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Synthesis and Alkali Metal Picrate Extraction Studies of *p-tert*-Butylcalix[4]arene Crown Ethers Bridged at the Lower Rim with Pyridyl Units

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Abstract—The syntheses of pyridyl containing calix[4]arene receptors (**4**, **5**, and **11**) that adopt the cone conformation are reported. The complexation properties of these host molecules were estimated via the results of alkali metal picrate extraction experiments. A singly-bridged bis-calix[4]arene, i.e. **4** does not appear to be an efficient alkali metal picrate extractant. A doubly-bridged bis-calix[4]arene, i.e. **5**, displays elevated extraction avidity toward Rb^+ and Cs^+ picrates when compared with that of **4**. A pyridyl containing calix[4]arene-crown-5, i.e. **11**, shows improved avidity and selectivity toward extraction of K^+ and Rb^+ picrates vis-a-vis the corresponding behavior of **4** and **5**.

Introduction

In recent years, readily available calix[4]arenes[1] have been utilized extensively as starting materials for the synthesis of metal selective[1b] ionophores. A variety of calix[4]arene-based receptors that possess unusual cavity dimensions have been synthesized via 'upper' and 'lower' rim functionalization.[2] The complexation properties of these molecules appear to be highly dependent upon the nature and number of donor atoms and also upon the conformation of the calix[4]arene moiety.[3] In particular, calix[4]arenes that contain polyethylene glycol units attached to the lower rim have been synthesized,[4] and their behavior as alkali metal extractants has been examined.[5]

The ability of pyridine-containing crown ethers to form complexes with a variety of guests has been studied in several laboratories.[6] However, pyridine moieties have been incorporated into the lower rim of calixarenes only relatively recently.[7] Furthermore, the complexation properties of pyridine-containing calix[4]arene crowns have not been studied extensively.

In the present study, we report the synthesis and alkali metal picrate extraction capabilities of novel bis-calix[4]arene[8] receptors, i.e. **4** and **5**, in which the lower rim of each calix[4]arene moiety has been linked covalently with one or more pyridine moities. In addition, a pyridine-containing calix[4]arene-crown-5 (**11**) has been prepared, and its alkali metal picrate extraction profile has been investigated.

The objectives of the present study are as follows: (i) to investigate whether lower-rim pyridine-bridged bis-calix-[4]arenes **4** and **5** display noteworthy ability to enter into complexation with alkali metal cation guests; and (ii) to determine the avidity and selectivity with which novel host system **11** is able to extract alkali metal picrates from aqueous solution into an organic phase ($CHCl_3$).

Preparation of Host Systems 4 and 5

The methods used to prepare lower rim functionalized, pyridine-containing bis-calix[4]arenes **4** and **5** are shown in Schemes 1 and 2, respectively. Thus, base-promoted reaction of *p-tert*-butylcalix[4]arene (**1a**) with 2,6-bis-(bromomethyl)pyridine (**2**)[9] in toluene/benzene produced both singly-bridged (**4**) and doubly-bridged bis-calix[4]-arenes (**5**) in 25 and 6% yield, respectively (Scheme 1). Interestingly, when **1a** was reacted with **2** in the presence of K_2CO_3 as the templating base for 5 days, only **5** was obtained in 30% yield.

It was anticipated that *mono*calix[4]arene crown-3 (**3**) might be formed via 1,3-bridging of **2** to **1a** (Scheme 1). However, in view of the steric strain that would become incorporated into the resulting crown ether (**3**), it seems likely that **2** as a bifunctional reagent prefers intermolecular 'linking' rather than intramolecular 'bridging'.

