8 H, β-pyrrole); UV-vis 418, 520, 554, 600, 658 nm.

***meso*-Tetradecylporphyrin (25)**: $C_{60}H_{94}N_4$ 870.7 calcd mass (M), 871.8 (M + H^+); ^1H NMR ($CDCl_3$) δ −2.62 (br s, 2 H, NH), 0.91 (s, 12 H, CH_3), 1.00, 1.45 (m, 56 H, $(CH_2)_7$), 2.31, 2.72 (m, 8 H, $C_\beta H_2$), 4.82, 5.02 (t, J = 8.0 Hz, 16.0 Hz, 8 H, $C_\alpha H_2$), 9.48 (s, 8 H, β-pyrrole); UV-vis 418, 520, 554, 600, 658 nm.

***meso*-Tetraphenethylporphyrin (26)**: $C_{52}H_{46}N_4$ 726.4 calcd mass (M), 727.5 (M + H^+); ^1H NMR (300 MHz) ($CDCl_3$) δ −2.62 (br s, 2 H, NH), 3.83, 3.88 (t, J = 8.1 Hz, 16.2 Hz, 8 H, $C_\alpha H_2$), 5.25, 5.30 (t, J = 8.4 Hz, 16.8 Hz, 8 H, $C_\beta H_2$), 7.33, 7.52 (m, 20 H, C_6H_5), 9.50 (s, 8 H, β-pyrrole); UV-vis 420, 520, 556, 600, 658 nm.

Solubility Studies. The concentration range which brackets the solubility limit was estimated by visual examination for precipitate formation of several samples prepared at different concentrations. The samples were briefly sonicated and allowed to stand at room temperature for at least 6 h. Results listed as compound, solvent (concentration range which brackets the solubility limit): **24**, CH_2Cl_2 (0.070–0.099 M), decane (0.0016–0.0022 M); Zn chelate of **24**, CH_2Cl_2 (0.019–0.038 M), decane (0.0026–0.0032 M); **25**, CH_2Cl_2 (0.047–0.052 M), decane (0.006–0.012 M); Zn chelate of **25**, CH_2Cl_2 (0.014–0.035 M), decane (0.0008–0.0015 M); **26**, CH_2Cl_2 (0.016–0.027 M), decane (<3.8 × 10^{-6} M).

5,10,15-Tridecyl-20-[(4-(phenacyloxy)carbonyl)phenyl]-porphyrin (27). Into a 500-mL, three-necked, round-bottomed flask equipped with nitrogen purge was placed 250 mL of CH_2Cl_2. Samples of pyrrole (17.4 μL, 2.5 mmol, 10^{-3} M), undecylic aldehyde (38.7 μL, 0.188 mmol, 7.5 × 10^{-4} M), and phenacyl 4-formylbenzoate (**16**) (16.7 mg, 0.062 mmol, 2.5 × 10^{-4} M) were added with magnetic stirring at room temperature. The reaction was initiated by addition of TFA (97 μL, 5 × 10^{-3} M) and allowed to proceed for 2–2.5 h. Aliquots were removed and oxidized by DDQ in the standard manner to monitor the progress of the reaction. The reaction was terminated by addition of DDQ (42.5 mg, 0.187 mmol) in solid form. After 30 min at room temperature the overall yield of porphyrins was 27.3% (assuming ϵ_{420} = 500 000 M^{-1} cm^{-1} for all porphyrin species). TLC analysis (silica gel, CH_2Cl_2/petroleum ether, 3:2) showed the presence of at least five porphyrin species. The fastest moving component was determined by cochromatography to be tetradecylporphyrin **25**. The next porphyrin was assigned as the tridecylmonoarylporphyrin **27**. The crude reaction mixture was concentrated and chromatographed on silica gel to remove quinone and polypyrrylmethene species. The porphyrins were eluted with CH_2Cl_2 steadily enriched with ethyl acetate. Further purification was achieved by preparative centrifugal TLC. The porphyrins were chromatographed on a 1-mm-thick silica gel rotor by using CH_2Cl_2–ethyl acetate, affording a fraction enriched with **25** and **27**. Rechromatography via centrifugal TLC of this fraction using CH_2Cl_2/petroleum ether (3:2) afforded **27** in 14.2% overall yield. The structural assignment of the title compound was verified by ^1H NMR spectroscopy and ^{252}Cf fission fragment mass spectrometry. The NMR assignments were confirmed by standard decoupling experiments. **27**: $C_{65}H_{82}N_4O_3$ 968.6 calcd mass (M), 969.7 (M + H^+); ^1H NMR (300 MHz) ($CDCl_3$) δ −2.65 (s, 2 H, NH), 0.80, 0.91 (m, 9 H, CH_3), 1.13, 1.45 (m, 36 H, $(CH_2)_6$), 1.75, 1.90 (m, 6 H, $C_\gamma H_2$), 2.45, 2.52 (m, 6 H, $C_\beta H_2$), 4.90, 5.05 (m, 6 H, $C_\alpha H_2$), 5.80 (s, 2 H, OCH_2), 7.51, 7.56 (m, 2 H, phenacyl C_3H, C_5H), 7.62, 7.65 (m, 1 H, phenacyl C_4H), 8.02, 8.05 (d, J = 4.3 Hz, 2 H, phenacyl C_2H, C_6H), 8.25, 8.53 (dd, J = 9.1 Hz, 73.4 Hz, 4 H, phenacyl C_6H_4), 8.74, 8.76 (d, J = 4.8 Hz, 2 H, C_2H, $C_{18}H$), 9.37, 9.38 (d, J = 4.8 Hz, 2 H, C_3H, $C_{17}H$), 9.45, 9.50 (dd, J = 4.8 Hz, 9.0 Hz, 4 H, C_7H, C_8H, $C_{12}H$, $C_{13}H$); IR (KBr) 2955, 2924, 2853 ($C_{10}H_{21}$), 1731 ($PhCO_2$), 1702 (PhC=O), 1275 (COC).

Other Reaction Conditions. The following notes refer to modification of one variable in the standard room temperature reaction described in general conditions for porphyrin synthesis.

Solvents: Chloroform in place of methylene chloride gave 40% yields. Toluene/ethanol (3:1) with 10^{-2} M HCl gave about 20% yields over the course of 24 h. No reaction occurred in tetrahydrofuran.

Catalysts: $ZnCl_2$ in methanolic THF gave no reaction. CH_2Cl_2 saturated with gaseous HCl gave low yields (≤10%) in 30 s. BCl_3 (10^{-3} M) in place of BF_3 gave good yields (40%) in 30 min. $HClO_4$ in glacial acetic acid gave low yields (<5%).

Oxidants: I_2 was found ineffective in oxidizing the porphyrinogens under these conditions, in contrast to its utility in the oxidation of uroporphyrinogen.[10]

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Synthesis and Cation-Extraction Study of Lithium-Selective Chromogenic 14-Crown-4 Derivatives

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Various proton-dissociable chromogenic crown ethers have been synthesized, which possess a 14-crown-4 ring and a nitrophenol or azophenol chromophore. Proton-dissociation of the chromogenic crown ethers and extraction equilibria between the crown ether dichloroethane solutions and basic aqueous solutions of alkali and alkaline-earth metal ions have been investigated spectrophotometrically. Most of the chromogenic 14-crown-4 derivatives extract Li^+ selectively and efficiently into the organic phase, thus showing marked spectral changes of the chromophores. Slight and no extractions of Na^+ and the other alkali and alkaline-earth metal ions, respectively, were found with the 14-crown-4 derivatives. Replacement of the 14-crown-4 cycle by other crown rings and a noncyclic analogue resulted in drastic decrease of the Li^+ extractability and selectivity. The high Li^+ extractability is lost even in the corresponding 13-crown-4 derivative. The location of the phenoxide anion in the chromophores attached to the 14-crown-4 ring is also important for the effective Li^+ extraction. Excellent Li^+/Na^+ selectivity ratios in the extraction equilibrium constant, which range from 45 to 240, were attained with most of the chromogenic 14-crown-4 derivatives.

