Synthesis, structure and inclusion properties of *distal*-bis{[(5'-methyl-2,2'-bipyridyl)-5-yl]methoxy}tetrathiacalix[4]arene with 1,3-*alternate* conformation

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distal-Tetrathiacalix[4]arene having [(5'-methyl-2,2'-bipyridyl)-5-yl]methoxy group with 1,3-*alternate* conformation was prepared, which shows strong Ag^+ affinity and the high Ag^+ selectivity. The conformational change of 2,2'-bipyridyl moiety from the original outward orientation of the ring nitrogen to the inside orientation toward the thiacalixarene cavity was observed in the process of Ag^+ complexation.

Keywords: thiacalix[4]arene, *O*-alkylation, 2,2'-bipyridyl group, conformation, ionophores, metal complexation

The introduction of larger alkyl groups on the phenolic oxygens of calix[4]arenes led to a situation where the OR groups within a cyclophane ring cannot pass each other by oxygen-through-the-annulus rotation.[1–4] There exist four possible conformational isomers in calix[4]arenes; *i.e.* cone, partial-cone, 1,2-alternate and 1,3-alternate.[1–4] Similarly, four conformational isomers are possible in the case of tetrathiacalix[4]arene.[5–7] The inhibition of interconversion between conformers derived from tetrathiacalix[4]arene by *O*-substitution differs from that of the calix[4]arenes. On the other hand, the regioselective *O*-alkylation of hydroxy groups in calixarenes is important for many purposes, in particular for the construction of multiple binding receptors or larger molecules starting from several calixarene building units.[8,9] In fact, we previously reported[10] that 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrahydroxytetrathiacalix[4]arene when treated with 2-(chloromethyl)pyridine in the presence of Na_2CO_3 under THF reflux yielded none of the pure regioselective isomers such as 1,2- or 1,3-di-*O*-substitution. Only a trace amount of a mixture of partial (2-pyridyl) methylation products were obtained along with the recovery of the starting compound. Recently, we have reported that regioselective synthesis of *distal*-bis[(2-pyridylmethyl)oxy] thiacalix[4]arenes is accomplished by a protection-deprotection method using benzyl groups as a protecting group.[11]

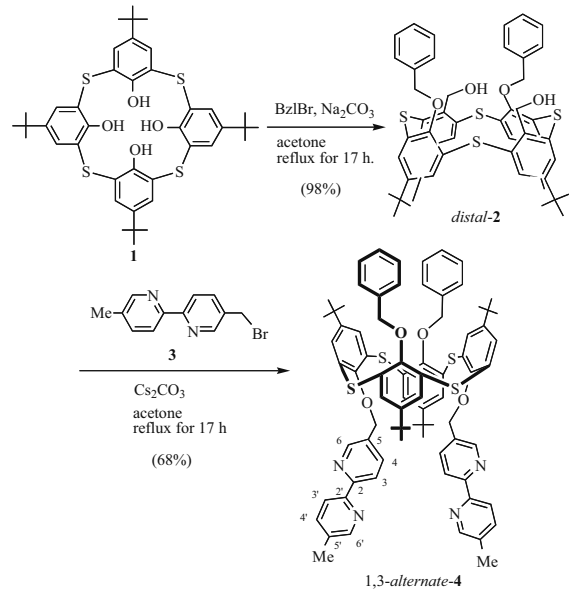
On the other hand, Nabeshima *et al.*[12] reported a novel calix[4]arene derivative bearing two 2,2'-bipyridine moieties and two ester groups at the lower rim in cone conformation to construct sophisticated molecular devices and systems. Bipyridyl containing calixarenes have been extensively used to complex various metal ions.[13–22] Di- or polytopic receptors are those constructed with two or more binding subunits within the same macrocyclic structure.[23–25] It is well known that these kinds of systems are suitable candidates for the allosteric regulation[13–16] of host-guest interactions with metal cations which play a major role in biological systems. We now report on the synthesis of *distal*-bis{[(5'-methyl-2,2'-bipyridyl)-5-yl] methoxy}tetrathiacalix[4]arene from *O*-alkylation of *distal*-di-*O*-alkoxythiacalix[4]arene with 5-bromomethyl-5'-methyl-2,2'-bipyridine. Conformational studies of *distal*-bis{[(5'-methyl-2,2'-bipyridyl)-5-yl]methoxy}tetrathiacalix[4]arene in solution and its inclusion properties are also described.