The structures of **4** and **5** were confirmed via analysis of

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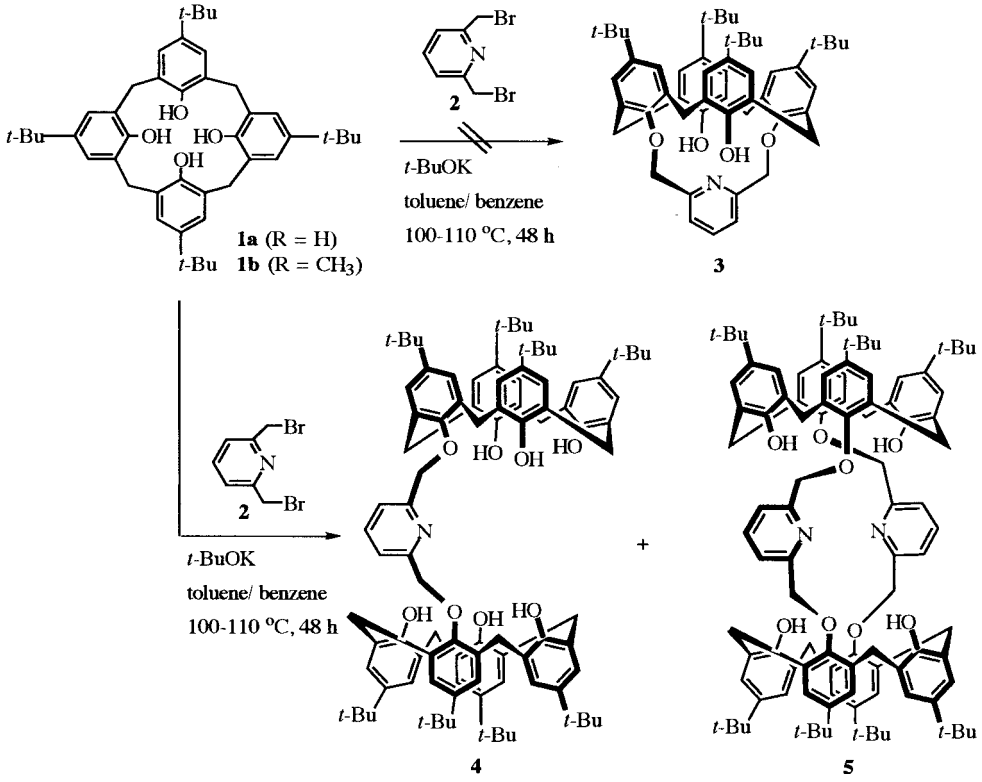
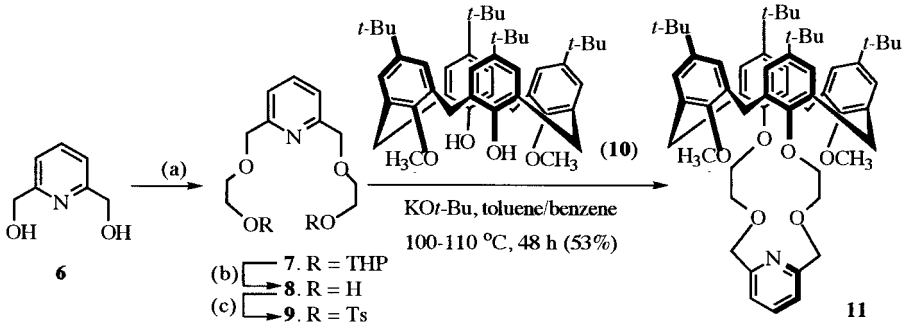


Scheme 1.

their respective ^{1}H NMR and ^{13}C NMR spectra and via HRMS analysis (see Experimental). Inspection of their respective ^{1}H NMR and ^{13}C NMR spectra suggests that the calix[4]arene moieties in **4** and **5** each adopt cone conformations.[10] Thus, the ^{1}H NMR spectrum of **4** contains overlapping AB spin systems at δ 3.45, 4.24 and δ 3.45, 4.52, respectively, that correspond to the two different types of Ar–CH_2–Ar methylene protons. In the ^{1}H NMR spectrum of **5**, a pair of doublets (δ 3.33 and 4.36, Ar–CH_2–Ar methylene protons) and two singlets (δ 0.93 and 1.24, *tert*-butyl protons) are observed. These results suggest that the two calix[4]arene moieties in **4** and **5** remain in the cone conformation.[10]

1,3-Dimethoxy-*p*-*tert*-butylcalix[4]arene crown-5 (**11**), which contains one pyridyl unit, was prepared in four synthetic steps by starting with commercially available 2,6-bis(hydroxymethyl)pyridine (**6**) (Scheme 2). The OH groups in **6** were protected via NaH promoted reaction of this diol with $BrCH_2CH_2OTHP$,[9] thereby affording **7**. Next, the *O*-tetrahydropyranyl protecting groups were removed via treatment with *p*-TsOH. This procedure afforded **8**, which subsequently could be converted into the corresponding ditosylate (**9**). Finally, KO*t*-Bu promoted reaction of **9** with tetra-*p*-*tert*-butyl-26,28-dimethoxycalix[4]arene[5c] (**10**) afforded **11** in 53% yield (Scheme 2).

