δ 2.7–3.07 (m, 5 H, ArCH$_2$CHH and C$_{13}$H); 3.94, 4.07 (2s, 6 H, 2 × OMe); 4.52–5.23 (m, 2 H, C$_6$ and C$_{13a}$H's); 6.05 (s, 2 H, OCH$_2$O); 6.8 (s, 2 H, ArH); 7.13 (s, 2 H, ArH). IR (Nujol): ν 1662 cm^{-1}. MS m/z: 354 (M$^+$ + 1, 11); 353 (51); 352 (9); 351 (10); 179 (12); 178 (100); 176 (36); 135 (22). HRMS calcd for $C_{20}H_{19}NO_5$: m/z 353.1263, obsd m/z 353.1278.

(±)-Tetrahydropalmatine (22a). To a solution of **21d** (0.05 g, 0.13 mmol) in dry ether (10 mL) was added lithium aluminium hydride (0.05 g, 0.15 mmol), and the reaction mixture was refluxed for 2 h. After the solution was cooled, the excess LAH was destroyed by addition of water (0.5 mL) and 10% sodium hydroxide (1 mL). It was filtered, and the filtrate was washed with water, dried, and evaporated to give berbine **22a** (0.045 g, 94%), mp 150–151 °C (lit.[16] mp 149.5–150.5 °C).

(±)-Canadine (22b). Reduction of **21e** with LAH as described above afforded **22b** in 98% yield, mp 172–173 °C (lit.[18b] mp 171 °C).

Registry No. **5a**, 78752-29-1; **5b**, 144192-07-4; (±)-**6a**, 34696-49-6; (±)-**6b**, 144192-08-5; (±)-**6c**, 144192-09-6; (±)-**6d**, 144192-10-9; (±)-**6e**, 82780-51-6; (±)-**6f**, 82780-52-7; (±)-**6**(R^1 = R^3 = OH, R^2 = R^4 = H), 80394-92-9; (±)-**6**(R^1=R^4=OH,R^2+-H,R^3=OMe), 55555-33-4; (±)-**7**, 144192-11-0; **8**, 6161-65-5; **9**, 144192-12-1; **10a**, 91416-33-0; **10b**, 93007-01-3; **11**, 73318-30-6; **12**, 71435-93-3; (±)-**14**, 144192-13-2; (±)-**15**, 144192-14-3; **16**, 144192-15-4; **18**, 144192-16-5; **19a**, 3947-78-2; **19b**, 30045-07-9; **19c**, 35287-11-7; (±)-**21a**, 41173-73-3; (±)-**21b**, 58093-70-2; (±)-**21c**, 76177-40-7; (±)-**21d**, 76177-39-4; (±)-**21e**, 76177-41-8; (±)-**22a**, 2934-97-6; (±)-**22b**, 29074-38-2; **23**, 104270-87-3; **24**, 144192-17-6; **25**, 5653-57-6; **26**, 144192-18-7; C_6H_5CHO, 100-52-7; $Br(CH_2)_3CH{=}CH_2$, 1119-51-3; *o*-tolualdehyde, 529-20-4; *p*-anisaldehyde, 123-11-5; veratraldehyde, 120-14-9; chloral, 75-87-6; isovanillin, 621-59-0; dimethyl fumarate, 624-49-7; diethyl fumarate, 623-91-6.

Supplementary Material Available: Spectroscopic and analytical data of known compounds (**6a**, **6b**, **6c**, **6e**, **6f**, **7**, **10a**, **11**, **21a–d**, and **22a,b**) (4 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Novel Cryptand Chromoionophores for Determination of Lithium Ions

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The syntheses and chromogenic properties of three novel chromogenic (*p*-nitrophenyl)azo-labeled cryptands **1–3**, having inward-facing phenolic groups, are described. Cryptand chromoionophore **1** has the smallest cavity of the three cryptands and exhibits total selectivity for Li$^+$ over Na$^+$ ions in 10% aqueous diethylene glycol monoethyl ether (DEGMEE). The association constant of 3200 M^{-1} was obtained in 10% aqueous DEGMEE/TMA(OH) for the **1**$^-$·Li$^+$ complex. Compound **1** is potentially applicable for the colorimetric analysis of lithium ions in largely aqueous solutions. The slightly larger chromoionophore **2**, in which diaza-12-crown-4 moiety is connected with the aromatic subunit via three-carbon bridges, is highly selective for Li$^+$ ions in the extraction mode and shows no cation response in homogeneous aqueous media. A larger analog of **1**, chromogenic cryptand **3**, which incorporates diaza-18-crown-6 moiety, exhibits K$^+$ ion selectivity in aqueous solutions.

Introduction

Over the past 15 years indicator systems derived from macrocyclic compounds capable of selective ion binding have seen much interest due to their potential application in the determination of physiologically important cations.[1] Reagents for colorimetric determination of sodium and potassium ions in aqueous solutions, based on cryptahemispherands and hemispherands, have recently been reported.[2] Several attempts have been made to design an indicator system for the determination of lithium ions.[3] Lithium carbonate is a therapeutic drug used in treatment of psychiatric disorders.[4] Flame photometry and ion-selective electrodes are currently used for determination of lithium in human serum.[5] Some of the lithium chromoionophores reported thus far are capable of highly selective Li$^+$ complexation in organic solvents but cannot be applied in homogeneous, aqueous media.

In this paper we report the design and synthesis of an indicator system based on a chromogenic cryptand. This novel chromoionophore exhibits extraordinary selectivity for Li$^+$ over Na$^+$ in largely aqueous solutions, allowing for the first time the practical colorimetric determination of lithium in blood and other physiological fluids.[6]

Results and Discussion

Design and Syntheses of Chromoionophores 1–3. The design of lithium-selective ionophores is an intricate task, especially when the complexation of lithium ions is expected to occur in aqueous media. High selectivity of Li$^+$ over Na$^+$ could be anticipated only with ionophores which incorporate small, rigid cavities which restrict complexation with Na$^+$ and other ions. To ensure strong binding, which is a prerequisite for high sensitivity of the

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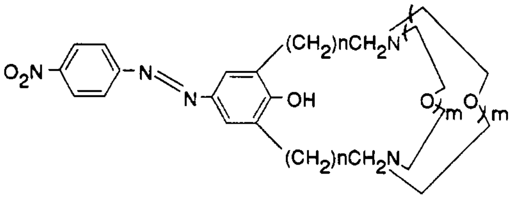
chromoionophore, the cavity should contain binding sites highly preorganized for interaction with Li^+.

All three new chromoionophores studied incorporate a [(*p*-nitrophenyl)azo]phenol chromophore system built into a cryptand structure. Examination of a CPK molecular model of chromoionophore 1 shows an extremely small and rigid cavity of the binding moiety. The highly convergent binding sites consist of two oxygen and two nitrogen atoms and an intraannular phenolic hydroxyl. The model guarantees high lithium selectivity over the larger-size sodium ion which would not be able to enter the cavity.



1 (n=m=1)

2 (n=2, m=1)

3 (n=1, m=2)

Despite the insertion of two additional carbon atoms, the cavity of chromoionophore 2 became only slightly larger and more flexible and promised the retention of propensity for binding Li^+ ions. This preference was expected to be absent for chromoionophore 3 whose cavity is clearly larger than those of 1 and 2. Thus, compound 3 was synthesized in order to compare its cation response with responses of smaller analogs 1 and 2.

Compounds 4–6 were common intermediates in the syntheses of all three chromoionophores. In the synthesis of chromoionophore 1, photochemical bromination of 2,6-dimethylanisole with *N,N'*-dibromo-5,5-dimethylhydantoin afforded 2,6-bis(bromomethyl)anisole (4) (72%), previously obtained by bromination of the same substrate with NBS.[7] Dibromide 2 was reacted with NaCN in a phase-transfer catalysis reaction to produce dinitrile 5 (95%). Basic hydrolysis of 5 gave acid 6 (91%), which was reacted with $(COCl)_2$ to give chloride 7 in an almost quantitative yield. A key intermediate, the bicyclic cryptand diamide 8, was synthesized from diacid chloride 7 and diaza-12-crown-4[8] under high dilution conditions in 57% yield. The last three reactions of the synthesis involved reduction of the cryptand diamide 8 to the corresponding cryptand, demethylation, and diazotization coupling reaction with *p*-nitrobenzenediazonium chloride. Reduction of bicyclic diamides is well documented in the field of macrocyclic chemistry.[9] It has usually been accomplished by reduction with diborane or $LiAlH_4$. However, we have found that cryptand diamide 8 could not be reduced efficiently by this and other commonly used reducing agents in typical reaction conditions. For example, treatment of 8 with $BH_3{\cdot}Me_2S$ afforded the dihydroborane adduct 9 (80%) which upon treatment with 6 N HCl (room temperature, 20 h) gave a hydrochloride of the monohydroborane adduct 10. In fact, one of the hydroborane groups could be cleaved just by stirring 9 in a water–THF mixture to give monohydroborane adduct 11. Attempts to cleave the second hydroborane group using an extended contact with the acid at room temperature failed, whereas refluxing with 6 N HCl led to decomposition. A very similar situation, in which the monohydroborane of [1.1.1]cryptand could not by cleaved easily, was reported by Lehn.[10] Treatment of 10 or 11 with methanolic KOH according to Lehn's procedure gave free cyptand 12 in about 90% yields (method A).