Results and discussion

1,3-*distal*-Bis(benzyloxy)tetrathiacalix[4]arene, *distal*-**2**, was prepared by *O*-alkylation of thiacalix[4]arene **1** with benzyl bromide in the presence of Na_2CO_3 according to the reported procedure.[11] *O*-Alkylation of *distal*-**2** with 5-bromomethyl-5'-methyl-2,2'-bipyridine **3** in the presence of Cs_2CO_3 as base in acetone under reflux for 17 h yielded the desired product 1,3-*alternate*-**4** in 68% yield. Similarly, *O*-alkylation of *distal*-**2** with 5-bromomethyl-5'-methyl-2,2'-bipyridine **3** in the presence of NaH or K_2CO_3 afforded 1,3-*alternate*-**4** in 55 and 59% yields, respectively. However, no formation of the other possible conformational isomers such as partial-cone or cone isomers was observed. In the case of Na_2CO_3 only the recovery of starting compounds resulted in spite of the conditions of large excess of Na_2CO_3 and 5-bromomethyl-5'-methyl-2,2'-bipyridine **3**.

The ^{1}H NMR spectrum of 1,3-*alternate*-**4** shows two singlet peaks for *tert*-butyl protons, in which both *tert*-butyl protons were observed to higher field at δ 0.78 and 0.86 ppm due to the ring current effect arising from the two benzyl benzene rings and the two 2,2'-bipyridine rings introduced.

Interestingly, the hetero aromatic protons of the bipyridine rings of 1,3-*alternate*-**4** are exposed to the ring current shielding effect[26–28] operating in the opposing bipyridine ring among the diaryl thiaether linkage, and resonate at higher fields with respect to those of the reference compound **6**, which was prepared by



Scheme 1

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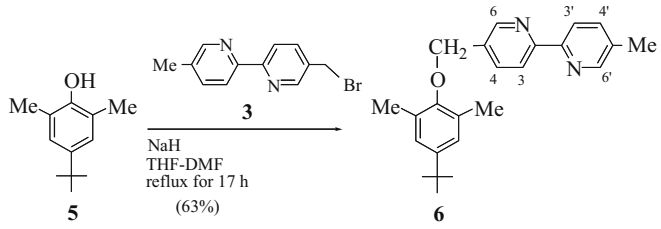


Scheme 2

O-alkylation of 4-*tert*-butyl-2,6-dimethylphenol **5**[29] with 5-bromomethyl-5'-methyl-2,2'-bipyridine **3** in the presence of NaH.

The magnitude of this shielding, computed as the difference between pertinent 2,2'-bipyridine protons of 1,3-*alternate*-**4** and reference compound **6**, increases significantly for the H_4, H_6 and $H_{6'}$ protons. The remarkable shielding effect experienced by the H_4 (–0.38 ppm) and H_6 (–0.26 ppm) protons of the 2,2'-bipyridine suggest that these protons are located much closer to the opposing bipyridine ring than are the H_3 proton and folded into the π-cavity formed by two thiacalix benzene rings and are thus shifted stronger upfield. Thus, one nitrogen atom (N_1) of the 2,2'-bipyridine ring might be orientated outwards with respect to the thiacalixarene cavity due to the electron repulsion between nitrogens at the distal positions. In contrast, the other nitrogen ($N_{1'}$) is oriented inwards due to the 2,2'-bipyridyl linkage.

Calixarene can be converted to neutral ligands by introduction of ester or amide groups into the OH groups.[1] The metal selectivity is dependent on the ring size and the *O*-alkylated substituents present. The ring size and the ring flexibility of thiacalix[4]arene are different from both calix[4]arene and hexahomotrioxacalix[3]arene.[1] Functionalisation of calix[4]arene by *O*-alkylation with halomethyl *N*-heterocyclic reagents in the presence of the base has been introduced in order to obtain "universal" ligands for both hard and soft metal ions, which in principle should exhibit some advantages over ester and amide structures, because of a high stability over a wide pH range.[30,31] Recently, Pappalardo has reported the synthesis of calix[4]arenes bearing pendant pyridine groups at the lower rim as potential ligands for transition metal cations.[32,33] Similar investigation was also carried out using hexahomotrioxacalix[3]arene and homocalix[3]arene as the platform.[34–37] Therefore, it is interesting to assess the type of ionophoric cavity provided by the bis{[(5'-methyl-2,2'-bipyridyl)-5-yl]methoxy} derivative 1,3-*alternate*-**4**. Usually, calixarenes form a 1 : 1 complex with guest molecules, but various other types of complexation were observed depending on the calix ring size and functional groups present. A 1 : 2 complex of calix[8]arene with ammonium ions was reported by Shinkai.[38-41] The 1,3-alternate conformer of calix[4]arene derivatives can also form a 1:2 complex with metal cations.[42]

