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# New Small-Cavity Cryptand Chromoionophores for Complexation of Lithium and Sodium Ions

EDDY CHAPOTEAU, BRONISLAW P. CZECH,* ANAND KUMAR and WOLODYMYR ZAZULAK
*Miles Incorporated, Tarrytown, NY 10591, U.S.A.*

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**Abstract.** Two new chromoionophores based on small-cavity cryptands with inward-facing phenolic groups have been synthesized. Both compounds incorporate a diaza-12-crown-4 moiety and bear a *p*-nitrophenylazo chromogenic group attached to the cryptand phenol framework, *para* to the phenolic group. Chromogenic cryptand **3** exhibits selectivity for $Li^+$ ions in the extraction mode but shows very little cation response in homogeneous aqueous media. A larger analog, chromogenic cryptand **4**, acts as a sodium scavenger and cannot be obtained in a sodium-free form.

**Key words:** Cryptands, chromoionophores, alkali metal cation complexation.

## 1. Introduction

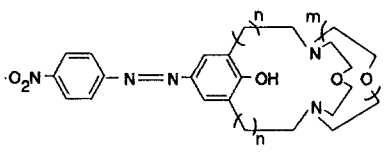
Chromogenic indicator systems for the determination of potassium, sodium, and lithium ions in biological fluids have been of interest for more than fifteen years [1]. Despite a multitude of chromogenic structures published during that time only those based on cryptahemispherands have proved to be of practical importance for use in homogeneous and largely aqueous media [2]. Indicators for the colorimetric determination of lithium in aqueous solutions have been even more elusive. We have recently reported chromoionophore **1**, based on a small-cavity cryptand phenol, which can be applied in practice for the determination of lithium in physiological fluids [3]. Another structurally-similar chromogenic cryptand, **2**, highly selective for lithium in extraction, has recently been reported by Sutherland and Sholl [4].

Chromogenic cryptand phenols having larger cavities have been reported before [5]. In this paper, we report the synthesis of two new chromoionophores, **3** and **4**, based on small-cavity cryptand phenols, and their spectroscopic responses to lithium, sodium, and potassium ions.

## 2. Experimental

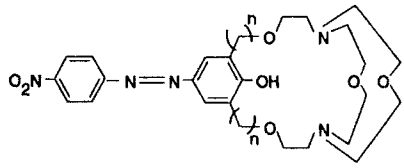
Melting points are uncorrected. $^1H$ and $^{13}C$-NMR spectra were recorded on a Varian Gemini spectrometer at 200 and 50 MHz, respectively. IR spectra were obtained

* Author for correspondence.



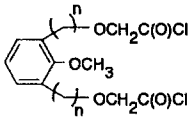
**1** (n=m=1)

**2** (n=0; m=2)



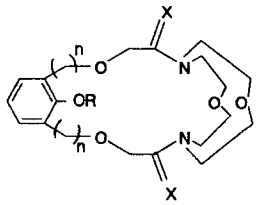
**3** (n=0)

**4** (n=1)

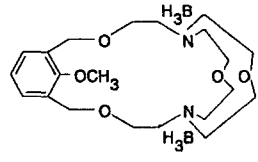


**5** (n=0)

**6** (n=1)



| | n | R | X |
|---|---|---|---|
| **7** | 0 | $CH_3$ | O |
| **8** | 1 | $CH_3$ | O |
| **9** | 0 | $CH_3$ | $H_2$ |
| **11** | 1 | $CH_3$ | $H_2$ |
| **12** | 0 | H | $H_2$ |
| **13** | 1 | H | $H_2$ |



**10**

Scheme.

with a Perkin-Elmer 267 spectrophotometer. The UV-visible spectra were recorded on a Cary-3 spectrophotometer. Fast atom bombardment (FAB) mass spectra were determined using *m*-nitrobenzyl alcohol (NOBA) as the matrix.

