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Calix[4]quinones Derived from Double Calix[4]arenes: Synthesis, Complexation, and Electrochemical Properties toward Alkali Metal Ions

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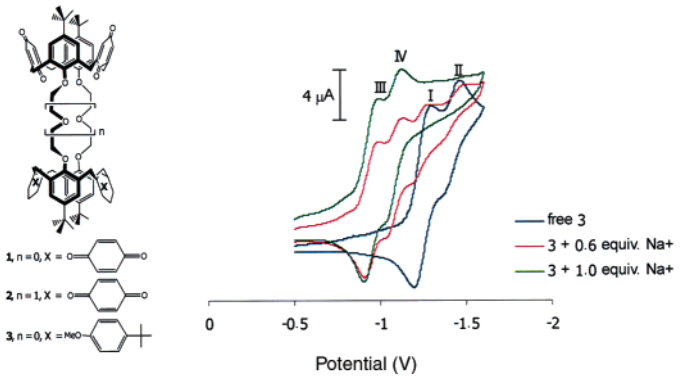

Bis(calix[4]diquinones) **1** and **2** and double calix[4]diquinone **3** have been synthesized from their corresponding double calix[4]arenes **4**, **5**, and **6**, respectively. Compounds **4**−**6** have been prepared from one-pot and stepwise syntheses under high pressure. Complexation studies of ligands **1**−**3** with alkali metal ions such as Li^+, Na^+, K^+, and Cs^+ were carried out by ^1H NMR titrations. Receptors **1** can selectively form 1:1 complexes with Na^+. Ligand **2** prefers to form 1:1 complexes with K^+ and Cs^+. Receptor **3** retained the cone conformation of the calix[4]arene unit upon binding K^+ but changed the conformation when complexing Li^+ and Na^+. Electrochemical studies using cyclic voltammetry and square wave voltammetry showed significant changing of voltammograms of **2** and **3** in the presence of alkali metal ions. Receptor **3** showed the electrochemically switched binding property toward Na^+ and K^+.

Introduction

Alkali metal ions such as Na^+ and K^+ are found in human organisms and found their importance in ion channels and ion pumps.[1] The great importance of the cations mentioned is also evident from the fact that disorders in the metabolism of these ions can severely affect the state of health. Radioactive cesium ion is found in nuclear waste solutions.[2] Therefore, detection or sensing of these metal ions is crucial to health and environmental concerns. Typically, a chemical sensor comprises two important parts: a receptor unit or an ionophore and a signaling unit.[3] Receptors for alkali metal ions can be either naturally occuring ionophores such as valinomycin or synthetic polyether-type receptors such as crown ethers and their derivatives.[4] Signaling units frequently used by chemists are ferrocene and *p*-quinone.[5−8]

Calix[4]arene is one of the most versatile molecular building blocks suitable for attaching both receptor and sensory units on the same molecules.[9] Many calix[4]arene derivatives containing ferrocene[5,6] and *p*-quinone[7,8] have

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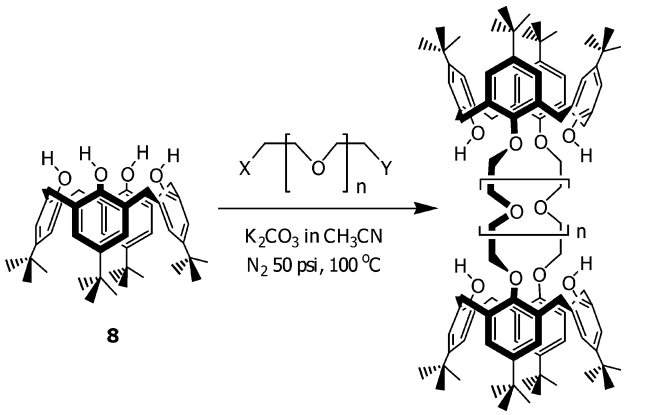
been synthesized, and their binding and sensing properties toward metal ions and anions have been studied. However, calix[4]quinones in particular have a superior property over ferrocene for the direct connection to the calixarene framework. Therefore, one can design and construct a molecular sensor from calix[4]quinones using its available oxygen atoms as donors for binding alkali cations.[10,11] Recently, a number of double calixarenes have been prepared and their binding studies with metal ions have been reported.[12,13] Shinkai and co-workers synthesized a series of double calix[4]arenes, each of which contains four ester or four ether groups. It was detected by variable-temperature ^{1}H NMR spectroscopy that alkali metal ions jumped between two metal-binding sites in the NMR time scale.[14−16] It is of interest to synthesize different double calix[4]arenes using ethylene glycol and diethylene glycol bridges connecting lower rim phenoxy groups. The substituents at the other *o*-phenoxy groups can also be varied to obtain a symmetric or a unsymmetric double calix[4]arene. Upon oxidation, we expect to obtain various kinds of double calix[4]quinones possessing a different number and various positions for the quinone moieties.

In this paper, we report the syntheses of three new calix[4]quinones, **1**−**3**. Complexation studies of receptors **1**−**3** with alkali metal ions such as Li^+, Na^+, K^+, and Cs^+ are investigated by means of ^{1}H NMR titrations. Electrochemical properties of the compounds in nonaqueous solutions in the absence and in the presence of alkali metal ions are studied by cyclic and square wave voltammetry.

Results and Discussion

Synthesis. The method to synthesize double calix[4]arene **4** was first reported by Tomapatanaget et al. in 1998 by nucleophilic substitution reactions of *p-tert*-butylcalix[4]arene with bromoethyl tosylate using anhydrous potassium carbonate as base and yielded **4** in 41%.[17] Janssen et al. found that use of pressure for selective alkylation of calix[6]arene resulted in a high yield of the alkylated products.[18] Ostaszewski and Jurczak also reported use of high pressure in the synthesis of simple and chiral bicyclic cryptands and diazacoronands that produced the desired products in high yield.[19]

SCHEME 1. Synthesis of Double Calix[4]arenes 4 and 5



Recently, our group applied high pressure in the coupling reaction and improved the yield of **4** to 69% (Scheme 1).[20]

Another biscalix[4]arene, **5**, possessing diethylene glycol as bridging groups can be synthesized by adapting the synthetic pathway reported by Asfari et al.[21] The coupling reaction of diethylene glycol ditosylate with *p-tert*-butylcalix[4]arene **8** in acetonitrile using anhydrous potassium carbonate as base and 18-crown-6 as phase transfer catalyst was carried out in a high-pressure tube compressed with N_2 at 50 psi (Scheme 1). Double calix[4]arene **5** was obtained in 14% yield as a white crystalline solid.