Due to the existence of the three potential metal-binding sites, namely the bipyridine moieties, two benzyloxy moieties and calix benzene rings, there are several possibilities for metal complexation for compound 1,3-*alternate*-**4** with guest molecules. Both 1 : 1 or 1 : 2 metal complexation might be possible attributable to the electrostatic interactions as well as cation–π interactions. The Job plots of compound 1,3-*alternate*-**4** were carried out in the H_2O/CH_2Cl_2 phases. The percent extractions reach maximum at 0.5 mole fraction when the 1,3-*alternate*-**4** and silver cation are changed systematically. This fact clearly indicates that the Ag^+ forms a 1:1 complex with 1,3-*alternate*-**4**. This result suggests the major contribution is from the nitrogen of 2,2'-bipyridine ring to Ag^+ binding, but not a cation–π-interaction with calix benzene rings nor the sulfur on the bridged linkage.

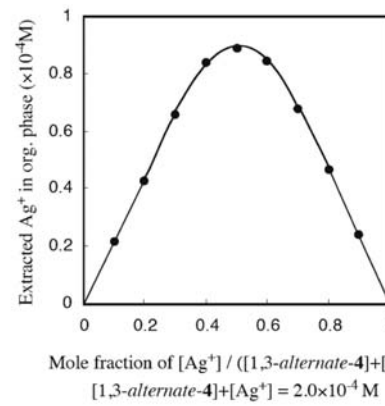


Fig. 1 Job plots of the extractions of Ag^+ with host 1,3-*alternate*-**4**.

Preliminary studies of the binding ability of 1,3-*alternate*-**4** are carried out by ion-pair extraction [M^+Pic^- ($M^+ = Ag^+$ or K^+)]. The *E*% value of 98% for 1,3-*alternate*-**4**, shows that 1,3-*alternate*-**4** strongly extract Ag^+. In contrast, no significant E% is observed for K^+ (1.5%) for 1,3-*alternate*-**4**. The association constant K_{ass} for the 1,3-*alternate*-**4**⊃Ag^+ is $K_{ass} = 3.1 \times 10^3\ M^{-1}$ calculated by non-linear fitting analysis of the observed chemical shift changes of OCH_2Bipy protons.[43]

^{1}H NMR titration experiments in $CDCl_3$–CD_3CN and with KSO_3CF_3 and $AgClO_4$ are carried out. The addition of an equiv. of KSO_3CF_3 to 1,3-*alternate*-**4** causes negligible chemical shift. On the other hand, titration with an equiv. of $AgClO_4$ causes a upfield shift for the methylene protons of OCH_2Bipy ($\Delta\delta = -0.20$ ppm) while the 2,2'-bipyridyl (*Bipy)* protons shifted to lower field with $\delta + 0.40$, + 0.43 ppm for H_4, $H_{4'}$ protons, and shifted to upper field with –0.13, –0.14 ppm for H_6, $H_{6'}$ protons, respectively (Fig. 2). These observations might be attributed to the conformational change of the 1,3-*alternate*-**4** upon complexation. Thus, the 1,3-*alternate*-**4** complexes Ag^+ through the both metal-nitrogen electrostatic interactions of bipyridyl group by tetrahedral Ag^+/heterocycle complex.[13–22] Interestingly, contrary to the observation of downfield shift of the methylene protons of OCH_2Bipy ($\Delta\delta = -0.20$ ppm), the chemical shift changes of the protons of OCH_2Ph moiety were negligibly small in the 1,3-*alternate*-**4** complexes Ag^+. These findings suggest the conformational change in the opposing OCH_2Ph moiety might be small after complexation with Ag^+ different from the reported 1,3-alternate-thiacalixarene derivatives.[11]

In order to study the present conformational behaviour more detail, we have prepared the corresponding *N,N*-diethylamide derivative 1,3-*alternate*-**8** by *O*-alkylation of *distal*-**2** with *N,N*-diethylchloroacetamide **7** in the presence of Cs_2CO_3 in 68% yield. Similar phenomena were also observed in the complexation of 1,3-*alternate*-**8** with Ag^+.