Benzene and DMF were kept over molecular sieves (4 Å). Tetrahydrofuran was distilled from sodium benzophenone ketyl. $BH_3 \cdot Me_2S$ complex was purchased from Aldrich. Diacid chlorides **5** [5a] and **6** [6], diaza-12-crown-4 [7], and sodium toluenethiolate-DMF reagent [8] were prepared according to literature procedures.

## 2.1. Preparation of Cryptand Diamides **7** and **8**

Solution A (100 mL) containing an acid chloride (7.00 mmol) in benzene and Solution B (100 mL) containing diaza-12-crown-4 (1.22 g, 7.00 mmol) [7] and triethylamine (1.74 g, 17.2 mmol) in benzene were added simultaneously to vigorously stirred benzene (230 mL), at an 8.3 mL/h addition rate. After the addition was completed, the mixture was stirred for 12 h. The solvent was removed *in vacuo* and the residue was dissolved in $CHCl_3$ and filtered. The solvent was removed

*in vacuo* and the residue was chromatographed on silica gel with $CH_2Cl_2$-EtOH (97 : 3 → 95 : 5) as eluent.

**7**: Yield: 30%; white solid with m.p. 230°C (dec). $^1$H-NMR($CDCl_3$): $\delta$ = 2.60–3.05 (m, $CH_2N$, 6H), 3.25–3.60 (m, $CH_2N$+$CH_2O$, 6H), 3.70–4.10 (m, $CH_2O$+$CH_3O$, 7H), 4.99 (ABq, $OCH_2CO$, 4H), 6.80–7.05 (m, Ar, 3H). $^{13}$C-NMR($CDCl_3$): $\delta$ = 45.62, 47.87 ($\underline{C}H_2N$), 61.54 ($\underline{C}H_3O$), 67.97, 69.45, 69.94 ($\underline{C}H_2O$), 117.83, 123.02, 151.16 (Ar), 169.27 (C=O). IR (deposit on NaCl plate): 1580 (C=O), 1128 (C-O) cm$^{-1}$. *Anal. Calcd.* for $C_{19}H_{26}N_2O_7$: C, 57.86; H, 6.64. *Found*: C, 57.92; H, 6.47.

**8**: Yield: 60%; white solid with m.p. 197.5–199°C. $^1$H-NMR($CDCl_3$): $\delta$ = 2.64–3.05 (m, $CH_2N$, 4H), 3.39–3.75 (m, $CH_2N$+$CH_2O$+$CH_3O$, 13H), 4.09 (ABq, $CH_2O$, 4H) 4.41 (t, $CH_2O$, 2H), 4.76 (ABq, $CH_2O$, 4H), 7.19 (t, ArH, 1H), 7.43 (d, ArH, 2H). $^{13}$C-NMR($CDCl_3$): $\delta$ = 48.87, 50.92 ($\underline{C}H_2N$), 62.68 ($\underline{C}H_3O$), 63.73, 64.86, 65.73 ($\underline{C}H_2O$), 72.19 (Ar$\underline{C}H_2$), 125.97, 126.86, 132.48, 133.11 (Ar), 172.04 (C=O). IR (deposit on NaCl plate): 1652 (C=O), 1124, 1100 (C-O) cm$^{-1}$. *Anal. Calcd.* for $C_{21}H_{30}N_2O_7$: C, 59.70; H, 7.16. *Found*: C, 59.81; H, 7.11.