The structure of **11** was confirmed via analysis of its ^{1}H NMR and ^{13}C NMR spectra and via HRMS analysis (see Experimental). The ^{1}H NMR spectrum of **11** displays an AB spin pattern (δ 3.10 and 4.23) for the Ar–CH_2–Ar methylene protons and two distinct singlets (δ 0.85 and 1.26) for the the *tert*-butyl protons. These results suggest that the *p*-*tert*-butylcalix[4]arene moiety in **11** preferentially adopts the cone conformation.[1a]



Scheme 2. (a) $BrCH_2CH_2OTHP$, NaH, DMF, 48 h (60%); (b) *p*-TsOH, MeOH (81%); (c) *p*-TsCl, KOH, THF (80%).

Table 1. Results of alkali metal picrate extraction experiments

Host molecule	Percent of picrate extracted (%)[a]				
	Li^+	Na^+	K^+	Rb^+	Cs^+
4	0.8±0.6	6.1±0.6	8.2±0.4	3.1±0.4	1.8±0.6
5	1.7±0.5	6.7±0.5	7.2±0.4	13.9±0.5	11.7±0.7
11	3.3±0.4	8.6±0.5	40.5±0.6	32.5±0.6	6.6±0.7

[a] Averages and standard deviations calculated for data obtained from three independent extraction experiments.

Alkali Metal Picrate Extraction Studies

In an effort to investigate the complexation properties of ligands **4**, **5**, and **11**, a series of alkali metal picrate extraction experiments was performed. The results thereby obtained are shown in Table 1.

Inspection of the data in Table 1 indicates that the bis-calix[4]arenes (**4** and **5**) are inefficient alkali metal picrate extractants. Among the bis-calix[4]arenes studied, the singly-bridged bis-calix[4]arene **4** displays slightly elevated extraction avidity toward K^+ picrate; however, **4** is an inefficient extractant toward Li^+ and Cs^+ picrates. The doubly-bridged bis-calix[4]arene **5** displays slightly higher extraction avidity toward all alkali metal picrates studied in comparison with **4**, with the exception of its behavior toward K^+ picrate.

It is interesting to note that **5** displays somewhat higher extracting ability toward Rb^+ and Cs^+ picrates vis-a-vis **4**. One possible rationale for this behavior is that the double-linking of calix[4]arene moieties to pyridyl units which is present in **5** results in a more favorable conformation for complexation of large metal cations in **5** when compared with that in **4**.

The data in Table 1 indicate that 1,3-dimethoxy-*p*-*tert*-butylcalix[4]arene-pyrido-crown-5 (**11**) displays appreciable extraction avidity toward K^+ and Rb^+ picrates. However, this host displays much lower corresponding avidities toward Li^+, Na^+ and Cs^+ picrates, respectively.

In view of the improved performance of **11** as an alkali metal picrate extractant in comparison with that of **4** and **5**, we considered the possibility of converting the phenolic hydroxyl groups in the latter two compounds into OCH_3 substituents. However, KO*t*-Bu promoted reaction of a di-*O*-methyl derivative of calix[4]arene (i.e. **1b**) with **2** afforded an intractable mixture of several products from which no single, pure compound could be isolated and characterized. Other attempts to *O*-methylate the phenolic OH groups in **5** by using standard procedures, i.e. (i) $(MeO)_2SO_2$–K_2CO_3 in acetone or (ii) NaH–THF followed by treatment with CH_3I were not successful.