A number of bis(calix[4]diquinone) receptors have been synthesized by Beer and co-workers. Interestingly, these receptors can possibly be used as electrochemical sensor for Cs^+ and Rb^+.[22] We are interested in preparing unsymmetric biscalix[4]arenes for further fabrication to double calix[4]quinones having different quinone moieties. However, this will need stepwise synthetic approaches. Compound **6** can be prepared in a stepwise manner as shown in Scheme 2.

Compound **6** was first synthesized from *p-tert*-butylcalix[4]arene (**8**). The reaction pathway proceeded through compounds **10**, **12**, and **14** as reported previously.[20] Then, the coupling reaction of **14** and **9** in THF using NaH as base resulted in the unsymmetric double calix[4]arene **6** in 18% yield. We found later that the main product of this reaction was compound **7** (78%) resulted from intramolecular cyclization. ^{1}H and ^{13}C NMR spectra of **7**[23] showed characteristic peaks due to 1,2-alternate conformation.[24,25] This conformation was rare and usually obtained from synthesis in limited yields.[26]

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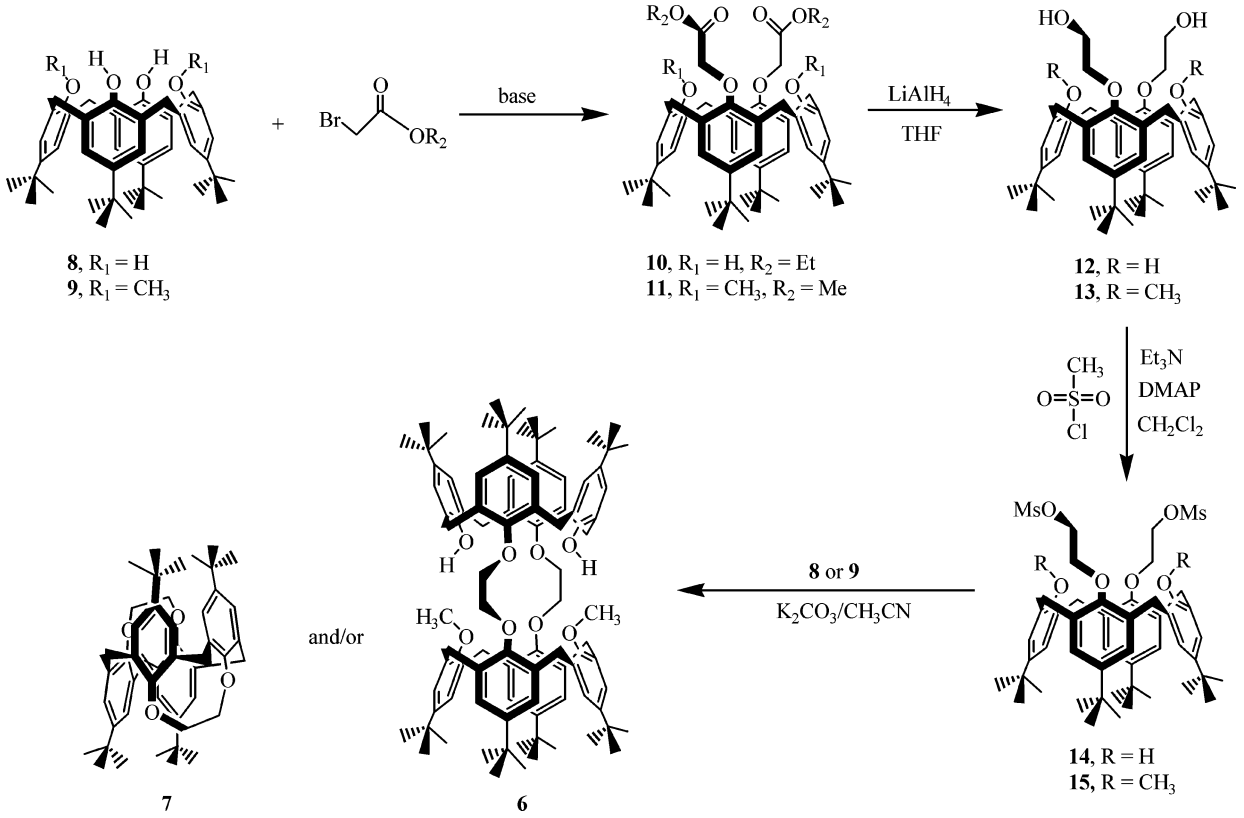
(23) Characterization for compound **7**: mp > 300 °C dec; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ippm) 7.06, 6.96 (m, 8H, RAr*H*), 4.57 (d, 2H, ArC*H*$_2$Ar axial), 4.05 (s, 4H, ArC*H*$_2$Ar), 3.58 (m, 4H, ArOC*H*$_2$-C*H*$_2$O), 3.32 (d, 2H, ArC*H*$_2$Ar equatorial), 3.14 (m, 4H, ArOC*H*$_2$-C*H*$_2$O), 1.25 (s, 36H, HOAr-*t*-C$_4$*H*$_9$); ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 153.10, 144.88, 134.73, 132.80, 125.21, 70.64, 34.19, 34.08, 31.46; FAB mass (*m*/*z*) 701 [$M^+ + H^+$].
(24) Arduini, A.; Domiano, L.; Pochini, A.; Secchi, A.; Ungaro, R.; Ugozzoli, F.; Struck, O.; Verboom, W.; Reinhoudt, D. N. *Tetrahedron* **1997**, *53*, 3767.