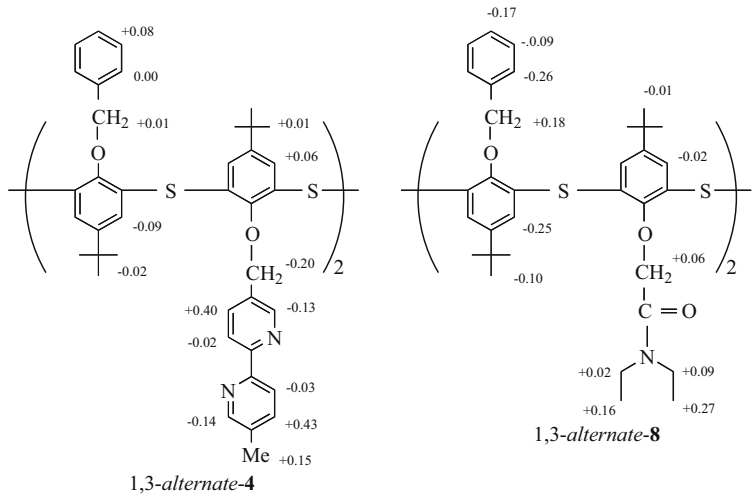
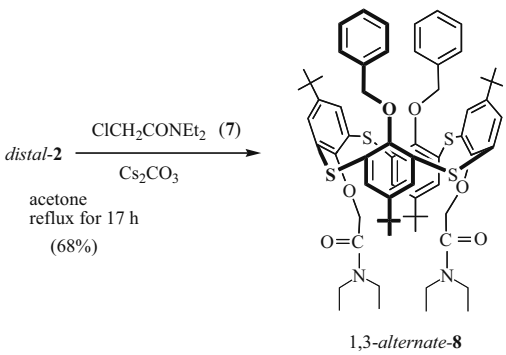


Fig. 2 Chemical shift changes of 1,3-*alternate*-**4** and 1,3-*alternate*-**8** induced in the presence of $AgClO_4$ in $CDCl_3$: CD_3CN (10:1); + denotes the downfield and – denotes the upfield shift.



Scheme 3

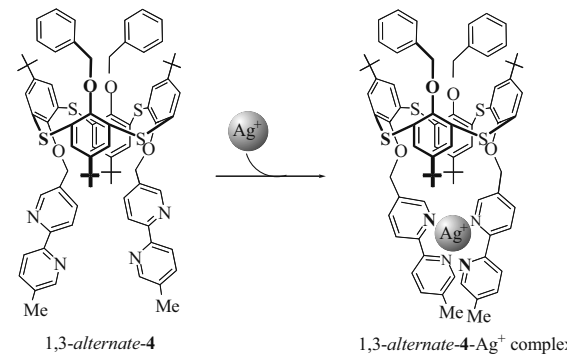


Fig. 3 Complexation mode of 1,3-*alternate*-4 with Ag^+.

The small down-field shifts of the methylene protons and ethyl protons of *N,N*-diethylamide moieties ($\Delta\delta$ = + 0.06 ppm for CH_2CONEt_2) were observed, which may be attributed to the smaller conformational change of the amide moieties upon complexation of 1,3-*alternate*-**8** with Ag^+ than that of 1,3-*alternate*-**4** (Fig. 2). In contrast, the chemical shift changes of the opposing inverted calix benzene protons and CH_2Ph protons are much larger than those of 1,3-*alternate*-**4**. These findings suggest the conformational change in the opposing OCH_2Ph moiety after complexation of 1,3-*alternate*-**8** with Ag^+ might be larger than that of 1,3-*alternate*-**4**.

As shown in Fig. 3, the nitrogen atom (N_1) in the bipyridine ring points away from the calix cavity in the free 1,3-*alternate*-**4** because of the electron repulsion between nitrogens. After complexation, the nitrogen turns inwards towards the cavity to complex with Ag^+ and thus affects H_4, $H_{4'}$ protons which shift to lower field and H_6, $H_{6'}$ protons which shift to upper field due to the tetrahedral interaction of N---Ag^+. However, the conformational change in the bipyridyl moieties does not affect that of the opposing benzyl moieties. Furthermore, the C_{2V}-symmetrical conformation of 1,3-*alternate*-**4** is still retained after complexation.