Table 2. Calculated (MMFF Force Field)[13] complexation energies for complexes of **5** and of **11** with alkali metal cations

Host Molecule	Li^+	Na^+	K^+	Rb^+
5	3.3	11.9	24.0	12.8
11	–	–	61.5	–

Results of Complexation Energy Calculations

Coordination studies of (i) **5** with Li^+, Na^+, K^+ and Rb^+ and (ii) **11** with K^+ were performed with gas-phase molecular mechanics calculations in SPARTAN®[11] by utilizing the Merck force field (MMFF)[12] and Monte Carlo conformational searches. Complexation energies were determined as the difference between the sum of the total energies of the host molecule (ligand) and that of the complex (ligand·M^+). The lowest energy complex was arrived at by manually docking the cation to various combinations of heteroatom donors within the host molecule.

The complexation energies thereby obtained are shown in Table 2. The results obtained for complexation of **5** suggests host–guest complex stability decreases in the order $K^+ > Rb^+$, $Na^+ > Li^+$. By way of contrast, our experimental picrate extraction results obtained by using **5** (Table 1) indicate the following order of decreasing host–guest complex stability: $Rb^+ > Na^+$, $K^+ > Li^+$. However, the significantly larger value calculated for **11**·K^+ complexation energy is qualitatively consistent with the experimental results shown in Table 1 for **11**.

Results of Molecular Modeling Studies

The appearance of the geometry-optimized structure of **5** suggests that potentially destabilizing nitrogen lone-pair interactions which occur when the pyridine moieties lie in a 'head-to-head' (coplanar) arrangement are reduced when the pyridine rings are mutually skewed. This 'twisting' results in minor defomation of the attached calix[4]arene moieties, with the result that the binding sites within **5** become exposed to the approaching cation guest.

The geometry-optimized structures that correspond to the lowest energy conformations of complexes of **5** with Li^+, Na^+, and K^+, respectively, indicate the existence of M^+ binding only to the pyridine ring nitrogens. Our attempts to direct coordination of the cation guest to additional Lewis base sites in host **5** resulted in a significant increase in complexation energy.

The energy-minized structure of **5**·Rb^+ is shown in Fig. 1. This structure reveals that Rb^+ is stabilized via coordination to the two pyridine ring nitrogen atoms and also to two hydroxyl groups in each of the two adjacent calix[4]arene moieties. This additional coordination lowers the energy of complex **5**·Rb^+ by ca. 10 kcal mol^{-1} relative to that of the corresponding complex in which Rb^+ is stabilized only via coordination to the two pyridine ring nitrogen atoms in **5**. It was also found that in the case of the smaller alkali metal cations, our attempts to impose additional coordination of M^+ to calix[4]arene OH groups results in severe bending of the calix[4]arene rings, with the result that C–H bonds situated in the upper rim *t*-butyl groups become forced into close proximity with an adjacent pyridine ring, thereby producing significant steric destabilization in the resulting **5**·M^+ complex. Consistent with this conclusion, for situations in which M^+ is docked to six heteroatoms in the complex **5**·M^+, we find that the calculated total energy of the complex decreases with increasing size of the alkali

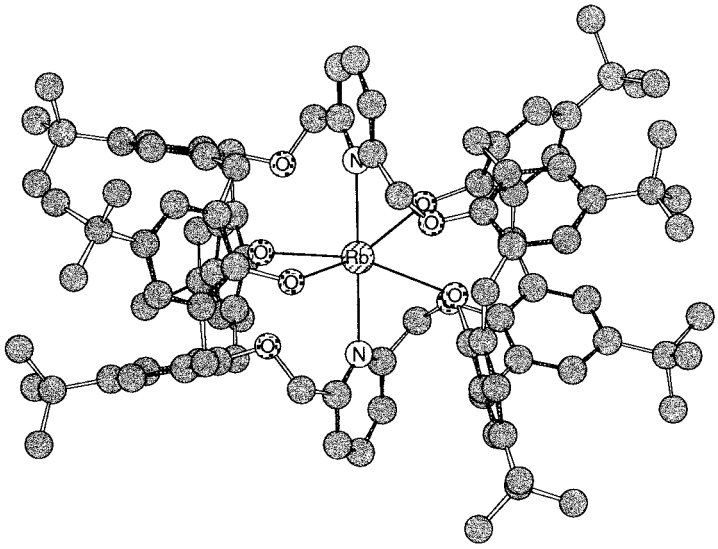


Figure 1. Geometry-optimized structure of **5**·Rb^+. Hydrogen atoms have been omitted for clarity. Calculated bond lengths in **5**·Rb^+: Rb–O, 2.83 Å; Rb–N, 2.77 Å.

metal cation guest. Importantly, our results suggest that **5** contains a clearly defined cavity wherein the cation guest resides in the **5**·M^+ complex.