SCHEME 2. Stepwise Synthesis of Unsymmetric Double Calix[4]arene 6

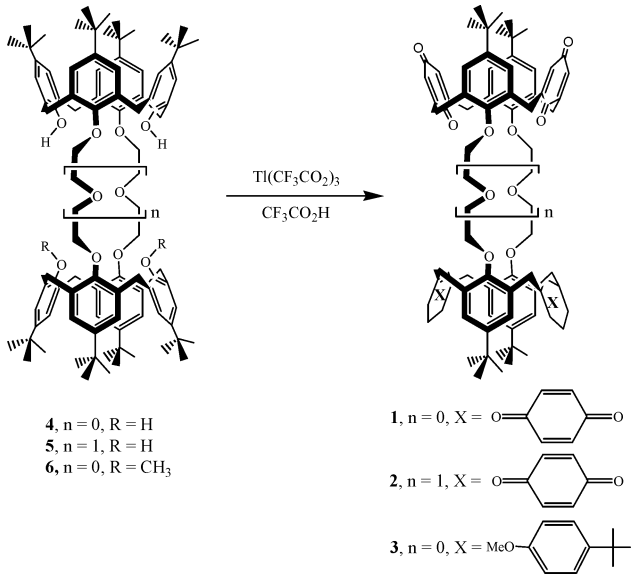


We, therefore, tried to improve the yield of **6** by starting from dimethoxy calixarene **9** to avoid intramolecular alkylation. Substitution of **9** with 3.0 equiv of methyl bromoacetate in the presence of 3.0 equiv of sodium hydride as base in dried tetrahydrofuran resulted in tetrasubstituted product **11** as a white powder in 80% yield. The diester product **11** was then reduced by 5 equiv of $LiAlH_4$ in dried THF to afford an alcohol derivative **13** as a white powder in 82% yield. The hydroxy protons of alcohol derivative **13** then underwent nucleophilic substitution with methanesulfonyl groups by treatment with 10 equiv of triethylamine and a catalytic amount of DMAP in dichloromethane. A white powder of **15** was obtained in 88% yield. Finally, the coupling reaction between the tetrasubstituted methane sulfonyl derivative **15** and *p-tert*-butylcalix[4]arene **8** in the presence of 2.5 equiv of anhydrous potassium carbonate as base in dried acetonitrile with a catalytic amount of 18-crown-6 as phase transfer was done by using the high-pressure technique. The reaction tube was compressed with nitrogen at 50 psi and heated at 80 °C for 4 days to give the unsymmetric double calix[4]arene **6** in 52% yield.

Double calix[4]arenes **4**−**6** were then transformed to their quinone derivatives as shown in Scheme 3 by using $Tl(CF_3CO_2)_3$ in CF_3CO_2H as oxidizing reagent in darkness under nitrogen. The final products **1**, **2** ,and **3** were obtained as yellow crystalline solids in 52%, 68%, and 38% yields, respectively.

Complexation Studies with Alkali Metal Ions. The complexation of ligands **1**, **2**, and **3** toward alkali metal ions can be studied by ^1H NMR titrations. ^1H NMR

SCHEME 3. Synthesis of Calix[4]quinones 1−3



spectra of the complexes suggest that all three receptors form complexes with alkali metal ions in a slow-exchange manner. Generally, addition of alkali metal ions such as Li^+, Na^+, and K^+ to the solution ($CDCl_3$) of **1** and **2** lowers the intensity of the signals due to aromatic and quinone protons and generates a new set of aromatic and quinone proton signals. The new doublet signal of methylene bridge protons of the calixarene unit in a complex arose in the spectrum while doublet signals of the methylene bridge protons of the free ligand disappeared. After addition of 1.0 equiv of the metal salt, the signal of aromatic protons and quinone protons of the free ligand

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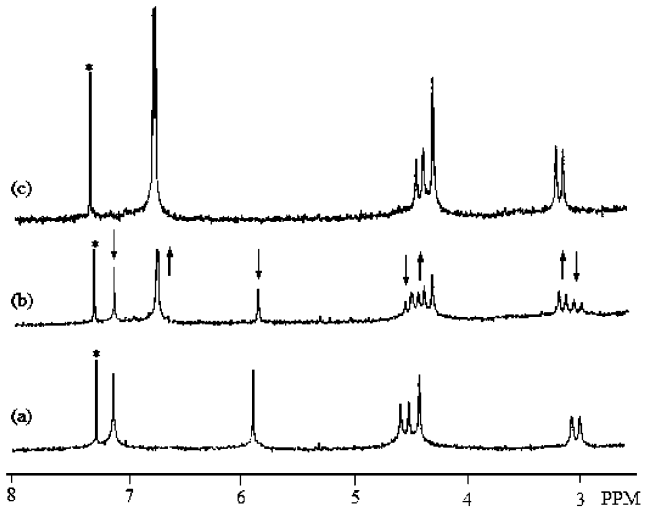

FIGURE 1. ^{1}H NMR spectra of (a) free **1** (b) **1** + 0.5 equiv of Na^+ and (c) **1** + 1.0 equiv of Na^+. * denotes the solvent peak.

totally disappeared and two new signals of aromatic and quinone protons of the complex were found instead. Addition of more than 1.0 equiv of the metal ion resulted in no change of the spectra. This indicated that **1** and **2** commonly formed complexes with alkali metal ions in a 1:1 stoichiometry.

Figure 1 illustrates ^{1}H NMR spectra of compound **1** upon addition of Na^+ in $CDCl_3$. The intensity of the signal of aromatic protons at 7.11 ppm and the signal of quinone protons at 5.88 ppm decreases while two new signals appear at 6.76 and 6.80 ppm. When 1.0 equiv of $NaClO_4$ was added, the signals of aromatic protons and quinone protons completely disappeared and only new signals at 6.76 and 6.80 ppm were found in the ^{1}H NMR spectrum. The signal of the glycolic chain at 4.42 ppm shifted upfield to 4.31 ppm. The doublet signals of the methylene bridge protons of the free ligand at 4.52 and 3.00 ppm also disappear and emerged at 4.42 and 3.20 ppm instead. Addition of more than 1.0 equiv of Na^+ showed no change of the spectra.

Titration experiments of **1**, **2**, and **3** with $CsPF_6$ in $CDCl_3$ were also carried out. Interestingly, it was found that in cases of **1** and **3** no new signal was observed in ^{1}H NMR spectra. The result showed that **1** and **3** cannot form complexes with cesium ion. Only compound **2** can form a complex with Cs^+ in a slow exchange manner (see the Supporting Information).