In a separate experiment, diamide 8 was treated with Lawesson's reagent in HMPA to obtain a dithio amide[11] which subsequently was to be reduced[12] to provide free cryptand 12. Surprisingly, no thio amide was formed, and only the intact cryptand diamide 8 was recovered from the reaction mixture. It has been shown earlier that some cryptand diamides having inward-facing methoxyl groups can selectively be reduced and demethylated in a one-pot reaction with $LiAlH_4$ in THF to provide corresponding cryptand–phenols.[13] However, treatment of diamide 8 with $LiAlH_4$ in boiling THF was found to be very unselective, producing only a small amount of the desired cryptand–phenol 13 and several byproducts. In the final step, the crude reduction–demethylation reaction product was coupled with *p*-nitrobenzenediazonium chloride to afford the target chromoionophore 1 in an overall 10% yield.

In an attempt to improve the reduction–demethylation step, the diamide 8 was treated with $LiAlH_4$ in a mixed, $THF–CH_2Cl_2$ solvent system[14] (method B). The free cryptand 12 was isolated in 42% yield. Demethylation of 12 was achieved with a EtSNa–LiBr mixture in boiling DMF.[15] The key intermediate cryptand–phenol 13 was isolated in 60% yield. Different runs produced 13 in yields ranging from 60% to 85%. The apolar character of the cryptand–phenol suggested by its CPK molecular model was confirmed by its abundant solubility in *n*-pentane. The subsequent diazotization coupling reaction produced the final product 1 in a much improved 72% yield.

In the synthesis of chromoionophore 2, diacid 6 was converted into its ethyl ester 14 (96%) which was reduced with $LiAlH_4$ to diol 15 in 67% yield. Diol 15 was treated with mesyl chloride to afford dimesylate 16 (85%) which under phase-transfer reaction conditions was converted into dinitrile 17 in 84% yield. Basic hydrolysis of 17 afforded diacid 18 (55%), which was reacted with $(COCl)_2$ to give acid chloride 19 in a quantitative yield. Cyclization of 19 with diaza-12-crown-4 provided bicyclic diamide 20 in 63% yield. Reduction of 20 was accomplished smoothly with $LiAlH_4$ in a $THF–CH_2Cl_2$ mixture after an 8-h reflux. Methoxycryptand 21 was isolated in 88% yield. Attempted demethylation of 21 with LiI in pyridine[16] (100 °C, 15 h) or EtSNa–LiBr in DMF (150 °C) either gave back the unreacted substrate or led to a complicated mixture of products, respectively. On the other hand,

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Chart I

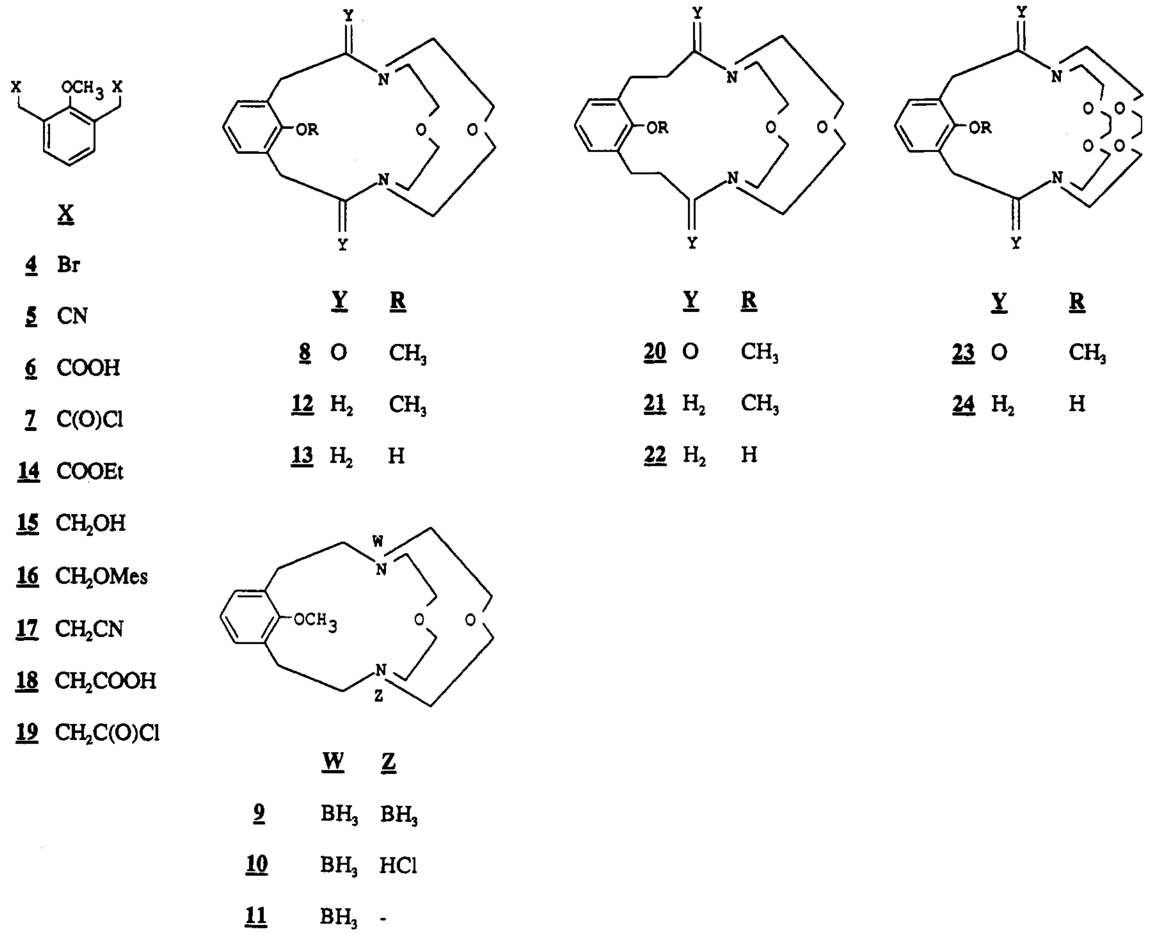

Table I. Selected Chemical Shifts in ^{13}C NMR Spectra of Cryptands 12, 13, and 21 and Their Lithium Complexes in CDCl$_3$

	^{13}C NMR, δ								
compd	C_{AR}-OMe	CH_2O	CH_2O	CH_3O	$ArCH_2CH_2N$	CH_2N	CH_2N	$ArCH_2$	CH_2
12	161.6	72.1	69.7	62.3	61.3	55.3	54.2	27.5	
12·LiClO$_4$	153.3	67.6	67.3	62.6	60.7	53.9	53.8	27.5	
21	158.4	69.5	69.3	60.9	55.4	52.9	52.6	28.9	28.4
21·LiClO$_4$	153.2	67.3	66.8	61.6	57.6	53.9	51.8	29.2	25.7
13	155.7[b]	72.0	69.7		61.6	55.4	53.1	28.7	
13^-·Li^+[a]	166.1[b]	68.2	68.1		61.7	55.4	54.1	29.5	

[a] 9 wt % LiOD in D$_2$O was used to ionize the phenolic group. [b] These signals are assigned to aromatic carbons linked with the phenolic oxygen atom.

when diamide **20** was refluxed for 10 h with LiAlH$_4$ in THF some cryptand phenol **22** was formed, as evidenced by ^{1}H NMR. Thus, the crude reaction product was treated directly with *p*-nitrobenzenediazonium chloride to produce chromoionophore **2** in an overall 40% yield.