Crown ether derivatives bearing chromophores in the periphery of the crown ring, which are referred to as chromogenic crown ethers or crown ether dyes, are great candidates for cation-detecting and -determining reagents.

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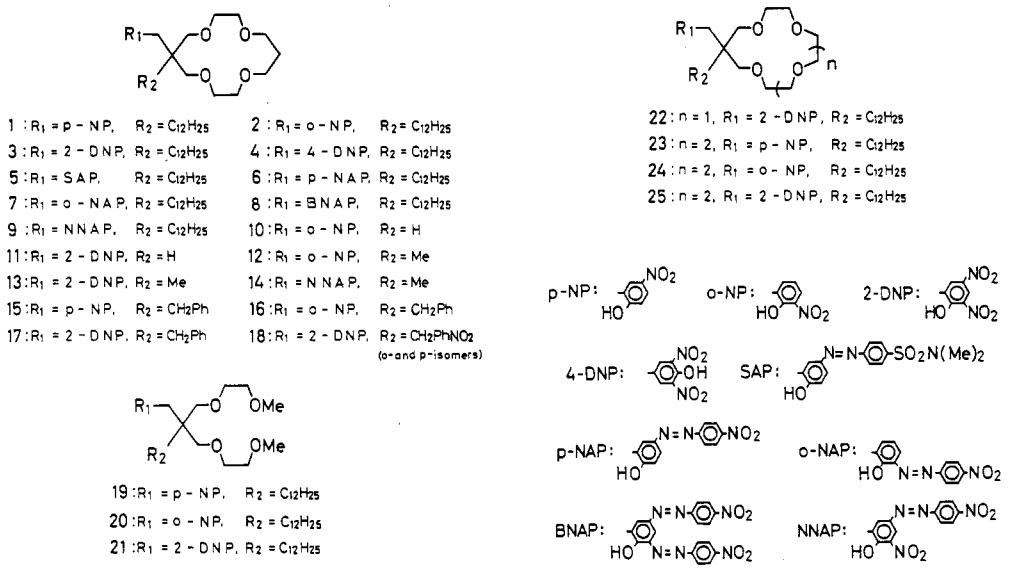


Figure 1. Chromogenic crown ethers and noncyclic analogues synthesized here.

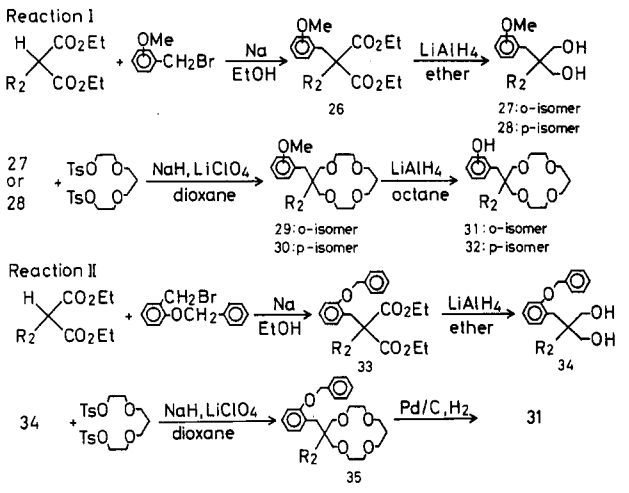
When chromogenic crown ethers complex certain cations, absorption of the chromophores in the electronic spectra or emission in the fluorescence spectra is perturbed considerably. The perturbation in turn causes more or less change in the spectra. The spectral change of the chromophores generally depends on the kind of cations complexed by the crown ether moieties. As a result, with chromogenic crown ethers, cations which the crown ether moieties complex strongly can be detected and determined by the spectral change of the chromophores and also recognized visually by specific coloration if the chromophores absorb in the visible region.

Pioneering works about chromogenic crown ethers have been made by Vögtle[1] and Takagi,[2] who have extensively synthesized uncharged and charged (or proton-dissociable) chromogenic crown ethers, respectively. Specifically, the proton-dissociable chromogenic crown ethers are quite attractive for selective cation determination in aqueous solutions, that is, extraction spectrophotometry. Crown ethers with proton-dissociable chromophores are capable of extracting certain cations selectively from a basic aqueous phase into an organic phase and then serving as spectrophotometric reagents.

Chromogenic crown ethers selective for Li^+ are gaining increasing interest as tools for Li^+ assay in biological systems. Kaneda et al.[3] have synthesized Li^+-selective "crowned" azophenols, which can be applied for spectrophotometric Li^+ determination in nonaqueous systems.[4] Very recently, Katayama et al.[5] and Sasaki and Pacey[6] have reported independently that a monoaza-12-crown-4 nitrophenol derivative possesses high Li^+ selectivity, being applicable to Li^+ extraction spectrophotometry.[6]

14-Crown-4, or 1,4,8,11-tetraoxacyclotetradecane, derivatives, when employed as neutral carriers for membrane electrodes[7,8] and as reagents for ion-pair extraction,[9,10] are highly selective for Li^+. It occurred to us that incorporation of proton-dissociable chromophores into the 14-crown-4 ring affords Li^+-selective reagents for extraction spectrophotometry. We have thus designed and synthesized 14-crown-4 derivatives bearing nitrophenol and azophenol chromophores. We recently outlined excellent Li^+ selectivity of some chromogenic 14-crown-4 derivatives on cation extraction.[11] This paper reports in details synthesis of various 14-crown-4 nitrophenols and azophenols and their extraction behavior toward alkali and alkaline-earth metal ions. Comparison with corresponding 13-crown-4 and 16-crown-5 derivatives and noncyclic analogues is also described.

Scheme I

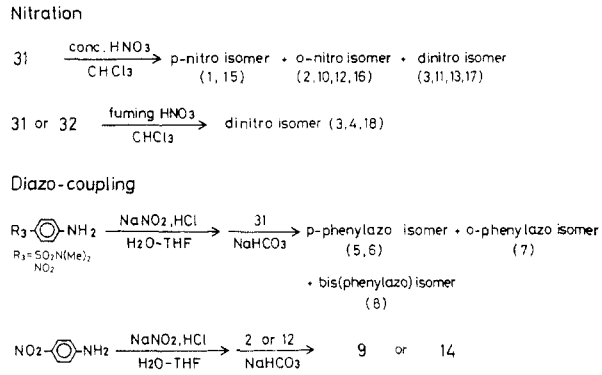


Results and Discussion

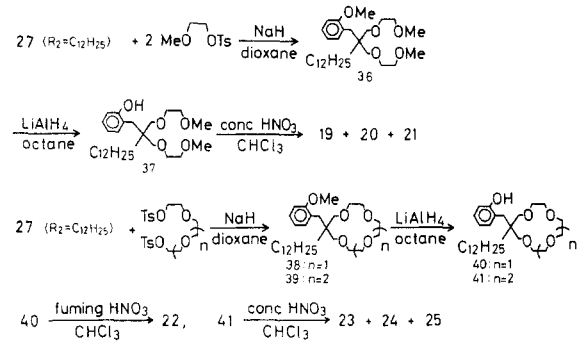
Synthesis. Eighteen chromogenic 14-crown-4 derivatives 1 through 18, as shown in Figure 1, were synthesized here. As the chromophores were chosen several nitrophenols and azophenols. Incorporation of dodecyl, methyl, and benzyl groups geminal to the chromogenic substituent