It should be noted that the calix[4]arene unit in free **3** stays in a cone conformation (Figure 2a). In the presence of 1 equiv of Li^+ and Na^+, ^{1}H NMR spectra of the complexes showed complicate signals in the aromatic and methylene bridge regions suggesting a slow conformation exchange of the calix[4]arene dimethoxy units which lack of intramolecular hydrogen bonding (Figure 2b,c) resulted in mixed conformations. However, in the presence of K^+ only two sets of methylene bridge protons and three sets of aromatic protons are found in the spectrum (Figure 2d) indicating that the calix[4]arene unit is in the cone conformation. This conformation behavior is also pertinent to that of 1,3-dimethyl-*p-tert*-butylcalix[4]arene-crown-5 where the free ligand was reported to be in a cone conformation.[27] Upon complexing with K^+, the calix[4]arene framework became a flattened partial cone conformation.[28] Shinkai[29] and Kochi[30] also reported the effect of Ag^+ and NO^+, respectively, to the conformation of the calix[4]arene frameworks.

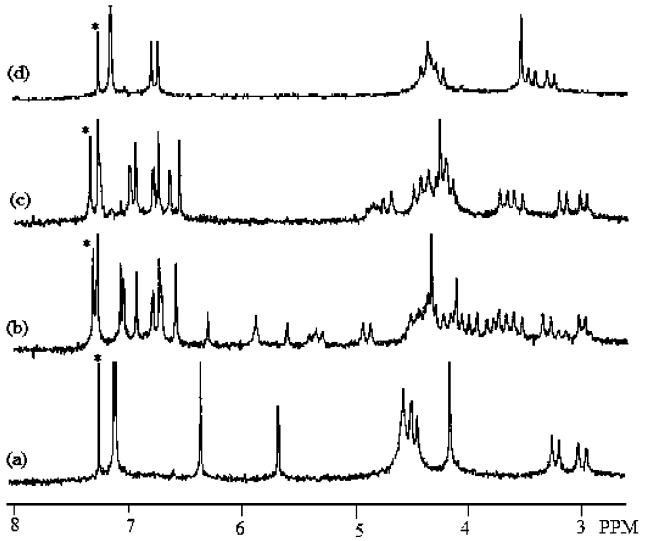

FIGURE 2. ^{1}H NMR spectra of (a) free **3** (b) **3** + 1 equiv of Li^+ (c) **3** + 1 equiv of Na^+ (d) **3** + 1 equiv of K^+. * denotes the solvent peak.

TABLE 1. Association Constants of 1−3 toward Various Alkali Metal Ions[a]

	association constant (M^{-1})		
metal ions	**1**	**2**	**3**
Li^+	30415	897	*b*
Na^+	44335	9771	*b*
K^+	1421	12993	458
Cs^+	*c*	13748	*c*

[a] Experiments were carried out in 4:1 $CDCl_3/CD_3CN$. [b] Association constant cannot be calculated due to mixed conformations. [c] No complexation was observed.

Since both complexes and free species of compounds **1**, **2**, and **3** are distinguishable in ^{1}H NMR spectra, binding constants can thus be determined by direct integration of host and complex resonances in ^{1}H NMR spectra as described by Macomber.[31] Association constants of **1**, **2,** and **3** toward various alkali metal ions are presented in Table 1.

According to the results shown in Table 1, receptor **1** shows high selectivity to Na^+ probably due to the optimal spatial fit of Na^+ within the cavity of the ligand. Furthermore, both ligands **1** and **3** exhibit low complexation constants with K^+ and no complexation with Cs^+ due to limited cavity size. In the case of ligand **2**, it forms the most stable complexes with K^+ and Cs^+ and the least

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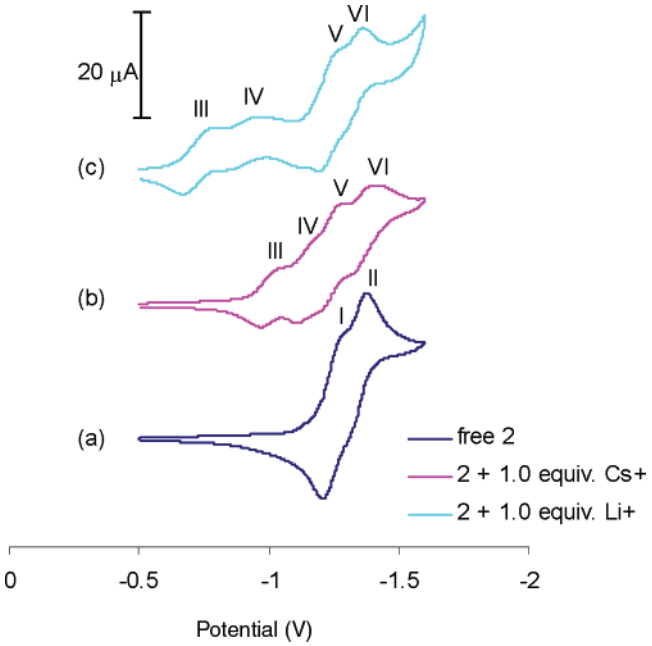


FIGURE 3. Cyclic voltammograms of (a) free **2**, (b) **2** + 1.0 equiv of Cs^+ (c) **2** + 1.0 equiv of Li^+.

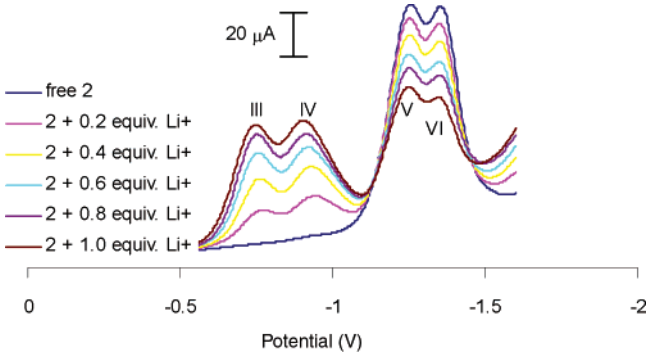


FIGURE 4. Square wave voltammograms of **2** in the presence of Li^+.

stable complex with Li^+ because of its large cavity. We expect that **1**, **2**, and **3** would exhibit interesting electrochemical recognition toward Li^+, Na^+, K^+, and Cs^+. These electrochemical properties are explored by cyclic and square wave voltammetry.