## 2.2. Preparation of Cryptand **9**

A solution of cryptand diamide **7** (1.00 g, 2.54 mmol) in $CH_2Cl_2$ (52 mL) was added dropwise to a solution of $LiAlH_4$ (0.39 g, 10.4 mmol) in THF (105 mL) and the mixture was refluxed for 8 h. The reaction was quenched by addition of EtOAc and water. The precipitate was filtered and the solvent was removed *in vacuo*. The residue was chromatographed on deactivated alumina with $CH_2Cl_2$-MeOH (95 : 5) to afford **9** (0.45 g, 48%) as a white solid which sinters at 150°C and slowly decomposes. $^1$H-NMR($CDCl_3$): $\delta$ = 2.38–3.09 (m, $CH_2N$+$CH_2O$, 16H), 3.42–3.55 (m, $CH_2O$, 2H), 3.65–3.79 (m, $CH_2O$, 2H), 3.94 (s, $CH_3O$, 3H), 4.06–4.38 (m, $CH_2O$, 4H), 6.57 (d, ArH, 2H), 6.83 (t, ArH, 1H). $^{13}$C NMR ($CDCl_3$): $\delta$ = 55.45, 57.24, 58.55 ($\underline{C}H_2N$), 62.71 ($\underline{C}H_3O$), 69.43, 69.85, 70.00 ($CH_2O$), 112.53, 122.59, 145.75, 154.12 (Ar). IR (deposit on NaCl plate): 1128, 1090 (C-O) cm$^{-1}$. *Anal. Calcd.* for $C_{19}H_{30}N_2O_5$: C, 62.27; H, 8.25. *Found*: C, 62.46; H, 8.15.

## 2.3. Preparation of Dihydroborane Cryptand **10**

10 M $BH_3 \cdot Me_2S$ complex (13.4 mL, 134 mmol) was slowly added to a solution of cryptand diamide **8** (2.00 g, 4.73 mmol) in THF (300 mL). The mixture was refluxed for 3 h. The reaction was quenched by careful addition of water and the solvent was removed *in vacuo*. The residue was redissolved in $CH_2Cl_2$, the solution was washed with water and filtered through a layer of anhydrous $CaSO_4$. The solvent was removed *in vacuo* and the residue was chromatographed on flash silica gel with $CHCl_3$-EtOH (99 : 1 → 95 : 5) to produce **10** (1.73 g, 86%) as a white solid with m.p. 173–175°C. $^1$H-NMR($CDCl_3$): $\delta$ = 1.50 (very br s, $BH_3$,

6H), 2.80–3.32 (m, $CH_2N$, 12H), 3.38–4.11 (m, $CH_2O$+$CH_3O$, 15H), 4.45 (ABq, $CH_2O$, 4H), 7.11 (t, ArH, 1H), 7.31 (d, ArH, 2H). $^{13}$C-NMR($CDCl_3$): $\delta$ = 57.19, 58.06, 63.59 ($\underline{C}H_2N$), 62.77 ($\underline{C}H_3O$), 66.30, 66.50, 67.12, 69.08 ($\underline{C}H_2O$), 124.91, 131.66, 133.07, 158.95 (Ar). IR (deposit on NaCl plate): 2339, 2312 (B-H), 1095, 1080, 1065 (C-O) cm$^{-1}$. *Anal. Calcd.* for $C_{21}H_{40}B_2N_2O_5$: C, 59.74; H, 9.55. *Found*: C, 59.74; H, 9.62.

### 2.4. Preparation of Cryptand **11**

Dihydroborane **10** (0.89 g, 2.46 mmol) was suspended in MeOH (200 mL) containing KOH (3.13 g, 55.8 mmol) and the mixture was stirred at room temperature for 4 days. The solvent was removed *in vacuo* and the residue was repeatedly extracted with petroleum ether. The solvent was removed *in vacuo* from the combined extracts to give a solid which was redissolved in $CH_2Cl_2$ and shaken several times with deionized water. The organic layer was separated and the solvent was removed *in vacuo* to give pure cryptand **11** (0.73 g, 89%) as a white solid with m.p. 143.5–145°C. $^1$H-NMR($CDCl_3$): $\delta$ = 2.28–2.65 (m, $CH_2N$, 12H), 3.04–3.52 (m, $CH_2O$, 12H), 4.12 (s, $CH_3O$, 3H), 4.55 (br s, $ArCH_2$, 4H), 7.08 (t, ArH, 1H), 7.28 (d, ArH, 2H). $^{13}$C-NMR($CDCl_3$): $\delta$ = 58.80, 60.45 ($\underline{C}H_2N$), 67.05 ($\underline{C}H_3O$), 69.28, 70.02, 71.33 ($\underline{C}H_2O$), 124.90, 133.95, 134.24, 161.89 (Ar). IR (deposit on NaCl plate): 1125, 1095 (C-O) cm$^{-1}$. *Anal. Calcd.* for $C_{21}H_{34}N_2O_5$: C, 63.94; H, 8.69. *Found*: C, 63.93; H, 8.76.