Conclusions

We have demonstrated for the first time that the stereoselective synthesis of *distal*-bis{[(5'-methyl-2,2'-bipyridyl)-5-yl]methoxy} tetrathiacalix[4]arene **4** with 1,3-*alternate* conformation has been accomplished by *O*-alkylation of 25,27-bis(benzyloxy)-26,28-dihydroxy-5,11,17,23-tetra-*tert*-butyl-2,8,14,20-tetrathiacalix[4]arene, *distal*-**2** with 5-bromomethyl-5'-methyl-2,2'-bipyridine. C_{2V}-Symmetrical bipyridyl-substituted thicalix[4]arene, 1,3-*alternate*-**4** can bind Ag^+ ion and the complexation mode has been elucidated clearly. The nitrogen atom in bipyridine ring turned from outward against the cavity to inside the cavity to interact with Ag^+ in 1,3-*alternate*-**4**. After complexation of 1,3-*alternate*-**4** with Ag^+, the original C_{2V}-symmetry has been remained. Further studies on the application to the synthetic receptors for use in metal controlled biomimetic systems are now in progress.

Experimental

All melting points are uncorrected. ^1H NMR spectra were recorded at 300 MHz on a Nippon Denshi JEOL FT-300 NMR spectrometer in deuteriochloroform with Me_4Si as an internal reference. IR spectra were measured as KBr pellets on a Nippon Denshi JIR-AQ2OM spectrometer. Mass spectra were obtained on a Nippon Denshi JMS-HX110A Ultrahigh Performance Mass Spectrometer at 75 eV using a direct-inlet system. Elemental analyses were performed by Yanaco MT-5.

Materials

distal-25,27-Bis(benzyloxy)-26,28-dihydroxy-5,11,17,23-tetra-*tert*-butyl-2,8,14,20-tetrathiacalix[4]arene *distal*-**2** was prepared according to the reported procedure.[7,11]

Synthesis of 5-bromomethyl-5'-methyl-2,2'-bipyridine: A solution of 5,5'-dimethyl-2,2'-bipyridine (500 mg, 2.84 mmol, 1 equiv.),

N-bromosuccinimide (NBS) (556 mg, 3.12 mmol, 1.1 equiv.) and 2,2'-azobis(2,4-dimethylpentanenitrile) (V_{65}) (300 mg, 1.20 mmol, 0.44 equiv.) in CH_2Cl_2(100 mL) was refluxed under argon for 12 h. The reaction mixture was allowed to rise to room temperature and solvent was evaporated. The residue dissolved in hot hexane and the solid part off out. The filtrate part keep 4 h at room temperature then dibromomethyl derivatives was precipitated and separated by filtration. The filtrate part again reduces one-third volume and put 12 h at room temperature and then white solid appears, which was recrystallisation from ethyl acetate–hexane(1 : 1) gave pure product as a white powder 433 mg (58%); m.p. 85–87 °C; δ_H ($CDCl_3$): 2.39 (3H, s, Bipy*CH*$_3$), 4.53 (2H, s, –*CH*$_2$Br), 7.62 (1H, d, *J* = 7.8 Hz, Bipy$H_{4'}$), 7.83 (1H, d, *J* = 6.0 Hz, bipyH_4), 8.28(1H, d, *J* = 7.8 Hz, Bipy*H*$_{3'}$), 8.35 (1H, d, *J* = 8.4 Hz, Bipy*H*$_3$), 8.49 (1H, s, Bipy*H*$_6$) and 8.65(1H, s, Bipy*H*$_6$); *m/z*: 262, 264 (M^+) Found: C, 54.97; H, 4.42; N, 10.88. $C_{12}H_{11}BrN_2$ (263.14) requires C, 54.77; H, 4.21; N, 10.65%.

