was refluxed for an additional 24 hours. The solvent was then removed by a rotary evaporator to obtain a dark brown solid. The solid was dissolved in CH_2Cl_2 (100 mL) and subsequently washed with 0.5 M HCl (150 mL) and 1 M $NaHCO_3$ (150 mL). The organic layer was then separated, dried over anhydrous sodium sulfate and solvent was removed under reduced pressure to afford a red brown solid. The solid was dissolved in a minimum amount of dichloromethane and placed on a silica gel column. Unreacted reagents were eluted with 2% acetone/dichloromethane. The desired product was eluted with 10% acetone/dichloromethane and was purified by adding diethylether to precipitate a white solid (1.13 g, 44%).

Characterization for **L**: ^{1}H NMR (δ in $CDCl_3$): 8.60 (d, 4H, J_{H-H} = 6.1 Hz, Py-2-proton); 7.64 (d, 4H, J_{H-H} = 5.9 Hz, Py-3-proton); 7.05 (s, 4H, HOAr*H*); 6.99 (s, 2H, ArO*H*); 6.77 (s, 4H, ROAr*H*); 5.05 (s, 4H, OCH_2Py); 4.23, 3.31 (dd (AB system), 8H, J_{H-H} = 13.1 Hz, $ArCH_AH_BAr$); 1.28 (s, 18H, HOAr-*t*-C_4H_9); 0.91 (s, 18H, ROAr-*t*-C_4H_9). ^{13}C NMR (δ in $CDCl_3$): 30.93, 31.55, 31.68, 33.84, 33.94, 75.93, 121.33, 125.13, 125.71, 127.52, 132.23, 141.85, 146.13, 147.57, 149.36, 150.11, 150.47. MALDI-TOF MS (M^+, m/z): 830.3. *Anal Calcd.* for $C_{56}H_{66}O_4N_2$: C, 80.93; H, 8.00; N, 3.37. *Found*: C, 80.60; H, 7.92; N, 3.21. Melting Point: 107 °C.

Host–guest chemistry studies

Host–guest studies of **L** *with ketones, aldehydes and amines*

Typically, a solution of **L** (0.1039 g, 0.125 mmol) in $CDCl_3$ (2.5 mL) was prepared. To each NMR tube containing 0.2 mL of the **L** solution was added 0–4 equivalents of a guest (0.250 mmol) in $CDCl_3$ (2.5 mL). The solution in each NMR tube was adjusted by adding $CDCl_3$ to the same volume before the NMR measurements. NMR spectra were then recorded. The chemical shifts of the signals were followed and plotted against the equivalents of the added guest.

Host–guest studies of **L** *with catechol*

A solution of **L** (0.1039 g, 0.125 mmol) in $CDCl_3$ (2.5 mL) and a solution of catechol (0.0275 g, 0 250 mmol) in $CDCl_3$ (2.5 mL) were prepared. To each NMR tube containing 0.2 mL of the **L** solution was added 0-4 equivalents of catechol. In the case of 5–10 equivalents, a solution of **L** (0.0623 g, 0.0750 mmol) in $CDCl_3$ (1.5 mL) was prepared. Solid 1,2-Dihydroxybenzene (0–4 equivalents) was added to each NMR tube containing 0.2 mL of the **L** solution. The solution in each NMR tube was adjusted by adding $CDCl_3$ to the same volume before the NMR measurements.

Host–guest studies of **L** *with resorcinol, hydroquinone and benzene dicarboxylic acids*

Typically, a solution of **L** (0.0707 g, 0.0851 mmol) in $CDCl_3$ (1.7 mL) was prepared. Solid guest compounds (0-4 equivalents) were added to each NMR tube containing 0.2 mL of the **L** solution. The solution in each NMR tube was adjusted by adding $CDCl_3$ to the same volume before the NMR measurements. Association constants were determined using a curve fitting method [20, 21].

Competitive study between catechol and resorcinol

A solution of **L** (0.0707 g, 0.0851 mmol) and a solution of catechol (0.0275 g, 0.250 mmol) in $CDCl_3$ (1.7 and 2.5 mL, respectively) were prepared. In each NMR tube, 0.2 mL of the prepared **L** solution was mixed with the prepared solution of catechol (0–4 equiv.), and the mixture was subsequently transferred to an NMR tube containing 0–4 equiv. of solid resorcinol. The solution in each NMR tube was adjusted by adding $CDCl_3$ to the same volume before the NMR measurements. Chemical shifts of the mixture were compared to the known chemical shifts of **L**-catechol and **L**-resorcinol.

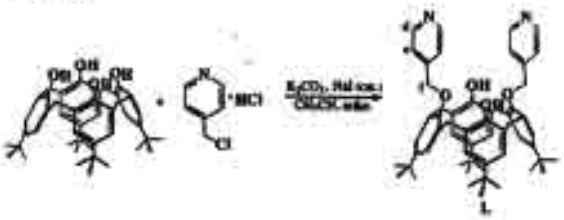
Theoretical calculations

Quantum calculations using a molecular mechanics method (MM+) were performed to obtain a gas phase structure of **L** [22]. An empirical method, PM3, was used to calculate the structures of benzene dialcohols and benzene dicarboxylic acids [23, 24].

Results and discussion

Synthesis and characterization

A *p-tert*-butylcalix[4]arene derivative, 5,11,17,23-tetra-*tert*-butyl-25,27-bis[(4-pyridyl methyl)oxy]-26,28-dihydroxycalix[4]arene (**L**) was synthesized by alkylating calix[4]arene with 2 equivalents of 4-(chloromethyl)pyridine hydrochloride in acetonitrile in the presence of K_2CO_3 as base and NaI (5 equivalents) as catalyst (Equation (1)). Separation of the products by column chromatography (SiO_2) using 10% acetone in dichloromethane as eluent gave **L** in 44% yield. Compared to other pyridylmethoxy derivatives such as *ortho* [13] and *meta* [14] derivatives, the *para* derivative (**L**) was obtained in lower yield because the N-donor in a *para* position could not chelate the K^+ ion to form a template framework that may facilitate the nucleophilic substitution reaction. A ^{1}H-NMR spectrum of **L** composed of a singlet signal of Ar-OCH_2-Py (f) at 5.05 ppm and two doublets of the aromatic protons on the pyridine moieties at 8.60 (d) and 7.64 ppm (e) as well as the signals of the *p-tert*-butyl calix[4]arene unit which showed a doublet of doublet signal at 4.23 and 3.31 ppm (designating the cone conformation). Furthermore, elemental analysis and MALDI-TOF MS results agree well with the proposed structure.



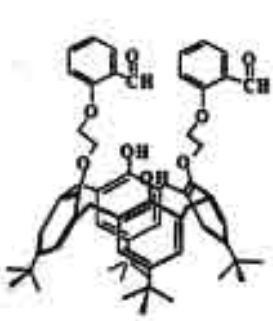
(1)

The compound **L** can possibly form a dimeric structure in a similar fashion with the bis(ureido)calix[4]arene as reported by Reinhoudt and colleagues [8]. However, the NOESY spectrum of **L** in $CDCl_3$ showed no NOE connectivity between the proton d and the proton f, methylene bridge and -O*H* protons, *vide infra*. This evidence suggests that **L** remains a single molecule in the solution.

Host–guest chemistry studies

^{1}H-NMR titrations have been carried out to investigate the host–guest chemistry of **L** towards neutral molecules. A series of compounds containing different types of hydrogen bond donor groups such as 1,3-bis(ethoxybenzaldehyde)-*p-tert*-butylcalix[4]arenes (**3** and **4**), 1,2-diaminoethane, 2,6-diaminopyridine, 1,2-dihydroxybenzene (catechol), 1,3-dihydroxybenzene (resorcinol), 1,4-dihydroxybenzene (hydroquinone), benzene-1,2-dicarboxylic acid (phthalic acid), benzene-1,3-dicarboxylic acid (isophthalic acid) and benzene-1,4-dicarboxylic acid (terephthalic acid) has been used in the investigation. In addition, a host–guest chemistry study between **L** and 2,4-pentanedione or acetylacetone has also been conducted. Generally, acetylacetone occurs in solution as an equilibrium mixture of 87% enol and 13% diketone [25]. The keto form contains acidic methylene

protons which may be suitable for hydrogen bonding with L. The change in the keto:enol proportion due to hydrogen bonding interactions is anticipated.



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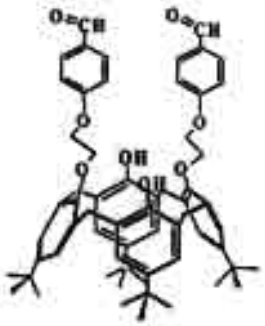

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^{1}H-NMR titrations of L with various hydrogen bond donors were performed in $CDCl_3$ solution at 25 °C. The results showed that the proton on the *ortho* and *meta* positions of the pyridine pendant groups (d and e) only slightly shifted upon addition of ligands 3 and 4, 1,2-diaminoethane, 2,6-diaminopyridine and acetylacetone and suggested that L had no recognition towards such compounds. In the case of compounds 3 and 4, the hydrogen bonding interactions may be too weak to be observed by NMR spectroscopy. For moderate hydrogen bond donors, 1,2-diaminoethane and 2,6-diaminopyridine, the absence of hydrogen bonding interaction with L may stem from the electron repulsion between *N*-amine and *N*-pyridine. It was surprising that no hydrogen bonding interaction between L and acetylacetone was observed. The intramolecular hydrogen bonding between –OH and O=C– in the enol form of acetylacetone must be very strong and prevents the intermolecular hydrogen bonding to occur.

In the light of the fascinating molecular structures of 1 and 2 which showed molecular assemblies by hydrogen bonding and van der Waals interactions, host–guest studies of L towards dihydroxybenzenes and benzene dicarboxylic acids containing two hydrogen bond donor groups at different positions are the subject of our interest. A relationship between the positions or orientations of the hydrogen bond donors and the structures/stabilities of the complexes is expected. Host–guest studies between dihydroxybenzenes and L were performed by adding various amounts of the guests into a deuterated chloroform solution of the host (L), and interactions of host and guest molecules were investigated by ^{1}H-NMR spectroscopy. Due to the insolubility of dihydroxybenzenes except catechol, they were added directly as solid into NMR tubes. Dissolution of the solids into the solution of L indicates that the alcohols have interacted with or formed complexes with L. It was found that the solution of L could not dissolve hydroquinone, and the Py-2-proton and Py-3-proton (d and e) were only slightly shifted. Therefore, L did not form a complex with hydroquinone. For catechol and resorcinol, each ^{1}H-NMR spectrum of the complexes with L possessed a doublet of doublet signal at approximately 3.34 and 4.23 ppm ($J \sim 13$ Hz) suggesting that L retained the cone conformation of calix[4]arene upon complexation.

Addition of resorcinol into the deuterated chloroform solution of L led to the evolution of a new set of proton resonances at 7.13 (t), 6.59 (d) and 6.46 (dd) ppm. All signals except the one for proton d shifted continuously downfield until 1 equivalent of the guest was added. A plot of chemical induced shift (CIS) against the equivalent of resorcinol is displayed in Figure 1a. The plot suggests that L forms a complex with resorcinol in a 1 : 1 fashion. The stability or complex formation constant of L towards resorcinol has been estimated using a curve-fitting program to be log K = 3.13 [20, 21].

The complexation of L and resorcinol was also studied in methanol-d_4 and DMSO-d_6. Unfortunately, the results showed that L did not complex resorcinol in these solvents. In deuterated methanol, the complexation of L and resorcinol may be disrupted and replaced by the stronger hydrogen bonding interactions of methanol towards L and resorcinol because the hydroxy group of methanol acted as both hydrogen bond donors and hydrogen bond acceptors. In the case of tetrapyridinocalix[4]arene, the crystal structure of the compound showed that a methanol of solvation was hydrogen bonded to one pyridine N atom [13]. Either the hydrogen bond donor character of the O-atom or the presence of H_2O in deuterated DMSO accounted for the absence of an interaction between L and resorcinol in this solvent.

Interestingly, addition of up to 10 equivalents of catechol produced continuous shifts of all proton signals of L (Figure 1b) except Py-3-proton (e). It should also be noted that catechol was completely dissolved in the solution of L in spite of the low solubility of catechol (>10 equivalents of catechol were added). The CIS of the protons and the evidence from the increasing solubility of catechol suggested that the interactions between the aromatic protons of catechol and the aromatic protons of L may be in a polymeric manner. Therefore, the stability constant was not able to be calculated using our curve-fitting program.

The abilities of L to form complexes with benzene dicarboxylic acids such as phthalic acid, isophthalic acid and terephthalic acid have been studied by ^{1}H-NMR titrations which were carried out by direct addition of the acid as solid into $CDCl_3$ solutions of L. It was found that isophthalic acid and terephthalic acid did not dissolve in the solution of L and, thus, did not form complexes with L. Only phthalic acid dissolved in a solution ($CDCl_3$) of L and a complex formation constant was able to be estimated by ^{1}H-NMR spectroscopy. In addition, each ^{1}H NMR spectrum contained a pair of doublet signals ($J \sim 13$ Hz) due to the methylene bridge protons (ArCH_2Ar) signifying a cone conformation of calix[4]arene. The titration results shown in Figure 1c suggested a 1 : 1 stoichiometry of the L·phthalic acid complex. The protons d, e and ArOH were used for determining a stability constant of L·phthalic acid which was estimated to be log $K = 5.41$.

Although the stability constant of the L·catechol complex could not be determined, the comparative binding ability of catechol and resorcinol was conducted. Addition

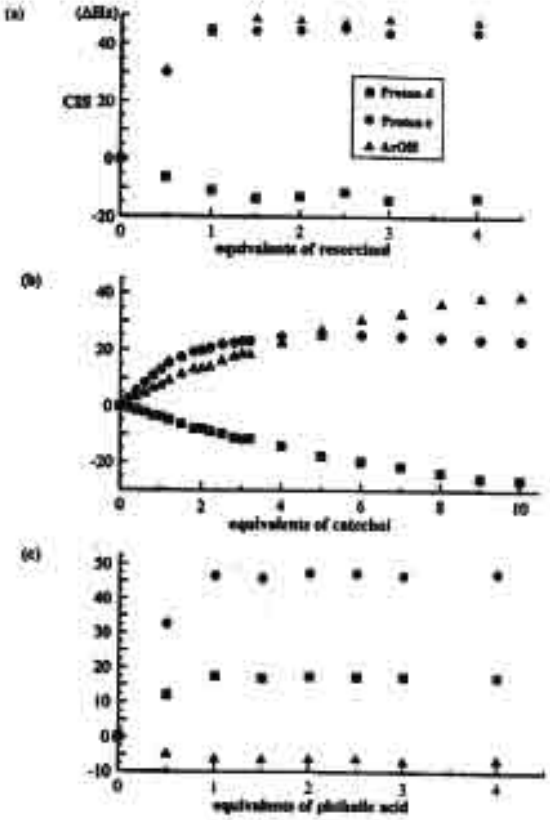

Figure 1. Titration curves for (a) resorcinol (b) catechol (c) phthalic acid (1equivalent of L present in the solutions). The negative ΔHz denotes the upfield shift of the signal.

of various stoichiometries of L-catechol in $CDCl_3$into the same various ratios of resorcinol resulted in the shifting of proton signals which was similar to the chemical shifts of L-resorcinol. The result signified that L formed a more stable complex with resorcinol.

Solution structures of complexes

In order to understand the factors that control the stability of the complexes, the solution structures of the host–guest complexes must be determined. Thus, NOESY experiments for L and the mixture of L and guests in $CDCl_3$ have been carried out. It can be clearly seen from the NOESY spectra of L that the proton e on the pyridine pendant groups has interacted with ArO*H* and the methylene bridge protons (g) on the calix[4]arene unit. We have calculated a structure of L by MM+ and found that the pyridine pendant arms organize themselves by bending towards the calix[4]arene unit. This is pertinent to the connectivity of the protons observed in NOESY. The distance between N_{py}–N_{py} of the pyridine groups was 6.34 Å. Figure 2 displays connectivities among protons of L as deduced from the NOESY spectra and the calculated structure of L which shows the preorganized cavity of the ligand.