### 2.5. Preparation of Cryptand Phenol **12**

Lithium bromide (0.17 g, 1.99 mmol) and sodium thioethoxide (0.23 g, 2.67 mmol) were added to a solution of cryptand **9** (0.38 g, 1.04 mmol) in DMF (14 mL) and the mixture was heated at 150°C for 9 h. The solvent was removed *in vacuo* and the residue was chromatographed on deactivated alumina with $CH_2Cl_2$-MeOH (99 : 1 → 96 : 4) to afford **12** (0.28 g, 77%) as a white solid with m.p. 136–138°C. $^1$H-NMR($CDCl_3$): $\delta$ = 2.35–2.90 (m, $CH_2N$, 12H), 3.05–3.40 (m, $CH_2O$, 8H), 4.15 (t, $CH_2O$, 4H), 6.56 (d, ArH, 2H), 6.73 (t, ArH, 1H), 7.88 (br s, OH, 1H). $^{13}$C-NMR($CDCl_3$): $\delta$ = 56.86, 59.06 ($\underline{C}H_2N$), 69.85, 71.03 ($\underline{C}H_2O$), 112.29, 120.66, 141.44, 153.88. IR (deposit on NaCl plate): 3310 (O-H), 1108 (C-O) cm$^{-1}$. *Anal. Calcd.* for $C_{18}H_{28}N_2O_5$: C, 61.34; H, 8.01. *Found*: C, 61.26; H, 7.94.

### 2.6. Preparation of Cryptand Phenol **13**

A solution of cryptand **11** (0.90 g, 2.28 mmol) and sodium toluenethiolate (1.46 g, 10.0 mmol) in DMF (20 mL) was heated under argon for 4 h at 100°C. The solvent was removed *in vacuo* and the residue was chromatographed on alumina with $CH_2Cl_2$-MeOH (98 : 2) as eluent to give **13** (0.64 g, 74%) as a light-yellow viscous oil. $^1$H-NMR($CDCl_3$): $\delta$ = 2.55–2.88 (m, $CH_2N$, 12H), 3.45–3.92 (m,

$CH_2O$, 12H), 4.55 (s, $PhCH_2$, 4H), 6.80 (t, ArH, 1H), 7.13 (d, ArH, 2H), 9.20 (br s, OH, 1H). $^{13}$C-NMR($CDCl_3$): $\delta$ = 58.83, 59.66 ($\underline{C}H_2N$), 69.63, 71.14, 71.35 ($\underline{C}H_2O$), 121.41, 128.64, 132.27, 158.32 (Ar). IR (neat): 3290 (O-H), 1111 (C-O) $cm^{-1}$. *Anal. Calcd.* for $C_{20}H_{32}N_2O_5$: C, 63.14; H, 8.48. *Found*: C, 63.11; H, 8.59.

## 2.7. Preparation of Chromogenic Cryptands 3 and 4

A solution of *p*-nitrobenzenediazonium chloride (prepared at 0–5°C from *p*-nitroaniline (114 mg, 0.825 mmol), 1 M HCl (2.5 mL), and $NaNO_2$ (68 mg, 0.985 mmol) was added dropwise to a solution of the cryptand phenol (0.84 mmol) in 0.25 M NaOH (4.2 mL). After the addition was completed, the pH of the mixture was adjusted to 8.5 with 5% aqueous NaOH and the mixture was stirred overnight at room temperature. Dichloromethane and water were added and the organic layer was separated. The solvent was removed *in vacuo* and the residue was chromatographed on deactivated neutral alumina with EtOAc-MeOH (98 : 2) as eluent.