To synthesize chromoionophore **3**, acid chloride **7** was reacted with diaza-18-crown-6 under high dilution conditions to provide cryptand diamide **23** in 32% yield. As indicated by its CPK molecular model, despite the larger cavity, diamide **23** lacks expected flexibility. In comparison with its smaller diamide analog **8**, the ^{1}H and ^{13}C NMR spectra of **23** are quite complicated and indicate the presence of conformers. Unexpectedly, the one-pot reduction–demethylation of **23** with LiAlH$_4$ in THF (reflux, 10 h) proceeded cleanly, affording cryptand–phenol **24** in 74% yield. This result showed that the presence of additional oxygen atoms in the proximity of the methoxyl group is highly desired in order to facilitate coordination of lithium ions and the subsequent demethylation. Apparently this requirement is not met in the case of cryptand diamide **20** or cryptand **21** where oxygen atoms are too distant from the methoxyl group to participate in the coordination of Li$^+$. On the other hand, in cryptand **9**, which undergoes demethylation easily, oxygen atoms of the azacrown moiety are close enough for coordination. The diazotization coupling reaction with *p*-nitrobenzenediazonium chloride gave chromogenic cryptand **3** in 70% yield.

Complexation of Lithium. The lithium ion complexation by methoxycryptands **12** and **21** and cryptand–phenol **13** was followed by ^{1}H and ^{13}C NMR. In general, upon complexation of **12** and **21** with Li$^+$, signals of methylene protons adjacent to nitrogen and oxygen atoms were shifted downfield by about 0.2 ppm. Singlets of the inward-facing methoxyls were also shifted downfield from δ 3.50 (free) to δ 3.78 (complex) for **12** and from δ 3.64 (free) to δ 3.84 (complex) for **21**. The ^{13}C NMR spectra of **12** and **21** (Table I) shed some light on the symmetry of these two cryptands and their respective lithium complexes. The spectrum of **12** consisted of seven signals in the aliphatic region and four benzene ring resonances. The presence of three signals assigned to CH$_2$N protons and two signals from CH$_2$O protons indicated a lack of symmetry. Interestingly, complexation of Li$^+$ seems to improve sym-

Table II. UV-Vis Spectral Characteristics (λ_{max} and $\epsilon(\lambda_{max})$) of Chromogenic Compounds 1-3 in H_2O-DEGMEE (90 + 10, v/v)

compd	form[a]	λ_{max}, nm	$\epsilon(\lambda_{max})$
1	L^-	575; 378	8000; 8000
	HL	494; 363	8800; 8000
2	L^-	561	27640
	HL	492	42600
3	L^-	566	30200
	HL	483	43150

[a] L^- is fully ionized ligand in 1.0 M (TMA)OH and HL is nonionized ligand in 0.1 M HCl.

metry of the molecule as evidenced by almost full coalescence of two CH_2N and two CH_2O resonances. In contrast, free **21** exhibited eight aliphatic signals, but the differences in chemical shifts of CH_2CH_2, CH_2N, and CH_2O were very small. These differences became more pronounced upon encapsulation of Li^+, suggesting decreased symmetry of the complex. In the aromatic regions, the largest changes were observed for the carbons linked with the methoxyl groups.

When a $CDCl_3$ solution of cryptand-phenol **13** was vortexed for 30 min with 9% LiOD in D_2O, only partial deprotonation was observed. The ^{13}C NMR spectrum exhibited two sets of resonances which were assigned to free, unprotonated **13** and its lithium phenolate complex, respectively (Table I).

The association constant $K_a = 3200\ M^{-1}$ in 10% aqueous DEGMEE/TMA(OH) was determined for the lithium complex $1^-{\cdot}Li^+$ using a literature procedure,[18] while association constants for Na^+ and K^+ could not be obtained due to the lack of chromogenic response. This result is in agreement with the data reported for a nonchromogenic cage aza macrocycle ($K_a = 1585\ M^{-1}$) which was found to complex Li^+ selectively in aqueous solutions.[19,20]

Spectral Characteristics of Chromogenic Compounds 1-3. Wavelength maxima (λ_{max}) and molar absorptivities (ϵ) of the acid (HL) and base (L^-) forms of chromogenic cryptands **1-3** were taken in 10% aqueous DEGMEE and are recorded in Table II. To suppress ionization of the phenolic hydroxyl and thereby obtain the HL spectra, absorbances were determined in 0.1 M HCl. Likewise, 0.1 M TMA(OH) was used when obtaining the L^- spectra to induce ionization of the O-H bond.

There are two wavelength maxima at 363 and 494 nm observed for nonionized **1**. According to the literature data and our earlier observations for analogous indicator systems,[3i] the maximum at 363 nm can be attributed to the azo form of **1**, which is stabilized by intraannular hydrogen bonding. The tautomeric hydrazone form gives an absorption maximum at 494 nm. In going from the HL form to L^-, a bathochromic shift to 575 nm is observed. The second maximum, now at 378 nm, probably represents the nonionized portion of **1**.

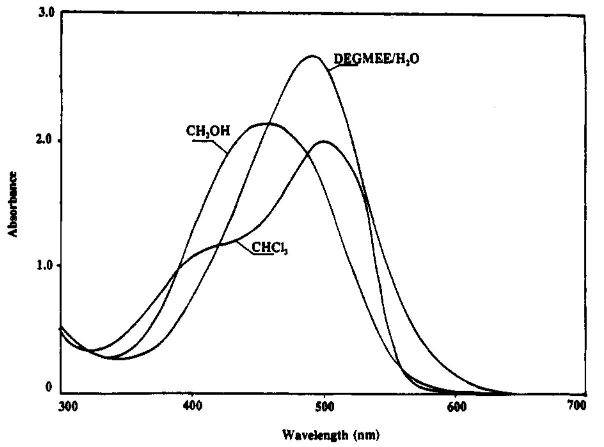

Figure 1. Solvent dependance of chromogenic cryptand **2**: 10% DEGMEE (λ_{max} 492 nm), $CHCl_3$ (λ_{max} 500 nm), and CH_3OH (λ_{max} 457 nm).

Table III. Spectral Responses of Chromogenic Cryptands to Lithium, Sodium, and Potassium Ions at pH Optimum[a] and Their pK_a Values in H_2O-DEGMEE (90 + 10, v/v) for Compounds 1 and 3 and in CH_2Cl_2-H_2O for Compound 2 at 25 °C

compd	optimum pH	form[b]	λ_{max}, nm	$\epsilon(\lambda_{max})$	pK_a[c]
1	12.0	L	379	13300	12.6 ± 0.15
		LiL	512; 379	8800; 12600	
		NaL	379	13300	
		KL	379	13300	
2	11.0	L	408	12400	11.5 ± 0.15
		LiL	561; 405	14670; 7590	
		NaL	407	12700	
		KL	408	12740	
3	11.1	L	498	16000	11.1 ± 0.20
		LiL	498	16100	
		NaL	501	15920	
		KL	523	21800	

[a] Buffers: 0.1 M CAPS (3-(cyclohexylamino)-1-propanesulfonic acid) adjusted with (TMA)OH. [b] L is the uncomplexed ligand; LiL, NaL, and KL are the compound in the presence of large excesses of lithium, sodium and potassium ions, respectively. [c] pK_a values are averages of three determinations ± standard deviation.

Acid forms of chromogenic cryptands **2** and **3** exhibit single absorption maxima at 492 and 483 nm, respectively. This is consistent with the presence of their hydrazone tautomers. Chromogenic cryptand **2** has no oxygen atoms close to the phenolic hydroxyl, and therefore, its azo form cannot be stabilized efficiently. It is known that the (phenylazo)phenol-quinone phenylhydrazone tautomeric equilibrium depends on the solvent.[17] The UV-visible spectra of compound **2** measured in 10% aqueous DEGMEE, $CHCl_3$, and MeOH are compared in Figure 1. While the spectrum measured in 10% aqueous DEGMEE shows a distinct absorption maximum at 492 nm indicative of the hydrazone form, the shapes of the spectra obtained in $CHCl_3$ and MeOH indicate the existence of both tautomeric forms. Thus ^1H and ^{13}C NMR signals obtained for compounds **1-3** in deuteriochloroform represent a mobile equilibrium between the azo and hydrazone forms.