(1) Löhr, H.-G.; Vögtle, F. *Acc. Chem. Res.* **1985**, *18*, 65 and references cited therein.
(2) Takagi, M.; Ueno, K. *Top. Curr. Chem.* **1984**, *121*, 39 and references cited therein.
(3) Kaneda, T.; Sugihara, K.; Kamiya, H.; Misumi, S. *Tetrahedron Lett.* **1981**, 4407.
(4) Nakashima, K.; Nakatsuji, S.; Akiyama, S.; Kaneda, T.; Misumi, S. *Chem. Lett.* **1982**, 1781.
(5) Katayama, Y.; Nita, K.; Ueda, M.; Nakamura, H.; Takagi, M. *Anal. Chim. Acta* **1985**, *173*, 193.
(6) Sasaki, K.; Pacey, G. *Anal. Chim. Acta* **1985**, *174*, 141.
(7) Kitazawa, S.; Kimura, K.; Yano, H.; Shono, T. *J. Am. Chem. Soc.* **1984**, *106*, 6978.
(8) Kitazawa, S.; Kimura, K.; Yano, H.; Shono, T. *Analyst (London)* **1985**, *110*, 295.
(9) Czech, B. P.; Babb, D. A.; Son, B.; Bartsch, R. A. *J. Org. Chem.* **1984**, *49*, 4805.
(10) Kobiro, K.; Matsuoka, T.; Takada, S.; Kakiuchi, K.; Tobe, Y.; Odaira, Y. *Chem. Lett.* **1986**, 713.
(11) Kimura, K.; Tanaka, M.; Kitazawa, S.; Shono, T. *Chem. Lett.* **1985**, 1239.

Scheme II



Scheme III



was also made to elucidate effects of lipophilicity and steric hindrance on the cation complexation and extraction.

Crown phenols **31** and **32**, which are precursors for the crown nitrophenols and azophenols, were prepared by reactions I and II in Scheme I. The cyclization procedures are similar to that for previous 14-crown-4 derivatives.[7] The cyclization for reaction I using 2-(methoxybenzyl)-1,3-propanediol derivatives **27** and **28** proceeded in yields of 20–55% when the R_2 substituent is dodecyl or benzyl group. On the other hand, in the case that R_2 is H or methyl group, the 14-crown-4 derivatives **29** were obtained in only poor cyclization yields (~3%). Reaction II using 2-[(benzyloxy)benzyl]-1,3-propanediol derivatives **34** (R_2 = H, CH_3), however, afforded cyclization yields comparable to those for reaction I using **27** (R_2 = $C_{12}H_{25}$, CH_2Ph). The result for the two cyclization reactions implies that the yields depend on the bulkiness of the substituents on the propanediols. Some back hindrance on the propanediols might facilitate the cyclization to the corresponding 14-crown-4 derivatives. Both reductive demethylation of **29** and **30** and debenzylation of **35** gave crown phenols **31** (R_2 = $C_{12}H_{25}$, H, CH_3, CH_2Ph) and **32** (R_2 = $C_{12}H_{25}$) in high yields.

Nitration of **31** (R_2 = $C_{12}H_{25}$, CH_2Ph) by concentrated HNO_3 gave the corresponding 14-crown-4 nitrophenols as mixtures of the *p*-nitro (**1**, **15**), *o*-nitro (**2**, **16**), and dinitro (**3**, **17**) isomers in good total yields, which were then separated to one another (Scheme II). The similar reaction using **31** (R_2 = H, CH_3), however, yielded only the *o*-nitro (**10**, **12**) and dinitro (**11**, **13**) isomers but no detectable amount of corresponding *p*-nitro isomers were obtained in this case. Instead of the *p*-nitro isomer were isolated a small quantity of corresponding *p*-quinone derivatives, the formation of which seems to depress nitration on the para position. The isomer composition on the nitration with concentrated HNO_3 was varied by the reaction time. In general, the longer reaction time brought about the higher content of the dinitro isomers. Crown dinitrophenols **3** and **4** were also prepared directly by nitration of **31** (R_2 = $C_{12}H_{25}$) and **32** (R_2 = $C_{12}H_{25}$) using fuming HNO_3. On treatment of **31** (R_2 = CH_2Ph) with fuming HNO_3, nitration of the benzene rings of the R_2 substituent as well as the hydroxybenzyl group occurred to yield crown dinitrophenol **18**.

The 14-crown-4 azophenol derivatives were synthesized by conventional diazo coupling as also illustrated in Scheme II. Diazo coupling of **31** (R_2 = $C_{12}H_{25}$) using *p*-nitroaniline as the diazo component afforded a mixture of the *p*-phenylazo (**6**), *o*-phenylazo (**7**), and bis(phenylazo) (**8**) isomers, the yield decreasing in the order **6** > **7** > **8**. The isomers were separated from one another. Employment of *p*-(*N*,*N*-dimethylsulfamoyl)aniline as the diazo component elicited formation of crown azophenol **5**. In this case, we did not try to isolate the other isomers due to their poor yields. Diazo coupling with *p*-nitroaniline was also attempted by using crown *o*-nitrophenols **2** and **12** to obtain **9** and **14**, respectively.

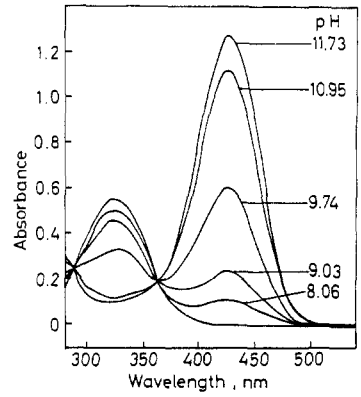


Figure 2. pH-dependent spectral change of crown *p*-nitrophenol **1** in water–dioxane (1/1).

For comparison with the 14-crown-4 derivatives, noncyclic crown (**19**–**21**), 13-crown-4 (**22**), and 16-crown-5 (**23**–**25**) nitrophenols were synthesized in good yields for each reaction step, according to procedures similar to those for the 14-crown-4 derivatives (Scheme III).

Acidity Constant. Proton dissociation on the phenol moieties of the chromogenic crown ethers was examined in water–dioxane (1/1) by using visible spectra. Tetramethylammonium hydroxide (TMAOH) was used as the base for controlling pH, in order to eliminate any effect of metal ion binding by the crown ether moiety on the proton dissociation.

Figure 2 depicts spectral change of crown *p*-nitrophenol **1** at various pH. Below pH 6, only absorption based on the undissociated species (HL) was observed at 327 nm. Increasing pH promotes the proton dissociation of the chromophore, thus augmenting absorption based on the dissociated species (L^-) at 428 nm. Similar pH-dependent spectral changes were found in the other chromogenic crown ethers and noncyclic analogues (**2**–**25**). Such significant spectral changes allowed determination of acidity constants (K_a) for the crown ether derivatives, which are summarized in Table I, together with the spectral data.

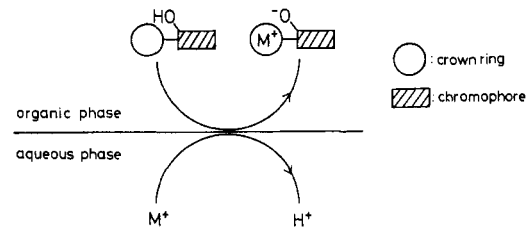
The *p*- and *o*-nitrophenol derivatives generally possess quite high pK_a values above 9. As expected, the pK_a values for the dinitrophenol derivatives are much lower than the other corresponding isomers, ranging from 4 to 5.2. Crown azophenols **5**–**8**, which absorb strongly at the longer wavelengths, also show high pK_a values. The introduction of nitro group into the *ortho* position of the *p*-azophenol moiety decreases the pK_a values markedly as seen in **9** and **14**.