**3**: Yield 36%, dark-red glass. $^1$H-NMR($CDCl_3$): $\delta$ = 2.40–3.65 (m, $CH_2N$+ $CH_2O$, 20H), 4.27 (t, $CH_2O$, 4H), 7.35 (s, ArH, 2H), 8.15 (ABq, ArH, 4H), 8.98 (br s, OH, 1H). $^{13}$C-NMR($CDCl_3$): $\delta$ = 56.56, 58.36 ($\underline{C}H_2N$), 69.76 ($\underline{C}H_2O$), 108.74, 123.54, 125.19, 153.07 (Ar). IR (film): 3200 (O-H), 1097 (C-O) $cm^{-1}$. MS: 502.3 ($M^+$). *Anal. Calcd.* for $C_{24}H_{31}N_5O_7$: C, 57.48; H, 6.23. *Found*: C, 57.21; H, 6.28.

**4**$^-\cdot Na^+$: Yield 63%, dark-violet glass. $^1$H- NMR($CDCl_3$): $\delta$ = 2.55–2.85 (m, $CH_2N$, 12H), 3.40–3.75 (m, $CH_2O$, 12H), 4.51 (s, $PhCH_2O$, 4H), 7.85 (s, ArH, 2H), 8.01 (ABq, ArH, 4H). $^{13}$C-NMR($CDCl_3$): $\delta$ = 54.36, 57.40 ($\underline{C}H_2N$), 68.38, 72.79 ($\underline{C}H_2O$), 123.44, 126.75, 129.81, 131.05, 141.40, 147.61, 160.53 (Ar), 181.61 (C=O). IR (film): 1092 (C-O) $cm^{-1}$. MS: 552.3 ($M+Na^+$). *Anal. Calcd.* for $C_{26}H_{34}N_5O_7Na$: C, 56.62; H, 6.21. *Found*: C, 57.04; H, 6.35.

A nearly sodium-free **4** was obtained by dissolving its sodium complex in toluene and washing several times with deionized water until almost complete disappearance of the band from the NaL form at ~530 nm.

## 2.8. UV-Vis Spectroscopic Properties of Chromogenic Cryptands 3 and 4

The UV-vis spectra of the acid (HL) and base ($L^-$) forms of chromogenic cryptands **3** and **4** were determined in $5.0 \times 10^{-5}$ M solutions of chromoionophore **3** in 1% v/v diethylene glycol monoethyl ether (DEGMEE) in water; $5 \times 10^{-3}$ M stock solutions of **3** and **4** were prepared in DEGMEE. Typically, the solutions were prepared as follows: for the spectral characteristics in 1% v/v DEGMEE, 0.02 mL of the stock solution was added to 1.98 mL of the appropriate reagent and mixed. HCl (1N) was used to obtain the acid form (HL) and 1 M tetramethylammonium hydroxide

(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.

### 2.9. Responses of Chromoionophores 3 and 4 to Lithium, Sodium and Potassium in $CH_2Cl_2$-Water

Equal volumes (3.0 mL) of a dichloromethane solution of **3** ($5.0 \times 10^{-5}$ M) and an aqueous solution made of 0.1 M CAPS for pH 12.0, containing 0.01 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). Similarly, a dichloromethane solution of **4** ($1.0 \times 10^{-4}$ M) and an aqueous solution of 0.2 M HEPES for pH 8.0, containing 0.02 M LiCl, NaCl, and KCl, respectively, were vortexed and the organic layer was scanned.