Certain regions of the NOESY spectra of the mixture of L and resorcinol in a 1 : 1 stoichiometry are shown in Figures 3a and 3b. The proton H_c of resorcinol is found to have a connectivity with the proton d while the protons

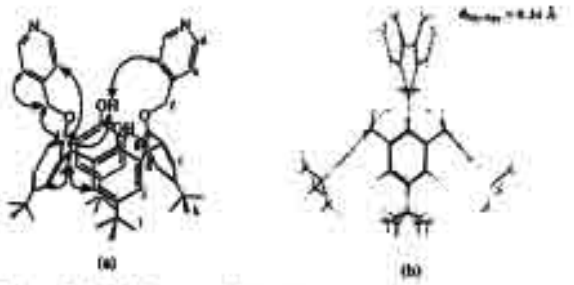

Figure 2. (a) NOE connectivities of L, (b) calculated structure of L.

H_a and H_b do not show any connectivities with the proton d. In addition, there is no connectivity between H_a/H_b and the proton e. The resorcinol molecule must arrange its H_c into the cavity of the pyridine pendant arms and pointing H_b and H_a outwards. This orientation should be stabilized by hydrogen bonding interactions between resorcinol-O*H* and *N*-pyridine of L. Unexpectedly, connectivities of the proton H_b with ROAr*H* (i) and HOAr*H* (j) of the calix[4]arene framework are detected. Furthermore, the NOESY spectrum in Figure 3b shows that the proton H_c has a connectivity with *t*-butyl protons (l) of the ArOH rings. These connectivities cannot result from through space interactions within a single aggregate because these protons are too far from each other. They must arise from interactions with hydrogens of another molecule. The interactions summarized in Figure 3c imply that a resorcinol molecule must also be included into the hydrophobic upper rim cavity of another calix[4]arene unit of L. Recently, Hosseini and coworkers have demonstrated use of the double fusion of two calix[4]arenes and *p*-xylene to form a unidirectional supermolecule in the solid state [26]. The possible solution structure of L-resorcinol is thus proposed in Figure 3d accounting for the 1:1 stoichiometry of L-resorcinol suggested by the titration results. The structure also corresponds with the upfield shifts of the proton d and all protons of resorcinol due to the diamagnetic anisotropy of the neighboring ring currents.

NOESY experiments of the 1 : 1 mixture of L and phthalic acid have also been performed in $CDCl_3$ and a spectrum is depicted in Figure 4a. The signal due to H_a on phthalic acid is superimposed on the signal of the proton e. Therefore, some interactions related to these two protons cannot be distinguished. From Figure 4a, only the connectivity between H_b of phthalic acid and the proton j of L can be unambiguously assigned. In addition, an interaction of the proton b towards *H*OArH can also be observed (Figure 4b). However, no intermolecular NOE connectivity encountered in L-resorcinol has been detected in the phthalic acid case. The results imply that phthalic acid resides within the cavity of L close to the lower rim ArO*H* and HOAr*H*. The possible solution structure of the L-phthalic acid complex can be drawn as shown in Figure 4c. The structure also agrees with the fact from titrations that ArO*H* shifted upfield (due to the anisotropic effect of the phthalic ring current).

NOESY spectra of the mixture of L and catechol have also been obtained. We observed that a proton of catechol had connectivities with protons d, e, f and g of L. However,

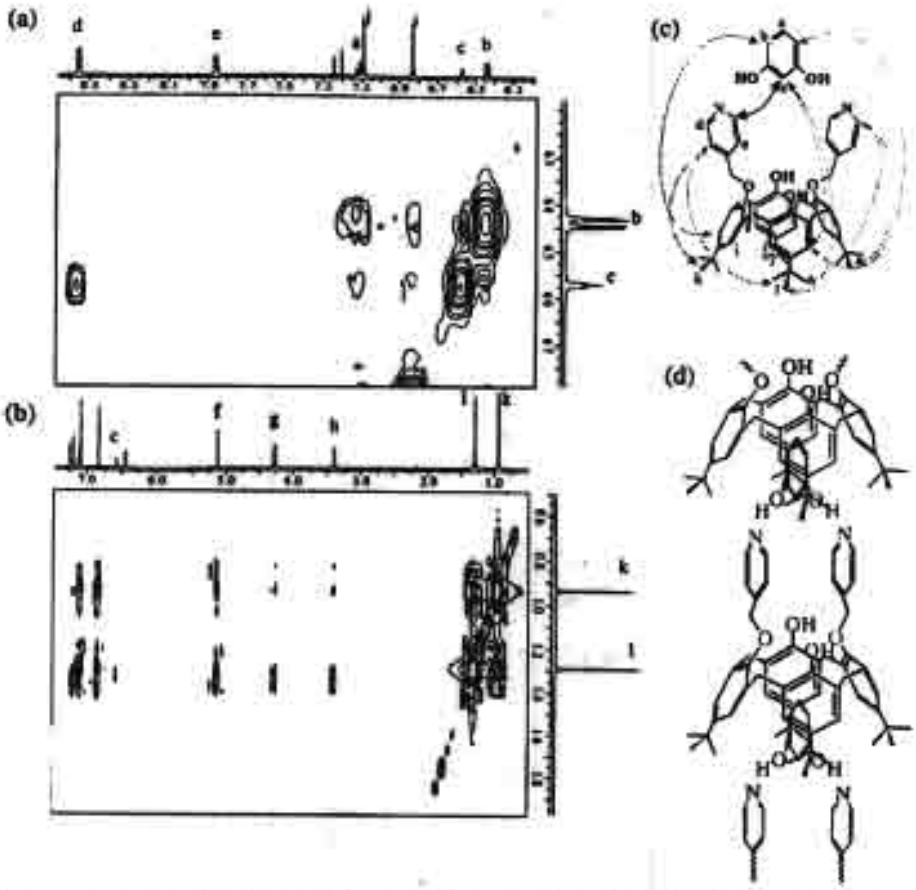

Figure 3. (a), (b) NOESY spectra of L-resorcinol in $CDCl_3$ (c) summary of interactions deduced from NOESY spectra. (d) possible solution structure of L-resorcinol.

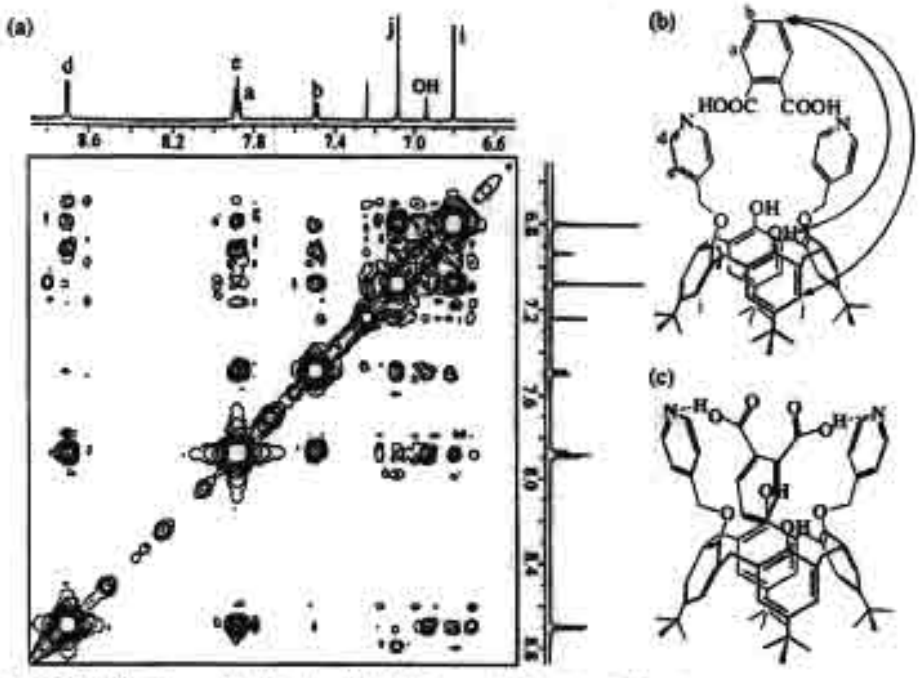

Figure 4. (a) NOESY spectrum of L-phthalic acid (b) NOE connectivities, (c) possible solutions structure of L-phthalic acid.

the NMR titration results indicated the polymeric structure of the complex. The data obtained from NOESY are, therefore, not conclusive enough for deducing the solution structure of L·catechol.

Effects of size, shape and interaction between host/guest towards aggregated molecules

The structures of dicarboxylic acids and benzene dialcohols used in these studies were calculated by the PM3 method. The results show that the H–H distances of HO–Ar–OH in catechol, resorcinol and hydroquinone are 3.29, 4.58 and 6.39 Å, respectively. For the acids, the H–H distances of HO–(C=O)–Ar–(C=O)–OH in phthalic acid, isophthalic acid and terephthalic acid are 5.82, 8.68 and 9.13 Å, respectively. Our results show that catechol, resorcinol and phthalic acid can form complexes with L. The size and dimensionality of hydroquinone, isophthalic acid and terephthalic acid may be unsuitable to form hydrogen bonding with L or fit into the cavity of L. Phthalic acid may have a suitable geometry for its hydroxy groups to form hydrogen bonding with *N*-pyridine of L and simultaneously be included into the lower rim cavity of L. The combination of hydrogen bonding and the preorganized structure of L for inclusion of phthalic acid may account for the high stablity constant of the L·phthalic acid complex. In contrast, the geometry of catechol and resorcinol are probably too constrained to organize such an alignment in the phthalic acid case. Nevertheless, the dimensionality of resorcinol must be appropriate for the inclusion into an upper rim cavity of calix[4]arene. In this case L requires a dramatic disturbance of the calix[4]arene compartment and this may result in the lower stability constant of the L·resorcinol complex. In the case of catechol, the polymeric structure of L·catechol may stem from the versatility of catechol to form both homonuclear hydrogen bonding (catechol-catechol) and heteronuclear hydrogen bonding (catechol-L). The structure of the catechol complex cannot be deduced from the present data. More experiments will be carried out in due course to elucidate its solution structure.

Conclusion

The compound 25,27-di-(4-pyridylmethoxy)-*p*-*tert*-butylcalix[4]arene (L) has been synthesized and found by NMR studies to interact with some dialcohols and diacids. The recognition of L towards dialcohols and diacids is as follows: phthalic acid (log K = 5.41) > resorcinol (log K = 3.13) > catechol. L selectively binds resorcinol in a 1 : 1 fashion by hydrogen bonding and van der Waals interactions to form a supramolecular structure. L also forms a 1 : 1 complex with phthalic acid. The phthalic acid molecule was included into the lower rim cavity of L, and the complex was stabilized by hydrogen bonding. Catechol was also found to form a complex with L in a polymeric manner *via* hydrogen bonding interactions. We have demonstrated thus far that a combination of hydrogen bonding and van der Waals interactions between L and certain neutral guests can result in interesting supramolecular structures.

Acknowledgements

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Graphical Abstract

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Aza crown ether calix[4]arenes containing cation and anion binding sites: effects of metal ions towards anion binding ability

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Thawatchai Tuntulani,[a,*] Sirilux Poompradub,[a] Praput Thavornyutikarn,[a] Nongnuj Jaiboon,[a] Vithaya Ruangpornvisuti,[a] Narongsak Chaichit,[b] Zouhair Asfari[c] and Jacques Vicens[c]

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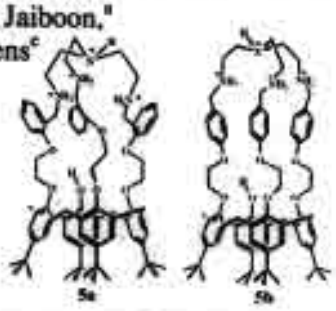

Compounds **5a** and **5b** were synthesised, and their complexation with halide anions in the presence of various countercations was studied by ^{1}H NMR titrations.

Pergamon

TETRAHEDRON LETTERS

Aza crown ether calix[4]arenes containing cation and anion binding sites: effects of metal ions towards anion binding ability

Thawatchai Tuntulani,[a,*] Sirilux Poompradub,[a] Praput Thavornyutikarn,[a] Nongnuj Jaiboon,[a] Vithaya Ruangpornvisuti,[a] Narongsak Chaichit,[b] Zouhair Asfari[c] and Jacques Vicens[c]

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Abstract— Tripodal aza crown ether calix[4]arenes containing both cation and anion binding sites (**5a** and **5b**) have been synthesised. The X-ray analysis shows that **5a** forms a self-threaded rotaxane-like structure in the solid state. ^{1}H NMR titrations of the two ligands with various halide anions indicate that **5a** and **5b** can form complexes with Br^- and I^- but not F^-. However, both compounds form more stable complexes with I^- than with Br^- in the presence of Bu_4N^+. The presence of K^+ enhances the binding ability of **5a** towards Br^-. © 2001 Elsevier Science. All rights reserved.

Keywords: aza crown; calix[4]arene; anion binding; proton nmr titration.

Molecular recognition of abiotic anions by synthetic receptors has received increasing attention in the past few years according to recent reviews written by Beer and Gale.[1] Many of receptors have been used successfully as sensors for anions.[2] Recently, synthetic receptors containing two individual recognition sites for a cation and an anion have attracted chemist attention. Applications of such receptors may be found in metal-controlled anion sensing devices. Reinhoudt and coworkers have elegantly demonstrated that a calix[4]arene derivative with cation binding ester groups on the lower rim and anion binding urea on the upper rim can efficiently bind Cl^- only in the presence of Na^+.[3] Beer and coworkers have synthesised a number of ditopic receptors that can undergo selective ion pair recognition.[4]

In 1997, polyaza crown ether derivatives of *p-tert*-butylcalix[4]arene have been synthesised in our lab. The ammonium derivatives are found to form complexes with CO_3^{2-}, NO_3^-, AsO_2^- and Cl^- in a different extent using electrostatic interactions.[5] We are interested in constructing a three dimensional anion receptor by combining the calix[4]arene framework with tris(2-amino) ethylamine, **tren**, and glycolic chains to obtain a compound that have both a cation and an anion binding sites in the same molecule. This compound may have great potential to bind a metal ion and an anion cooperatively and selectively.

Tripodal aza crown ether calix[4]arenes, **5a** and **5b**, were synthesised according to the procedure shown in Scheme 1. Substitution reactions of *p-tert*-butylcalix[4]arene with 3.0 equiv. of 2-(2′-bromoethoxy)benzaldehyde, **1a**, and 4-(2′-bromo ethoxy)benzaldehyde, **1b**, respectively, were carried out in the presence of a base to produce trialdehyde precursors, **3a** and **3b**, for preparing the tripodal amine capped calix[4]arene. The synthesis of **3a** was reported previously in acetonitrile using K_2CO_3 as base. This reaction gave only 6% yield of the desired trialdehyde derivative.[6] Furthermore, substitution reactions using K_2CO_3 always gave the dialdehyde derivatives, **2a** and **2b**, in high yields.[7] Since then, a number of bases and solvents have been employed to optimize the yields of the desired products. However, it was found that reactions in the presence of strong bases such as NaH and KOH underwent Cannizzaro reactions and gave both alcohol and carboxylic acid derivatives instead.[8] Finally, we found that reactions using BaO in DMF gave higher yields of trialdehyde calix

[4]arenes, **3a**[6] (21%) and **3b**[9] (46%), than those of dialdehyde calix[4]arenes, **2a** (20%) and **2b** (2%). It should be noted that the yield of **3b** was twice as much as that of **3a** probably due to the less steric hindrance of the *para* isomer facilitating the substitution reaction. Compounds **2** and **3** were separated by silica gel chromatography using CH_2Cl_2 as eluent. Condensation reactions of **3a** and **3b** with 1.1 equiv. of tris(2-amino) ethylamine in acetronitrile precipitated imine or Schiff base products, **4a**[6] (95%) and **4b**[10] (97%). Reduction of **4a** and **4b** by 20 equiv. of $NaBH_4$ and subsequent acidifying with HCl/CH_3OH (0.74% v/v) yielded the desired tripodal ammonium derivatives, **5a**[6] (86%) and **5b**[11] (95%). ^1H NMR spectra of compounds **3b**-**5b** possessed four sets of doublet due to the methylene bridge protons on the calix[4] arene moiety suggesting the existence of the cone conformation.