Table I. Acidity Constants of Chromogenic Crown Ether Derivatives[a]

compd	pK_a[b]	λ_{max}, nm (ϵ, mol^{-1} dm^3 cm^{-1}) HL	λ_{max}, nm (ϵ, mol^{-1} dm^3 cm^{-1}) L^-
1	9.64	327 (7890)	428 (16 400)
2	10.74	293 (5770)	444 (4970)
		362 (2900)	
3	4.92	270 (11 800)	380 (14 200)
4	4.71	358 (4140)	455 (7660)
5	10.50	372 (11 100)	493 (32 200)
6	10.43	386 (23 700)	540 (35 800)
7	11.96	360 (15 000)	566 (14 800)
8	8.79	370 (31 500)	593 (32 400)
9	6.54	364 (16 600)	497 (27 000)
10	9.06	287 (6430)	434 (5580)
		358 (3140)	
11	4.59	266 (13 300)	374 (15 200)
12	9.49	288 (6570)	439 (5940)
		360 (3230)	
13	4.83	268 (13 700)	377 (16 100)
14	5.90	358 (26 800)	495 (29 600)
15	8.96	328 (9030)	425 (22 000)
16	9.76	291 (6090)	442 (5950)
		362 (3040)	
17	4.95	271 (12 200)	381 (13 500)
18	4.60	273 (20 900)	378 (15 300)
19	9.05	325 (8230)	424 (19 000)
20	10.06	290 (6300)	442 (6070)
		362 (3130)	
21	5.06	269 (12 400)	377 (12 600)
22	5.17	270 (12 700)	379 (14 900)
23	9.12	325 (8660)	424 (20 400)
24	9.91	290 (6270)	442 (5790)
		362 (3170)	
25	5.12	269 (13 800)	378 (15 200)

[a] In H_2O/dioxane (1/1). [b] $pK_a = -\log K_a$.

Scheme IV



Cation Extraction. The proton-dissociable chromogenic crown ethers are able to extract certain cations by complexation from a basic aqueous phase to an organic phase, as shown schematically in Scheme IV. On the complex formation the crown ethers undergo proton dissociation on the phenol moiety of the chromophores to yield an anion, which in turn interacts intramolecularly with a metal ion complexed by the crown ether moiety. Thus the cation complexation and thereby extraction leads to drastic spectral changes in the organic phase. Cation extractabilities of the chromogenic crown ethers can, therefore, be examined easily by the spectral changes. Extractions of alkali and alkaline-earth metal ions were carried out from an aqueous solution containing one of the metal ions at the same concentration into 1,2-dichloroethane solution of the chromogenic crown ether. The pH conditions in the aqueous phase are concerned with the acidity constants of the chromogenic crown ethers employed. Naturally, higher pH conditions are required for the cation extraction by the crown ethers with higher pK_a values. In addition, the pH was adjusted so that in the absence of any of the metal ions the spectra of the chromophores in the organic phase do not change at all.

Figure 3 and 4 give typical examples for the extraction behavior of the 14-crown-4 nitrophenols and azophenols,

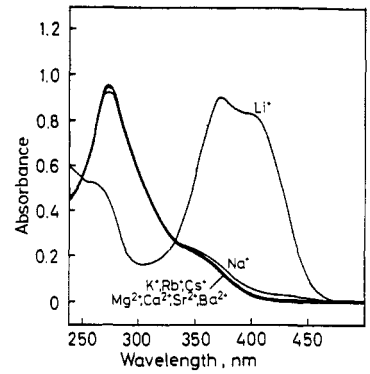


Figure 3. Spectral change in organic phase on cation extraction with 2-(14-crown-4)dinitrophenol **3**; at pH 7.26 (MOPS/TMAOH buffer).

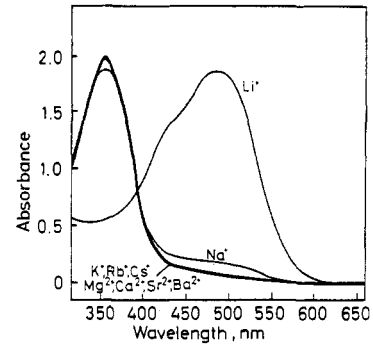


Figure 4. Spectral change in organic phase on cation extraction with (14-crown-4)azophenol **9**; at pH 9.12 (TAPS/TMAOH buffer).

qualitatively demonstrating extremely high Li^+ selectivities on the cation extraction with **3** and **9**. Only Li^+ can be extracted efficiently in the 14-crown-4 systems. Although Na^+ is extracted slightly, there is no detectable spectral change on the extraction of the other alkali and alkaline-earth metal ions. Such Li^+-selective cation extraction was also found in the other chromogenic 14-crown-4 derivatives except **4**. The visible spectral data for the Li^+ or Na^+ complexes of the chromogenic 14-crown-4 derivatives in the organic phase can be seen in Table II. Surprisingly enough, crown dinitro-4-phenol **4** exhibited only poor cation extractability even for Li^+. Two of the 14-crown-4 dinitrophenols, **3** and **4**, are quite different in the extraction behavior despite that they both consist of dodecyl-14-crown-4 and dinitrophenol moieties. CPK molecular model examination suggested that the phenoxide anion is located farther from the crown ether complexed Li^+ in **4** than in **3**. The longer distance between the anion and the metal ion probably destabilizes the intramolecular cation complexes of **4**, especially with highly charged cations such as Li^+, thus being reflected in the poor Li^+ extractability.

Noncyclic crown ethers **19–21**, 13-crown-4 derivative **22**, 16-crown-5 derivatives **23–25** and 2,6-dinitro-4-nonylphenol were tested for their cation extractabilities to see how the crown ether moiety affects the ion selectivity of the chromogenic crown ethers on the extraction. Extraction of any alkali and alkaline-earth metal ions hardly occurred by using noncyclic analogues **19–21** and 2,6-dinitro-4-nonylphenol which does not carry any crown ether moiety. Very interestingly, 13-crown-4 derivative **22** exhibited such poor cation extractability as observed on the extraction with **4**. That is to say, cation extractability was drastically decreased in **22** compared to the corresponding 14-crown-4 derivative, **3**, irrespective of their slight structural difference by a methylene unit. Na^+ selectivity was observed

Table II. Extraction Equilibrium Constants and Ion Selectivity Ratios of Chromogenic Crown Ethers[a]

compd	pK_{ex}(Li)[c]	pK_{ex}(Na)[c]	K_{ex}(Li)/K_{ex}(Na)	ϵ_{ML} (at λ_{max}, nm)[b] LiL	NaL
1	11.29	13.66	240	19300 (413)	19800 (415)
2	11.93	nd[d]		5610 (424)	
3	6.93	8.87	87	13600 (374)	13400 (376)
5	12.66	nd		31800 (488)	
6	12.31	nd		36600 (538)	
7	12.12	nd		14900 (560)	
8	10.91	12.87	91	34200 (582)	33900 (584)
9	8.62	10.45	68	27600 (488)	26600 (490)
10	12.45	nd		5660 (430)	
11	7.03	8.72	49	15800 (370)	15500 (372)
12	12.02	nd		5450 (436)	
13	6.90	8.78	76	15800 (374)	15500 (376)
14	8.39	10.04	45	31300 (490)	31900 (492)
15	10.85	13.16	200	21000 (411)	20800 (413)
16	11.79	nd		6130 (420)	
17	6.76	8.76	100	15200 (371)	15800 (373)
18	7.20	nd		15400 (368)	
23	12.27	10.54	0.019[e]	21300 (413)	20100 (419)
24	nd	11.32	e		5490 (436)
25	8.24	6.14	0.0079[e]	15700 (375)	15800 (375)

[a] In $ClCH_2CH_2Cl$–H_2O system, at 25 °C. [b] In the organic phase, mol^{-1} dm^3 cm^{-1}. [c] $pK_{ex} = -\log K_{ex}$. [d] The pK_e value marked with nd and any pK_e value for 4 and **19–22** could not be determined due to the poor extractability. [e] $K_{ex}(Na)/K_{ex}(K)$: 43 for **23**, 17 for **24**, and 14 for **25**.