## 3. Results and Discussion

### 3.1. Syntheses

Cyclization of diacid chlorides **5** [5a] and **6** [6] with diaza-12-crown-4 [7] under high dilution conditions in benzene gave cryptand diamides **7** and **8** in yields of 30 and 60%, respectively. Reduction of **7** with $LiAlH_4$ in a mixed THF-$CH_2Cl_2$ solvent system [3a] afforded cryptand **9** in 48% yield. When these conditions were applied to diamide **8** only a complicated mixture of products was obtained. Thus, diamide **8** was first treated with a $BH_3 \cdot Me_2S$ complex to give dihydroborane **10** (86%), which subsequently was converted in 89% yield into cryptand **11** by treatment with methanolic KOH according to Lehn's procedure [9]. Demethylation of cryptand **9** with a EtSNa-LiBr mixture in DMF at 150°C [10] gave cryptand phenol **12** in 77% yield.

Cryptand phenol **13** was obtained in 74% yield from its precursor **11** in reaction with sodium toluenethiolate in DMF [8] at 100°C after a 4 h period. Higher temperatures and/or longer reaction times lead to fast decomposition of the product. Cryptand phenols **12** and **13** were coupled with *p*-nitrobenzenediazonium chloride to produce chromogenic cryptands **3** and $\mathbf{4}^- \cdot Na^+$ in yields of 36 and 63%, respectively. When cryptand phenol **13** was treated with *p*-nitrobenzenediazonium tetrafluoroborate in the presence of 5% aqueous LiOH, chromogenic cryptand **4** was obtained as a mixture of its sodium complex and a free ligand, as evidenced by the FAB mass spectrum of the product. This result indicates that **4** easily scavenges traces of sodium present in solvents, reagents, and chromatographic materials. Such behavior has been previously observed with spherands [11] and cryptahemispherands [2b]. Although most of the complexed sodium can be removed by extensive washing of organic solvent solutions of **4** with deionized water, full removal of $Na^+$ is impossible since the cryptand nitrogen atoms freed from the complex become protonated and the chromogenic compound is lost to the aqueous phase.

TABLE I. Chemical shifts of methoxyl groups in $^{1}H$- and $^{13}C$-NMR spectra of cryptands and their lithium, sodium, and potassium complexes in $CDCl_3$.

| Compd. | $^{1}H$ NMR, $\delta$ | | $^{13}C$ NMR, $\delta$ | |
|---|---|---|---|---|
| | $ArOC\underline{H}_3$ | $ArC\underline{H}_2O$ | $ArO\underline{C}H_3$ | $\underline{C}_{AR}$-OMe |
| **9** | 3.94 | — | 62.71 | 145.75 |
| **9** · $LiClO_4$ | 3.99 | — | 64.66 | 141.02 |
| **9** · $NaClO_4$ | 4.01 | — | 64.99 | 143.42 |
| **9** · $KClO_4$ | NB[a] | — | NB[a] | NB[a] |
| **11** | 4.12 | 4.55 (br s) | 67.05 | 161.89 |
| **11** · $LiClO_4$ | 3.92 | 4.58 (ABq, $\Delta\nu_{AB}$0.58) | 63.73 | 159.67 |
| **11** · $NaClO_4$ | 3.93 | 4.55 (ABq, $\Delta\nu_{AB}$0.63) | 63.13 | 158.84 |
| **11** · $KClO_4$ | 3.91 | 4.45 (ABq, $\Delta\nu_{AB}$0.55) | 63.82 | 159.09 |

[a] No binding was observed.

TABLE II. UV-vis spectral characteristics ($\lambda_{max}$ and $\varepsilon(\lambda_{max})$) of chromogenic compounds **3** and **4** in $H_2O$-DEGMEE (99+1, v/v).

| Compd. | Form[a] | $\lambda_{max}$, nm | $\varepsilon(\lambda_{max})$ |
|---|---|---|---|
| **3** | $L^-$ | 578 | 32300 |
| | HL | 499 | 66000 |
| **4**[b] | $L^-$ | 516 | 31940 |
| | HL | 368 | 23550 |
| | | 467 | 7400 |

[a] $L^-$ is fully ionized in 1.0 M TMAOH and HL is nonionized ligand in 0.1 M HCl.
[b] Compound **4** contained residual sodium.