Benzylation of **1** *with benzyl bromide in the presence of* Na_2CO_3: A mixture of **1** (200 mg, 0.276 mmol) and Na_2CO_3 (293 mg, 2.8 mmol) in acetone (15 mL) was heated at reflux for 1 h. Benzyl bromide (0.34 mL, 2.8 mmol) was then added and the mixture heated at reflux for 17 h. After cooling the reaction mixture to room temperature, it was filtered. The filtrate was concentrated and the residue was extracted with CH_2Cl_2 (100 mL × 2) and washed with water (50 mL × 2), and dried (Na_2SO_4). The filtrate was concentrated to give a yellow oil, which was then distilled under reduced pressure to remove the excess unreacted benzyl bromide using a Kugelrohr apparatus. The residue was washed with methanol to give the crude *distal*-**2** (247 mg, 98%) as a colourless solid. Recrystallisation from MeOH:$CHCl_3$ (3:1) gave 25,27-bis(benzyloxy)-26,28-dihydroxy-5,11,17,23-tetra-*tert*-butyl-2,8,14,20-tetrathiacalix[4]arene, *distal*-**2** as colourless prisms; m.p. 250–252 °C; ν_{max} (KBr)/cm^{-1} 3383 (OH), 2962, 2867, 1478, 1448, 1437, 1363, 1260, 1244, 886 and 756; δ_H ($CDCl_3$) 0.79 (18H, s, *t*Bu), 1.34 (18H, s, *t*Bu), 5.49 (4H, s, O*CH*$_2$Ph), 6.96 (4H, s, Ar*H*), 7.24–7.36 (6H, m, Ph*H*), 7.61–7.64 (4H, m, Ph*H*), 7.68 (4H, s, Ar*H*) and 7.98 (2H, s, *OH*); *m/z* 901 (M^+) Found: C, 72.08; H, 6.86. $C_{54}H_{60}O_4S_4$ (901.28) requires C, 71.96; H, 6.71%.

O-Alkylation of distal-**2** *with 5-bromomethyl-5'-methyl-2,2'-bipyridine* **3** *in the presence of* Cs_2CO_3: A mixture of *distal*-**2** (200 mg, 0.22 mmol) and Cs_2CO_3 (720 mg, 2.22 mmol) in dry acetone (15 mL) was heated at reflux for 1 h under N_2. A solution of 5-bromomethyl-5'-methyl-2,2'-bipyridine **3** (353 mg, 1.34 mmol) in DMF (5 mL) was then added and the mixture heated at reflux for an additional 20 h. After cooling the reaction mixture to room temperature, it was acidified with 1 M HCl (10 mL) and extracted with CH_2Cl_2 (100 mL × 2). The combined extracts were washed with water (50 mL × 2), and dried (Na_2SO_4) and condensed under reduced pressure to give a yellow oil. The residue was washed with methanol to give 1,3-*alternate*-**4** (198 mg, 68%) as a colourless solid. Recrystallisation from MeOH:$CHCl_3$ (3:1) gave 1,3-*alternate*-**4** as a colourless prisms.

1,3-*alternate*-25,27-Bis(benzyloxy)-26,28-bis{[(5'-methyl-2,2'-bipyridinyl)-5-yl]methoxy}-5,11,17,23-tetra-*tert*-butyl-2,8,14,20-tetrathiacalix[4]arene (1,3-*alternate*-**4**) was obtained as colourless prisms, m.p. 253–255 °C; ν_{max} (KBr)/cm^{-1} 3468, 2962, 1653, 1558, 1471, 1375, 1265, 1085, 1015 and 827; δ_H ($CDCl_3$) 0.78 (18H, s, *t*Bu), 0.86 (18H, s, *t*Bu), 2.38 (6H, s, Bipy*CH*$_3$), 5.06 (4H, s, O*CH*$_2$Ph), 5.36 (4H, s, O*CH*$_2$Bipy), 6.92 (4H, d, *J* = 9.0 Hz, Ph*H*), 6.97–7.02 (6H, m, Ph*H*), 7.07 (4H, s, Ar*H*), 7.11 (4H, s, Ar*H*), 7.53 (2H, d, *J* = 6.0 Hz, Bipy$H_{4'}$), 7.56 (2H, d, *J* = 6.0 Hz, BipyH_4), 8.16 (2H, s, BipyH_6), 8.25 (2H, d, *J* = 6.0 Hz, Bipy$H_{3'}$), 8.28 (2H, d, *J* = 6.0 Hz, BipyH_3) and 8.49 (2H, s, BipyH_6); *m/z* 1265.52 (M^+) Found: C, 73.37; H, 6.32; N, 4.23. $C_{78}H_{80}N_4O_4S_4$ (1265.77) requires C, 74.01; H, 6.37; N, 4.43%.

Similarly, *O*-alkylation of *distal*-**2** with 5-bromomethyl-5'-methyl-2,2'-bipyridine **3** in the presence of NaH or K_2CO_3 afforded 1,3-*alternate*-**4** in 55 and 59% yields, respectively.