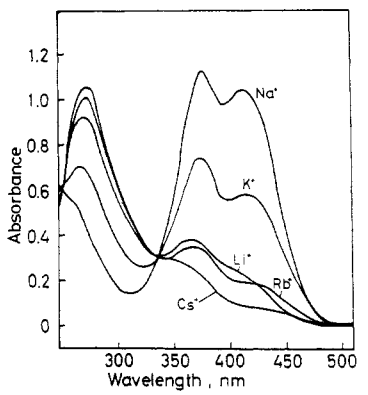


Figure 5. Spectral change in organic phase on cation extraction with (16-crown-5)dinitrophenol **25**; The same pH condition as for Figure 3.

on the cation extraction with chromogenic 16-crown-5 derivative **25** (Figure 5), the extractability decreasing in the order $Na^+ > K^+ > Li^+ \geq Rb^+ > Cs^+$. This was the case with the other 16-crown-5 derivatives, **23** and **24**.

Accordingly, the 14-crown-4 cycle, combined with the chromophores containing proton-dissociable 2-phenol moieties, is essential to the highly selective, efficient Li^+ extraction.

Extraction Equilibrium. On the assumption that crown ethers bearing proton-dissociable chromophores form only 1:1 complexes with metal ions, the extraction equilibrium as shown in Scheme IV is discussed by the extraction equilibrium constant, K_{ex}, in eq 1, where ML

$$K_{ex} = ([ML]_o[H^+]_a)/([HL]_o[M^+]_a) \quad (1)$$

stands for complexes of L^- with M^+ and subscript o and a denote the organic and aqueous phases, respectively. If the following assumptions are made, i.e., $[HL]_t \simeq [HL]_o + [ML]_o + [L^-]_a$, $[M^+]_t \simeq [M^+]_a$ (t means total), $[HL]_a \simeq 0$, $[ML]_a \simeq 0$, and $[L^-]_o \simeq 0$, eq 1 can be rewritten as shown in eq 2, where ϵ_{L^-} and A_a stand for molar absorp-

$$[H^+]_a/[M^+]_t = \{K_{ex}\epsilon_{ML}(\epsilon_{L^-}[HL]_t - A_a)/\epsilon_{L^-}A_o\} - K_{ex} \quad (2)$$

tivity and absorbance for L^- in the aqueous phase. Also, ϵ_{ML} and A_o denote molar absorptivity and absorbance for ML in the organic phase at a wavelength where HL does not absorb. Furthermore, if distribution of chromogenic crown ethers to the aqueous phase is negligible on account of their high lipophilicity, eq 2 can be simplified as shown in eq 3. Equation 3 can be applied for most of the

$$[H^+]_a/[M^+]_t = (K_{ex}\epsilon_{ML}[HL]_t/A_o) - K_{ex} \quad (3)$$

chromogenic crown ether derivatives with dodecyl and benzyl groups as the R_2 substituent (**1–9**, **14**, **16–25**). In contrast, eq 2 should be employed for the other chromogenic crown ethers (**10–13**, **15**) due to their more or less distribution to the aqueous phase on the cation complexation. In the extraction systems where significant cation extraction was realized, plots of $[H^+]_a/[M^+]_t$ against $(\epsilon_{L^-}[HL]_t - A_a)/\epsilon_{L^-}A_o$ or $1/A_o$ gave straight lines, indicating that the assumptions made here are reasonable. The K_{ex} values for Li^+ and Na^+ were thus obtained from the intercepts of the straight lines, being listed in Table II, together with the Li^+/Na^+ selectivity ratios. In chromogenic crown ethers **4**, **22**, and **24**, noncyclic analogues **19–21**, and 2,6-dinitro-4-nonylphenol, which showed poor or no extractability toward Li^+, the K_{ex}(Li) value could not be determined. The same holds for the Na^+ extraction with chromogenic 14-crown-4 derivatives **2**, **4–7**, **10**, **12**, **16**, and **18** and the noncyclic analogues. Of course, the K_{ex} values for the other alkali and alkaline-earth metal ions could not be obtained with the crown ethers and noncyclic analogues except the 16-crown-5 derivatives, which extract K^+ to some extent.

Now one can compare quantitatively the Li^+ selectivity on the cation extraction among the chromogenic crown ethers. The K_{ex} values themselves are hard to compare among the crown ethers since the values are related considerably to their acidity constants. On comparison of their Li^+/Na^+ ratios, $K_{ex}(Li)/K_{ex}(Na)$, it seems reasonable to discuss the Li^+ selectivities of the chromogenic crown ethers on the cation extraction. The Li^+/Na^+ selectivity ratio for the chromogenic 14-crown-4 derivatives ranges from 45 to 240, clearly indicating their excellent Li^+ selectivities. Presumably, the 14-crown-4 derivatives, the $K_{ex}(Na)$ value of which could not be determined, **2**, **5–7**, **10**, **12**, **16**, and **18**, are also qualified for such high Li^+/Na^+ selectivities by the already mentioned Li^+-selective spectral changes on the cation extraction. The Li^+ selectivity over Na^+ is reversed in the 16-crown-5 derivatives, which are Na^+ selective against K^+ as well. Undoutedly, the 14-

crown-4 cycle makes a great contribution to the high Li^+ selectivities for the chromogenic 14-crown-4 derivatives. The variation of lipophilicity based on the R_2 substituent ($C_{12}H_{25}$, CH_3, CH_2Ph) does not appear to affect essentially the Li^+/Na^+ selectivity of the chromogenic 14-crown-4 derivatives. Yet, in 14-crown-4 dinitrophenol **11** which has no R_2 substituent, the Li^+ selectivity is weakened more or less as compared to the other corresponding derivatives with dodecyl, methyl, and benzyl groups (**3**, **13**, **17**). This might be because the incorporation of the R_2 substituents geminal to the chromogenic ones causes projection of the chromophore moiety over the 14-crown-4 ring plane,[12,13] thus allowing easy intramolecular interaction of the phenoxide anion and the complexed Li^+.

In conclusion, most of the chromogenic 14-crown-4 derivatives are highly Li^+ selective on the cation extraction, being quite promising for Li^+-extraction spectrophotometry. Crown *p*-nitrophenols **1** and **15** are excellent at the point of the Li^+ selectivity. Crown dinitro-2-phenols **3**, **13**, and **17**, which have small pK_a values, may be preferable to the crown *p*-nitrophenols in case that the cation extraction should be performed under mild pH conditions of the aqueous phase. The high molar absorptivities of crown azophenols **8**, **9**, and **14** are desirable for the sensitivity on the spectrophotometry. Studies are now under way regarding analytical applications of these Li^+-selective chromogenic crown ethers.