### 3.2. Complexation of Lithium, Sodium, and Potassium Ions by Cryptands **9** and **11**

Complexation of lithium, sodium and potassium ions by methoxycryptands **9** and **11** was followed by $^{1}H$ and $^{13}C$-NMR in $CDCl_3$. In the proton spectra, upon complexation of **9** with $Li^+$ and $Na^+$, singlets of the inward-facing methoxyls were shifted only slightly downfield (Table I). Downfield shifts by about 2 ppm were observed in the corresponding $^{13}C$-NMR spectra for the methyl carbon signals. There was no detectable interaction between **9** and $K^+$, most probably due to cavity-ion incompatibility. More pronounced effects were caused by complexation in spectra of **11**. In general, upon complexation, signals of methylene protons

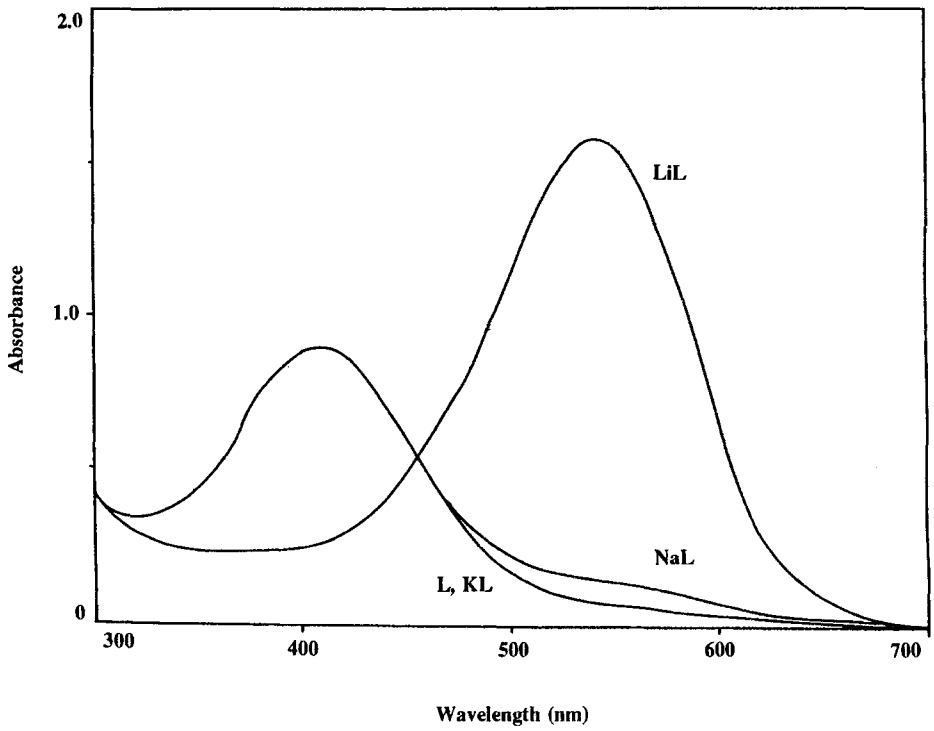



Fig. 1. UV-vis spectra of lithium (LiL), sodium (NaL), and potassium (KL) responses of cryptand **3** (L) in $CH_2Cl_2$-0.1 M TMAOH.

adjacent to nitrogen and oxygen were shifted downfield. The largest shift by about 0.5 ppm was observed for $CH_2N$ protons due to complexation of $Li^+$. Singlets assigned to the methoxyl protons were shited upfield by about 0.2 ppm from $\delta$ 4.12 (free) to about $\delta$ 3.92 (complexes). A broad singlet of $ArCH_2O$ protons became an AB quartet upon complexation with all three ions. In the aromatic regions, the largest changes were observed for the carbons linked with the methoxyl groups.