Preparation of 4-tert-butyl-2,6-dimethyl{[(5'-methyl-2,2'-bipyridinyl)-5-yl]methoxy}benzene **6**: A mixture of 4-*tert*-butyl-2,6-dimethylphenol **5**[29] (400 mg, 2.25 mmol) and NaH (580 mg, 14.5 mmol, 60 wt%) in dry THF (20 mL) was heated at reflux for 1 h under N_2. Then a solution of 5-bromomethyl-5'-methyl-2,2'-bipyridine **3** was added at room temperature and the mixture heated at reflux for an additional 17 h. After cooling the reaction mixture to room temperature, it was acidified with 1 M HCl (10 mL) and extracted with CH_2Cl_2 (100 mL × 2). The combined extracts were washed with water (50 mL × 2), dried (Na_2SO_4) and condensed under reduced pressure to give a yellow oil. The residue was treated with MeOH (5 mL) to give the crude **6** (373 mg, 46%) as a white solid. Recrystallisation from $CHCl_3$:MeOH (3:1) gave **6** as colourless prisms; m.p. 81–82 °C; δ_H ($CDCl_3$) 1.30 (9H, s, *t*Bu), 2.30 (6H, s, *CH*$_3$), 2.40 (3H, s, Bipy*CH*$_3$), 4.87 (2H, s, O*CH*$_2$), 7.04 (2H, s, Ar*H*), 7.63 (1H, dd, *J* = 8.1, 1.8 Hz, Bipy$H_{4'}$), 7.91 (1H, dd, *J* = 8.1, 1.8 Hz, BipyH_4), 8.30 (1H, d, *J* = 8.1 Hz, Bipy$H_{3'}$), 8.39 (1H, d, *J* = 8.1 Hz, BipyH_3), 8.51 (1H, d, *J* = 1.8 Hz, Bipy$H_{6'}$) and 8.75 (1H, d, *J* = 1.8, BipyH_6); *m/z*: 360 (M^+) Found: C, 80.05; H, 7.79; N, 7.68. $C_{24}H_{28}N_2O$ (360.50) requires C, 79.95; H, 7.83; N, 7.77%.

O-Alkylation of distal-**2** *with N,N-diethylchloroacetamide in the presence of* Cs_2CO_3: A mixture of *distal*-**2** (680 mg, 0.754 mmol) and Cs_2CO_3 (2.46 g, 7.54 mmol) in dry acetone (30 mL) was heated at reflux for 1 h under N_2. A solution of *N,N*-diethylchloroacetamide **7** (1.13 g, 7.54 mmol) was then added and the mixture heated at reflux for an additional 17 h. After cooling the reaction mixture to room temperature, it was acidified with 1 M HCl (10 mL) and extracted with CH_2Cl_2 (100 mL × 2). The combined extracts were washed with water (50 mL × 2), and dried (Na_2SO_4) and condensed under reduced pressure to give a yellow oil. The residue was washed with methanol to give 1,3-*alternate*-**8** (510 mg, 60%) as a colourless solid. Recrystallisation from MeOH : $CHCl_3$ (3 : 1) gave 1,3-*alternate*-**8** as a colourless prisms.

1,3-*alternate*-25,27-Bis(benzyloxy)-26,28-bis[(*N,N*-diethylamino-carbonyl)methoxy]-5,11,17,23-tetra-*tert*-butyl-2,8,14,20-tetrathiacalix[4]arene (1,3-*alternate*-**8**) was obtained as colourless prisms, m.p. 255–256 °C; ν_{max} (KBr)/cm^{-1} 1664; δ_H ($CDCl_3$) 0.83 (18H, s, *t*Bu), 0.89–1.00 (6H, m, CH_2CH_3), 1.10–1.20 (6H, m, CH_2CH_3), 1.30 (18H, s, *t*Bu), 3.12–3.19 (4H, m, CONC*H*$_2$), 3.35–3.42 (4H, m, CONC*H*$_2$), 4.70 (4H, s, C*H*$_2$CON), 4.95 (4H, s, C*H*$_2$Ph), 7.18 (4H, s, Ar*H*), 7.17–7.23 (10H, m, Ph*H*) and 7.62 (4H, s, Ar*H*); *m/z* 1127.5 (M^+) Found: C, 70.25; H, 7.28; N, 2.44. $C_{66}H_{82}N_2O_6S_4$ (1127.74) requires C, 70.3; H, 7.33; N, 2.48%.