Experimental Section

Chemicals. Commercially available reagents were used without further purification unless otherwise specified. 1,2-Dichloroethane for the cation extraction was purified by distillation. Deionized water was used. Alkali and alkaline-earth metal chlorides were analytical grade.

Apparatus. Infrared spectra were recorded on a Hitachi 215 grating spectrophotometer. Melting points were determined with a YANACO melting point apparatus and were uncorrected. Mass spectra were measured at 70 eV with a Hitachi RMU-6E instrument. ^1H NMR spectra were recorded on a JEOL JMN-PS-100 spectrometer as CCl_4 solutions of 0.5–10 wt % concentrations. Electronic spectra were obtained on a Hitachi 340 recording spectrophotometer. Preparative reversed-phase liquid chromatography was conducted with a Kyowaseimitsu K-880 liquid chromatograph, a Waters R-40 differential refractometer, and a 20 × 250 mm column packed with 15-μm irregular-type octadecylsilanized silica. The eluent was pure methanol unless otherwise noted.

Synthesis. General Procedure for Preparation of Crown and Noncyclic Crown Phenols via Reactions I and II. The methoxybenzyl crown ethers **29**, **30**, **38**, and **39**, the (benzyloxy)benzyl crown ether **35**, and the noncyclic analogue **36** were prepared with modifications to the reported method.[7] The 2,2-disubstituted or 2-substituted propanediols **27**, **28**, and **34** were obtained by the reaction of the corresponding diethyl malonate derivatives with methoxybenzyl or (benzyloxy)benzyl bromide, followed reduction with $LiAlH_4$.[7] The preparation of *o*- and *p*-methoxybenzyl bromide was performed starting from *o*- and *p*-salicylaldehyde, successively by methylation with dimethyl sulfate, reduction with $NaBH_4$, and bromination with HBr. Similarly, *o*-(benzyloxy)benzyl bromide can be obtained by adopting benzylation ($PhCH_2Cl$, KOH) instead of the methylation.

Demethylation of **29**, **30**, **36**, **38**, and **39** was achieved as follows: In an octane solution (300 mL) of the methoxybenzyl derivative (6.3 mmol) was suspended $LiAlH_4$ (63 mmol), and the mixture was refluxed for 8 h. After the reaction the excess of $LiAlH_4$ was decomposed with dilute HCl while cooling. Water (200 mL) was added, the mixture stirred vigorously, and the organic phase separated. The aqueous phase was extracted with $CHCl_3$ (50 mL × 2). The combined extract was washed with water and dried over $MgSO_4$. Rotary evaporation of the solvent afforded a crude product, which was then purified by recrystallization or reversed-phase liquid chromatography.

Debenzylation of **35** was carried out in a glass autoclave under a hydrogen pressure of 4 atm at room temperature for about 3 h, using **35** (12 mmol), ethanol (200 mL), 5% Pd/C (2 g), and *p*-toluenesulfonic acid (1 g). After removal of the Pd/C the solvent was evaporated off. The resulted crude product was subjected to reversed-phase liquid chromatography ($MeOH/H_2O$ (10/1)).

2-(Dodecyl-14-crown-4)phenol 31 ($R_2 = C_{12}H_{25}$): colorless liquid (38% for cyclization, 60% for demethylation); ^1H NMR δ 0.87 (t, 3 H, CH_3), 1.1–1.5 (m, 22 H, $CH_3(CH_2)_{11}$), 1.6–1.8 (m, 2 H, $(OCH_2)_2CH_2$), 2.37 (s, 2 H, $PhCH_2$), 3.2–3.4 (m, 4 H, $(OCH_2)_2C$), 3.5–3.8 (m, 12 H, $(OCH_2)CH_2$ and OCH_2CH_2O), 6.6–7.1 (m, 4 H, Ar H), 7.86 (s, 1 H, OH); MS, *m/e* 478 (M^+).

2-(Benzyl-14-crown-4)phenol 31 ($R_2 = CH_2Ph$): colorless solid (21% for cyclization, 88% for demethylation); mp 123.5 °C (from MeOH); ^1H NMR δ 1.7–1.8 (m, 2 H, $(OCH_2)_2CH_2$), 2.48 (s, 2 H, $PhCH_2$), 2.60 (s, 2 H, $HOPhCH_2$), 3.34 (s, 4 H, $(OCH_2)_2C$), 3.4–3.7 (m, 12 H, $(OCH_2)_2CH_2$ and OCH_2CH_2O), 6.6–7.3 (m, 9 H, Ar H), 7.88 (s, 1 H, OH); MS, *m/e* 400 (M^+).

2-(14-Crown-4)phenol 31 ($R_2 = H$): colorless liquid (38% for cyclization, 60% for debenzylation); ^1H NMR δ 1.5–1.8 (m, 2 H, $(OCH_2)_2CH_2$), 1.8–2.1 (m, 1 H, $(OCH_2)_2CH$), 2.48 (d, 2 H, $PhCH_2$), 3.3–3.8 (m, 16 H, OCH_2), 6.6–7.1 (m, 5 H, Ar H and OH); MS, *m/e* 310 (M^+).

2-(Methyl-14-crown-4)phenol 31 ($R_2 = Me$): colorless liquid (27% for cyclization, 74% for debenzylation); ^1H NMR δ 0.81 (s, 3 H, CH_3), 1.5–1.8 (m, 2 H, $(OCH_2)_2CH_2$), 2.38 (s, 2 H, $PhCH_2$), 3.32 (s, 4 H, $(OCH_2)_2C$), 3.4–3.8 (m, 12 H, $(OCH_2)_2CH_2$ and OCH_2CH_2O), 6.6–7.1 (m, 4 H, Ar H), 7.36 (s, 1 H, OH); MS, *m/e* 324 (M^+).

4-(Dodecyl-14-crown-4)phenol 32 ($R_2 = C_{12}H_{25}$): colorless liquid (56% for cyclization, 92% for demethylation); ^1H NMR δ 0.87 (t, 3 H, CH_3), 1.1–1.4 (m, 22 H, $CH_3(CH_2)_{11}$), 1.6–1.8 (m, 2 H, $(OCH_2)_2CH_2$), 2.34 (s, 2 H, $PhCH_2$), 3.20 (s, 4 H, $(OCH_2)_2C$), 3.4–3.8 (m, 12 H, $(OCH_2)_2CH_2$ and OCH_2CH_2O), 5.70 (s, 1 H, OH), 6.5–7.0 (m, 4 H, Ar H); MS, *m/e* 478 (M^+).

Noncyclic crown 2-phenol 37: colorless liquid (63% for **36**, 52% for demethylation); ^1H NMR δ 0.87 (t, 3 H, CH_3CH_2, 1.1–1.4 (m, 22 H, $CH_3(CH_2)_{11}$), 2.48 (s, 2 H, $PhCH_2$), 3.12 (s, 4 H, $(OCH_2)_2C$), 3.30 (s, 6 H, OCH_3), 3.4–3.6 (m, 8 H, OCH_2), 6.6–7.1 (m, 4 H, Ar H), 7.60 (s, 1 H, OH); MS, *m/e* 466 (M^+).

2-(Dodecyl-13-crown-4)phenol 40: colorless liquid (55% for cyclization, 79% for demethylation); ^1H NMR δ 0.87 (t, 3 H, CH_3), 1.1–1.5 (m, 22 H, $CH_3(CH_2)_{11}$), 2.37 (s, 2 H, $PhCH_2$), 3.2–3.4 (m, 4 H, $(OCH_2)_2C$), 3.5–3.8 (m, 12 H, OCH_2CH_2O), 6.4–7.1 (m, 4 H, Ar H), 7.88 (s, 1 H, OH); MS, *m/e* 464 (M^+).