Electrochemical Studies. The electrochemistry of compounds **1**−**3** was investigated in 4:1 CH_2Cl_2/CH_3CN. Cyclic voltammograms of receptor **2** are presented in Figure 3a. Compound **2** exhibits clearly two redox waves at −1269 and −1370 mV assigned as I/I′ and II/II′. Although we scanned up to 2000 mV, no further redox wave was observed.[32] These two waves are the potential due to two two-electron-transfer processes.[22] Addition of Cs^+ and Li^+ (1 equiv) to electrochemical solutions of **2** led in all cases to the evolution of four new redox waves as shown in parts b and c, respectively, of Figure 3. Two of the new couples III/III′ and IV/IV′ are substantially anodic shifted as compared to the original waves I/I′ and II/II′. The other two new couples, V/V′ and VI/VI′, occur at a potential similar to that of I/I′ and II/II′. Square wave voltammograms of **2** in the presence of Li^+ in Figure 4 clearly show the disappearance of waves I and II and the emergence of III, IV, V, and VI. Half-wave potentials of couples III/III′, IV/IV′, V/V′, and VI/VI′ of **2** in the presence of 1 equiv. of Li^+, Na^+, K^+, and Cs^+ are summarized in Table 2. The magnitude of the anodic shifts of the redox couple III/III′ and IV/IV′ reflects the polarizing power of the cation involved. Li^+ produces the largest shift while Cs^+ gives the smallest. The cyclic voltammogram of ligand **1** shows unresolved waves probably due to the insolubility of this compound in the solvent system used. Addition of Li^+, Na^+, and K^+ to the solutions of **1** leads to the evolution of broad redox waves which redox potentials can hardly be assigned.

TABLE 2. Redox Waves of 2 upon Addition of 1 Equiv of Li^+, Na^+, K^+, and Cs^+[a]

	redox couples (mV)					
compd	I/I′	II/II′	III/III′	IV/IV′	V/V′	VI/VI′
free **2**	−1236	−1337				
2 + Li^+			−718	−900	−1224	−1332
2 + Na^+			−876	−1010	−1196	−1313
2 + K^+			−984	−1118	−1255	−1368
2 + Cs^+			−996	−1133	−1237	−1364

[a] Experiments were carried out in 4:1 CH_2Cl_2/CH_3CN using Ag/$AgNO_3$ as reference electrode and $TBAPF_6$ as supporting electrolyte.

In light of Beer's model of electrochemical reduction of the bis(calix[4]diquinone) compounds,[22] electrochemical recognition behavior of receptors **2** and **3** toward metal ions can be rationalized. The first step involves complexation of the cation by the ligand. Second, electron transfer to one of the calix[4]diquinone groups proceeds leading to the complex cation moves to the reduced end. These two reductions account for waves III/III′ and IV/IV′. In the last step, two further one-electron reductions occur at the other calix[4]diquinone group. The reductions give rise to couple V/V′ and VI/VI′. The reason the waves III/III′ and IV/IV′ shifted more anodically as compared to couples V/V′ and VI/VI′ can be explained. The presence of a metal ion caused the first reduction occurred more easily due to the stabilization of the reduced quinone species with a metal ion. This makes the reduction waves shifted significantly to less negative potentials. The metal ion does not effect much to the second electron transfer and therefore caused the reduction couples appear almost the same as those of the free ligand. This rational is supported by the electrochemical behavior of **3** upon complexing metal ions.

The cyclic voltammogram of ligand **3** presented in Figure 5 shows two redox waves, I/I′ and II/II′, at −1251 and −1433 mV. This agrees with two one-electron-transfers found in simple calix[4]diquinones.[33] Upon addition of Na^+ and K^+ to electrochemical solutions of ligand **3**, only two new redox waves, III/III′ and IV/IV′, appear at −940 and −1082 mV as well as −906 and −1081 mV corresponding to the electron transfer of the

(32) In our system, we can observe only two two-electron reduction waves but cannot see the four-electron waves probably due to the presence of a trace of H_2O in the solvent used. The water probably destroyed all radical species that occurred upon reduction of the quinones.

(33) Beer, P. D.; Gale, P. A.; Chen, Z.; Drew, M. G. B., Heath, J. A.; Ogden, M. I.; Powell, H. R. *Inorg. Chem.* **1997**, *36*, 5880. Similar to **2**, the irreversible wave due to two-electron transfer upon further reduction of **3** was not observed.

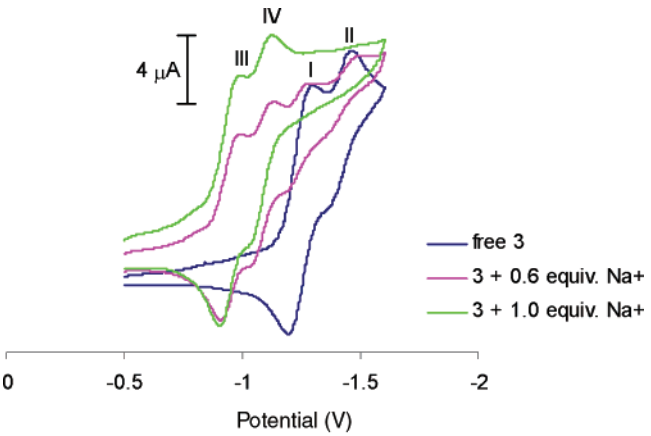
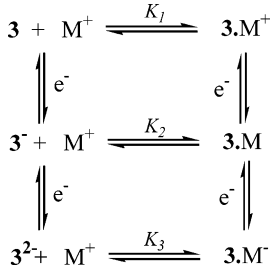


FIGURE 5. Cyclic voltammograms of free **3**, **3** + 0.6 equiv of Na^+, and **3** + 1.0 equiv of Na^+.

SCHEME 4. Electrochemically Switched Binding toward Metal Ions of 3 and Reduced 3



complexes **3**·Na^+ and **3**·K^+, respectively.[34] These new redox waves gradually emerge while the original redox couples of the free ligand disappear. Upon addition of 1 equiv of Na^+, the waves due to the free ligand completely disappear and the voltammogram shows only new waves of the complex as shown in Figure 5.

Compound **3** can also be considered as an electrochemically switched binding receptor toward Na^+ and K^+.[35] In the case of **3**, the ability to bind Na^+ and K^+ was enhanced upon electrochemical reduction of the ligand to form anion species as shown in Scheme 4. The binding enhancement may be calculated by considering the shift in the $E_{1/2}$ for the bound and free **3** using the equation $K_2/K_1 = \exp\{-(nF/RT)\Delta E_{1/2(I-III)}\}$ and $K_3/K_2 = \exp\{-(nF/RT)\Delta E_{1/2(II-IV)}\}$.[36−38] The binding enhancement, K_2/K_1 and K_3/K_2, for Na^+ and K^+ complexes with ligand **3** can be evaluated as shown in Table 3. Interestingly, it was found that the K_2/K_1 value of K^+ is higher than that of Na^+. This signifies the polarizing ability of the $-OCH_3$ group that can stabilize softer K^+.