Scheme 1.

The solid state structure of compound **5a** has been determined by X-ray crystallography (Figure 1).[12] The calix[4]arene unit is in a pinched cone conformation. One of the ethoxy benzyl chains connecting to the **tren** unit threads through the cavity of the other two ethoxy benzyl chains. This structure resembles a self-threaded rotaxane derivatised from two homooxacalix[3]arenes.[13] Recently, Vicens and colleagues have also reported a similar structure of tripodal calix[4](azo)crowns.[14]

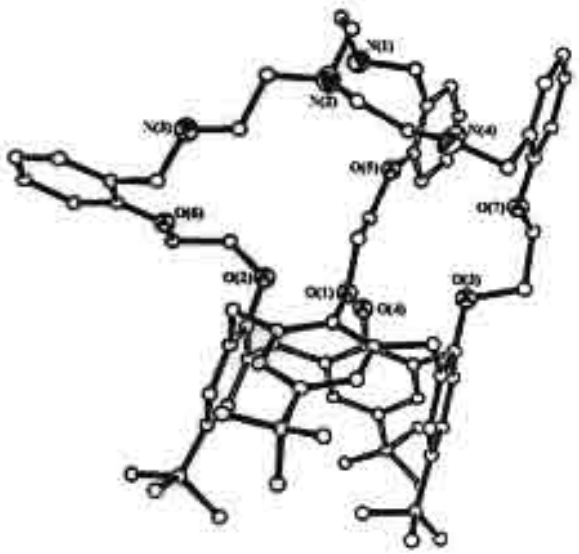


Figure 1. Crystal structure of **5a**. Hydrogen atoms were omitted for clarity.

Although suitable crystals of **5b** for *X*-ray analysis cannot be obtained, the ^1H NMR spectrum of **5b** suggests a more symmetrical orientation of the glycolic chains.[11] Both **5a** and **5b** possess N_4-tripodal ammonium units for binding anions and O_6-crown ether cavities for binding alkali cations. However, the N_4-tripodal ammonium cavity of the *para* isomer, **5b**, should have more space than that of the *ortho* isomer, **5a**. This leads to the different selectivity of **5a** and **5b** towards various anions.

^1H NMR (200 MHz) titrations were employed in complexation studies of **5a** and **5b** towards halide anions (F^-, Br^- and I^-) in the presence of various countercations.[15] It was found that no displacement of any proton signals of **5a** and **5b** occurred upon addition of F^-. The result indicates that **5a** and **5b** do not form complexes with F^-. Addition of Br^- and I^- to **5a** and **5b**, however, resulted in the displacement of signals due to -$OArCH_2N\boldsymbol{H}_2^+$- and -$OAr\boldsymbol{H}CH_2$-. The plot showing the relationship between chemical shifts of the signal due to -$OAr\boldsymbol{H}CH_2$- and concentrations of iodide anion is depicted in Figure 2. Job plot analysis indicates that **5a** and **5b** bind Br^- and I^- in a 1:1 ligand/anion ratio. Association constants of **5a** and **5b** towards Br^- and I^- in the presence of various countercations such as Bu_4N^+, Na^+ and K^+ calculated by the program EQNMR[16] are collected in Table 1.

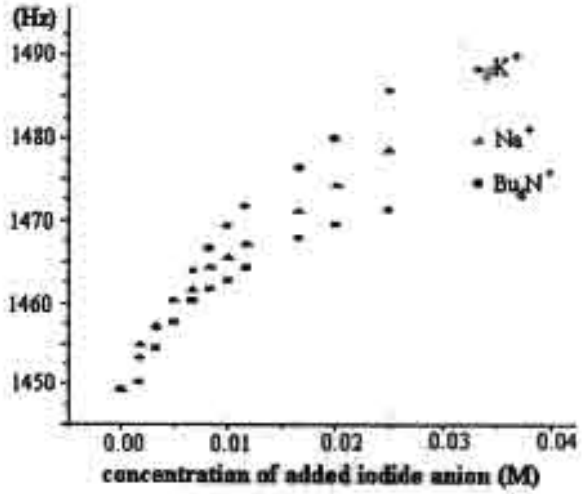


Figure 2. Titration curves of **5b** with I^- in the presence of Bu_4N^+, Na^+ and K^+.

Table 1. Association constants of ligands **5a** and **5b** towards Br^- and I^- in the presence of various countercations.[a]

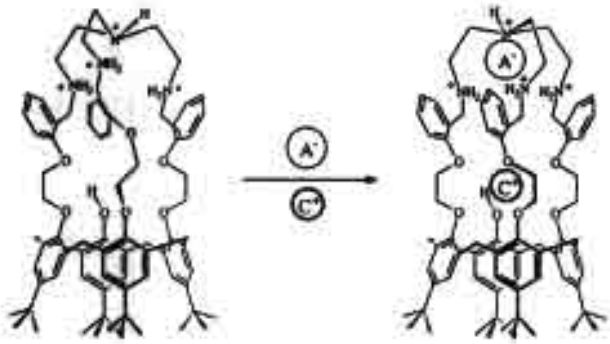
Metal	Anion	K_{assoc} (M^{-1})	
		5a	**5b**
None[b]	Br^-	84.2	76.5
Na^+	Br^-	58.6	53.0
K^+	Br^-	120.1	34.9
None[b]	I^-	108.9	137.9
Na^+	I^-	77.2	57.3
K^+	I^-	103.3	66.3

[a]all experiments were carried out at 298 K; errors estimated to be less than 15%. [b]Using Bu_4N^+ as countercation.

The result implies that the tripodal ammonium cavities of **5a** and **5b** are not suitable for binding F^-. With Bu_4N^+ as

countercation, **5a** and **5b** can form more stable complexes with I^-. However, the stability of **5b** towards I^- is higher than **5a**. This signifies that the cavity of **5b** is more suitable for binding a big anion such as I^-. In the presence of K^+, **5a** shows an increase in binding affinity towards Br^- by nearly 1.5 folds. On the other hand, Na^+ does not show any enhancement in anion binding ability of **5a**. The result suggests that the crown ether unit of **5a** prefers binding K^+ over Na^+. A similar crown ether cavity found in biscalix[4]arene in which two molecules of calix[4]arene linked by four glycolic units has been reported to bind K^+ selectively.[17] From the crystal structure of **5a**, it is also possible that an alkali metal ion can coordinate to the crown ether unit and induces the structural reorganization of **5a** to be more appropriate for binding anions (Scheme 2). Interestingly, the binding ability of **5b** towards Br^- and I^- decreases in the presence of Na^+ and K^+. The observation in which the presence of alkali metal ions decreases the anion binding ability of **5a** and **5b** can be rationalised in term of the binding competition. Alkali metal ions (Na^+ or K^+) that cannot fit into the cavity size of the crown ether unit in **5a** or **5b** retain alkali metal-anion pairs and compete in binding with the tripodal ammonium unit of the ligands.

Scheme 2. A metal ion can possibly induce the structural reformation of **5a** to bind an anion more efficiently.



In summary, we have synthesised two tripodal aza crown ether calix[4]arenes, **5a** and **5b**, and shown that both can bind Br^- and I^- in a different extent depending on coutercations. We are currently investigating the complexation of **5a** and **5b** towards other anions and also preparing new ion pair receptors for better understanding of such cooperative behaviour and for possible applications in metal ion-controlled anion extraction.

Acknowledgments

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9. **3b**: ^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ 9.76 and 9.68 (s each, 2H and 1H, -Ar(C=O)*H*), 7.57 and 7.43 (d each, J_{H-H} = 8.7 Hz, 4H and 2H, -OArH_a), 7.19 (s, 2H, HOAr*H*), 7.14 (s, 2H, ROAr*H*), 6.70 and 6.63 (d each, J_{H-H} = 8.7 Hz, 4H and 2H, -OArH_b), 6.54 (s, 4H, ROAr*H*), 5.40 (s, 1H, *H*OAr), 4.86 (m, 2H, OCH_2CH$_2$O), 4.45 and 3.32 (d each, J_{H-H} = 12.4 Hz, 4H each, ArCH_AH$_B$Ar), 4.28 (m, 2H, OCH$_2$CH_2O), 4.13 (s ,8H, OCH_2CH_2O), 1.36 (s, 18H, HOAr-*t*-C$_4$H$_9$ and ROAr-*t*-C$_4$H$_9$), 0.82 (s, 18H, ROAr-*t*-C$_4$H$_9$). FAB MS (m/z): 1092.5. *Anal. Cald.* for **3b** ($C_{71}H_{88}O_{10}$): C,77.99; H, 7.37%. *Found*: C, 77.91; H, 7.52%.
10. **4b**:^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ 8.07 and 7.86 (s each, 1H and 2H, -C*H*=N), 7.38 (d, J_{H-H} = 8.7 Hz , 4H, -OArH_a), 7.20 (s, 2H, HOAr*H*), 7.18 (s, 2H, ROAr*H*), 6.73 (d, J_{H-H} = 8.7 Hz, 4H, -OArH_b), 6.62 (d, J_{H-H} = 2.4 Hz, 2H, ROArH_a), 6.52 (d, J_{H-H} = 2.4 Hz, 2H, ROArH_b), 6.32 (s, 1H, *H*OAr), 6.13 (d, J_{H-H} = 8.8 Hz, 2H, ROAr*H*), 6.02 (d, J_{H-H} = 8.8 Hz, 2H,ROAr*H*), 4.92 and 3.32 (d each, J_{H-H} = 13.0 Hz, 4H, ArCH_AH$_B$Ar), 4.56 (m, 2H, OCH_2CH$_2$O), 4.33 and 3.23 (d each, J_{H-H} = 13.0 Hz, 4H, ArCH_AH$_B$Ar), 4.28-4.02 (m, 10H, OCH_2CH_2O), 3.74 (m, 4H, CH=NCH_2CH$_2$N), 3.64 (m, 2H, CH=N CH_2CH$_2$N), 2.83 (m, 4H, CH=NCH$_2$CH_2N), 2.59 (m, 2H, CH=NCH$_2$CH_2N), 1.39 (s, 9H, HOAr-*t*-C$_4$H$_9$), 1.36 (s, 9H, ROAr-*t*-C$_4$H$_9$), 0.83 (s, 18H, ROAr-*t*-C$_4$H$_9$). *Anal. Cald.* for **4b** ($C_{71}H_{92}N_4O_{10}$): C, 78.01; H, 7.82; N, 4.73%. *Found*: C, 77.95; H, 7.66; N, 4.77%.
11. **5b**: ^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ 8.71 and 8.23 (s each, broad, 4H and 2H, ArCH$_2$NH_2^+Cl$^-$), 7.79 (d, J_{H-H} = 8.6 Hz, 4H, -OArH_a), 7.36 (d, J_{H-H} = 8.5 Hz, 2H, -OArH_a), 7.14 (s, 2H, HOAr*H*), 7.10 (s, 2H, ROAr*H*), 6.92 (d, J_{H-H} = 8.7 Hz, 4H, -OArH_b), 6.54 (m, 6H, ROAr*H* and -OArH_b), 6.12 (s, 1H, HOAr), 4.56 and 3.30 (d each, J_{H-H} = 13.3 Hz, 4H, ArCH_AH$_B$Ar), 4.55-4.40 (m, 14H, OCH_2CH_2O, ArCH_2N and ArCH_AH$_B$Ar), 4.20-3.98 (m, 6H, OCH_2CH_2O, ArCH_2N), 3.70 (s, br, 2H, NCH$_2$CH_2N), 3.41-3.10 (m, 10H, NCH_2CH_2N), 3.25 (d, J_{H-H} = 13.0 Hz, 2H, ArCH_AH$_B$Ar), 1.34 (s, 9H, HOAr-*t*-C$_4$H$_9$), 1.32 (s, 9H, ROAr-*t*-C$_4$H$_9$), 0.82 (s, 18H, ROAr-*t*-C$_4$H$_9$). *Anal. Cald.* for **5b** ($C_{71}H_{102}N_4O_7Cl_2$): C, 69.15; H, 7.69; N, 4.19%. *Found*: C, 69.19; H, 7.76; N, 4.16%.
12. Crystal data for **5a**, $C_{71}H_{102}N_4O_7Cl_2(OH)_2$•(CH$_3$OH)(H$_2$O)$_5$, *M* = 1368.7, monoclinic, space group *C*2/*c*, *Z* = 8, *a* = 43.6552 (14), *b* = 15.9085 (5), *c* = 25.1856 (7) Å, β = 109.4630 (10)°, *V* = 16491.6 (9) Å^3, *Dc* = 1.119 g cm^{-3}, 23606 unique data, *R1* = 0.1355, *wR2* = 0.3402.
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15. A solution of **5a** (0.0250 M) and a solution of **5b** (0.0083M) in DMSO-d_6 and in a mixture of $CDCl_3$ and CD_3OD, respectively, were prepared. To a solution of a ligand in each NMR tube was added 0.0-4.0 equivalents of 0.1 M anion salts. Spectra were recorded every 24 hours until the complexation reached the equilibrium. The result of the experiment was a plot of displacement in chemical shift as a function of the amount of added anion. The program EQNMR was then used to analyse the resulting titration curves and calculate stability constant values for 1:1 anion complexes in M^{-1}. Titration experiments were repeated twice with at least 12 data points for each anion.
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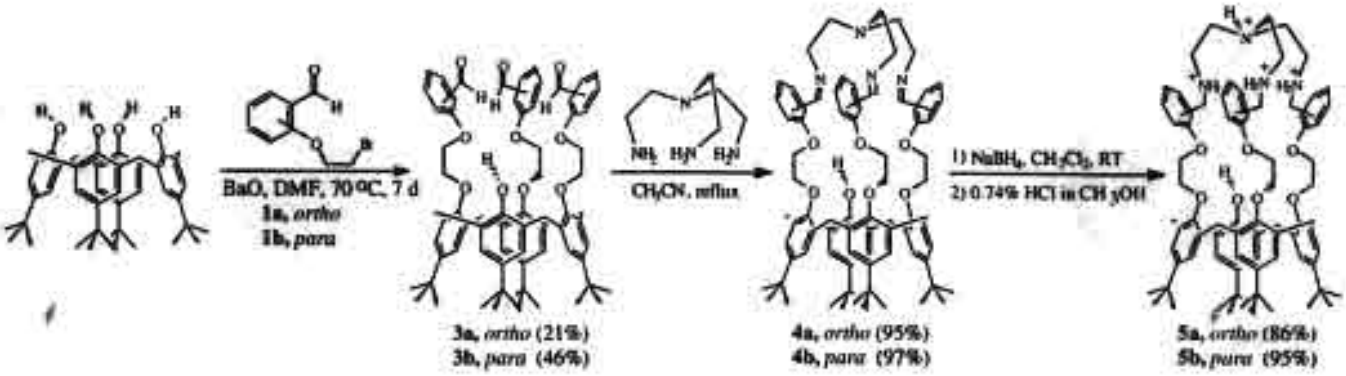
Supplementary Material

Crystallographic data for **5a** are available upon request from the editorial office.

Scheme 1. Synthetic procedure of compounds **5a** and **5b**.