Similar reasoning may apply to explain the absence of the azo form absorption maximum of compound **3**. Ether oxygens of the crown ether moiety are not close enough to the phenolic group to stabilize the azo form by hydrogen bonding. For both cryptands **2** and **3**, ionization causes bathochromic shifts to 560 and 566 nm, respectively, with reduced molar absorptivity (Table II).

The pK_a values for chromogenic cryptands **1-3** in 10% aqueous DEGMEE are listed in Table III. For compound **1**, the pK_a value of 12.6 is consistent with the presence of a strong intraannular hydrogen bonding. Compounds **2** and **3** exist predominantly in hydrazone forms, and their lower pK_a values are 11.6 and 11.1, respectively.

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Cation Responses. Responses of chromogenic cryptands 1 and 3 to large excesses (100–200-fold) of physiologically important lithium, sodium, and potassium ions in 10% diethylene glycol monoethyl ether (DEGMEE) were determined. Absorption maxima and molar absorptivities at the pH optima are presented in Table III. (The pH optimum is defined as the pH at which the largest wavelength shift is observed.) At pH 12.0 for chromoionophore 1, there is a 133-nm bathochromic shift in the absorption maximum in the presence of Li^+ (LiL).

Chromogenic cryptand 3 responds at pH 11.1 to K^+ with a 23-nm bathochromic shift and a substantial increase in the molar absorptivity. Interestingly, chromogenic cryptand 2 is inactive toward Li^+, Na^+, and K^+ in 10% DEGMEE but exhibits a high preference for Li^+ in CH_2Cl_2–water extractions. Shaking a CH_2Cl_2 solution of 2 with aqueous LiCl at pH 11.0 results in a 153-nm shift in the absorption maximum to a longer wavelength and a slightly higher molar absorptivity for the LiL form versus the L form.

For comparison, spectral cation responses of chromogenic cryptands 1–3 are shown in Figure 2.

In conclusion, chromogenic cryptand 1 shows extraordinary selectivity for lithium over physiologically important cations in largely aqueous solutions. This feature provides an opportunity to use compound 1 in reagents for the colorimetric determination of lithium as an alternative to ion-selective electrodes and atomic absorption spectrometry. In instances where the extraction mode is applicable, both chromoionophores 1 and 2 can be used.

Experimental Section

Melting points are uncorrected. ^1H and ^{13}C NMR spectra were recorded at 200 and 50 MHz, respectively. Fast atom bombardment (FAB) mass spectra were determined using *m*-nitrobenzyl alcohol (NOBA) as the matrix.

Materials. Unless specified otherwise, reagent-grade reactants and solvents were used as received from chemical suppliers. Benzene was dried over molecular sieves (4-Å). Tetrahydrofuran was distilled from sodium benzophenone ketyl. Diaza-12-crown-4 was prepared according to the literature procedure.[8] Organic solutions were dried over anhydrous $MgSO_4$. Solutions were evaporated under reduced pressure using a rotary evaporator.

2,6-Bis(bromomethyl)anisole (4).[7] A refluxing solution of 2,6-dimethylanisole (13.6 g, 0.10 mol), *N,N'*-dibromo-5,5-dimethylhydantoin (31.5 g, 0.11 mol), and benzoyl peroxide (0.46 g) in CCl_4 (215 mL) was irradiated for 2 h with a 500-W tungsten lamp. The reaction mixture was cooled to room temperature and washed with water, the organic layer was dried, and the solvent was removed. The obtained orange oil was treated with cold CH_3OH, and a white crystalline solid (52.16 g, 72%) was collected, mp 83.5–85.5 °C (lit.[7] mp 85 °C). ^{13}C NMR ($CDCl_3$): δ 27.77 (CH_2), 62.59 (CH_3), 125.58, 132.47, 132.78, 157.19 (Ar).

2,6-Bis(cyanomethyl)anisole (5). A solution of dibromide 4 (10.0 g, 34.0 mmol) in benzene (40 mL) was added to a flask containing NaCN (8.33 g, 0.17 mol) and hexadecyldimethylethylammonium bromide (1.00 g, 2.66 mmol) in 20 mL of water. The heterogeneous solution was rapidly mixed at reflux for 5 h. To the reaction mixture was added 100 mL each of benzene and water. The aqueous layer was extracted with an additional 50 mL of benzene, and the organic layers were combined and dried. The solvent was removed to give a yellow oil which was chromatographed on alumina with CH_2Cl_2 as eluent to afford 6.00 g (95%) of dinitrile 5 as a white solid, mp 58–59.5 °C. IR (melt): 2252 (CN) cm^{-1}. ^1H NMR ($CDCl_3$): δ 3.78 (s, $ArCH_2$, 4 H), 3.84 (s, CH_3, 3 H), 7.20 (t, ArH, 1 H), 7.43 (d, ArH, 2 H); ^{13}C NMR ($CDCl_3$): δ 18.67 (CH_2), 61.80 (CH_3), 118.02, 125.01, 126.02, 130.68 (Ar), 156.29 (CN). Anal. Calcd for $C_{11}H_{10}N_2O$: C, 70.95; H, 5.41. Found: C, 71.01; H, 5.39.

2,6-Bis(carboxymethyl)anisole (6). Dinitrile 5 (11.0 g, 59.0 mmol) in 7% aqueous NaOH (300 mL) was refluxed overnight. After cooling to room temperature, the solution was extracted with CH_2Cl_2 (2 × 80 mL) to remove any unreacted starting material. The pH of the aqueous layer was adjusted to 2 by careful addition of concentrated HCl. After 1 h, the white precipitate was filtered, redissolved in THF (200 mL), and filtered again to remove NaCl. The solvent was removed to give a white solid which was washed with ether to produce 11.9 g (91%) of diacid 6 with mp 184–186 °C. IR (deposit on NaCl plate): 3500–2750 (OH), 1698 (C=O) cm^{-1}. ^1H NMR (DMSO-d_6): δ 3.57 (s, $ArCH_2$, 4 H), 3.69 (s, CH_3, 3 H), 6.95–7.10 (m, ArH, 1 H), 7.13 (d, ArH, 2 H). ^{13}C NMR (DMSO-d_6): δ 35.24 (CH_2), 60.9 (CH_3O), 124.00, 128.72, 130.60, 156.92 (Ar), 173.12 (C=O). Anal. Calcd for $C_{11}H_{12}O_5$: C, 58.93; H, 5.39. Found: C, 59.11; H, 5.51.

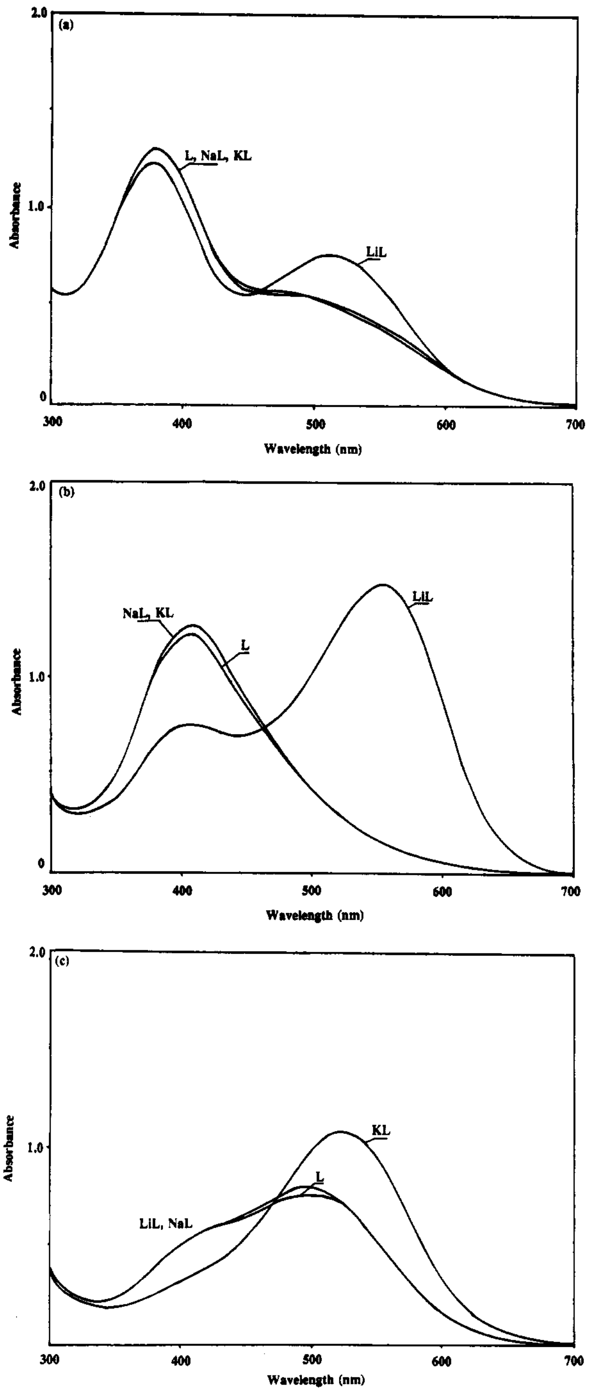

Figure 2. UV–visible spectra of lithium (LiL), sodium (NaL), and potassium (KL) responses of (a) cryptand 1 (L) in 10% aqueous DEGMEE, pH 12.0; (b) cryptand 2 (L) in CH_2Cl_2–H_2O, pH 11.0; and (c) cryptand 3 in 10% aqueous DEGMEE, pH 11.1.