The corresponding energy-minized structure of **11**·K^+ is shown in Fig. 2. Here, it can be seen that K^+ binds to the pyridine ring nitrogen atom and also to both ether oxygen atoms at the lower rim of the adjacent calix[4]arene moiety. When coordination of K^+ is restricted only to the pyridine ring nitrogen atom in the **11**·K^+ complex, the calculated complexation energy is reduced to only ca. 25 kcal mol.

Summary and Conclusions

Novel pyridyl containing calix[4]arene receptors (**4**, **5**, and **11**) were prepared. Inspection of their respective ^1H NMR and ^{13}C NMR spectra suggests that calix[4]arene moieties in **4**, **5**, **11** occupy the cone conformation. The complexation properties of these host molecules were estimated via the results of alkali metal picrate extraction experiments.

Among the three host systems studied, only the doubly-bridged bis-calix[4]arene **5** displays significant avidity toward complexation with K^+ and Rb^+ picrates. The singly-bridged bis-calix[4]arene **4** is not an efficient host toward alkali metal picrates, although it displays slightly elevated extraction avidity toward K^+ picrate. The results presented herein do not provide compelling evidence that cooperativity exists among the two calix[4]arene moieties and the pyridyl unit(s) in **4** and **5** when they function as donor ligands toward alkali metal cation guests.

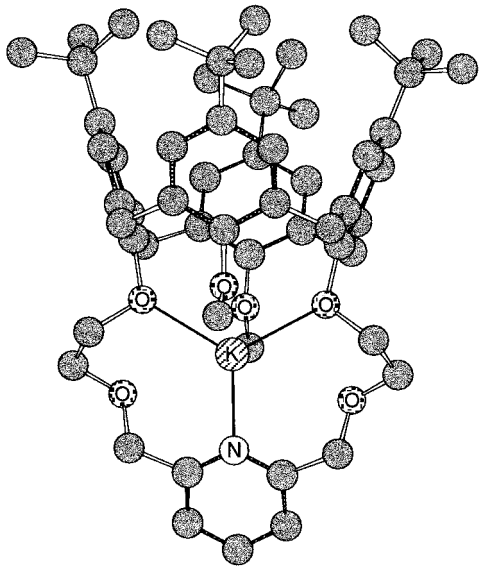


Figure 2. Geometry-optimized structure of **11**·K^+. Hydrogen atoms have been omitted for clarity. Calculated bond lengths in **11**·K^+: K–O, 2.52 Å; K–N, 2.47 Å.

Experimental

Melting points are uncorrected. Absorption intensities of alkali metal picrate solutions were measured at λ=374 nm by using a Hewlett-Packard Model 84524 Diode Array UV-visible spectrophotometer. High-resolution mass spectral data reported herein were obtained by Professor Jennifer S. Brodbelt at the Mass Spectrometry Facility at the Department of Chemistry and Biochemistry, University of Texas at Austin by using a ZAB-E double sector high-resolution mass spectrometer (Micromass, Manchester, England) that was operated in the chemical ionization mode.