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Design and Synthesis of Tripodal Aza Crown Ether Calix[4] arenes: Anion Binding Studies and Role of Countercations towards Anion Binding Ability

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Introduction

During the past decade, chemists have synthesized many types of anion receptors and studied their anion binding properties as appeared in recent review articles.[1-7] Anion receptors can be subdivided into two classes: positively charge and electroneutral anion hosts. The anion binding role of macrocyclic compounds such as cryptands can be dated back to the early year of anion recognition studies. Park and his coworkers have demonstrated that the preorganized molecular cages so called katapinands can encapsulate halide anions into the cavity.[8] The selectivity towards a particular anion can be controlled by the lengths of the alkyl spacers. Later, Lehn and colleagues have found that macrobicyclic and macrotricyclic polyamine ligands can selectively bind Cl^- and N_3^-, respectively.[9-11]

Recently, receptors containing two individual recognition units, one for a cation and one for an anion have attracted chemist attention.[12] Applications of such receptors may be found in metal-controlled anion sensing devices. Reinhoudt and coworkers have synthesized an elegant calix[4]arene derivative with cation binding ester groups on the lower rim and anion binding urea on the upper rim. The compound can efficiently bind Cl^- in the presence of Na^+.[13] Beer and coworkers have synthesized a number of ditopic receptors that can undergo selective ion pair recognition. Rhenium(I) bipyridyl amide crown ether receptors were found to complex KCl ion pairs.[14] A tripodal *tris*(amido benzo-15-crown-5) ligand was found to cooperatively bind chloride, iodide and perrhenate anions via co-bound crown ether complexed sodium cations.[15] Later, a heteroditopic bis(calix[4]arene) ferrocene receptor was

found to give a significant electrochemical response to bromide anions in the presence of Li ion.[16]

Reinhoudt and coworkers have shown that the tripodal urea podand derivatized form tris(2-amino)ethylamine, **tren**, can bind $H_2PO_4^-$ selectively by hydrogen bonding.[17] Recently, polyaza crown ether derivatives of *p-tert*-butylcalix[4]arene have been synthesized in our lab. The ammonium derivatives were found to form complexes with CO_3^{2-}, NO_3^-, AsO_2^- and Cl^- in a different extent.[18] It is of interest to expand the cavity of our compounds to three dimension by combining the calix[4]arene framework with the cage constructing unit such as tris(2-amino)ethylamine, **tren**, to synthesize a compound that has great potential to bind metal ions and anions cooperatively. We report herein the synthesis of the tripodal-amine capped benzo crown *p-tert*-butylcalix[4]arenes, **5a** and **5b**. The complexation of **5a** and **5b** towards anions has been studied in the presence of various countercations in order to understand the role of cations towards anion binding ability.

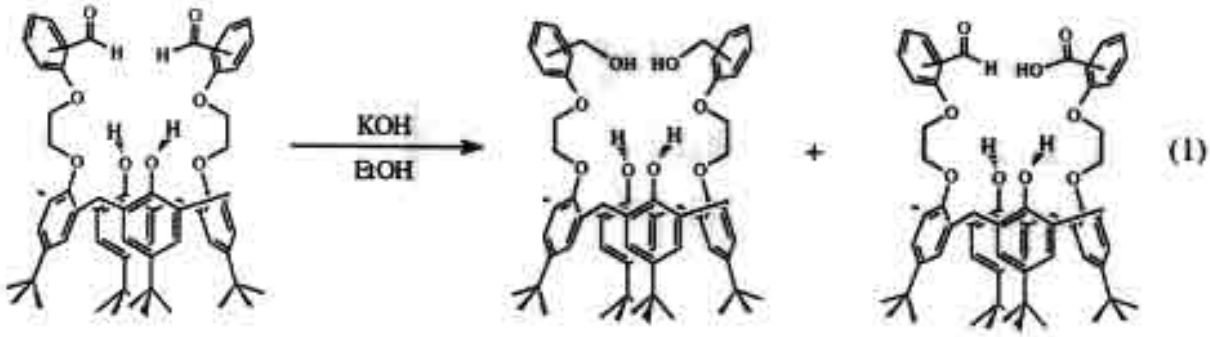
Results and Discussion

Design, synthesis and characterization. Our desired receptors must contain both cation and anion binding size. Ammonium groups and crown ether are well-known to bind anions via electrostatic interactions and cations via coordination bond, respectively. In this paper, we employ *p-tert*-butylcalix[4]arene as a supramolecular building block. Three ethoxy benzaldehyde groups have been attached to the calix[4]arene unit to form a crown ether-like cation ionophore. Subsequent reactions of trialdehyde calix[4]arene with tris(2-amino) ethylamine generated tripodal ammonium receptor unit for binding anions. Compounds **5a** and **5b** thus possess both metal ion and anion ionophores next to each other separating by a spacer such as benzene unit. Both **5a** and **5b** can thus possibly exhibit appealing host-guest chemistry with both metal ions and anions.

Scheme 1

The synthesis of compounds **5a** and **5b** was carried out as shown in Scheme 1. Substitution reactions of *p-tert*-butylcalix[4]arene with 3.0 equiv. of 2-(2′-bromoethoxy) benzaldehyde, **1a**, and 4-(2′-bromo ethoxy)benzaldehyde, **1b**, respectively, were carried out in the presence of a base to produce trialdehyde precursors, **3a** and **3b**, for preparing the tripodal amine capped calix[4]arene. The synthesis of **3a** was reported previously in

acetonitrile using K_2CO_3 as base.[19] This reaction gave only 6% yield of the desired trialdehyde derivative. Furthermore, substitution reactions using K_2CO_3 always gave the dialdehyde derivatives, **2a** and **2b**, in high yields.[20,21] Since then, a number of bases and solvents have been employed to optimize the yields of the desired products. However, it was found that reactions in the presence of strong bases such as KOH underwent Cannizzaro reactions and gave both alcohol and carboxylic acid derivatives instead (Eq. 1).[22] Finally, we found that reactions using BaO in DMF gave higher yields of trialdehyde calix[4]arenes, **3a** (21%) and **3b** (46%), than those of dialdehyde calix[4]arenes, **2a** (20%) and **2b** (2%). It should be noted that the yield of **3b** was twice as much as that of **3a** probably due to the less steric hindrance of the *para* isomer facilitating the substitution reaction. The ^{1}H-NMR spectrum of **3a** showed (C=O)*H* at 10.41 and 9.74 ppm and at 9.76 and 9.68 ppm for **3b** in 1:2 integral ratio. FAB MS and elemental analysis results of **3a** and **3b** were agreeable with the proposed structure.



(1)

Condensation reactions of **3a** and **3b** with 1.1 equivalents of *tris*(2-amino)ethylamine in a mixture of CH_3CN and CH_2Cl_2 (high dilution) precipitated imines or Schiff base products, **4a** (95%) and **4b** (97%). The signals due to (C=O)*H* proton disappeared, and the signals due to RN=C*H* protons showed at 8.83 and 8.93 ppm in the ^{1}H-NMR spectrum of **4a** and at 8.07 and 7.68 ppm for **4b**. FAB MS and elemental analysis results were pertinent to the proposed structures. Reduction of **4a** and **4b** by 20 equivalents of $NaBH_4$ in CH_2Cl_2 and subsequent protonation with HCl/CH_3OH (0.74% v/v) yielded ammonium derivatives, **5a** (86%) and **5b** (95%), which showed very broad signals in the ^{1}H-NMR spectrum due to the effect of positive charges. Signals due to $ArCH_2NH_2^+CH_2$- appeared at 9.78 and 9.39 ppm with an integral ratio of 2:1 for **5a** and at 8.71 and 8.23 ppm for **5b**. Although, mass spectra of **5a** and **5b** showed a strong signal at m/z 1192.1 corresponding to the molecular weight of the neutralized species. Nevertheless, elemental analysis result agreed with the proposed structures. It is interesting that the position of (C=O)*H*, RN=C*H* and $ArCH_2NH_2^+CH_2$- protons in **3a**-**5a** appear more downfield than those of **3b**-**5b** probably due to the effect of

magnetic anisotropy of the adjacent phenyl ring. Neutralization of **5a** and **5b** with NaOH in methanol provided the neutral tripodal-amine capped benzocrown calix[4]arene, **6a** (72%) and **6b** (80%). Spectroscopic and elemental analysis results of **6a** and **6b** agreed well with the proposed structures.

The solid state structure of compound **5a** was determined by X-ray crystallography (Figure 1). The structure was solvated by one molecule of CH_3OH and two molecules of H_2O. The phenyl rings of the calix[4]arene unit is in a pinched cone conformation. Interestingly, one of the ethoxy benzyl chains connecting to the **tren** unit threads through the cavity of the other two ethoxy benzyl chains. This structure resembles a self-threaded rotaxane derivatised from two homooxacalix[3]arenes.[23] Recently, Vicens and colleagues have also reported a similar structure of tripodal calix[4](azo)crowns.[24] Although suitable crystals of **5b** for X-ray analysis cannot be obtained, the ^{1}H NMR spectrum of **5b** suggests a more symmetrical orientation of the glycolic chains. Difference in structure and size of the cavity of 5a and 5b lead to the different in anion binding ability, *vide infra*.

Figure 1

Anion binding studies. Charge and geometry of anions were considered in our investigation. Therefore, we chose to investigate spherical anions (F^-, Br^- and I^-), trigonal planar anions (AsO_2^- and CO_3^{2-}) and tetrahedral anions ($H_2PO_4^-$, HPO_4^{2-}, SO_4^{2-} and PO_4^{3-}). ^{1}H NMR (200 MHz) titrations were employed in complexation studies of **5a** and **5b** towards anions. NMR titrations for **5a** were carried out in DMSO-d_6 due to the great solubility of **5a** and anion salts in that solvent. The compound **5b**, however, were not soluble in DMSO-d_6 but soluble in $CDCl_3$. Anion salts dissolved quite well in CD_3OD. The NMR titrations for **5b** were thus carried out in the mixture of $CDCl_3$ and CD_3OD.

Although excess NaF and Na_2SO_4 was added to solutions of **5a** and **5b**, no chemical shift displacement of any signals in NMR spectra was observed. The result shows that F^- and SO_4^{2-} cannot form complexes with **5a** and **5b**. This is probably due to the size of F^- and SO_4^{2-} which is not appropriate for the ligand cavity.

In case of anions such as AsO_2^-, CO_3^{2-}, PO_4^{3-}, HPO_4^{2-} and $H_2PO_4^-$ (using sodium salts), we observed interesting phenomena when complexation studies of ligand **5a** were performed. Upon increasing the mole ratio of anions, white solids precipitated from the mixture of **5a** and AsO_2^-, CO_3^{2-} and PO_4^{3-} . Therefore, NMR titrations cannot be completed with these anions and the association constants cannot be calculated. However, the solution

of **5a** and HPO_4^{2-} and $H_2PO_4^-$ did not precipitate white solids. Upon addition of HPO_4^{2-} and $H_2PO_4^-$ into the solution of **5a**, moderate upfield shifts of the signal $ArCH_2NH_2^+CH_2$- at δ 9.39 and 9.78 ppm were observed. Nevertheless, when the anion ratio increased the spectrum changed to the same as that of the neutral compound (**6a**) implying that the deprotonation of **5a** took place upon complexing HPO_4^{2-} and $H_2PO_4^-$. Association constants of the complexes of **5a** with HPO_4^{2-} and $H_2PO_4^-$ thus cannot be calculated.

The complexation studies of **5b** towards AsO_2^-, CO_3^{2-} and PO_4^{3-} were also carried out. It was found that complexation occurred along with the deprotonation to give the nuetral compound **6b**. Therefore, the association constants for these complexes cannot be calculated. Although addition of Na_2HPO_4 into ligand **5b** causes the displacement of the aromatic signal (at 6.5-8.0 ppm) of **5b**, Na_2HPO_4 cannot be completely dissolved into solution. The association constant of the complex of **5b** and HPO_4^{2-} cannot be determined correctly. Furthermore, upon addition of excess $NaH_2PO_4{\cdot}H_2O$ to a solution of **5b**, no chemical shift displacement in the NMR spectra was observed. The result shows that **5b** cannot form a complex with $H_2PO_4^-$.

Upon addition of NaBr, NaI and $NaNO_3$ to the solutions of **5a**, moderate upfield shifts of the signal $ArCH_2NH_2^+CH_2$- at δ 9.39 and 9.78 ppm and slightly shifts of aromatic regions at δ 7.00–8.00 ppm were observed in the ^{1}H-NMR spectra. This indicates that anions form complexes with **5a** in the cavity of the tripodally capped unit using the electrostatic interactions. Job's plots indicated that **5a** formed complexes with these anions in a 1:1 fashion. The association constants were obtained from the resulting titration curves using the program EQNMR[25] and the values are presented in Table 1.

Table 1

In case of **5b**, the signal of the $ArCH_2NH_2^+CH_2$- protons in ligand **5b** disappeared because the protons on ammonium position exchanged with CD_3OD. Nevertheless, the moderate downfield shift of protons on *para* position of $-CH_2ArH_a$ and $ROArH_b$ was monitored upon addition of various ratios of NaBr, NaI and $NaNO_3$. The interaction that occurred between host **5b** and guests such as Br^-, I^- and NO_3^- was electrostatic interaction and hydrogen bonding. Job's plots indicated that **5b** also formed complexes with anions in a 1:1 ratio. The association constants of the various anions calculated by the program EQNMR were shown in Table 1. It is found that using Na^+ as countercation **5a** and **5b** form

complexes with Br^-, I^- and NO_3^- and the stability of the complexes varies as $NO_3^- > I^- > Br^-$. This must stem from the fact that both electrostatic and hydrogen bonding interactions are presented in the case of NO_3^- while Br^- and I^- have only electrostatic interactions with **5a** and **5b**. It should also be noted that the interaction of **5a** towards NO_3^- is stronger than that of **5b**. The results indicate that **5b** possess a bigger cavity for anion binding.

We are also interested in the effects of metal ions towards anion binding. Upon addition of tetrabutylammonium and potassium salts of Br^- and I^- to **5a** moderate upfield shifts of the signal $ArCH_2NH_2^+CH_2$- at δ 9.39 and 9.78 ppm and to **5b** strongly downfield shifts of the signal -CH_2ArH_a and $ROArH_b$ at δ 7.38 and 6.93 ppm were observed in the ^{1}H-NMR spectra. The plot showing the relationship between chemical shifts of the signal due to -$OArHCH_2$- and concentrations of iodide anion in the presence of various countercations are depicted in Figure 2. Association constants of **5a** and **5b** towards Br^-, I^- and NO_3^- in the presence of various countercations such as Bu_4N^+ and K^+ calculated by the program EQNMR are collected in Table 1.

Figure 2

With Bu_4N^+ as countercation, **5a** and **5b** can form more stable complexes with I^-. However, the stability of **5b** towards I^- is higher than **5a**. This signifies that the cavity of **5b** is more suitable for binding a big anion such as I^-. In the presence of K^+, **5a** shows an increase in binding affinity towards Br^- by nearly 1.5 folds. On the other hand, Na^+ does not show any enhancement in anion binding ability of **5a**. The result suggests that the crown ether unit of **5a** prefers binding K^+ over Na^+. A similar crown ether cavity found in biscalix [4]arene in which two molecules of calix[4]arene linked by four glycolic units has been reported to bind K^+ selectively.[26] From the crystal structure of **5a**, it is also possible that an alkali metal ion can coordinate to the crown ether unit and induces the structural reorganization of **5a** to be more appropriate for binding anions (Scheme 2). Interestingly, the binding ability of **5b** towards Br^- and I^- decreases in the presence of Na^+ and K^+. The observation in which the presence of alkali metal ions decreases the anion binding ability of **5a** and **5b** can be rationalised in term of the binding competition. Alkali metal ions (Na^+ or K^+) that cannot fit into the cavity size of the crown ether unit in **5a** or **5b** retain alkali metal-anion pairs and compete in binding with the tripodal ammonium unit of the ligands.