Conclusion

Two bis(calix[4]diquinone) compounds, **1** and **2**, and one double calix[4]diquinone, **3**, have been synthesized from their corresponding double calix[4]arenes. We have demonstrated that double calix[4]arenes **4**−**6** can be synthesized in reasonable yields under high pressure. Receptors **1**−**3** have been found to form complexes with various alkali metal ions. Receptor **1** selectively binds Na^+ while compound **2** prefers K^+ and Cs^+. The dimethoxycalix[4]arene unit in **3** retains its cone conformation upon complexing K^+ and turns to mixed conformations upon binding Li^+ and Na^+. Receptors **2** and **3** show significant changes in cyclic and square wave voltammetry in the presence of alkali metal ions. Shifts of voltammograms were found to depend on the poralizing abilities of metal ions. Interestingly, receptor **3** exhibited electrochemical switchable binding toward Na^+ and K^+ in which the reduced form of **3** forms more stable complexes with the metal ions. Moreover, we can explain and support the reduction mechanism of biscalix[4]-diquinones presented by Beer and colleague.

TABLE 3. Redox Waves of 3 upon Addition of 1 Equiv of Na^+ and K^+ and Binding Enhancement[a]

	redox couples (mV)				binding enhancement	
compd	I/I′	II/II′	III/III′	IV/IV′	K_2/K_1	K_3/K_2
free **3**	−1251	−1433				
3 + Na^+			−940	−1082	1.82×10^5	8.71×10^5
3 + K^+			−906	−1081	6.85×10^5	9.00×10^5

[a] Experiments were carried out in 4:1 CH_2Cl_2/CH_3CN using Ag/$AgNO_3$ as reference electrode and $TBAPF_6$ as supporting electrolyte.

Experimental Section

Double Calix[4]arenes 4 and 5. In a high-pressure tube equipped with valves and pressure gauge were suspended *p-tert*-butylcalix[4]arene, **8**, (3.0 g, 4.62 mmol), a catalytic amount of 18-crown-6, bromoethyl tosylate (1.3 g, 4.62 mmol), and K_2CO_3 (1.3 g, 9.24 mmol) in anhydrous acetonitrile (10 mL). The tube was then pressurized with N_2 at 50 psi. The mixture was stirred and heated at 100 °C for 4 days. The solution was allowed to cool to room temperature. The pressure in the tube was then released. The solvent was evaporated to dryness to yield a yellow residue. The residue was dissolved in dichloromethane (100 mL), and an aqueous solution of 3 M hydrochloric acid was subsequently added until the pH of the solution reached pH 1. The mixture was extracted with dichloromethane (3 × 50 mL). The combined organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated on a rotary evaporator to obtain a white solid **4**. The product was recrystallized in dichloromethane upon addition of methanol to afford a white crystalline solid (2.16 g, 69%). In the case of **5**, *p-tert*-butylcalix[4]arene (3 g, 4.62 mmol), diethyleneglycol ditosylate (1.91 g, 4.62 mmol), a catalytic amount of 18-crown-6, and potassium carbonate (1.28 g, 9.24 mmol) were suspended in dried acetonitrile (10 mL). The workup procedure was similar to that of **4**. Compound **5** was obtained as a white crystalline solid (0.44 g, 14%).

4: mp > 300 °C dec; ^{1}H NMR ($CDCl_3$, 200 MHz) δ (ppm) 7.65 (s, 4H), 7.00 (s, 8H), 6.82 (s, 8H), 4.55 (s, 8H), 3.35, 4.50 (dd, J = 14.0 Hz, 16H), 1.25 (s, 36H), 0.99 (s, 36H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 151.2, 150.4, 147.1, 141.3, 132.3, 127.8, 127.7, 125.5, 124.6, 75.9, 33.7, 33.5, 32.1, 31.3, 30.7; FAB mass (*m/z*) 1367.8 [$M^+ + NH_4^+$]. Anal. Calcd for $C_{92}H_{116}O_8$: C, 81.86; H, 8.66. Found: C, 81.86; H, 8.86.

5: mp > 300 °C dec; ^{1}H NMR ($CDCl_3$, 200 MHz) δ (ppm) 8.09 (s, 4H), 7.00 (s, 8H), 6.85 (s, 8H), 4.50−4.10 (m, 24H), 3.18, (dd, J = 14.0 Hz, 8H), 1.25 (s, 36H), 1.05 (s, 36H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 150.5, 149.5, 147.2, 141.4, 133.5, 127.8, 125.6, 125.1, 74.8, 70.4, 34.0, 33.8, 31.6, 31.1; FAB

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mass (*m/z*) 1437 [M^+]. Anal. Calcd for $C_{96}H_{124}O_{10}$: C, 80.18; H, 8.69. Found: C, 80.21; H, 8.43.

25,27-Dimethoxy-26,28-di(carbomethoxymethoxy)-*p-tert*-butylcalix[4]arene (11). In a 100 mL, two-necked round-bottom flask were suspended 25,27-dimethoxy-*p-tert*-butylcalix[4]arene, **9** (3 g, 4.32 mmol), and sodium hydride (0.31 g, 12.96 mmol) in dried tetrahydrofuran (60 mL). The mixture was stirred for 30 min. Methyl bromoacetate (1.23 mL, 12.96 mmol) was then added. The mixture was stirred overnight and heated at 70 °C under nitrogen. After the reaction was completed, the solution was allowed to cool to room temperature and evaporated to dryness under reduced pressure. The residue was dissolved in dichloromethane (50 mL), and a saturated solution of ammonium chloride (50 mL) was subsequently added to destroy excess methyl bromoacetate and followed by washing with saturated sodium chloride solution (50 mL). Water (50 mL) was added, and the mixture was stirred for 30 min and extracted with dichloromethane (2 × 50 mL). The organic layer was dried over anhydrous sodium sulfate, filtered, and evaporated to dryness. The residue was dissolved in a minimum amount of dichloromethane, and methanol was added to precipitate a white powder **11** (2.82 g, 80% yield): mp 170−172 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.13 (br, 4H), 6.95−6.42 (br, 4H), 4.03 (s, 4H), 3.82 (br, 6H), 3.40−3.10 and 4.70−4.10 (br, 8H), 1.37 (s, 18H), 1.03 (2s, 18H), 0.8 (s, 6H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 169.9, 155.7, 153.7, 145.2, 144.7, 135.7, 131.9, 127.7, 125.4, 124.6, 72.0, 70.8, 60.4, 58.1, 51.6, 37.6, 34.1, 33.6, 31.6, 31.2; FAB mass (*m/z*) 821 [$M^+ + H^+$]. Anal. Calcd for $C_{52}H_{68}O_8$: C, 76.06; H, 8.35. Found: C, 76.14; H, 8.18.