2-(Dodecyl-16-crown-5)phenol 41: colorless liquid (50% for cyclization, 55% for demethylation); ^1H NMR δ 0.87 (t, 3 H, CH_3), 1.0–1.4 (m, 22 H, $CH_3(CH_2)_{11}$), 2.44 (s, 2 H, $PhCH_2$), 3.29 (s, 4 H, $(OCH_2)_2C$, 3.4–3.7 (m, 16 H, OCH_2CH_2O), 6.6–7.1 (m, 4 H, Ar H), 7.80 (s, 1 H, OH); MS, *m/e* 508 (M^+).

General Procedure for Nitration to Crown Nitrophenols. To a chloroform solution (600 mL) of crown or noncyclic crown phenol (7 mmol) was added concentrated HNO_3 (400 mL) while stirring. The stirring was continued at room temperature for several more minutes after the reaction mixutre turned pale yellow. The total reaction time was 5–15 min after complete addition of the HNO_3. Water (400 mL) was added, then the mixture was stirred vigorously, and the organic phase was separated. The aqueous phase was extracted with $CHCl_3$ (200 mL × 2). The combined extract was washed with water, and then the solvent was evaporated off. The isomers were separated and purified by reversed-phase liquid chromatography ($MeOH/H_2O$ (10/1) for **10–18**). The retention time of the isomers on the chromatography generally increases in the order para > dinitro > ortho isomers. The solid products can be also purified by recrystallization.

The procedure for nitration with fuming HNO_3 was as follows: Fuming HNO_3 (70 mL) was added to a chloroform solution (300 mL) of crown phenol (1 mmol) while stirring. The stirring was continued for an additional 5 min. The workup was similar to that for the above nitration.

6-Dodecyl-6-(2-hydroxy-5-nitrobenzyl)-, 6-dodecyl-6-(2-hydroxy-3-nitrobenzyl)-, and 6-dodecyl-6-(2-hydroxy-3,5-

(12) Nakatsuji, Y.; Nakamura, T.; Okahara, M.; Dishong, D. M.; Gokel, G. W. *Tetrahedron Lett.* **1982**, 1351.

(13) Kimura, K.; Yano, H.; Kitazawa, S.; Shono, T. *J. Chem. Soc., Perkin Trans. 2* **1986**, 1945.

dinitrobenzyl)-1,4,8,11-tetraoxacyclotetradecane (1, 2, and 3) were prepared concurrently with **31** ($R_2 = C_{12}H_{25}$), as described in the general procedure for the nitration with concentrated HNO_3. Nitration with fuming HNO_3 gave only **3**. **1**: reddish brown solid (41%); mp 53.5 °C (from MeOH/H_2O (10/1)); IR (KBr) 3100, 1520, 1280, 1120 cm^{-1}; ^1H NMR δ 0.88 (t, 3 H, CH_3), 1.0–1.5 (m, 22 H, $CH_3(CH_2)_{11}$), 1.5–1.8 (m, 2 H, $(OCH_2)_2CH_2$), 2.44 (s, 2 H, $PhCH_2$), 3.1–3.8 (m, 16 H, OCH_2), 6.7–8.1 (m, 3 H, Ar H), 8.96 (s, 1 H, OH); MS, *m/e* 524 (M^+). Anal. Calcd for $C_{29}H_{49}NO_7$: C, 66.51; H, 9.43; N, 2.67. Found: C, 66.46; H, 9.37; N, 2.50. **2**: deep red liquid (29%); IR (neat) 3140, 1535, 1250, 1120 cm^{-1}; ^1H NMR δ 0.88 (t, 3 H, CH_3), 1.0–1.5 (m, 22 H, $CH_3(CH_2)_{11}$), 1.5–1.8 (m, 2 H, $(OCH_2)_2CH_2$), 2.64 (s, 2 H, $PhCH_2$), 3.1–3.8 (m, 16 H, OCH_2), 6.7–8,.0 (3 H, m, Ar H), 11.02 (s, 1 H, OH); MS, *m/e* 524 (M^+). Anal. Calcd for $C_{29}H_{49}NO_7$: the same as for **1**. Found: C, 66.42; H, 9.67; N, 2.73. **3**: yellow solid (10% with concentrated HNO_3, 77% with fuming HNO_3); mp 60.5 °C (from MeOH); IR (KBr) 3200, 1540, 1260, 1128, 1100 cm^{-1}; ^1H NMR δ 0.89 (t, 3 H, CH_3), 1.1–1.5 (m, 22 H, $CH_3(CH_2)_{11}$), 1.5–1.8 (m, 2 H, $(OCH_2)_2CH_2$), 2.72 (s, 2 H, $PhCH_2$), 3.2–3.7 (m, 16 H, OCH_2), 8.5–8.9 (m, 2 H, Ar H), 11.51 (s, 1 H, OH); MS, *m/e* 569 (M^+). Anal. Calcd for $C_{29}H_{48}N_2O_9$: C, 61.25; H, 8.51; N, 4.93. Found: C, 61.25; H, 8.51; N, 4.86.

6-Dodecyl-6-(4-hydroxy-3,5-dinitrobenzyl)-1,4,8,11-tetraoxacyclotetradecane (4) was prepared by the nitration of **32** ($R_2 = C_{12}H_{25}$) with fuming HNO_3 and isolated as a yellowish orange solid (28%): mp 64.5 °C (from MeOH); IR (KBr) 3225, 1536, 1297, 1112 cm^{-1}; ^1H NMR δ 0.87 (t, 3 H, CH_3), 1.1–1.5 (m, 22 H, $CH_3(CH_2)_{11}$, 1.5–1.8 (m, 2 H, $(OCH_2)_2CH_2$), 2.52 (s, 2 H, $PhCH_2$), 3.24 (dd, 4 H, $(OCH_2)_2C$), 3.5–3.7 (m, 12 H, OCH_2CH_2O and $(OCH_2)_2CH_2$), 8.04 (s, 2 H, Ar H), 11.20 (s, 1 H, OH); MS, *m/e* 569 (M^+). Anal. Calcd for $C_{29}H_{48}N_2O_9$: C, 61.25; H, 8.51; N, 4.93. Found: C, 61.25; H, 8.53; N, 4.66.

6-(2-Hydroxy-3-nitrobenzyl)- and 6-(2-hydroxy-3,5-dinitrobenzyl)-1,4,8,11-tetraoxacyclotetradecane (10 and 11) were obtained concurrently by the concentrated HNO_3 nitration of **31** (R_2 = H). **10**: deep yellow liquid (11%); IR (neat) 3200, 1540, 1250, 1125 cm^{-1}; ^1H NMR δ 1.5–1.8 (m, 2 H, $(OCH_2)_2CH_2$), 1.9–2.1 (m, 1 H, $(OCH_2)_2CH$), 2.64 (d, 2 H, $PhCH_2$), 3.3–3.6 (m, 16 H, OCH_2), 6.7–8.0 (m, 3 H, Ar H), 10.96 (s, 1 H, OH); MS, *m/e* 355 (M^+). Anal. Calcd for $C_{17}H_{25}NO_7$: C, 57.45; H, 7.09; N, 3.94. Found: C, 57.27; H, 7.11; N, 3.82. **11**: pale yellow solid (49%); mp 107 °C (from MeOH/H_2O (10/1)); IR (KBr) 3400, 1520, 1262, 1130, 1090 cm^{-1}; ^1H NMR δ 1.5–1.8 (m, 2 H, $(OCH_2)_2CH_2$), 2.0–2.2 (m, 1 H, $(OCH_2)_2CH$), 2.78 (d, 2 H, $PhCH_2$), 3.3–3.7 (m, 16 H, OCH_2), 8.2–8.9 (m, 2 H, Ar H), 11.40 (s, 1 H, OH); MS, *m/e* 400 (M^+). Anal. Calcd for $C_{17}H_{24}N_2O_9$: C, 51.00; H, 6.04; N, 7.00. Found: C, 50.90; H, 6.01; N, 6.85.