Diacid Chloride 7. Oxalyl chloride (1.13 g, 9.80 mmol) and two drops of dry pyridine were added to a suspension of diacid 6 (0.50 g, 2.20 mmol) in benzene (25 mL). The mixture was stirred at room temperature for 2 days and filtered, and the solvent was removed to give 0.59 g (98% yield) of 7 as a light-yellow oil. IR (neat): 1801 ($C{=}O$) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 3.64 (s, $ArCH_2$, 3 H), 4.09 (s, CH_3, 4 H), 7.00–7.20 (m, ArH, 3 H). ^{13}C NMR ($CDCl_3$): δ 47.90 (CH_2), 62.02 (CH_3), 125.52, 126.57, 132.30, 157.56 (Ar), 172.45 ($C{=}O$).

Cryptand Diamide 8. A solution (400 mL) of diacid chloride 7 (2.71 g, 10.4 mmol) in benzene and a solution (400 mL) of diaza-12-crown-4[8] (1.81 g, 10.4 mmol) and triethylamine (2.58 g, 25.5 mmol) in benzene were added simultaneously at room temperature with two syringe pumps at the addition rate of 20 mL/h to 415 mL of vigorously stirred benzene. After the addition was completed, the stirring was continued for 6 h. The solvent was removed, and the residue was chromatographed on flash silica gel with CH_2Cl_2–CH_3OH (95:5) as eluent to afford 2.10 g (57%) of diamide 8 as a white solid, mp 278–280 °C. IR (deposit on NaCl): 1630 ($C{=}O$), 1142 (CO) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 2.58–2.76 (m, $ArCH_2$, 4 H), 3.05–3.26 (m, CH_2N, 4 H), 3.40–3.95 (m, $CH_2N + CH_2O + CH_3$, 15 H), 7.00 (s, ArH, 3 H). ^{13}C NMR ($CDCl_3$): δ 41.57 ($ArCH_2$), 45.85, 49.69 (CH_2N), 59.33 (CH_3), 68.09, 69.19 (CH_2O), 124.68, 130.22, 131.16, 160.57 (Ar), 172.12 ($C{=}O$). MS: *m/e* 334 (M^+, 15.8). Anal. Calcd for $C_{19}H_{26}N_2O_5$: C, 62.97; H, 7.23. Found: C, 63.05; H, 7.26.

Dihydroborane Cryptand 9. A 10 M $BH_3{\cdot}Me_2S$ solution (3.9 mL, 39.0 mmol) was added to a refluxing suspension of cryptand diamide 8 (0.50 g, 1.38 mmol) in THF (160 mL). The reaction was quenched after 3 h by careful addition of water, the solvent was removed, and the residue was partitioned between CH_2Cl_2 and water. The organic layer was washed with water and filtered through a layer of anhydrous $CaSO_4$, and the solvent was removed. The crude product was purified on silica gel with petroleum ether–CH_2Cl_2 (3:1 → 1:1) as eluent to afford 9 (0.40 g, 80%) as a white solid with mp 179–180 °C (bubbles). IR (film): 2375, 2330, 2280 (BH), 1162, 1068, 1018 (CO) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 0.90–2.20 (m, BH_3, 6 H), 2.30–2.60 (m, CH_2O, 2 H), 2.80–4.25 (m, $ArCH_2 + CH_2N + CH_2O + CH_3O$, 25 H), 6.98–7.30 (m, ArH, 3 H). ^{13}C NMR ($CDCl_3$): δ 26.76 ($ArCH_2$), 57.55, 60.95, 62.81 (CH_2N), 65.88 (CH_3O), 66.45, 68.40 (CH_2O), 126.46, 130.17, 133.40, 156.35 (Ar). MS: *m/e* 347 ($M^+ - CH_3$, 100). Anal. Calcd for $C_{19}H_{36}B_2N_2O_3$: C, 63.02; H, 10.02. Found: C, 62.93; H, 10.17.

Monohydroborane Hydrochloride Cryptand 10. A 6 N HCl solution (30 mL) was added to a solution of dihydroborane 9 (0.60 g, 1.66 mmol) in THF (50 mL) at 0 °C. The mixture was stirred overnight at room temperature, concentrated in vacuo to a small volume, treated with 5% aqueous LiOH, and extracted with CH_2Cl_2. The solvent was removed, and the residue was chromatographed on deactivated, basic alumina with $CHCl_3$–EtOH (gradual polarization) as eluent to give 10 (0.16 g, 29%) as white crystals with mp 148–150 °C. IR (film): 2427, 2362 (BH), 1130, 1102 (CO) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.96–2.66 (m, $BH_3 + ArCH_2 + CH_2O$, 9 H), 2.85 (m, $CH_2N + CH_2O$, 13 H), 3.61–3.88 (m, $CH_3O + CH_2O$, 6 H), 3.96–4.20 (m, CH_2O, 2 H), 6.97–7.15 (m, ArH, 3 H). ^{13}C NMR ($CDCl_3$): δ 27.36, 29.71 ($ArCH_2$), 54.95, 55.70, 57.12, 57.37, 58.87, 61.24 (CH_2N), 59.93 (CH_3O), 66.23, 67.68, 70.27, 71.28 (CH_2O), 125.30, 129.65, 130.40, 132.76, 134.49, 159.20 (Ar). Anal. Calcd for $C_{19}H_{34}BClN_2O_3$: C, 59.31; H, 8.91; Cl, 9.21. Found: C, 59.52; H, 8.57; Cl, 9.26.

Monohydroborane Cryptand 11. Dihydroborane 9 (0.17 g, 0.49 mmol) was stirred for 48 h in a mixture of THF (8 mL), CH_2Cl_2 (3 mL), and water (2 mL). The solvent was removed, and the residue was purified by passing through a short layer of silica gel with petroleum ether–EtOAc (1:1) as eluent to give 11 (0.12 g, 70%) as a white solid which slowly sintered at 165–175 °C and melted at 189–190 °C (bubbles). IR (Nujol): 2380–2280 (BH), 1103, 1010 (CO) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 0.70–2.05 (m, BH_3, 3 H), 2.15–4.35 (m, $ArCH_2 + CH_2N + CH_2O + CH_3O$, 27 H), 6.95–7.14 (m, ArH, 3 H). ^{13}C NMR ($CDCl_3$): δ 27.34, 29.41 ($ArCH_2$), 55.93, 58.06, 58.40, 58.68, 59.67, 61.39 (CH_2N), 65.48 (CH_3O), 66.63, 68.76, 69.69, 71.13 (CH_2O), 125.24, 129.52, 130.03, 132.77, 134.68, 158.99 (Ar). MS: *m/e* 348 (M^+, 3.9). Anal. Calcd for $C_{19}H_{33}BN_2O_3$: C, 65.52; H, 9.55. Found: C, 65.45; H, 9.49.

Cryptand 12. Method A. Dihydroborane 9 (0.89 g, 2.46 mmol) was suspended in a 0.28 M KOH solution in methanol (200 mL) and stirred at room temperature over 4 days. The solvent was evaporated to dryness, and the solid residue was extracted with petroleum ether. The solvent was removed to give 0.73 g (89%) of cryptand 12 as white crystals which decomposed above 130 °C. IR (film): 1164, 1132, 1079 (CO) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.98–2.58 (m, $ArCH_2 + CH_2N$, 12 H), 2.88–3.34 (m, $CH_2N + CH_2O$, 10 H), 3.51 (s, CH_3, 3 H), 3.55 (t, CH_2O, 1 H), 3.60 (t, CH_2O, 1 H), 6.98 (s, ArH, 3 H). ^{13}C NMR ($CDCl_3$): δ 27.49 ($ArCH_2$), 54.29, 55.42, 61.25 (CH_2N), 62.29 (CH_3O), 69.70, 72.03 (CH_2O), 123.41, 127.21, 134.81, 161.61 (Ar). MS: *m/e* 334 (M^+, 100). Anal. Calcd for $C_{19}H_{30}N_2O_3$: C, 68.23; H, 9.04. Found: C, 68.11; H, 9.18.