Scheme 2

Conclusion

In summary, we have synthesised two tripodal aza crown ether calix[4]arenes, **5a** and **5b**. We have studied anion complexation of **5a** and **5b** with various anions such as F^-, Br^-, I^-, NO_3^-, SO_4^{2-}, CO_3^{2-}, PO_4^{3-}, AsO_2^-, HPO_4^{2-} and $H_2PO_4^-$ using Na^+ countercation. In case of basic anionic guests such as AsO_2^-, CO_3^{2-} and PO_4^{3-}, two phenomena have occurred. The first one is complexation and the second one is deprotonation. We, therefore, cannot calculate the stability constants of these complexes. This is the most crucial defect of anion hosts using ammonium receptors. However, the main advantage of using the electrostatic interaction for anions is the various choice of solvent can be chose, unlike the hydrogen bonding interaction which depended on the solvent employed. Our results also show the effect of K^+ ion towards anion binding of **5a** and **5b** and also demonstrate an example of metal ion controlled anion binding receptors.

Experimental Section

Analytical instruments. The ^{1}H-NMR spectra were recorded on a Bruker ACF 200 MHz nuclear magnetic resonance spectrometer and 400 MHz on a Bruker DRX 400 spectrometer. In all cases, samples were dissolved in deuterated chloroform or methyl sulfoxide, and chemical shifts were recorded using a residual proton signal as internal reference.

Elemental analyses were analyzed on a Perkin Elmer CHON/S analyzer (PE2400 series II). Mass spectra were determined using VG-Analytical ZAB HF Mass Spectrometer. The ESI-TOF mass spectra were obtained from a Micromass LCT Mass Spectrometer and the electrospray ion trap mass spectra were recorded on a Bruker Mass Spectrometer. Melting points were taken on an Electrothermal 9100 apparatus. The FT-IR spectra were recorded on a Nicolet Impact 410 FT-IR spectrophotometer.

Materials for synthesis. All materials and reagents were standard analytical grade, purchased from BDH, Fluka, J.T. Baker or Merck, and used without further purification. Commercial grade solvents such as acetone, dichloromethane, ethyl acetate, hexane and methanol were distilled and stored over 4 Å molecular sieves. DMF was dried according to

the published procedure and distilled before used.[27] Chromatographic separations were performed on silica gel column (kieselgel 60, 0.063-0.200 mm, Merck). Thin layer chromatography (TLC) was carried out using silica gel plates (kieselgel 60 F_{254}, 1 mm, Merck). 2-(2′-Bromoethoxy)benzaldehyde, **1a**,[28] 4-(2′-bromoethoxy)benzaldehyde, **1b**,[21] and *p-tert*-butylcalix[4]arene[29] were prepared according to the literature.

Preparation of 25,26,27-tri((2-ethoxy)benzaldehyde-*p-tert*-butylcalix[4]arene, 3a and 25,26,27-tri((4-ethoxy)benzaldehyde-*p-tert*-butylcalix[4]arene, 3b. Into a 250-mL two-necked round bottom flask equipped with a magnetic bar and a reflux condenser, a mixture of *p-tert*-butylcalix[4]arene (6.05 g, 9.34 mmol), barium oxide (5.20 g, 33.90 mmol) and dry DMF (150 mL) was stirred for 1 hour. Into this mixture, 2-(2′-bromoethoxy) benzaldehyde, **1a**, (6.56 g, 28.64 mmol) in DMF (50 mL) was then added dropwise through an addition funnel. The mixture was stirred and heated at 70 °C under nitrogen atmosphere for 7 days. The reaction was allowed to cool to room temperature, and the solvent was evaporated under reduced pressure to give an orange-brown residue. The residue was dissolved in dichloromethane and it was then added 3M hydrochloric acid until the pH of the solution reached 1. The organic phase was separated, and the aqueous layer was extracted again with dichloromethane. The combined organic layer was dried over sodium sulfate anhydrous. After filtration of sodium sulfate, the solvent was removed to give an oily orange-brown residue. The residue was redissolved in a minimum amount of dichloromethane. The orange-brown solution was eluted through a silica gel column with dichloromethane as eluent. The 25,26,27-tri((2-ethoxy)benzaldehyde-*p-tert*-butylcalix[4]arene, **3a**, eluted out of the column after 25,27-di((2-ethoxy)benzaldehyde-*p-tert*-butylcalix[4]arene, **2a**. White needle crystals of **3a** can be obtained by adding CH_3OH into its (CH_2Cl_2) solution (2.17 g, 21%).

In a similar manner to **3a**, the reaction between *p-tert*-butylcalix[4]arene (7.03 g, 10.83 mmol) and 4-2(2′-bromoethoxy)benzaldehyde (7.42 g, 32.63 mmol) in dry DMF (50 mL) resulted in compounds **2b** (0.20 g, 2%) and **3b** (5.53 g, 46%).

3a: ^{1}H-NMR spectrum (200 MHz, $CDCl_3$) δ (ppm) 10.41 and 9.74 (s each, 2H and 1H, -Ar(C=O)*H*); 7.63-6.32 (m, 20H, aromatic protons); 5.22 (s, 1H, ArO*H*); 4.90, 4.42 and 4.16 (m, 12H, -OCH_2CH_2O-); 4.24 and 3.29 (m, 4H each, ArCH_AH_BAr); 1.36-0.82 (m, 36H, -Ar-*t*-C_4H_9). FAB MS (m/z): 1092.5. *Anal. Cald.* for **4a** ($C_{77}H_{80}O_{10}$): C,77.99; H, 7.37. *Found*: C, 78.11; H, 7.17.

3b: ^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ (ppm) 9.76 and 9.68 (s each, 2H and 1H, -Ar(C=O)*H*), 7.57 and 7.43 (d each, $J_{H\text{-}H}$ = 8.7 Hz, 4H and 2H, -OArH_a), 7.19 (s, 2H, HOAr*H*), 7.14 (s, 2H, ROAr*H*), 6.70 and 6.63 (d each, $J_{H\text{-}H}$ = 8.7 Hz, 4H and 2H, -OArH_b), 6.54 (s, 4H, ROAr*H*), 5.40 (s, 1H, *H*OAr), 4.86 (m, 2H, OCH_2CH$_2$O), 4.45 and 3.32 (d each, $J_{H\text{-}H}$ = 12.4 Hz, 4H each, ArC$H_A H_B$Ar), 4.28 (m, 2H, OCH$_2$CH_2O), 4.13 (s ,8H, OCH_2CH_2O), 1.36 (s, 18H, HOAr-*t*-C$_4H_9$ and ROAr-*t*-C$_4$H$_9$), 0.82 (s, 18H, ROAr-*t*-C$_4H_9$). MALDI-TOF MS (m/z): 1093.6. *Anal. Cald.* for **3b** ($C_{77}H_{80}O_{10}$): C,77.99; H, 7.37. *Found*: C, 77.91; H, 7.52.

Preparation of 25,26,27-*N,N′,N″*-tri-((2-ethoxy)benzyl)ethylenetriimine-*p*-*tert*-butylcalix[4]arene, 4a, and 25,26,27-*N,N′,N″*-tri-((4-ethoxy)benzyl)ethylenetriimine-*p*-*tert*-butylcalix[4]arene, 4b. Into a 500-mL two-necked round bottom flask equipped with a magnetic bar and a reflux condenser, a mixture of **3a**, (1.00 g, 0.92 mmol) and acetonitrile (250 mL) was stirred. tris(2-amino)ethylamine (0.16 g, 1.10 mmol) in dichloromethane (10 mL) and acetronitrile (50 mL) was then added dropwise through an addition funnel over 30 minutes. The mixture was refluxed under nitrogen atmosphere for 8 hours. White solid precipitated from the solution. The mixture was allowed to cool to room temperature and filtered. The white solid residual of **4a** was washed with acetronitrile and dried *in vacuo* (1.03 g, 95 %).

Compound **4b** was synthesized from the reaction between **3b** (3.05 g, 2.79 mmol) and tris(2-aminoethyl)amine (0.50 g, 3.43 mol) in acetonitrile (250 mL). (3.23 g, 97%)

4a: ^{1}H-NMR spectrum (200 MHz, $CDCl_3$) δ (ppm) 8.93 and 8.83 (s each, 1H and 2H, -C*H*=N-); 7.91-6.45 (m, 20H, aromatic protons); 5.30 (s, 1H, -ArO*H*); 5.16, 4.53 and 4.04 (m, 12H, -OCH_2CH_2O); 2.89 (m, 12H, -NCH_2CH_2N-); 4.39 and 4.33, 3.39 and 3.32 (d each, 2H each, $J_{H\text{-}H}$ = 13 Hz, ArC$H_A H_B$Ar); 1.36, 1.27 and 0.79 (s each, 9H, 9H and 18H, ROAr-*t*-C$_4H_9$ and HOAr-*t*-C$_4H_9$). FAB MS (m/z): 1185.7 *Anal. Cald.* for **4a**·H_2O ($C_{77}H_{94}N_4O_8$): C, 76.84; H, 7.87; N, 4.65. *Found*: C, 76.70; H, 7.61; N, 4.24.

4b: ^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ (ppm) 8.07 and 7.86 (s each, 1H and 2H, -C*H*=N), 7.38 (d, $J_{H\text{-}H}$ = 8.7 Hz , 4H, -OArH_a), 7.20 (s, 2H, HOAr*H*), 7.18 (s, 2H, ROAr*H*), 6.73 (d, $J_{H\text{-}H}$ = 8.7 Hz, 4H, -OArH_b), 6.62 (d, $J_{H\text{-}H}$ = 2.4 Hz, 2H, ROArH_a), 6.52 (d, $J_{H\text{-}H}$ = 2.4 Hz, 2H, ROArH_b), 6.32 (s, 1H, *H*OAr), 6.13 (d, $J_{H\text{-}H}$ = 8.8 Hz, 2H, ROAr*H*), 6.02 (d, $J_{H\text{-}H}$ = 8.8 Hz, 2H,ROAr*H*), 4.92 and 3.32 (d each, $J_{H\text{-}H}$ = 13.0 Hz, 4H, ArC$H_A H_B$Ar), 4.56 (m, 2H, OCH_2CH$_2$O), 4.33 and 3.23 (d each, $J_{H\text{-}H}$ = 13.0 Hz, 4H, ArC$H_A H_B$Ar), 4.28-4.02 (m, 10H, OCH_2CH_2O), 3.74 (m, 4H, CH=NCH_2CH$_2$N), 3.64 (m, 2H, CH=N CH_2CH$_2$N), 2.83 (m, 4H,

CH=NCH$_2$C*H*$_2$N), 2.59 (m, 2H, CH=NCH$_2$ C*H*$_2$N), 1.39 (s, 9H, HOAr-*t*-C$_4$*H*$_9$), 1.36 (s, 9H, ROAr-*t*-C$_4$*H*$_9$), 0.83 (s, 18H, ROAr-*t*-C$_4$*H*$_9$). MALDI-TOF MS (m/z): 1184.6 *Anal. Cald.* for **4b** ($C_{77}H_{92}N_4O_7$): C, 78.01; H, 7.82; N, 4.73. *Found*: C, 77.95; H, 7.66; N, 4.77.

Preparation of 25,26,27-*N,N′,N″*-tri((2-ethoxy)benzyl)ethylenetetraamine-*p*-*tert*-butylcalix[4]arene·4HCl, 5a and 25,26,27-*N,N′,N″*-tri((4-ethoxy)benzyl) ethylenetetraamine-*p*-*tert*-butylcalix[4]arene·4HCl, 5b. Into a 500-mL one-necked round bottom flask equipped with a magnetic bar and a reflux condenser, **4a** (1.00 g, 0.84 mmol) was dissolved in dry dichloromethane (50 mL). The solution was added excess sodium borohydride (0.63 g, 0.02 mmol) and stirred overnight under nitrogen atmosphere. A copious amount of deionized water was then added to destroy excess sodium borohydride. The organic phase was separated and washed again with deionized water until the pH of the aqueous layer became neutral. The combined organic layer was dried over sodium sulfate anhydrous. After filtration of sodium sulfate, the solvent was removed to dryness. The solid residue was dissolved in a minimum amount of methanol and acidified with 0.74% V/V hydrochloric acid in methanol until the pH of the solution reach 1. Upon slow evaporation of the solvent, the white crystals of **5a** were precipitated (0.92 g, 81 %).

In a similar fashion, the reaction between **4b** (1.52 g, 1.283 mmol) and $NaBH_4$ (0.92 g, 24.35 mmol) in dry CH_2Cl_2 (300 mL) yielded **5b.** (1.44 g, 84%)

5a: ^{1}H-NMR spectrum (DMSO-d_6) δ (ppm) = 9.78 and 9.38 (s each, broad, 4H and 2H, ArCH$_2$N*H*$_2^+$Cl$^-$); 7.86, 7.66, 7.57, 7.34 and 7.03 (m, 12H, H_a, H_b, H_c and H_d); 7.17 and 7.11 (s each, 2H each, ROAr*H* and HOAr*H*); 6.54 and 6.46 (s each, 2H each, ROAr*H*); 5.80 (s, 1H, ArO*H*); 5.13 (m, broad, 2H, OC*H*$_2$C*H*$_2$O); 4.62-4.39 (m, 6H, H$_2$N$^+$C*H*$_2$-Ar and 4H, ArC*H*$_2$Ar); 4.18 (m, broad, 10H, OC*H*$_2$C*H*$_2$O and 4H, ArC*H*$_2$Ar); 2.82-2.75 (m, 12H, $^+$NHC*H*$_2$C*H*$_2$N$^+$H$_2$); 1.30, 1.20 and 0.73 (s each, 9H, 9H and 18H, HOAr-*t*-C$_4$*H*$_9$ and ROAr-*t*-C$_4$*H*$_9$). ESI-TOF MS (m/z): 1192.1 *Anal. Cald.* for **5a**·4H$_2$O ($C_{77}H_{110}N_4O_{11}Cl_4$): C, 65.69; H, 8.44; N, 3.78. *Found*: C, 65.61; H, 7.87; N, 3.97.

5b: ^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ 8.71 and 8.23 (s each, broad, 4H and 2H, ArCH$_2$N*H*$_2^+$Cl$^-$), 7.79 (d, $J_{H\text{-}H}$ = 8.6 Hz, 4H, -OArH_a), 7.36 (d, $J_{H\text{-}H}$ = 8.5 Hz, 2H, -OArH_a), 7.14 (s, 2H, HOAr*H*), 7.10 (s, 2H, ROAr*H*), 6.92 (d, $J_{H\text{-}H}$ = 8.7 Hz, 4H, -OArH_b), 6.54 (m, 6H, ROAr*H* and -OArH_b), 6.12 (s, 1H, HOAr), 4.56 and 3.30 (d each, $J_{H\text{-}H}$ = 13.3 Hz, 4H, ArCH_AH_BAr), 4.55-4.40 (m, 14H, OC*H*$_2$C*H*$_2$O, ArC*H*$_2$N and ArCH_AH_BAr), 4.20-3.98 (m, 6H, OC*H*$_2$C*H*$_2$O, ArC*H*$_2$N), 3.70 (s, br, 2H, NCH$_2$C*H*$_2$N), 3.41-3.10 (m, 10H, NC*H*$_2$C*H*$_2$N), 3.25 (d, $J_{H\text{-}H}$ = 13.0 Hz, 2H, ArCH_AH_BAr), 1.34 (s, 9H, HOAr-*t*-C$_4$H$_9$), 1.32 (s, 9H, ROAr-*t*-

C_4H_9), 0.82 (s, 18H, ROAr-*t*-C_4H_9). MALDI-TOF MS (m/z): 1191.8 *Anal. Cald.* for **5b** ($C_{77}H_{102}N_4O_7Cl_4$): C, 69.15; H, 7.69; N, 4.19. *Found*: C, 69.19; H, 7.76; N, 4.16.