25,27-Dimethoxy-26,28-di(2-hydroxyethoxy)-*p-tert*-butylcalix[4]arene (13). In a 100 mL two-necked round-bottom flask was stirred a solution of **11** (1.6 g, 1.95 mmol) in dried tetrahydrofuran (40 mL) for 10 min at 10 °C under nitrogen. $LiAlH_4$ (0.37 g, 9.75 mmol) was then added gradually. The mixture was allowed to stir overnight at room temperature under nitrogen atmosphere. After the reaction was complete, an aqueous solution of 3 M hydrochloric acid was subsequently added until a precipitate formed, which was then filtered. Water (30 mL) was added and the mixture stirred for 30 min and extracted with dichloromethane (2 × 30 mL). The organic layer was dried over anhydrous sodium sulfate, filtered, and evaporated to dryness under reduced pressure. The residue was dissolved in a minimum amount of dichloromethane, and methanol was added to precipitate a white powder **13** (1.23 g, 82% yield): mp 135 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.20−6.50 (m, 8H), 5.30−4.90 (m, 2H), 4.07 (m, 8H), 3.72 (s, 6H), 4.30 and 3.20 (dd, J = 12.0 Hz, 8H), 1.25 (s, 18H), 0.82 (s, 18H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 153.7, 153.4, 151.9, 146.2, 145.7, 145.0, 135.3, 133.7, 133.3, 132.2, 131.7, 126.4, 125.6, 124.9, 75.7, 62.9, 61.7, 61.5, 58.8, 38.4, 33.9, 33.9, 33.6, 31.6, 31.5, 31.0, 30.4; FAB mass (*m/z*) 765 [$M^+ + H^+$]. Anal. Calcd for $C_{50}H_{68}O_6$: C, 78.49; H, 8.96. Found: C, 78.41; H, 8.88.

25,27-Dimethoxy-26,28-di(methanesulfonyloxyethoxy)-*p-tert*-butylcalix[4]arene (15). In a 50 mL two-necked round-bottom flask was chilled a dichloromethane solution (30 mL) of **13** (0.5 g, 0.65 mmol), triethylamine (1.02 mL, 6.5 mmol), and a catalytic amount of DMAP to 10 °C with an ice bath and the mixture stirred under nitrogen for 30 min. MsCl (0.45 mL, 6.5 mmol) was then added. The reaction mixture was stirred at room temperature under nitrogen for 3 h. After the reaction was complete, an aqueous solution of 3 M hydrochloric acid (30 mL) was added and the mixture stirred for 30 min and extracted with dichloromethane (2 × 30 mL). The organic layer was dried over anhydrous sodium sulfate, filtered, and evaporated to dryness. The residue was dissolved in a minimum amount of dichloromethane, and methanol was added to precipitate a white powder **15** (0.52 g, 88% yield): mp 234−236 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.05 (br, 4H), 6.54 (br, 4H), 4.61 (br, 4H), 4.30 (br, 4H), 3.95 (br, 6H), 3.18 (br, 6H), 4.10 and 3.03 (br, 8H), 1.32 (br, 18H), 1.10−0.90 (br, 18H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm) 155.2, 152.6, 145.0, 134.7, 132.3, 125.4, 71.5, 68.2, 60.2, 34.0, 33.6, 37.6, 31.6, 31.1; FAB mass (*m/z*) 921 [$M^+ + H^+$]. Anal. Calcd for $C_{52}H_{72}O_{10}S_2$: C, 67.79; H, 7.88. Found: C, 67.83; H, 7.84.

Double Calix[4]arene 6. In a high-pressure tube equipped with valves and a pressure gauge were suspended *p-tert*-butylcalix[4]arene, **8** (0.21 g, 0.33 mmol), compound **15** (0.3 g, 0.33 mmol), catalytic amount of 18-crown-6, and potassium carbonate (0.11 g, 0.82 mmol) in dried acetonitrile (5 mL). The tube was then pressurized with N_2 at 50 psi. The mixture was stirred and heated at 80 °C for 4 days. The solution was allowed to cool to room temperature and evaporated to dryness under reduce pressure. The residue was dissolved in dichloromethane (50 mL), and an aqueous solution of 3 M hydrochloric acid (50 mL) was subsequently added, stirred for 30 min, and then extracted with dichloromethane (2 × 50 mL). The organic layer was dried over anhydrous sodium sulfate, filtered, and evaporated to dryness. The residue was dissolved in a minimum amount of dichloromethane, and methanol was added to precipitate a white crystalline solid **6** (0.23 g, 52% yield): mp > 300 °C dec; ^{1}H NMR ($CDCl_3$, 200 MHz) δ (ppm) 10.37 (s, 2H), 7.09−6.70 (m, 16H), 4.78−4.12 (m, 22H), 3.40−3.15 (m, 8H), 1.30 (s, 18H), 1.25 (s, 18H), 0.95 (s, 36H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 154.6, 144.5, 144.3, 141.3, 134.5, 133.0, 132.6, 127.9, 127.7, 125.8, 125.2, 124.9, 75.4, 72.8, 62.5, 33.9, 33.8, 33.6, 32.7, 32.5, 31.6, 31.5, 31.4, 31.3, 31.1, 31.0; ESI mass (*m/z*) 1395.2 ($M^+ + NH_4^+$). Anal. Calcd for $C_{94}H_{120}O_8$: C, 80.01; H, 8.43. Found: C, 80.40; H, 8.43.