Method B. A solution of diamide 8 (1.00 g, 2.76 mmol) in CH_2Cl_2 (55 mL) was added dropwise to a cold (ice bath) suspension of $LiAlH_4$ (0.42 g, 11.07 mmol) in THF (95 mL). The mixture was stirred at room temperature, and the reaction was followed by TLC. The substrate disappeared after 22 h, and the reaction was quenched by addition of EtOAc and a small amount of water. The inorganic material was filtered and washed extensively with CH_2Cl_2, and the residue obtained after evaporation of the solvent was chromatographed on deactivated, basic alumina with CH_2Cl_2–CH_3OH (100:0 → 85:15) to give a yellow solid which was extracted several times with ethyl ether. The solvent was removed in vacuo to produce 12 (0.44 g, 47%).

Cryptand–Phenol 13. A mixture of cryptand 12 (0.44 g, 1.31 mmol), EtSNa (0.28 g, 3.38 mmol), and LiBr (0.22 g, 2.51 mmol) in DMF (9 mL) was heated at 150–155 °C over 5 h. The solvent was removed in vacuo, and the residue was redissolved in CH_2Cl_2 and filtered. The solvent was evaporated, and the crude product was chromatographed on alumina with CH_2Cl_2–CH_3OH (1%) to give cryptand–phenol 13 (0.25 g, 60%) as a white crystalline solid with mp 116.5–117.5 °C. IR (film): 3224, 3177 (OH), 1128, 1110 (CO) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.85–2.6 (m, $ArCH_2 + CH_2N$, 12 H), 2.85–3.8 (m, $CH_2N + CH_2O$, 12 H), 6.8–7.0 (m, ArH, 3 H), 7.58 (s, OH, 1 H). ^{13}C NMR ($CDCl_3$): δ 28.71 ($ArCH_2$), 53.08, 55.47, 61.58 ($ArCH_2$), 69.69, 72.00 (CH_2O), 122.12, 126.97, 135.32, 155.74 (Ar). MS: *m/e* 320 (M^+, 6.4). Anal. Calcd for $C_{18}H_{28}N_2O_3$: C, 67.47; H, 8.81. Found: C, 67.30; H, 8.92.

Chromoionophore 1. Method A. Cryptand diamide (8, 0.95 g, 2.62 mmol) was added portionwise to a suspension of $LiAlH_4$ (0.82 g, 21.61 mmol) in THF (80 mL), and the mixture was refluxed over 15 h. After cooling, 5% aqueous LiOH (2.5 mL) was added carefully, and the inorganic material was filtered and washed extensively with THF. The solvent was removed to give a red viscous oil which was redissolved in THF (5 mL), and five drops of 32% aqueous NaOH was added. The solvent was removed, and glacial acetic acid (4 mL) was added to the residue. To this solution was added dropwise *p*-nitrobenzenediazonium chloride (prepared at 0–5 °C from *p*-nitroaniline (0.35 g), 1 N HCl (7.8 mL), and $NaNO_2$ (0.21 g)). The reaction mixture turned from colorless to red-brown and was stirred overnight at room temperature. The solvent was removed, and the residue was partitioned between CH_2Cl_2 and water. The organic layer was washed several times with deionized water, the solvent was evaporated, and the residue was chromatographed twice on deactivated basic alumina with $CHCl_3$ and $CHCl_3$–EtOH (95:5) as eluents to afford 1 (0.12 g, 10% yield from two steps) as a red crystalline solid which decomposed over 210 °C. IR (film): 3095 (OH), 1517, 1339 (NO), 1129, 1112 (CO) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.5–3.5 (m, $ArCH_2 + CH_2N + CH_2O$, 24 H), 7.68 (s, ArH, 2 H), 8.17 (AB q, ArH, 4 H). ^{13}C NMR ($CDCl_3$): δ 28.96 ($ArCH_2$), 54.23 (br, CH_2N), 61.30 (CH_2N), 70.71 (br, CH_2O), 123.16, 123.49, 125.18, 136.65, 148.40, 148.64, 156.87, 161.05 (Ar). MS: *m/e* 469 (M^+, 10.9). Anal. Calcd for $C_{24}H_{31}N_5O_5$: C, 61.39; H, 6.65. Found: C, 61.07; H, 6.66.

Method B. Cryptand–phenol 13 (380 mg, 1.19 mmol) was dissolved in THF (5 mL), and 32% aqueous NaOH (3 drops) was added. The mixture was sonicated, the solvent was removed in vacuo, and the residue was redissolved in glacial acetic acid (2 mL). A solution of *p*-nitrobenzenediazonium chloride (made from *p*-nitroaniline (172 mg, 1.245 mmol), 1 N HCl (3.7 mL), and $NaNO_2$ (97 mg, 1.41 mmol)) was added dropwise. The red-colored solution was stirred overnight at room temperature. The workup and purification of method A gave 400 mg (72%) of pure 1.

Diester 14. Diacid 6 was esterified with ethanol in the presence of *p*-toluenesulfonic acid. The crude reaction product was purified on silica gel with petroleum ether–EtOAc (5:1) as eluent to give 14 (93%) as a colorless liquid. IR (neat): 1736 ($C{=}O$) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.23 (t, CH_3, 6 H), 3.64 (s, $ArCH_2$, 4 H), 3.72 (s, OCH_3, 3 H), 4.14 (q, OCH_2, 4 H), 7.04 (t, ArH, 1 H), 7.18 (d, ArH, 2 H). ^{13}C NMR ($CDCl_3$): 14.35 (CH_3), 35.87 ($ArCH_2$), 61.17 (OCH_2), 61.81 (OCH_3), 124.82, 128.52, 130.87, 157.36 (Ar), 172.29

(C=O). Anal. Calcd for $C_{15}H_{20}O_5$: C, 64.27; H, 7.19. Found: C, 64.39; H, 7.19.

Diol 15. A solution of ester 14 (5.80 g, 20.7 mmol) in ethyl ether (13 mL) was added dropwise at 0 °C to a suspension of $LiAlH_4$ (1.08 g, 28.5 mmol) in ethyl ether (80 mL). The reaction was quenched after stirring for 2 h at room temperature by subsequent addition of ethyl ether saturated with water (24.3 mL), water (1.2 mL), 15% aqueous NaOH (1.2 mL), and water (3.6 mL). The inorganic material was filtered, the solvent was removed, and the residue was chromatographed on silica gel with CH_2Cl_2–MeOH (95:5) to afford diol 15 (3.4 g, 84%) as a colorless oil. IR (neat): 3320 (OH) cm^{-1}. ^1H NMR ($CDCl_3$): 2.11 (br s, OH, 2 H), 2.87 (t, $ArCH_2$, 4 H), 3.74 (s, OCH_3, 3 H), 3.81 (q, OCH_2, 4 H), 6.97–7.12 (m, ArH, 3 H). ^{13}C NMR ($CDCl_3$): 33.84 ($ArCH_2$), 61.54 (CH_3), 63.55 (CH_2O), 125.17, 129.88, 132.58, 157.72 (Ar). Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.33; H, 8.22. Found: C, 67.17; H, 8.28.

Dimesylate 16. A solution of mesyl chloride (4.89 g, 41.8 mmol) in CH_2Cl_2 (75 mL) was added dropwise to a solution of diol 15 (3.37 g, 17.1 mmol) and triethylamine (5.65 g, 55.3 mmol) in CH_2Cl_2 at below 0 °C. After stirring for 1 h at 0 °C the reaction mixture was diluted with cold CH_2Cl_2 (90 mL), washed subsequently with 5% HCl, water, 5% aqueous $NaHCO_3$, and water again, and dried. The solvent was removed, and the residue was chromatographed on silica gel with CH_2Cl_2–MeOH (98:2) as eluent to give 16 (6.0 g, 100%) as a colorless oil. IR (neat): 1355, 1180 (S=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.86 (s, 6 H, SCH_3), 3.07 (t, 4 H, $ArCH_2$), 3.75 (s, 3 H, OCH_3), 4.41 (t, 4 H, OCH_2), 6.97–7.17 (m, 3 H, Ar). ^{13}C NMR ($CDCl_3$): δ 30.57 (SCH_3), 37.57 ($ArCH_2$), 61.68 (OCH_3), 69.66 (OCH_2), 125.19, 130.28, 130.65, 157.95 (Ar). Anal. Calcd for $C_{13}H_{20}O_7S_2$: C, 44.31; H, 5.72. Found: C, 44.23; H, 5.59.