Preparation of 25,26,27-*N,N',N''*-tri((2-ethoxy)benzyl)ethylenetetraamine-*p*-*tert*-butylcalix[4]arene, 6a and 25,26,27-*N,N',N''*-tri((4-ethoxy)benzyl)ethylenetetraamine-*p*-*tert*-butylcalix[4]arene, 6b. Into a 50-mL round bottom flask equipped with a magnetic bar, 25,26,27-*N,N',N''*-tri-((2-ethoxy)benzyl)ethylenetetraamine-*p*-*tert*-butylcalix[4]arene·4HCl, **6a**, (0.10 g, 0.07 mmol) was dissolved in dry methanol (30 mL). NaOH solution (CH_3OH) was then slowly added until the pH of the solution reached 10. The reaction was stirred under nitrogen atmosphere for 1 hour. The solvent was subsequently removed under reduced pressure. The residue was redissolved in dichloromethane and extracted with deionized water until the aqueous phase contained no Cl^-. The organic layer was then dried over sodium sulfate anhydrous and concentrated on a rotary evaporator. Upon slow evaporation of the solvent, the white solid of **6a** precipitated (0.06 g, 72 %).

6a: ^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ(ppm) 7.20 and 6.56 (s each, 4H, *t*-C(CH_3)$_3$Ar*H*CH_2-); 7.47, 7.15, 6.93 and 6.25 (m, 12 H, -OAr*H*OCH_2-); 5.19 (s, 1H, -ArO*H*); 4.98,4.32, 4.03 and 3.86 (m, 12H, -OCH_2CH_2O-); 4.18 and 3.75 (d, 2H and 4H, $J_{H\text{-}H}$ = 14 Hz, ArCH_2NR); 7.34 (t, 3H, H_c aromatic); 4.85, 4.45, 3.37 and 3.23 (d, 2H each, $J_{H\text{-}H}$ = 13 Hz, ArCH_ACH_BAr); 2.66-1.99 (m, broad, 12H, RNCH_2CH_2NR); 1.41, 1.39 and 0.86 (s each, 9H, 9H and 18H, HOAr-*t*-C_4H_9 and ROAr-t-C_4H_9). FAB MS (m/z): 1191.7 *Anal. Cald.* for **6a** ($C_{77}H_{98}N_4O_7$): C, 77.61; H, 8.29; N, 4.70. *Found*: C, 77.57; H, 7.85; N, 4.32.

6b: ^{1}H-NMR spectrum (200 MHz, $CDCl_3$) δ(ppm) 7.18, 7.07, 7.05 and 7.01 (s each, 8H, *t*-C(CH_3)$_3$Ar*H*CH_2-); 6.70-6.30 (m, 12 H, -OAr*H*OCH_2-); 5.39 (s, 1H, -ArO*H*); 4.85-4.60 (m, 6H, -OCH_2CH_2O-, ArCH_AH_BAr); 3.27 (m, 2H, ArCH_AH_BAr); 3.74-3.45 (m, 6H, -OArCH_2N-); 2.86, 2.67, 1.92 (m, broad, 12H, RNCH_2CH_2NR); 1.32 and 0.83 (s each, 18H and 18H, HOAr-*t*-C_4H_9 and ROAr-t-C_4H_9). FAB MS (m/z): 1191.7 *Anal. Cald.* for **6b** ($C_{77}H_{98}N_4O_7$): C, 77.61; H, 8.29; N, 4.70. *Found*: C, 77.57; H, 7.85; N, 4.32.

X-ray crystallography. The crystal of **5a** (0.20 x 0.20 x 0.10 mm^3) was mounted on the end of a hollow glass fiber approximately parallel to the long dimension of the crystal using cyanoacrylate glue. Preliminary examination and data collection were performed using MoK_α X-radiation (λ = 0.71073 Å) on Bruker AXS SMART area detector diffractrometer. The collected data were reduced using the program SAINT.[30] Empirical absorption correction was done by the program SADABS.[31] A total of 58283 reflections were measured within the θ range of 0.99-30.46°. The structure was solved by direct methods and refined

with anisotropic thermal parameters for all non-hydrogen atoms by full matrix least square using SHELX-97 package.[32] All hydrogen atoms were found in different Fourier maps and were included in the refinement. Due to vibrational disorder of the solvent of crystallization, refinement converged with rather high *R* and *wR* values (0.1355 and 0.402, respectively).[33]

^{1}H NMR titrations. Complexation of **5a** and **5b** towards various anions such as arsenite, bromide, carbonate, fluoride, hydrogen phosphate, dihydrogen phosphate, iodide, nitrate, sulfate and phosphate were studied employing ^{1}H NMR titrations. For **5a**, typically, a 0.0250 M solution of ligand **5a** (0.0836 g, 0.0625 mmol) in DMSO-d_6 (2.50 mL) was prepared. To 0.20 mL of this solution in NMR tubes were added 0.0-4.0 equivalents of 0.1000 M sodium salts (0.1500 mmol) in DMSO-d_6 (1.50 mL). In each NMR tube, the amount of DMSO-d_6 was then adjusted to the same quantity. For **5b**, typically, a 0.1000 M solution of a sodium salt (0.1500 mmol) in CD_3OD (1.50 mL) was prepared. Ligand **5b** was brought into the NMR tubes and 0.0-4.0 equivalents of 0.1000 M sodium salt were added. In each NMR tube, the amount of the solvents was adjusted to the same quantity. The spectra were recorded every 24 hours until the complexation reached the equilibrium. Job's plots between the complex concentration and the mole fraction of ligands and anions (Br^-, I^- and NO_3^-) indicated 1:1 ligand:anion complexes. The result of the experiment was a plot of displacement in chemical shift as a function of the amount of added anion, which was subjected to analysis by a non-linear curve-fitting method using the program EQNMR.[25] Titration experiments were repeated at least twice for each anion.

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33. Crystal data for **5a**, $C_{77}H_{102}N_4O_7Cl_2(OH)_2 \cdot (CH_3OH)(H_2O)_2$, M = 1368.7, monoclinic, space group *C2/c*, *Z* = 8, *a* = 43.6552 (14), *b* = 15.9085 (5), *c* = 25.1856 (7) Å, β = 109.4630 (10)°, *V* = 16491.6 (9) Å^3, *Dc* = 1.119 g cm^{3-}, 23606 unique data, *R1* = 0.1355, *wR2* = 0.3402.

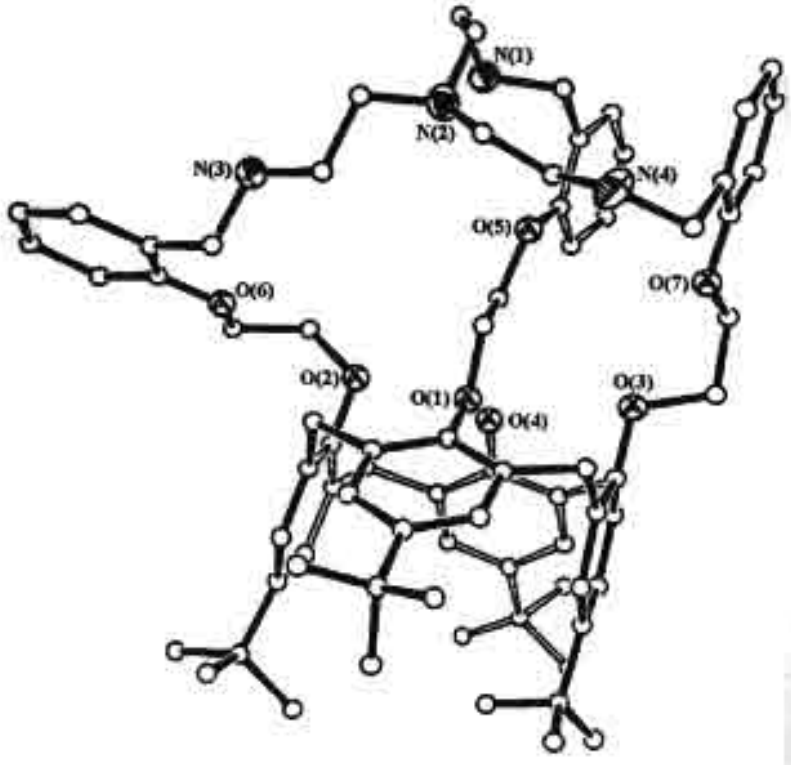


Figure 1. Crystal structure of **5a**. Hydrogen atoms were omitted for clarity.

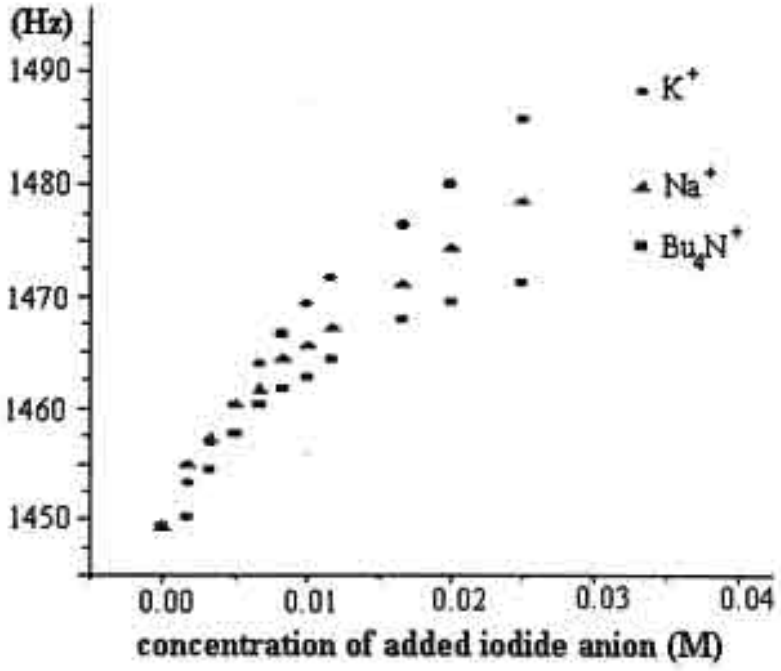
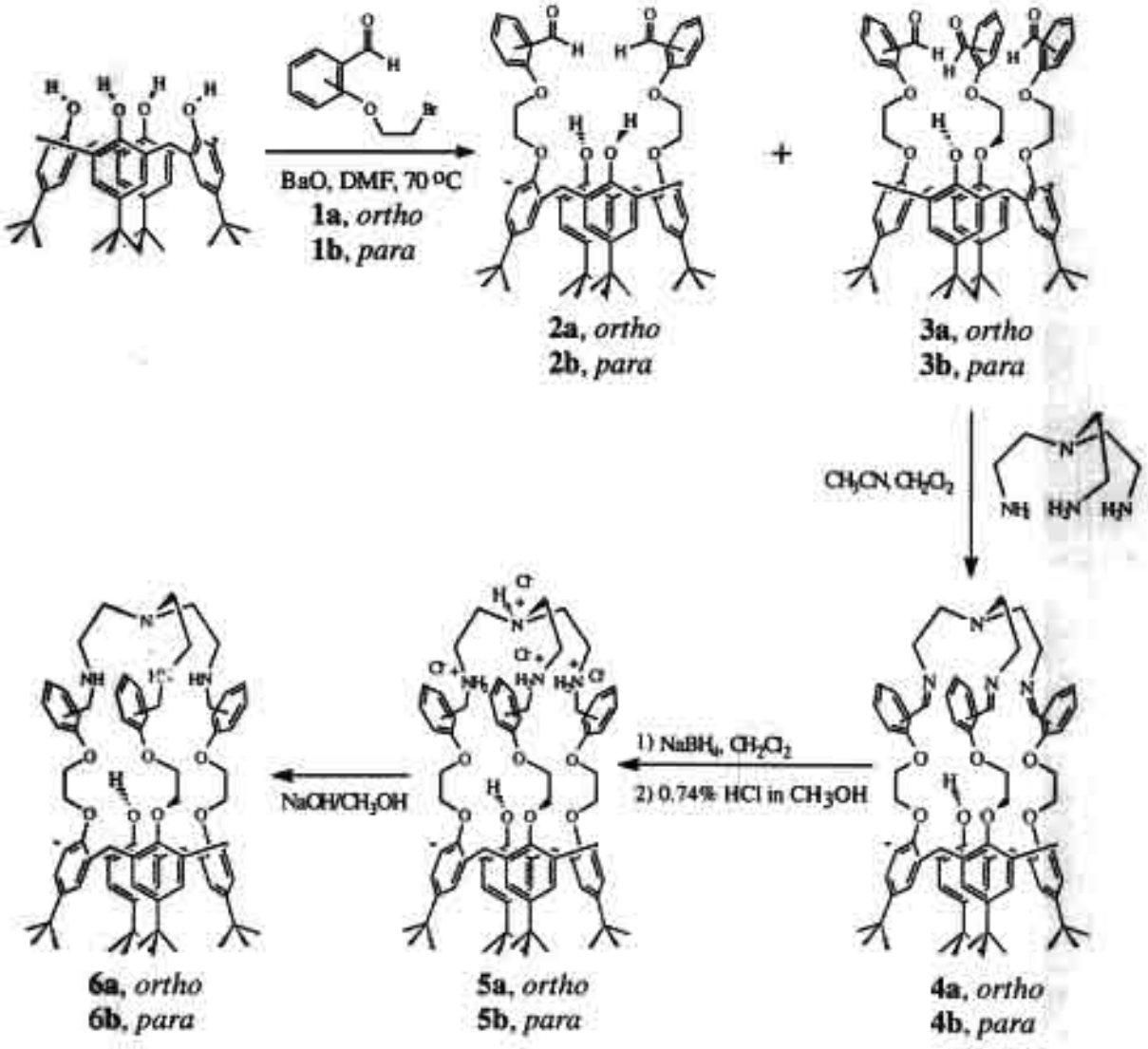


Figure 2. Titration curves of **5b** with I^- in the presence of Bu_4N^+, Na^+ and K^+.

Scheme 1. Synthetic procedure of compounds **5a** and **5b**.



Scheme 2. A metal ion can possibly induce the structural reformation of **5a** to bind an anion more efficiently.

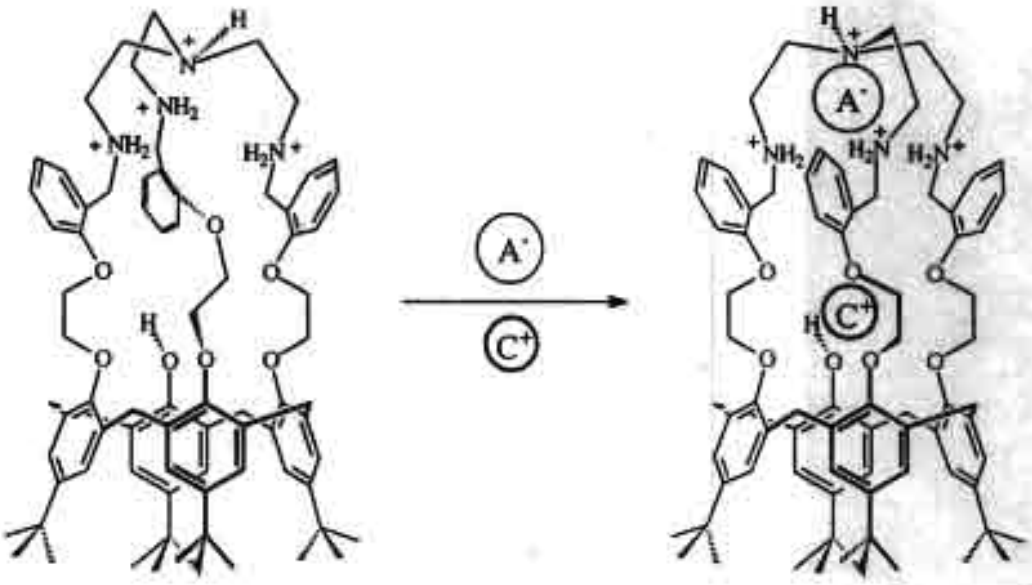


Table 1. Summary of association constants of ligands **5a** and **5b** towards various anions.[a]

Metal	Anion	K_{assoc} (M^{-1})	
		5a	**5b**
None[b]	Br^-	84.2	76.5
Na^+	Br^-	58.6	53.0
K^+	Br^-	120.1	34.9
None[b]	I^-	108.9	137.9
Na^+	I^-	77.2	57.3
K^+	I^-	103.3	66.3
Na^+	NO_3^-	190.2	106.3

[a]all experiments were carried out at 298 K; errors estimated to be less than 15%. [b]Using Bu_4N^+ as countercation.