### 3.3. Spectral Characteristics of Chromogenic Crytands **3** and **4**

Wavelength maxima ($\lambda_{max}$) and molar absorptivities ($\varepsilon$) of the acid (HL) and base ($L^-$) forms of chromogenic cryptands **3** and **4** were taken in 1% 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 1.0 M HCl. Likewise, 1.0 M TMA(OH) was used when obtaining the $L^-$ spectra to induce ionization of the O-H bond.

Previously, it has been observed that chromogenic cryptands having inward-facing hydroxyl groups can exist in solutions in the (phenylazo)phenol-quinone

TABLE III. Spectral responses of chromogenic cryptand **3** to lithium, sodium and potassium ions in $CH_2Cl_2$-0.1 M TMAOH and in $CH_2Cl_2$-$H_2O$, pH 8.0 for compound **4**.

| Compd. | Form[a] | $\lambda_{max}$, nm | $\varepsilon(\lambda_{max})$ |
|---|---|---|---|
| **3** | L | 409 | 18000 |
| | LiL | 543 | 32000 |
| | NaL | 408 | 18000 |
| | KL | 410 | 18300 |
| **4**[b,c] | L | 521 | 12200 |
| | LiL | 518 | 11500 |
| | NaL | 524 | 15600 |
| | KL | 523 | 12700 |

[a] 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.

[b] The aqueous phase (pH 8.0) was buffered with 0.2 M *N*-2-hydroxyethylpiperazine-*N'*-3-ethanesulfonic acid, adjusted with TMAOH.

[c] Compound **4** contained residual sodium.

phenylhydrazone tautomeric equilibrium which depends on the solvent [3a, 5b]. A wavelength maximum at 499 nm with an unusual high molar absorptivity of 66,000 for nonionized **3** is consistent with the presence of its hydrazone tautomer (Table II). In going from HL form to $L^-$, a bathochromic shift to 578 nm accompanied by a typical reduction of absorptivity is observed.

There are two wavelength maxima at 368 and 467 nm observed for nonionized **4**. According to the literature data [12], the maximum at 368 nm can be attributed to the azo form of **4**, which is stabilized by intraannular hydrogen bonding. The tautomeric hydrazone form gives the higher wavelength maximum. Ionization of **4** produced a smaller than expected bathochromic shift to 516 nm and an increase in molar absorptivity. It is possible that this rather anomalous behavior is due to the residual sodium contamination of **4**.

### 3.4. Cation Responses

Unlike chromogenic cryptand **1**, compound **3** is inactive toward $Li^+$, $Na^+$, and $K^+$ in homogeneous aqueous solutions but exhibits high preference for $Li^+$ in $CH_2Cl_2$-water extractions. Shaking a $CH_2Cl_2$ solution of **3** with aqueous LiCl at pH > 12

results in a 134-nm shift in the absorption maximum to a longer wavelength and a considerably higher molar absorptivity for the LiL form versus the L form (Table III). Neither $Na^+$ nor $K^+$ interact with **3** under these conditions. Spectral cation responses of chromogenic cryptand **3** are shown in Figure 1. Compound **4**, which scavenges $Na^+$ from the environment, does not seem to bind $Li^+$ or $K^+$: only slight changes in both wavelength maxima and absorptivities are observed in the presence of these ions (Table III).

In conclusion, chromogenic cryptand **3** exhibits very good selectivity for lithium over physiologically important sodium and potassium ions. In instances where the extraction mode is applicable **3** can be used for the colorimetric quantitation of lithium ions. The difficulty in obtaining sodium-free compound **4** makes it impractical for the colorimetric determination of sodium ions.

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