Dinitrile 17. A solution of dimesylate 16 (3.04 g, 8.63 mmol) in DMSO (8 mL) was added dropwise to a suspension of NaCN (1.02 g, 20.7 mmol) in DMSO (2 mL) at 80 °C. The mixture was heated at 80–85 °C for 18 h. The solvent was removed in vacuo, and the residue was chromatographed on alumina with petroleum ether–EtOAc (2:1 → 1:1) to afford dinitrile 17 (1.56 g, 84%) as a solid with mp 41–43 °C. IR (Nujol): 2240 (CN) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.62 (t, $ArCH_2$, 4 H), 2.96 (t, CH_2CN, 4 H), 3.75 (s, OCH_3, 3 H), 7.00–7.18 (m, Ar, 3 H). ^{13}C NMR ($CDCl_3$): δ 18.25 (CH_2CN), 26.63 ($ArCH_2$), 61.84 (OCH_3), 119.75, 125.59, 129.98, 132.25 (Ar), 157.21 (CN). Anal. Calcd for $C_{13}H_{14}N_2O$: C, 72.87; H, 6.59. Found: C, 72.69; H, 6.65.

Diacid 18. Dinitrile 17 (1.56 g, 7.28 mmol) was refluxed for 18 h with 7% aqueous NaOH (38 mL). The reaction mixture was acidified with concentrated HCl, and 18 (1.0 g, 55%) was collected as a white fluffy solid with mp 113–115 °C. IR (Nujol): 1710 (C=O) cm^{-1}. ^1H NMR ($(CD_3)_2CO$): δ 2.59 (t, $ArCH_2$, 4 H), 2.93 (t, CH_2CO_2, 4 H), 3.76 (s, OCH_3, 3 H), 6.97 (t, ArH, 1 H), 7.11 (d, ArH, 2 H). ^{13}C NMR ($(CD_3)_2CO$): δ 26.05 ($ArCH_2$), 34.94 (CH_2CO_2), 61.54 (OCH_3), 125.42, 129.37, 135.27, 158.14 (Ar), 174.59 (COOH). Anal. Calcd for $C_{13}H_{16}O_5$: C, 61.90; H, 6.39. Found: C, 61.55; H, 6.28.

Acid Chloride 19. A procedure similar to that used for the preparation of 7 gave chloride 19 (1.0 g, 100%) as a pale-yellow oil. IR (neat): 1790 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 3.00 (t, $ArCH_2$, 4 H), 3.21 (t, CH_2CO, 4 H), 3.75 (s, OCH_3, 3 H), 6.96–7.10 (m, ArH, 3 H). ^{13}C NMR ($CDCl_3$): δ 26.12 ($ArCH_2$), 47.62 (CH_2CO), 61.48 (OCH_3), 125.32, 129.61, 132.70, 157.29 (Ar), 173.93 (C=O).

Cryptand Diamide 20. Acid chloride 19 (1.04 g, 3.60 mmol) and diaza-12-crown-4 (0.63 g, 3.60 mmol) were reacted according to the procedure described for the preparation of 8 to provide diamide 20 (0.88 g, 63%) as white crystals with mp 218 °C dec. IR (deposit on NaCl): 1640 (C=O), 1128, 1110 (CO) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.32–4.12 (m, CH_2 + $ArCH_2$ + CH_2O + CH_2N, 27 H), 6.82 (t, ArH, 1 H), 7.20 (d, ArH, 2 H). ^{13}C NMR ($CDCl_3$): δ 27.67 (CH_2), 32.59 ($ArCH_2$), 48.13, 51.01 (CH_2N), 60.90 (OCH_3), 66.34, 70.70 (CH_2O), 123.26, 132.76, 133.59, 157.64 (Ar), 172.80 (C=O). MS: *m/e* 391 (M^+ + 1, 100). Anal. Calcd for $C_{21}H_{30}N_2O_5$: C, 64.60; H, 7.74. Found: C, 64.71; H, 7.83.

Cryptand 21. Diamide 20 (0.50 g, 1.28 mmol) was reduced with $LiAlH_4$ (0.19 g, 5.12 mmol) using the conditions described for the preparation of cryptand 12. Purification on deactivated, basic alumina with CH_2Cl_2–MeOH (98:2) as eluent afforded cryptand 21 (0.41 g, 88%) as a white solid which decomposed above 135 °C. IR (deposit on NaCl): 1130 (CO) cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.64–1.98 (m, 4 H, CH_2), 2.24–3.18 (m, 20 H, $ArCH_2$ + CH_2N + CH_2O), 3.32–3.70 (m, 4 H, CH_2O), 3.64 (s, 3 H, OCH_3), 6.88–7.03 (m, 3 H, ArH). ^{13}C NMR ($CDCl_3$): 28.42, 28.94 (CH_2), 52.60, 52.90, 55.37 (CH_2N), 60.92 (OCH_3), 69.30, 69.51 (CH_2O), 123.75, 128.92, 135.90, 158.43 (Ar). MS: *m/e* 363 (M^+ + 1, 100). Anal. Calcd for $C_{21}H_{34}N_2O_3$: C, 69.58; H, 9.45. Found: C, 69.48; H, 9.64.

Chromoionophore 2. Reacting cryptand diamide 20 with $LiAlH_4$ in a manner described for the preparation of 1 (method A) resulted in a mixture of products[21] which was directly treated with *p*-nitrobenzenediazonium salt. The crude product was chromatographed on deactivated, basic alumina with CH_2Cl_2–MeOH (99:1 → 85:15) as eluent to produce pure 2 (0.23 g, 40%) as a dark-red glass. IR (film): 3320 (OH), 1505, 1338 (NO), 1120, 1092 (CO) cm^{-1}. ^1H NMR (CD_3OD): δ 2.05–2.22 (t, CH_2, 4 H), 2.78–3.50 (m, CH_2N + $ArCH_2$, 16 H), 3.80–4.06 (m, CH_2O, 8 H), 7.67 (s, C_{quin}, 2 H), 8.04 (AB q, ArH, 4 H). ^{13}C NMR (CD_3OD): 27.09, 28.41 ($ArCH_2CH_2$), 55.64, 56.00 (CH_2N), 67.32 (CH_2O), 123.63, 125.99, 127.87, 129.47, 144.75, 148.71, 158.77 (=CH + Ar), 172.75 (C=O). MS: *m/e* 497 (M^+, 9.8). Anal. Calcd for $C_{28}H_{35}N_5O_5 \cdot CH_2Cl_2$: C, 55.67; H, 6.40. Found: C, 55.98; H, 6.79.

Diamide 23. Acid chloride 7 (2.00 g, 7.66 mmol) and diaza-18-crown-6 (2.01 g, 7.66 mmol) were reacted under the conditions used for the preparation of 8 to give after column chromatography (silica gel, CH_2Cl_2–MeOH (9:1)) cryptand 23 (1.20 g, 35%) as crystals with mp 210–212 °C. IR (deposit on NaCl): 1644 (C=O), 1123 (CO) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.06–2.21 (m, 1 H, CH_2O), 2.48–2.88 (m, 4 H, CH_2O), 2.99–4.27 (m, 27 H, $ArCH_2$ + CH_2O + CH_2N + CH_3O), 7.02–7.20 (m, 2 H, ArH), 7.40–7.55 (m, 1 H, ArH). ^{13}C NMR ($CDCl_3$): δ 34.00, 42.27 ($ArCH_2$), 46.37, 48.41, 50.23, 51.65 (CH_2N), 61.28 (CH_3O), 67.52, 69.27, 70.03, 70.10, 70.55, 70.70, 71.51, 73.69 (CH_2O), 125.75, 129.12, 129.45, 130.43, 131.12, 156.63 (Ar), 171.97, 172.14 (C=O). MS: *m/e* 451 (M^+ + 1, 100). Anal. Calcd for $C_{23}H_{34}N_2O_7$: C, 61.32; H, 7.61. Found: C, 61.43; H, 7.70.