ภาคผนวก ข

ข้อมูลและรายละเอียดทางคริสตัลโลกราฟฟีของสาร 5a

Supporting Data

for

Aza crown ether calix[4]arenes containing cation and anion binding sites: effects of metal ions towards anion binding ability

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Total of 14 pages.

Table 1S. Crystal data and structure refinement for **5a**.

Empirical formula	$C_{78}H_{112}Cl_2N_4O_{12}$
Formula weight	1368.67
Temperature	293(2) K
Wavelength	0.71073 A
Crystal system	monoclinic, C2/c
Unit cell dimensions	a = 43.6552(14) Å
	b = 15.9085(5) Å
	c = 25.1856(7) Å
	β = 109.4630(10) °
Volume	16491.6(9) A^3
Z, Calculated density	8, 1.119 g/cm^3
Absorption coefficient	0.136 mm^{-1}
F(000)	5976
Crystal size	0.40 x 0.40 x 0.40 mm
Theta range for data collection	0.99 to 30.46 °
Limiting indices	-56<=h<=60, -22<=k<=12, -34<=l<=31
Reflections collected / unique	58283 / 23606 [R(int) = 0.0954]
Completeness to theta = 30.46	94.2 %
Max. and min. transmission	0.9474 and 0.9474
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	23606 / 615 / 883
Goodness-of-fit on F^2	1.061
Final R indices [$I > 2\sigma(I)$]	R1 = 0.1355, wR2 = 0.3402
R indices (all data)	R1 = 0.3078, wR2 = 0.4380
Extinction coefficient	0.00088(15)
Largest diff. peak and hole	1.134 and -0.476 e.A^{-3}

Table 2S. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for **5a**.

	x	y	z	U(eq)
Cl(1)	152(1)	1141(1)	4840(1)	72(1)
Cl(2)	-526(1)	2677(3)	2698(2)	191(2)
O(1)	1370(1)	1961(2)	5308(1)	44(1)
O(2)	934(1)	2450(2)	6015(1)	48(1)
O(1W)	1167(2)	1580(6)	2821(5)	197(7)
O(3)	1854(1)	458(2)	5750(1)	52(1)
O(2W)	1049(5)	2489(17)	3532(6)	540(30)
O(4)	1472(1)	1417(2)	6602(1)	62(1)
O(3W)	-207(2)	2785(6)	6618(4)	152(5)
O(5)	929(1)	14(2)	5106(1)	60(1)
O(4W)	402(3)	2454(12)	7428(4)	281(9)
O(6)	305(1)	3233(2)	5249(1)	56(1)
O(7)	1619(1)	-770(2)	4827(2)	74(1)
O(8)	748(2)	-842(3)	2176(2)	76(2)
N(1)	271(1)	-671(3)	4448(2)	58(1)
N(2)	325(1)	420(3)	3527(2)	63(1)
N(3)	19(1)	2404(3)	3869(2)	61(1)
N(4)	1106(1)	-49(4)	3293(2)	80(2)
C(1)	1311(1)	4484(3)	5955(2)	49(1)
C(2)	1439(1)	4713(3)	6525(2)	57(1)
C(3)	1413(1)	4136(3)	6911(2)	55(1)
C(4)	1253(1)	3354(3)	6768(2)	47(1)
C(5)	1257(1)	2728(3)	7221(2)	54(1)
C(6)	1570(1)	2240(3)	7461(2)	46(1)
C(7)	1777(1)	2373(3)	8007(2)	46(1)
C(8)	2066(1)	1937(3)	8250(2)	49(1)

Table 2S. (continued) Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for **5a**.

	x	y	z	U(eq)
C(9)	2148(1)	1349(3)	7906(2)	50(1)
C(10)	1955(1)	1195(3)	7350(2)	47(1)
C(11)	2071(1)	654(3)	6968(2)	53(1)
C(12)	2182(1)	1221(3)	6571(2)	45(1)
C(13)	2387(1)	1889(3)	6787(2)	54(1)
C(14)	2469(1)	2483(3)	6455(2)	52(1)
C(15)	2331(1)	2396(3)	5885(2)	51(1)
C(16)	2122(1)	1727(3)	5636(2)	48(1)
C(17)	1944(1)	1718(3)	5003(2)	52(1)
C(18)	1732(1)	2488(3)	4832(2)	45(1)
C(19)	1825(1)	3155(3)	4563(2)	51(1)
C(20)	1658(1)	3919(3)	4458(2)	57(1)
C(21)	1391(1)	4002(3)	4643(2)	49(1)
C(22)	1291(1)	3353(3)	4921(2)	42(1)
C(23)	1018(1)	3508(3)	5158(2)	46(1)
C(24)	1146(1)	3727(3)	5785(2)	41(1)
C(25)	1458(1)	2603(3)	5000(2)	40(1)
C(26)	1106(1)	3195(3)	6191(2)	38(1)
C(27)	1663(1)	1624(3)	7138(2)	46(1)
C(28)	2059(1)	1128(3)	5990(2)	44(1)
C(29)	1778(2)	4645(4)	4184(3)	80(2)
C(30)	2006(6)	5133(14)	4657(7)	430(30)
C(31)	1962(4)	4402(7)	3831(7)	211(11)
C(32)	1513(3)	5190(7)	3860(6)	210(10)
C(33)	1586(2)	5594(4)	6699(3)	77(2)
C(34)	1937(2)	5485(6)	7114(5)	103(5)

Table 2S. (continued) Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for **5a**.

	x	y	z	U(eq)
C(35)	1572(2)	6137(5)	6208(4)	125(5)
C(36)	1380(2)	6048(5)	7023(4)	80(4)
C(37)	2293(1)	2089(4)	8850(2)	61(2)
C(38)	2629(2)	2087(9)	8905(4)	219(11)
C(39)	2182(5)	2717(12)	9128(5)	390(20)
C(40)	2315(3)	1250(7)	9198(4)	153(9)
C(41)	2917(5)	3077(10)	7267(8)	350(20)
C(42)	2782(6)	3731(12)	6372(6)	380(20)
C(43)	2480(5)	3818(11)	6897(12)	370(30)
C(44)	2675(2)	3245(4)	6720(3)	70(2)
C(45)	1159(1)	1328(3)	4982(2)	54(1)
C(46)	1083(1)	763(3)	5392(2)	57(1)
C(47)	915(1)	-651(3)	5449(2)	65(2)
C(48)	1066(2)	-682(5)	6026(3)	111(3)
C(49)	1048(3)	-1418(6)	6315(4)	158(5)
C(50)	865(2)	-2067(5)	6062(4)	140(4)
C(51)	707(2)	-2033(4)	5500(3)	85(2)
C(52)	727(1)	-1325(3)	5182(2)	63(2)
C(53)	536(1)	-1295(3)	4555(2)	63(2)
C(54)	25(2)	-688(4)	3859(2)	72(2)
C(55)	170(2)	-411(4)	3413(2)	73(2)
C(56)	84(1)	1093(4)	3384(2)	66(2)
C(57)	234(2)	1935(4)	3626(2)	68(2)
C(58)	154(1)	3247(4)	4086(2)	64(2)
C(59)	-52(1)	3668(3)	4377(3)	56(1)
C(60)	-340(2)	4088(4)	4061(3)	77(2)

Table 2S. (continued) Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for **5a**.

	x	y	z	U(eq)
C(61)	-537(2)	4460(4)	4305(4)	90(2)
C(62)	-456(2)	4451(4)	4879(4)	85(2)
C(63)	-167(1)	4060(3)	5224(3)	70(2)
C(64)	28(1)	3647(3)	4960(2)	53(1)
C(65)	389(1)	3140(4)	5843(2)	59(1)
C(66)	608(1)	2401(3)	6057(2)	58(1)
C(67)	567(2)	508(4)	3247(2)	69(2)
C(68)	881(2)	122(4)	3606(2)	77(2)
C(69)	1417(2)	-504(5)	3659(3)	93(2)
C(70)	1335(2)	-1296(5)	3920(3)	77(2)
C(71)	1152(2)	-1920(6)	3586(3)	97(2)
C(72)	1073(2)	-2618(6)	3791(4)	112(3)
C(73)	1165(2)	-2748(5)	4397(4)	110(3)
C(74)	1351(2)	-2127(4)	4744(3)	82(2)
C(75)	1439(1)	-1407(4)	4513(3)	71(2)
C(76)	1787(2)	-947(4)	5414(3)	80(2)
C(77)	2026(2)	-265(3)	5657(3)	75(2)
C(78)	684(4)	-1050(11)	2314(6)	450(30)

U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Table 3S. Bond lengths [Å] for **5a**.

Atoms	Bond lengths (Å)	Atoms	Bond lengths (Å)
O(1)-C(25)	1.411(5)	C(5)-C(6)	1.514(7)
O(1)-C(45)	1.426(5)	C(6)-C(7)	1.385(6)
O(2)-C(26)	1.394(5)	C(6)-C(27)	1.416(7)
O(2)-C(66)	1.462(6)	C(7)-C(8)	1.391(7)
O(3)-C(28)	1.394(6)	C(8)-C(9)	1.398(7)
O(3)-C(77)	1.437(6)	C(8)-C(37)	1.525(7)
O(4)-C(27)	1.369(5)	C(9)-C(10)	1.394(6)
O(5)-C(47)	1.378(6)	C(10)-C(27)	1.389(7)
O(5)-C(46)	1.437(6)	C(10)-C(11)	1.500(7)
O(6)-C(64)	1.357(6)	C(11)-C(12)	1.537(7)
O(6)-C(65)	1.423(6)	C(12)-C(13)	1.379(7)
O(7)-C(75)	1.362(7)	C(12)-C(28)	1.389(6)
O(7)-C(76)	1.441(7)	C(13)-C(14)	1.387(7)
N(1)-C(53)	1.480(7)	C(14)-C(15)	1.367(7)
N(1)-C(54)	1.513(7)	C(14)-C(44)	1.524(8)
N(2)-C(67)	1.459(7)	C(15)-C(16)	1.407(7)
N(2)-C(56)	1.461(7)	C(16)-C(28)	1.394(7)
N(2)-C(55)	1.470(8)	C(16)-C(17)	1.523(6)
N(3)-C(57)	1.483(7)	C(17)-C(18)	1.508(7)
N(3)-C(58)	1.492(7)	C(18)-C(19)	1.389(7)
N(4)-C(68)	1.472(7)	C(18)-C(25)	1.408(7)
N(4)-C(69)	1.545(8)	C(19)-C(20)	1.397(7)
C(1)-C(24)	1.397(6)	C(20)-C(21)	1.398(7)
C(1)-C(2)	1.403(7)	C(20)-C(29)	1.526(8)
C(2)-C(3)	1.369(7)	C(21)-C(22)	1.396(6)
C(2)-C(33)	1.543(8)	C(22)-C(25)	1.379(6)
C(3)-C(4)	1.414(7)	C(22)-C(23)	1.521(7)
C(4)-C(5)	1.509(7)	C(23)-C(24)	1.529(6)

Table 3S. (continued) Bond lengths [Å] for **5a**.

Atoms	Bond lengths (Å)	Atoms	Bond lengths (Å)
C(4)-C(26)	1.404(6)	C(52)-C(53)	1.519(8)
C(24)-C(26)	1.382(6)	C(54)-C(55)	1.525(8)
C(29)-C(31)	1.435(12)	C(56)-C(57)	1.526(8)
C(29)-C(32)	1.459(11)	C(58)-C(59)	1.495(8)
C(29)-C(30)	1.492(16)	C(59)-C(64)	1.391(8)
C(33)-C(35)	1.494(10)	C(59)-C(60)	1.409(7)
C(33)-C(34)	1.548(10)	C(60)-C(61)	1.351(10)
C(33)-C(36)	1.578(10)	C(61)-C(62)	1.369(10)
C(37)-C(39)	1.394(13)	C(62)-C(63)	1.416(9)
C(37)-C(38)	1.429(11)	C(63)-C(64)	1.406(8)
C(37)-C(40)	1.582(11)	C(65)-C(66)	1.500(7)
C(41)-C(44)	1.454(15)	C(67)-C(68)	1.498(8)
C(42)-C(44)	1.363(14)	C(69)-C(70)	1.519(10)
C(43)-C(44)	1.420(15)	C(71)-C(72)	1.317(12)
C(45)-C(46)	1.489(7)	C(71)-C(70)	1.372(10)
C(47)-C(52)	1.382(7)	C(72)-C(73)	1.458(12)
C(47)-C(48)	1.382(8)	C(73)-C(74)	1.389(10)
C(48)-C(49)	1.395(10)	C(74)-C(75)	1.395(10)
C(49)-C(50)	1.330(11)	C(75)-C(70)	1.421(9)
C(50)-C(51)	1.354(11)	C(76)-C(77)	1.490(8)
C(51)-C(52)	1.401(8)		

Table 4S. Bond angles [deg] for **5a**.

Atoms	Angles [deg]	Atoms	Angles [deg]
C(25)-O(1)-C(45)	115.9(3)	C(22)-C(23)-C(24)	112.2(4)
C(26)-O(2)-C(66)	117.1(4)	C(26)-C(24)-C(1)	118.7(4)
C(28)-O(3)-C(77)	112.9(4)	C(26)-C(24)-C(23)	122.1(4)
C(47)-O(5)-C(46)	115.7(4)	C(1)-C(24)-C(23)	119.2(4)
C(64)-O(6)-C(65)	119.1(4)	C(22)-C(25)-C(18)	122.1(4)
C(75)-O(7)-C(76)	116.6(5)	C(22)-C(25)-O(1)	118.6(4)
C(53)-N(1)-C(54)	115.0(4)	C(18)-C(25)-O(1)	119.1(4)
C(67)-N(2)-C(56)	112.9(5)	C(24)-C(26)-O(2)	118.3(4)
C(67)-N(2)-C(55)	110.7(4)	C(24)-C(26)-C(4)	122.0(4)
C(56)-N(2)-C(55)	111.3(5)	O(2)-C(26)-C(4)	119.6(4)
C(57)-N(3)-C(58)	112.2(5)	O(4)-C(27)-C(10)	116.1(4)
C(68)-N(4)-C(69)	112.3(5)	O(4)-C(27)-C(6)	122.6(4)
C(24)-C(1)-C(2)	121.8(5)	C(10)-C(27)-C(6)	121.4(4)
C(3)-C(2)-C(1)	116.9(5)	C(12)-C(28)-C(16)	120.9(4)
C(3)-C(2)-C(33)	122.1(5)	C(12)-C(28)-O(3)	120.4(4)
C(1)-C(2)-C(33)	120.9(5)	C(16)-C(28)-O(3)	118.6(4)
C(2)-C(3)-C(4)	124.1(5)	C(31)-C(29)-C(32)	108.5(8)
C(26)-C(4)-C(3)	116.0(4)	C(31)-C(29)-C(30)	105.8(14)
C(26)-C(4)-C(5)	123.4(4)	C(32)-C(29)-C(30)	109.3(14)
C(3)-C(4)-C(5)	120.6(4)	C(31)-C(29)-C(20)	115.2(6)
C(4)-C(5)-C(6)	115.0(4)	C(32)-C(29)-C(20)	112.0(6)
C(7)-C(6)-C(27)	117.4(4)	C(30)-C(29)-C(20)	105.8(7)
C(7)-C(6)-C(5)	121.4(4)	C(35)-C(33)-C(2)	113.0(6)
C(27)-C(6)-C(5)	121.2(4)	C(35)-C(33)-C(34)	112.4(7)
C(6)-C(7)-C(8)	123.8(4)	C(2)-C(33)-C(34)	108.4(6)
C(7)-C(8)-C(9)	116.2(4)	C(35)-C(33)-C(36)	106.8(7)
C(7)-C(8)-C(37)	123.5(4)	C(2)-C(33)-C(36)	107.9(5)
C(9)-C(8)-C(37)	120.4(4)	C(34)-C(33)-C(36)	108.0(6)

Table 4S. (continued) Bond angles [deg] for **5a**.