Base promoted reaction of 1a with 2. Method A

A solution of **1a** (738 mg, 1.00 mmol) and KO*t*-Bu (112 mg, 1.00 mmol) in dry $PhCH_3$ (15 mL) under argon was heated to reflux. To this refluxing solution was added dropwise with stirring a solution of 2,6-bis(bromomethyl)pyridine (**2**, 265 mg, 1.00 mmol) in dry benzene (15 mL) during 45 min. After all of this reagent had been added, the resulting mixture was refluxed during 24 h, at which time a

second portion of KO*t*-Bu (112 mg, 1.00 mmol) was added, and the resulting mixture was refluxed for an additional 24 h. The reaction mixture was allowed to cool gradually to ambient temperature, and H_2O (10 mL) then was added. The layers were separated, and the aqueous layer was extracted with $CHCl_3$ (3×30 mL). The combined organic layers were washed with water (20 mL), dried ($MgSO_4$), and filtered, and the filtrate was concentrated in vacuo. The residue was purified via column chromatography on silica gel by eluting with 10% EtOAc–hexane. Pure **4** (350 mg, 25%) was thereby obtained as a colorless microcrystalline solid: mp 249–251°C; IR (KBr) 3423 (br, s), 2961 (s), 1603 (m), 1489 (m), 1363 (m), 1192 (m), 1092 (m), 1048 (s), 841 cm^{-1} (m); ^1H NMR ($CDCl_3$) δ 1.24 (s, 72H), 3.45 (d, J=14.6 Hz, 8H), 4.24 (*A*B, J_{AB}=14.2 Hz, 4H), 4.52 (A*B*, J_{AB}=14.6 Hz, 4H), 5.40 (s, 4H), 6.92–7.16 (m, 16H), 8.03 (d, J=7.8 Hz, 2H), 8.13 (t, J=7.3 Hz, 1H), 9.43 (s, 4H), 10.12 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 31.2 (q), 31.5 (t), 32.3 (q), 33.0 (s), 33.8 (s), 34.0 (s), 34.2 (t), 78.7 (t), 122.3 (d), 125.6 (d), 126.5 (d), 127.4 (d), 128.1 (d), 128.3 (d), 133.6 (d), 138.6 (d), 143.0 (s), 143.5 (s), 147.8 (d), 148.1 (d), 148.4 (d), 149.7 (d), 155.8 (s), 158.3 (s). Exact mass (CI HRMS) Calcd for $C_{95}H_{117}NO_8$: $[M_r+H]^+$ *m/z* 1399.8779. Found: $[M_r+H]^+$ *m/z* 1399.8753.

Continued elution of the chromatography column afforded **5** (90 mg, 6%) as a colorless microcrystalline solid: mp 241–244°C; IR (KBr) 3354 (br, s), 2961 (s), 2870 (m), 1595 (m), 1482 (s), 1352 (m), 1205 (s), 1124 (m), 1012 (m), 879 cm^{-1} (m); ^1H NMR ($CDCl_3$) δ 0.93 (s, 36H), 1.24 (s, 36H), 3.33 (*A*B, J_{AB}=13.3 Hz, 8 H, $ArCH_2Ar$), 4.36 (A*B*, J_{AB}=13.3 Hz, 8H, $ArCH_2Ar$), 5.18 (s, 8H), 6.86 (s, 8H), 7.03 (s, 8H), 7.21 (s, 4H), 7.90 (t, J=8.5 Hz, 2H), 8.16 (d, J=8.9 Hz, 4H); ^{13}C NMR ($CDCl_3$) δ 31.5 (q), 32.2 (q), 34.3 (t), 34.4 (s), 78.7 (t), 120.5 (d), 125.5 (d), 126.1 (d), 128.0 (d), 128.2 (d), 132.9 (s), 139.2 (d), 142.0 (s), 147.5 (s), 150.5 (d), 151.2 (d), 157.5 (s), 158.3 (s). Exact mass (CI HRMS) Calcd for $C_{102}H_{122}N_2O_8$: $[M_r+H]^+$ *m/z* 1503.9280. Found: $[M_r+H]^+$ *m/z* 1503.9319.

Method B

A solution of **1a** (738 mg, 1.00 mmol), **2** (265 mg, 1 mmol), and K_2CO_3 (550 mg, 4.00 mmol) in CH_3CN (25 mL) was refluxed with stirring during 4 days. The reaction mixture was allowed to cool gradually to ambient temperature and then was filtered, and the filtrate was concentrated in vacuo. The residue was purified via column chromatography on silica gel by eluting with 10% EtOAc–hexane. Pure **5** (450 mg, 30%) was thereby obtained as a colorless microcrystalline solid: mp 241–244°C. The IR, ^1H NMR, and ^{13}C NMR spectra of the material thereby obtained are essentially identical with the corresponding spectral data reported above for authentic **5**.