Extraction experiments

Metal picrates (2.5×10^{-4} M) were prepared *in situ* by dissolving the metal hydroxide (0.01 mol) in 2.5×10^{-4} M picric acid (100 mL); triply distilled water was used for all aqueous solutions. Two-phase solvent extraction was carried out between water (5 mL, [metal picrate] = 2.5×10^{-4} M) and CH_2Cl_2 (5 mL, [ionophore] = 2.5×10^{-4} M). The two-phase mixture was shaken in a stoppered flask for 2 h at 25 °C. We confirmed that this period is sufficient to attain the distribution equilibrium. This was repeated three times, and the solutions were left standing until phase separation was complete. The extractability was determined spectrophotochemically from the decrease in the absorbance of the picrate ion in the aqueous phase as described by Pedersen.[44]

Stoichiometry of metal complexation

The method of continuous variation[44] was employed to determine the stoichiometry of 1,3-*alternate*-**4**. Two-phase solvent extraction was carried out between aqueous picrates (5 mL, [silver picrate] = 2×10^{-4} M) and 1,3-*alternate*-**4** (5 mL, [1,3-*alternate*-**4**] = 2×10^{-4} M in CH_2Cl_2). The molar ratios of the both 1,3-*alternate*-**4** and metal picrate were varied from 0 to 1, while the total concentration was kept at several constant levels. The two-phase mixture in a glass tube immersed in a thermostated water bath at 25 °C was shaken at 300 strokes per min for 1 h and then kept, at the same temperature, for 2 h, allowing the complete separation of the two phases. The absorbance of each solution was determined by UV spectroscopy (λ = 290 nm). Job plots were generated by plotting the extracted [Ag^+] versus the mole fraction of metal.

^{1}H NMR complexation experiments

To a $CDCl_3$ solution (4×10^{-3} M) of 1,3-*alternate*-4 in the NMR tube was added a CD_3CN solution (4×10^{-2} M) of $AgClO_4$ and KSO_3CF_3. The spectrum was registered after addition and the temperature of NMR probe kept constant at 25 °C.

The ^{1}H NMR data of the most representative complexes is given below.

1,3-*alternate*-**4**$\supset Ag^+$ *(1 : 1)*: δ_H ($CDCl_3$–CD_3CN, 10:1) 0.79 (18H, s, *t*Bu), 0.84 (18H, s, *t*Bu), 2.53 (6H, s, Bipy*CH*$_3$), 5.07 (4H, s, O*CH*$_2$Ph), 5.16 (4H, s, O*CH*$_2$Bipy), 6.98 (4H, s, Ar*H*), 6.92 (4H, d, *J* = 9.0 Hz, Ph*H*), 7.05–7.10 (6H, m, Ph*H*), 7.17 (4H, s, Ar*H*), 7.96 (4H, d, *J* = 6.0, Bipy-*H*$_4$, *H*$_{4'}$), 8.02 (2H, s, Bipy*H*$_6$), 8.22 (2H, dd, *J* = 6.0, Bipy$H_{3'}$), 8.26 (2H, d, *J* = 6.0 Hz, BipyH_3) and 8.36 (2H, s, BipyH_6).

1,3-*alternate*-**8**$\supset Ag^+$ *(1 : 1)*: δ_H ($CDCl_3$–CD_3CN, 10:1) 0.82 (18H, s, *t*Bu), 1.18–1.24 (6H, m, CH_2CH_3), 1.29–1.33 (6H, m, CH_2CH_3), 1.20 (18H, s, *t*Bu), 3.25–3.35 (4H, m, CONC*H*$_2$), 3.45–3.55 (4H, m, CONC*H*$_2$), 4.76 (4H, s, C*H*$_2$CON), 5.13 (4H, s, C*H*$_2$Ph), 6.94 (4H, d,

J = 7.0 Hz, PhH_2), 7.11 (4H, dd, J = 7.0, 7.0 Hz, PhH_3), 7.16 (4H, s, ArH), 7.21 (2H, t, J = 7.0 Hz, PhH_4) and 7.37 (4H, s, ArH).

Determination of association constants

The measurements were performed by ^{1}H NMR titration experiments in $CDCl_3$:CD_3CN 1 : 1 v/v) at 25 °C using a concentration of 4×10^{-3} M and a varying guest concentration of 0.3–30 mM. The association constants (K_{ass}) for the 1,3-*alternate*-**4** complexes were calculated by non-linear fitting analysis of the observed chemical shift of the methylene protons of OCH_2Bipy for 1,3-*alternate*-**4**⊃Ag^+ complex and 1,3-*alternate*-**4**⊃K^+ complex, respectively.[43]

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