Atoms	Angles [deg]	Atoms	Angles [deg]
C(3)-C(2)-C(33)	122.1(5)	C(39)-C(37)-C(38)	118.0(11)
C(39)-C(37)-C(8)	113.1(6)	N(3)-C(58)-C(59)	110.7(5)
C(38)-C(37)-C(8)	113.7(6)	C(64)-C(59)-C(60)	118.2(5)
C(39)-C(37)-C(40)	107.1(11)	C(64)-C(59)-C(58)	121.6(4)
C(38)-C(37)-C(40)	94.2(7)	C(60)-C(59)-C(58)	120.2(6)
C(8)-C(37)-C(40)	108.3(5)	C(61)-C(60)-C(59)	122.2(7)
C(42)-C(44)-C(43)	102.0(12)	C(60)-C(61)-C(62)	119.8(6)
C(42)-C(44)-C(41)	114.7(12)	C(61)-C(62)-C(63)	121.1(6)
C(43)-C(44)-C(41)	98.2(11)	C(64)-C(63)-C(62)	118.1(6)
C(42)-C(44)-C(14)	116.7(6)	O(6)-C(64)-C(59)	116.4(5)
C(43)-C(44)-C(14)	108.6(8)	O(6)-C(64)-C(63)	123.0(5)
C(41)-C(44)-C(14)	113.9(6)	C(59)-C(64)-C(63)	120.6(5)
O(1)-C(45)-C(46)	106.1(4)	O(6)-C(65)-C(66)	111.7(4)
O(5)-C(46)-C(45)	109.2(4)	O(2)-C(66)-C(65)	116.9(4)
O(5)-C(47)-C(52)	115.7(5)	N(2)-C(67)-C(68)	109.5(5)
O(5)-C(47)-C(48)	125.4(5)	N(4)-C(68)-C(67)	113.1(5)
C(52)-C(47)-C(48)	118.8(5)	C(70)-C(69)-N(4)	110.9(6)
C(47)-C(48)-C(49)	119.3(7)	C(72)-C(71)-C(78)	123.0(8)
C(50)-C(49)-C(48)	122.0(8)	C(71)-C(72)-C(73)	120.9(8)
C(49)-C(50)-C(51)	119.1(7)	C(74)-C(73)-C(72)	117.2(9)
C(50)-C(51)-C(52)	121.5(6)	C(73)-C(74)-C(75)	120.4(7)
C(47)-C(52)-C(51)	119.0(6)	O(7)-C(75)-C(74)	123.7(6)
C(47)-C(52)-C(53)	120.9(5)	O(7)-C(75)-C(70)	116.0(6)
C(51)-C(52)-C(53)	120.1(5)	C(74)-C(75)-C(70)	120.3(6)
N(1)-C(53)-C(52)	109.6(4)	O(7)-C(76)-C(77)	109.0(5)
N(1)-C(54)-C(55)	112.6(5)	O(3)-C(77)-C(76)	108.4(5)
N(2)-C(55)-C(54)	113.2(5)	C(71)-C(70)-C(75)	118.1(8)
N(2)-C(56)-C(57)	111.4(4)	C(71)-C(70)-C(69)	120.6(7)
N(3)-C(57)-C(56)	111.1(5)	C(75)-C(70)-C(69)	121.3(6)

Symmetry transformations used to generate equivalent atoms.

Table 5S. Anisotropic displacement parameters ($Å^2 \times 10^3$) for **5a**.

	U11	U22	U33	U23	U13	U12
Cl(1)	91(1)	62(1)	68(1)	-5(1)	30(1)	-1(1)
Cl(2)	160(3)	218(4)	158(3)	-5(2)	4(2)	30(3)
O(1)	54(2)	38(2)	39(2)	1(1)	13(2)	-5(2)
O(2)	42(2)	44(2)	54(2)	2(2)	10(2)	-2(2)
O(1W)	107(6)	215(10)	275(14)	125(9)	71(7)	10(5)
O(3)	64(2)	38(2)	49(2)	-4(2)	10(2)	6(2)
O(2W)	480(30)	800(50)	182(13)	143(19)	-105(15)	-450(30)
O(4)	72(3)	56(2)	40(2)	-7(2)	-5(2)	11(2)
O(3W)	132(8)	196(10)	134(8)	-34(6)	54(6)	-26(6)
O(5)	71(2)	40(2)	58(2)	-6(2)	8(2)	-17(2)
O(4W)	179(10)	480(20)	165(9)	73(10)	34(7)	56(11)
O(6)	49(2)	64(2)	53(2)	3(2)	14(2)	15(2)
O(7)	79(3)	62(3)	62(2)	-15(2)	-2(2)	11(2)
O(8)	93(4)	73(3)	45(3)	-26(2)	1(3)	8(3)
N(1)	55(3)	57(3)	51(3)	-3(2)	4(2)	8(2)
N(2)	66(3)	65(3)	59(3)	-5(2)	22(2)	9(2)
N(3)	53(3)	55(3)	69(3)	-13(2)	13(2)	5(2)
N(4)	50(3)	121(5)	62(3)	-7(3)	10(2)	17(3)
C(1)	43(3)	43(3)	64(3)	0(2)	21(2)	1(2)
C(2)	50(3)	47(3)	73(4)	-8(3)	20(3)	-5(2)
C(3)	50(3)	59(3)	49(3)	-11(3)	6(2)	1(3)
C(4)	37(3)	52(3)	48(3)	-2(2)	9(2)	3(2)
C(5)	42(3)	70(4)	47(3)	1(2)	10(2)	9(2)
C(6)	44(3)	49(3)	42(3)	3(2)	10(2)	1(2)
C(7)	47(3)	48(3)	39(3)	-8(2)	11(2)	-1(2)
C(8)	53(3)	42(3)	45(3)	-4(2)	5(2)	-4(2)

Table 5S. (continued) Anisotropic displacement parameters ($Å^2 \times 10^3$) for **5a**.

	U11	U22	U33	U23	U13	U12
C(9)	51(3)	46(3)	40(3)	8(2)	-2(2)	3(2)
C(10)	55(3)	37(3)	43(3)	4(2)	9(2)	2(2)
C(11)	71(4)	36(3)	44(3)	4(2)	8(2)	9(2)
C(12)	52(3)	34(2)	44(3)	0(2)	9(2)	14(2)
C(13)	58(3)	49(3)	46(3)	-2(2)	4(2)	7(3)
C(14)	50(3)	42(3)	61(3)	-7(2)	14(3)	3(2)
C(15)	60(3)	43(3)	55(3)	0(2)	26(3)	10(2)
C(16)	52(3)	46(3)	44(3)	1(2)	14(2)	16(2)
C(17)	63(3)	46(3)	48(3)	-2(2)	22(2)	7(2)
C(18)	51(3)	45(3)	37(2)	0(2)	12(2)	4(2)
C(19)	51(3)	57(3)	49(3)	8(2)	22(2)	10(2)
C(20)	64(4)	54(3)	52(3)	8(2)	20(3)	0(3)
C(21)	60(3)	39(3)	48(3)	8(2)	17(2)	7(2)
C(22)	40(3)	46(3)	35(2)	5(2)	9(2)	3(2)
C(23)	41(3)	43(3)	47(3)	10(2)	7(2)	7(2)
C(24)	36(2)	42(3)	43(3)	-1(2)	10(2)	5(2)
C(25)	42(3)	38(3)	37(2)	0(2)	7(2)	-1(2)
C(26)	29(2)	37(3)	44(3)	3(2)	7(2)	3(2)
C(27)	52(3)	42(3)	34(2)	-1(2)	1(2)	-9(2)
C(28)	46(3)	39(3)	42(3)	-1(2)	7(2)	9(2)
C(29)	85(5)	75(4)	87(5)	29(4)	39(4)	-1(4)
C(30)	600(40)	390(30)	183(18)	76(17)	-10(20)	-400(30)
C(31)	285(19)	129(10)	330(20)	110(11)	250(18)	53(10)
C(32)	170(12)	172(12)	350(20)	192(14)	169(14)	85(9)
C(33)	74(4)	62(4)	89(5)	-20(3)	21(4)	-21(3)
C(34)	51(6)	75(7)	161(10)	-46(6)	7(5)	-23(4)

Table 5S. (continued) Anisotropic displacement parameters ($Å^2 \times 10^3$) for **5a**.

	U11	U22	U33	U23	U13	U12
C(9)	51(3)	46(3)	40(3)	8(2)	-2(2)	3(2)
C(10)	55(3)	37(3)	43(3)	4(2)	9(2)	2(2)
C(11)	71(4)	36(3)	44(3)	4(2)	8(2)	9(2)
C(12)	52(3)	34(2)	44(3)	0(2)	9(2)	14(2)
C(13)	58(3)	49(3)	46(3)	-2(2)	4(2)	7(3)
C(14)	50(3)	42(3)	61(3)	-7(2)	14(3)	3(2)
C(15)	60(3)	43(3)	55(3)	0(2)	26(3)	10(2)
C(16)	52(3)	46(3)	44(3)	1(2)	14(2)	16(2)
C(17)	63(3)	46(3)	48(3)	-2(2)	22(2)	7(2)
C(18)	51(3)	45(3)	37(2)	0(2)	12(2)	4(2)
C(19)	51(3)	57(3)	49(3)	8(2)	22(2)	10(2)
C(20)	64(4)	54(3)	52(3)	8(2)	20(3)	0(3)
C(21)	60(3)	39(3)	48(3)	8(2)	17(2)	7(2)
C(22)	40(3)	46(3)	35(2)	5(2)	9(2)	3(2)
C(23)	41(3)	43(3)	47(3)	10(2)	7(2)	7(2)
C(24)	36(2)	42(3)	43(3)	-1(2)	10(2)	5(2)
C(25)	42(3)	38(3)	37(2)	0(2)	7(2)	-1(2)
C(26)	29(2)	37(3)	44(3)	3(2)	7(2)	3(2)
C(27)	52(3)	42(3)	34(2)	-1(2)	1(2)	-9(2)
C(28)	46(3)	39(3)	42(3)	-1(2)	7(2)	9(2)
C(29)	85(5)	75(4)	87(5)	29(4)	39(4)	-1(4)
C(30)	600(40)	390(30)	183(18)	76(17)	-10(20)	-400(30)
C(31)	285(19)	129(10)	330(20)	110(11)	250(18)	53(10)
C(32)	170(12)	172(12)	350(20)	192(14)	169(14)	85(9)
C(33)	74(4)	62(4)	89(5)	-20(3)	21(4)	-21(3)
C(34)	51(6)	75(7)	161(10)	-46(6)	7(5)	-23(4)

Table 5S. (continued) Anisotropic displacement parameters ($Å^2 \times 10^3$) for **5a**.

	U11	U22	U33	U23	U13	U12
C(35)	154(9)	89(7)	143(9)	-7(5)	65(7)	-51(6)
C(36)	77(6)	53(5)	105(7)	-35(4)	23(5)	0(4)
C(37)	60(4)	71(4)	41(3)	-15(3)	3(3)	-3(3)
C(38)	64(7)	410(30)	148(11)	-154(13)	-5(6)	-36(9)
C(39)	370(30)	420(30)	178(14)	-210(17)	-180(16)	270(20)
C(40)	219(17)	130(11)	43(6)	24(6)	-46(7)	-37(9)
C(41)	330(30)	185(17)	320(30)	55(14)	-170(20)	-171(19)
C(42)	590(50)	380(30)	172(15)	-136(16)	149(19)	-420(30)
C(43)	290(30)	260(20)	630(60)	-330(30)	250(30)	-140(20)
C(44)	83(4)	46(3)	76(4)	-6(3)	23(4)	-10(3)
C(45)	66(3)	40(3)	43(3)	-2(2)	0(2)	-11(2)
C(46)	61(3)	45(3)	59(3)	-8(2)	13(3)	-14(2)
C(47)	70(4)	45(3)	63(4)	7(3)	0(3)	-11(3)
C(48)	122(6)	80(5)	83(5)	25(4)	-30(4)	-44(4)
C(49)	191(10)	118(7)	98(6)	58(6)	-42(6)	-57(7)
C(50)	147(8)	79(6)	142(8)	54(5)	-21(7)	-33(5)
C(51)	84(5)	39(3)	114(6)	10(3)	9(4)	-7(3)
C(52)	63(4)	42(3)	73(4)	0(3)	8(3)	6(3)
C(53)	69(4)	43(3)	70(4)	-13(3)	14(3)	-9(3)
C(54)	75(4)	76(4)	60(4)	-15(3)	14(3)	-9(3)
C(55)	80(4)	73(4)	61(4)	-9(3)	16(3)	-4(3)
C(56)	60(4)	75(4)	56(3)	-8(3)	10(3)	11(3)
C(57)	64(4)	73(4)	65(4)	0(3)	19(3)	11(3)
C(58)	54(3)	67(4)	59(3)	3(3)	4(3)	0(3)
C(59)	42(3)	37(3)	79(4)	-2(2)	6(3)	4(2)
C(60)	60(4)	57(4)	87(4)	2(3)	-10(3)	8(3)

Table 5S. (continued) Anisotropic displacement parameters ($Å^2$ x 10^3) for **5a**.

	U11	U22	U33	U23	U13	U12
C(61)	54(4)	66(4)	125(7)	-16(4)	-2(4)	19(3)
C(62)	56(4)	55(4)	142(7)	-20(4)	32(4)	10(3)
C(63)	49(3)	58(4)	100(5)	-10(3)	23(3)	4(3)
C(64)	42(3)	41(3)	72(4)	2(2)	15(3)	7(2)
C(65)	46(3)	67(4)	64(4)	-7(3)	19(3)	-5(3)
C(66)	53(3)	65(4)	51(3)	8(3)	11(3)	-16(3)
C(67)	74(4)	70(4)	66(4)	3(3)	27(3)	14(3)
C(68)	73(4)	102(5)	56(4)	-15(3)	22(3)	14(4)
C(69)	63(4)	123(6)	86(5)	-9(4)	18(4)	15(4)
C(70)	59(4)	95(5)	67(4)	-33(4)	8(3)	22(3)
C(71)	95(6)	85(6)	95(5)	-32(5)	10(4)	12(5)
C(72)	99(6)	97(7)	114(7)	-53(5)	-1(5)	11(5)
C(73)	91(6)	76(5)	147(8)	-33(5)	17(5)	12(4)
C(74)	87(5)	57(4)	89(5)	-19(3)	13(4)	10(3)
C(75)	59(4)	66(4)	76(4)	-30(3)	6(3)	12(3)
C(76)	91(5)	52(4)	72(4)	-17(3)	-7(3)	28(3)
C(77)	76(4)	42(3)	81(4)	-17(3)	-8(3)	22(3)
C(78)	390(30)	670(50)	110(12)	-230(20)	-158(15)	470(40)

The anisotropic displacement factor exponent takes the form: $-2pi^2[h^2a^2*U11 + ... + 2hka*b*U12]$.