Preparation of 7

A suspension of NaH (60% dispersion in mineral oil, 960 mg, 20.0 mmol) in dry DMF (14 mL) under argon was cooled to 0°C via application of an external ice–water bath. To this cooled solution was added dropwise with stirring a solution of 2,6-pyridinedimethanol (**6**, 1.39 g, 10.0 mmol) in DMF (14 mL). The resulting white suspension was stirred at 0°C for 10 min, at which time the external ice–water bath was removed, and the reaction mixture was allowed to warm gradually to ambient temperature while stirring during 2 h. The reaction mixture again was cooled to 0°C via application of an external ice–water bath. To the cooled reaction mixture was added dropwise with stirring a solution of 1-(*O*-tetrahydropyranyl)-2-bromoethane (4.16 g, 20.0 mmol) in DMF (14 mL). The resulting suspension was stirred at 0°C for 10 min, at which time the external cold bath was removed, and the reaction mixture was allowed to warm gradually to ambient temperature and was stirred at that temperature for 72 h. The reaction mixture was concentrated in vacuo, and ice–water (50 mL) was added to the residue. The resulting aqueous suspension was extracted with CH_2Cl_2 (3×40 mL). The combined organic layers were dried ($MgSO_4$) and filtered, and the filtrate was concentrated in vacuo. The residue was purified via column chromatography on silica gel by using a 10–50% EtOAc–hexane gradient elution scheme. Pure **7** (2.67 g, 67%) was thereby obtained as a colorless, viscous oil; IR (film) 3028 (w), 2945 (s), 2873 (s), 1638 (s), 1448 (w), 1337 (w), 1118 (s), 1064 (m), 1027 (w), 782 (w), 639 cm^{-1} (w); ^1H NMR ($CDCl_3$) δ 1.42–1.96 (m, 12H), 3.42–4.01 (m, 12H), 4.8 (m, 6H), 7.3 (d, J=8.8 Hz, 2H), 7.61 (t, J=7.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 19.8 (t), 25.9 (t), 31.0 (t), 62.6 (t), 67.1 (t), 70.3 (t), 74.5 (t), 99.3 (s), 120.3 (d), 137.5 (d), 158.1 (s). Exact mass (CI HRMS) Calcd for $C_{21}H_{33}NO_6$: $[M_r+H]^+$ *m/z* 396.2386. Found: $[M_r+H]^+$ *m/z* 396.2392.

Preparation of 8

To a solution of **7** (320 mg, 0.81 mmol) in MeOH (8 mL) was added TsOH (50 mg), and the resulting mixture was stirred at ambient temperature during 24 h. The reaction mixture was filtered, and the filtrate was concentrated in vacuo. The residue was purified via column chromatography on basic alumina by eluting with MeOH. Pure **8** (810 mg, 81%) was thereby obtained as a colorless viscous oil; IR (film) 3868 (br, s), 3029 (s), 2878 (s), 1723 (s), 1652 (s), 1591 (m), 1454 (s), 1117 (s), 1068 (s), 766 (w), 632 cm^{-1} (w); ^1H NMR ($CDCl_3$) δ 3.51–3.70 (m, 8H), 4.50 (s, 4H), 7.16 (d, J=8.7 Hz, 2H), 7.54 (t, J=7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 60.6 (t), 72.5 (t), 72.7 (t), 120.1 (d), 137.2 (d), 157.5 (s). Exact mass (CI HRMS) Calcd for $C_{11}H_{17}NO_4$: $[M_r+H]^+$ *m/z* 228.1236. Found: $[M_r+H]^+$ *m/z* 228.1238.