Preparation of Bis(calix[4]quinones) 1 and 2 and Double Calix[4]diquinone 3. In a 50 mL two-necked round-bottom flask was stirred a suspension of thallium trifluoroacetate (0.8 g, 1.48 mmol) in trifluoroacetic acid (5 mL) in the dark under nitrogen for 1 h. Double calix[4]arene **4** (0.2 g, 0.15 mmol) was then added. The mixture was stirred in the dark for another 2 h. The solution was then poured into ice. Chloroform (50 mL) was added and the mixture stirred with water until the organic phase reached pH 7 and then extracted with chloroform (2 × 30 mL). The organic layer was dried over anhydrous magnesium sulfate, filtered, and evaporated to dryness. The residue was dissolved in a minimum amount of chloroform, and methanol was added to precipitate a yellow crystalline solid (0.091 g, 52% yield). Receptors **2** (68%) and **3** (38%) were synthesized from **5** and **6** in the same manner as **1**.

1: mp > 260 °C dec; ^{1}H NMR ($CDCl_3$, 200 MHz) δ (ppm) 7.10 (s, 8H), 5.86 (s, 8H), 4.39 (s, 8H), 4.52, 3.00 (dd, J = 13.9 Hz, 16H), 1.33 (s, 36H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 187.2, 185.0, 154.2, 149.7, 147.6, 134.0, 133.2, 126.7, 72.6, 33.6, 31.6, 30.8; ESI mass (*m/z*) 1203.4 ($M^+ + 4H^+ + NH_4^+$); IR (KBr (cm^{-1})): 1658 (C=O). Anal. Calcd for $C_{76}H_{76}O_{12}\cdot 2H_2O$: C, 74.98; H, 6.62. Found: C, 74.99; H, 6.20.

2: mp > 260 °C dec; ^{1}H NMR ($CDCl_3$, 200 MHz) δ (ppm) 6.95 (s, 8H), 6.39 (s, 8H), 4.35−3.90 (m, 24H), 3.12 (dd, J = 13.9 Hz, 8H), 1.20 (s, 36H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 188.0, 185.3, 154.0, 148.8, 146.5, 132.8, 131.1, 126.6, 74.3, 71.3, 34.1, 31.4; IR (KBr (cm^{-1})) 1661 (C=O). Anal. Calcd for $C_{80}H_{84}O_{14}\cdot 2H_2O$: C, 72.60; H, 6.85. Found: C, 72.86; H, 6.12.

3: mp > 260 °C dec; ^{1}H NMR ($CDCl_3$, 200 MHz) δ (ppm) 7.15 (s, 8H), 6.36 (s, 4H), 5.68 (s, 4H), 4.60−4.40 (m, 16H), 4.17 (s, 6H), 3.30−2.90 (m, 8H), 1.33 (s, 36H), 0.83 (s, 18H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 187.0, 185.5, 155.7, 154.7, 154.2, 150.9, 146.8, 145.0, 144.2, 135.2, 134.5, 132.6, 130.9, 126.6, 125.7, 124.2, 73.7, 71.4, 63.0, 34.3, 34.0, 33.6, 31.6, 31.5, 31.2, 30.9, 29.7; ESI mass (*m/z*) 1315.8 ($M^+ + 4H^+ + NH_4^+$); IR (KBr (cm^{-1})) 1660 (C=O). Anal. Calcd for $C_{86}H_{100}O_{10}\cdot CH_3OH\cdot H_2O$: C, 77.76; H, 7.95. Found: C, 77.20; H, 8.52.

Complexation Studies. Typically, a solution of 0.005 M receptor **1**, **2**, and **3** (2.5×10^{-6} mol) in $CDCl_3$ (0.5 mL) was prepared in NMR tubes. A solution of 0.05 M metal salt (5×10^{-5} mol) in CD_3CN (1 mL) was prepared in a vial. The solution of the metal salt was added directly to the NMR tube by a microsyringe to have desired cation:ligand ratios. ^{1}H NMR

spectra were recorded after each addition. Integrations of signals due to free ligands (I_h) and complexes (I_c) were used in calculation of K values by the following equations.[31]

$$K = \frac{n_c/[H]_o}{(1 - n_c)(R - n_c)}$$

where

$$n_c = \frac{I_c}{I_c + I_h}$$

and

$$R = [G]_o/[H]_o$$

$[H]_o$ and $[G]_o$ are initial concentrations of a host and a guest, respectively.

Electrochemical Studies. Cyclic voltammetry and square wave voltammetry were performed using an AUTOLAB PGSTAT 100 with a three electrode consisting of a glassy carbon electrode with a conducting area of 3 mm diameter, a platinum wire counter electrode, and a $Ag/AgNO_3$ reference electrode. All CV measurements were digitized using the GPES software (version 4.7). Unless otherwise indicated, all experiments were carried out in an electrolyte solution of 0.1 M tetrabutylammonium hexafluorophosphate ($TBAPF_6$) in 20% acetonitrile in dichloromethane. The reference electrode contained 0.01 M $AgNO_3$ and 0.1 M $TBAPF_6$ in 20% acetonitrile in dichloromethane. The background solution contained only 0.1 M $TBAPF_6$ (0.19372 g, 5×10^{-4} mmol) in 5 mL of 20% acetonitrile in dichloromethane.

All CV and SWV measurements were carried out in a cell compartment enclosed with a built-in Teflon cap. To avoid interference from O_2, all solutions were bubbled with nitrogen at least 5 min before each measurement. Typically, a solution of 0.001 M of a ligand (5×10^{-6} mol) and $TBAPF_6$ (0.1937 g, 5×10^{-4} mmol) in 5 mL of 20% acetonitrile in dichloromethane was prepared in a volumetric flask. A mixture of a metal salt (5×10^{-4} mol) and $TBAPF_6$ (0.1937 g, 5×10^{-4} mmol) in 5 mL of acetonitrile was prepared in a volumetric flask. All solutions were sonicated for 30 min before used. The solution of the metal salt was added directly to the cell by a microsyringe to have the desired cation/ligand ratios. Redox currents were determined from CV scans of the complex solutions at a scan rate of 0.050 V/s.

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Supporting Information Available: General experimental procedures and additional ^1H NMR spectra of **1** and **2** in the presence of alkali metal ions and square wave voltammograms of **2** and **3** in the presence of alkali metal ions. This material is available free of charge via the Internet at http://pubs.acs.org.

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