Cryptand–Phenol 24. A mixture of diamide 23 (0.40 g, 0.89 mmol) and $LiAlH_4$ (0.14 g, 3.69 mmol) in THF (30 mL) was refluxed for 15 h. The reaction was quenched by addition of 15% aqueous NaOH (0.5 mL), the inorganic salts were filtered, and the solvent was removed. The residue was purified on basic alumina with CH_2Cl_2–MeOH (99:1 → 96:4) as eluent to afford 24 (0.27 g, 75%) as a glass. IR (deposit on NaCl): 1118 (CO) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.53–2.86 (m, 16 H, CH_2N + $ArCH_2$), 3.32–3.58 (m, 12 H, CH_2O), 3.60–3.75 (m, 4 H, CH_2O), 6.71 (t, 1 H, ArH), 6.91 (d, 2 H, ArH). ^{13}C NMR ($CDCl_3$): δ 29.85 ($ArCH_2$), 55.26, 59.20 (CH_2N), 69.72, 71.62 (CH_2O), 119.79, 128.62, 130.62, 155.69. MS: *m/e* 409 (M^+ + 1, 100). Anal. Calcd for $C_{22}H_{36}N_2O_5$: C, 64.68; H, 8.88. Found: C, 64.70; H, 8.85.

Chromoionophore 3. Reacting cryptand–phenol 24 with *p*-nitrobenzenediazonium chloride in a manner described for the preparation of 1 (method B) produced after column chromatography (alumina, $CHCl_3$–EtOH (99:1)) compound 3 in 70% yield as a red glass. IR (film): 3360 (OH), 1514, 1338 (NO), 1140, 1103 (CO) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.58–3.00 (m, 16 H, CH_2N + $ArCH_2$), 3.22–3.84 (m, 16 H, CH_2O), 7.66 (s, 2 H, ArH), 8.13 (AB q, 4 H, ArH). ^{13}C NMR ($CDCl_3$): δ 30.16 ($ArCH_2$), 55.30, 58.80 (CH_2N), 69.64, 71.74 (CH_2O), 123.27, 125.18, 125.35, 131.29, 146.39, 148.35, 157.08, 162.34 (Ar). MS: *m/e* 558 (M^+ + 1, 100). Anal. Calcd for $C_{28}H_{39}N_5O_7 \cdot H_2O$: C, 58.42; H, 7.18. Found: C, 58.29; H, 7.20.

UV–Vis Spectroscopic Properties of Chromoionophores 1–3 and Determination of Their pK_a Values. The UV–vis spectra of the various forms of chromoionophores 1, 2, and 3 were determined in 5×10^{-5} M solutions of a chromoionophore in 10% v/v DEGMEE in water; 10^{-2} M stock solutions of 1, 2 and 3 were prepared in DEGMEE. Typically, the solutions were prepared as follows: for the spectral characteristics in 10% v/v DEGMEE,

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[21] A small amount of cryptand phenol 22 was isolated from the reaction mixture and characterized by NMR. ^1H NMR ($CDCl_3$): δ 1.70–1.90 (m, 4 H, CH_2), 2.40–2.70 (m, 12 H, $ArCH_2$ + CH_2N), 2.81 (t, 4 H, CH_2N), 3.13–3.32 (m, 4 H, CH_2O), 3.43–3.67 (m, 4 H, CH_2O), 6.80 (t, 1 H, ArH), 6.92 (d, 2 H, ArH), 9.87 (br s, 1 H, OH). ^{13}C NMR ($CDCl_3$): δ 28.11, 28.61 (CH_2 + $ArCH_2$), 56.72, 59.41 (CH_2N), 68.86 (CH_2O), 121.46, 127.19, 135.09, 153.48 (Ar).

0.05 mL of the stock solution was added to 0.95 mL of DEGMEE. The diluted sample was quantitatively transferred to 9.0 mL of the appropriate reagent and mixed. HCl (1 N) was used to obtain the acid form (HL) and 1 M TMAOH for the base form (L^-). The resulting solutions were scanned in a 1-cm path length cuvette from 700 to 300 nm on a Beckman DU-8B spectrophotometer.

For the pK_a determinations, absorbances were measured at the acid and base wavelength maxima of the chromogenic compounds in a zwitterionic buffer (3-(cyclohexylamino)-1-propanesulfonic acid, CAPS)) at pH values equal to the pK_a and the $pK_a \pm 0.5$ units. These absorbances were used in conjunction with the absorptivities of the acid and base forms to calculate the pK_a values of 1–3.[2b]

Responses of Chromoionophores 1 and 3 to Lithium, Sodium, and Potassium in 10% Aqueous DEGMEE. The reagents for obtaining lithium, sodium, and potassium responses consisted of 5.0×10^{-5} M chromoionophore in 10% DEGMEE/water and an appropriate buffer (Table III). The spectra of the cation complexes (L^-M^+) of 1 and 3 in 10% v/v DEGMEE were obtained by adding 0.02 mL of 1.0 M LiCl, NaCl, and KCl to their respective cuvettes containing 2 mL of reagent and scanned from 700 to 300 nm.

The association constant for the lithium complex of 1 in 10% aqueous DEGMEE/TMA(OH) was determined according to a literature procedure.[18]

Responses of Chromoionophore 2 to Lithium, Sodium, and Potassium in CH_2Cl_2–Water. Equal volumes (3.0 mL) of a dichloromethane solution of 2 (1.0×10^{-4} M) and an aqueous solution made of 0.1 M CAPS for pH 11.0, containing 0.05 M LiCl, NaCl, and KCl, respectively, were vortexed in a test tube for 2 min. The organic phase was separated and scanned from 700 to 300 nm (Table II).

For the Li^+ response curve with chromoionophore 2, equal volumes (3.0 mL) of a CH_2Cl_2 solution of 2 (2.0×10^{-4} M) and an aqueous solution made of 0.1 M CAPS for pH 11.6, containing from 0 to 0.01 M LiCl, were vortexed, and the organic layer was separated and scanned from 700 to 300 nm.

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Ionic Photodissociation of Polyenes via a Highly Polarized Singlet Excited State

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Several polyene acetates and polyene methyl ether were prepared. Upon direct excitation these polyenes undergo ionic photodissociation from their singlet excited states. Triplet-sensitization experiments on these polyenes revealed that the ionic photodissociation process is restricted to singlet excited states. The rationale put forward is that the polyene chromophore undergoes charge separation/polarization in the singlet excited state, which leads to ionic photodissociation.

Introduction

The spectroscopic and photochemical behavior of polyenes, polyenals, polyenones, and to a certain extent polyene esters and nitriles has been studied.[1] Deactivation of polyene excited states results in cis–trans isomerization, sigmatropic shifts, and electrocyclization reactions.[2] The involvement of a highly polarized excited states in these photochemical reactions has been suggested. Theoretical studies carried out by Salem and others[3] on polyenes revealed the polarized nature of their excited states. A zwitterionic excited state was put forward by Dauben[4] to explain the high stereospecificity observed in the photocyclization reaction of *trans*-ethylidenecyclooctene. The same hypothesis was extended to explain vitamin D and triene photochemistry.[5] Similarly, a highly polarized

Table I. Quantum Yield for Direct Excitation Reactions[a]

compd	cis isomers	tetraene	methyl ether
1	0.243	0.191	0.113
2	0.197	0.199	0.086
3	0.195		0.078
4	0.143	0.092	

[a] Quantum yields were determined using ferrioxalate actinometry in an Applied Photophysics quantum yield reactor (QYR-20); methanol is the solvent; at 280 nm using solution filters; values are averages of three runs.

Table II. Quantum Yield Data of Pentaene Acetate in Various Solvents[a]

entry no.	solvent	fluorescence	9-cis	13-cis	anhydroretinol	methyl ether
1	hexane	0.041	0.012	0.008	0.007	
2	CH_2Cl_2	0.011	0.047	0.017	0.028	
3	CH_3CN	0.003	0.032	0.029	0.106	
4	MeOH	0.004	0.039	0.026	0.019	0.104

[a] Quantum yield of fluorescence for entry 4 is from ref 11; quantum yield determined is relative to 9,10-diphenylanthracene; values are averages of three runs; product quantum yield was determined using potassium ferrioxalate actinometry, at 320 nm.

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