Preparation of 9

To a solution of **8** (290 mg, 1.29 mmol) in dry THF (2 mL) was added finely pulverized KOH (230 mg, 3.68 mmol). The mixture was cooled to 0°C via application of an external ice–water bath. To the resulting mixture was added dropwise with stirring a solution of TsCl (freshly recrystallized from hexane, 560 mg, 2.95 mmol) in dry THF (3 mL) at 0°C under argon. The resulting mixture was stirred at 0°C during 5 h, at which time the external ice–water bath was removed, and the reaction mixture was allowed to warm gradually to ambient temperature while stirring during 12 h. The resulting mixture was filtered, and the residue was washed with THF (10 mL). The combined filtrates were concentrated in vacuo. The residue was purified via column chromatography

on silica gel by eluting with 50% EtOAc–hexane. Pure **9** (480 mg, 80%) was thereby obtained as a colorless oil (480 mg, 80%); IR (film) 3053 (m), 2898 (m), 1625 (w), 1352 (m), 1176 (s), 1029 (m), 1012 (m), 919 (m), 814 (m), 782 (m), 677 cm^{-1} (m); ^1H NMR ($CDCl_3$) δ 2.34 (s, 6H), 3.80 (t, J=10.3 Hz, 4H), 4.21 (t, J=8.7 Hz, 4H), 4.54 (s, 4H), 7.15–7.32 (m, 6 H), 7.51 (t, J=6.8 Hz, 1 H), 7.73 (d, J=8.1 Hz, 4 H); ^{13}C NMR ($CDCl_3$) δ 20.7 (q), 67.74 (t), 68.6 (t), 73.3 (t), 119.5 (d), 127.4 (d), 129.3 (d), 136.2 (s), 138.3 (d), 142.1 (s), 156.4 (s). This material was observed to be somewhat unstable; accordingly, it was used immediately as obtained in the next synthetic step.

Preparation of 11

A solution of **10** (125 mg, 0.19 mmol) and KO*t*–Bu (11 mg, 0.18 mmol) in dry $PhCH_3$ (15 mL) was heated to reflux. To this refluxing solution was added dropwise with stirring a solution of **9** (89 mg, 0.19 mmol) in dry benzene (5 mL) during 0.5 h. The resulting mixture was refluxed for 24 h, at which time a second portion of KO*t*–Bu (20.7 mg, 0.19 mmol) was added, and the reaction mixture was refluxed for an additional 24 h. The reaction mixture was allowed to cool gradually to ambient temperature, and H_2O (10 mL) then was added. The layers were separated, and the aqueous layer was extracted with $CHCl_3$ (3×20 mL). The combined organic layers were washed with water (20 mL), dried ($MgSO_4$), and filtered, and the filtrate was concentrated in vacuo. The residue was purified via column chromatography on silica gel by eluting with 20% EtOAc–hexane. Pure **11** (85 mg, 53%) was thereby obtained as a colorless, viscous oil; IR (KBr) 3423 (br, s), 2961 (s), 1653 (m), 1603 (m), 1559 (m), 1468 (m), 1363 (m), 1222 (m), 1118 (m), 1032 (s), 882 cm^{-1} (m); ^1H NMR ($CDCl_3$) δ 0.85 (s, 18H), 1.26 (s, 18H), 3.10 (*A*B, J_{AB}=12.3 Hz, 4H), 3.60 (s, 6 H), 3.87–4.08 (m, 8 H), 4.23 (*A*B, J_{AB}=12.3 Hz, 4 H), 4.75 (s, 4H), 6.45 (s, 4H), 7.13 (s, 4H), 7.33 (d, J=8.5 Hz, 2H), 7.65 (t, J=7.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ(31.5 (q), 31.6 (t), 32.2 (q), 34.5 (s), 61.3 (q), 71.7 (t), 73.9 (t), 76.0 (t), 123.4 (d), 124.8 (d), 125.4 (d), 133.1 (s), 136.2 (s), 137.5 (d), 145.2 (s), 152.6 (s), 156. 3 (s), 157.7 (s, 2 C). Exact mass (CI HRMS) Calcd for $C_{57}H_{73}O_6N$: $[M_r+H]^+$ m/z 868.5516. Found: $[M_r+H]^+$ m/z 868.5525.

Alkali metal picrate extraction experiments

The extraction experiments were performed by using 5 mM solutions of each compounds in $CHCl_3$. The procedure that was used for this purpose has been described previously.[13]

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