6-(2-Hydroxy-3-nitrobenzyl)-6-methyl- and 6-(2-hydroxy-3,5-dinitrobenzyl)-6-methyl-1,4,8,11-tetraoxacyclotetradecane (12 and 13) were obtained concurrently by the concentrated HNO_3 nitration. **12**: reddish orange liquid (23%); IR (neat) 3180, 1535, 1250, 1120 cm^{-1}; ^1H NMR δ 0.74 (s, 3 H, CH_3), 1.5–1.8 (m, 2 H, $OCH_2)_2CH_2$), 2.66 (s, 2 H, $PhCH_2$), 3.30 (s, 4 H, $(OCH_2)_2C$), 3.4–3.7 (m, 12 H, $(OCH_2)_2CH_2$ and OCH_2CH_2O), 6.8–8.0 (m, 3 H, Ar H), 11.06 (s, 1 H, OH); MS, *m/e* 370 (M^+). Anal. Calcd for $C_{18}H_{27}NO_7$: C, 58.53; H, 7.37; N, 3.79. Found: C, 58.28; H, 7.37; N, 3.74. **13**: yellow solid (40%): mp 95 °C (from MeOH/H_2O (10/1)); IR (KBr) 3170, 1545, 1240, 1120, 1110 cm^{-1}; ^1H NMR δ 0.76 (s, 3 H, CH_3), 1.5–1.8 (m, 2 H, $(OCH_2)_2CH_2$), 2.75 (s, 2 H, $PhCH_2$), 3.2–3.4 (m, 4 H, $(OCH_2)_2C$), 3.5–3.7 (m, 12 H, $(OCH_2)_2CH2$ and OCH_2CH_2O), 8.4–8.9 (m, 2 H, Ar H), 11.50 (s, 1 H, OH); MS, *m/e* 415 (M^+). Anal. Calcd for $C_{18}H_{26}N_2O_9$: C, 52.17; H, 6.32; N, 6.76. Found: C, 52.03; H, 6.28; N, 6.67.

6-Benzyl-6-(2-hydroxy-5-nitrobenzyl)-, 6-benzyl-6-(2-hydroxy-3-nitrobenzyl)-, and 6-benzyl-6-(2-hydroxy-3,5-dinitrobenzyl)-1,4,8,11-tetraoxacyclotetradecane (15, 16, and 17) were obtained concurrently by the nitration of **31** (R_2 = CH_2Ph) with concentrated HNO_3. **15**: pale yellow solid (23%); mp 105 °C (from MeOH); IR (KBr) 3070, 1520, 1295, 1105 cm^{-1}; ^1H NMR δ 1.5–1.9 (m, 2 H, $(OCH_2)_2CH_2$), 2.60 (s, 4 H, $PhCH_2$), 3.2–3.8 (m, 16 H, OCH_2), 6.8–8.0 (m, 8 H, Ar H), 9.10 (s, 1 H, OH); MS, *m/e* 446 (M^+). Anal. Calcd for $C_{24}H_{31}NO_7$: C, 64.70; H, 7.01; N, 3.14. Found: C, 64.62; H, 7.06; N, 3.30. **16**: yellow liquid (28%); IR (neat) 3150, 1532, 1240, 1110 cm^{-1}; ^1H NMR δ 1.5–1.7 (m, 2 H, $(OCH_2)_2CH_2$), 2.64 (s, 2 H, $PhCH_2$), 2.72 (s, 2 H, $HOPhCH_2$), 3.2–3.7 (m, 16 H, OCH_2), 6.7–8.0 (m, 8 H, Ar H), 11.08 (s, 1 H, OH); MS, *m/e* 446 (M^+). Anal. Calcd for $C_{24}H_{31}NO_7$: the same as for **15**. Found: C, 64.64; H, 7.13; N, 2.95. **17**: yellowish brown liquid (15%); IR (neat) 3200, 1540, 1268, 1124, 1115 cm^{-1}; ^1H NMR δ 1.4–1.7 (m, 2 H, $(OCH_2)_2CH_2$), 2.64 (s, 2 H, $PhCH_2$), 2.80 (s, 2 H, $HOPhCH_2$), 3.2–3.7 (m, 16 H, OCH_2), 7.1–8.8 (m, 7 H, Ar H), 11.44 (s, 1 H, OH); MS, *m/e* 491 (M^+). Anal. Calcd for $C_{24}H_{30}N_2O_9$: C, 58.77; H, 6.17; N, 5.71. Found: C, 58.31; H, 6.03; N, 5.64.

6-(2-Hydroxy-3,5-dinitrobenzyl)-6-(*o*-nitrobenzyl)- and 6-(2-hydroxy-3,5-dinitrobenzyl)-6-(*p*-nitrobenzyl)-1,4,8,11-tetraoxacyclotetradecane (18) was produced by the nitration of **31** ($R_2 = CH_2Ph$) with fuming HNO_3. Compound **18**, which is a mixture of the *p*- and *o*-nitrobenzyl isomers (molar ratio of ca. 3/2), was isolated as a yellow solid (57%): mp 77–78 °C (from MeOH/H_2O (10/1)); IR (KBr) 3175, 1510, 1260, 1110 cm^{-1}; ^1H NMR δ 1.3–1.7 (m, 2 H, $(OCH_2)_2CH_2$), 2.7–2.9 (m, 4 H, $PhCH_2$), 3.1–3.7 (m, 16 H, OCH_2), 7.3–9.0 (m, 6 H, Ar H), 11.55 (s, 1 H, OH); MS, *m/e* 536 (M^+). Anal. Calcd for $C_{24}H_{29}N_3O_{11}$: C, 53.83; H, 5.46; N, 7.85. Found: C, 53.56; H, 5.44; N, 7.77.

7-Dodecyl-7-(2-hydroxy-5-nitrobenzyl)-, 7-dodecyl-7-(2-hydroxy-3-nitrobenzyl)-, and 7-dodecyl-7-(2-hydroxy-3,5-dinitrobenzyl)-2,5,9,12-tetraoxatridecane (19, 20, and 21) were obtained concurrently by the concentrated HNO_3 nitration of noncyclic crown phenol **37**. **19**: red liquid (32%); IR (neat) 3200, 1516, 1240, 1105, 1086 cm^{-1}; ^1H NMR δ 0.88 (t, 3 H, CH_3CH_2), 1.1–1.5 (m, 22 H, $CH_3(CH_2)_{11}$), 2.61 (s, 2 H, $PhCH_2$), 3.16 (s, 4 H, $(OCH_2)_2C$), 3.2–3.4 (m, 8 H, OCH_2CH_2O), 3.56 (s, 6 H, OCH_3), 6.8–8.0 (m, 3 H, Ar H), 8.63 (s, 1 H, OH); MS, *m/e* 511 (M^+). Anal. Calcd for $C_{28}H_{49}NO_7$: C, 65.72; H, 9.65; N, 2.74. Found: C, 65.98; H, 9.77; N, 2.54. **20**: red liquid (30%); IR (neat) 3150, 1540, 1254, 1106 cm^{-1}; ^1H NMR δ 0.88 (t, 3 H, CH_3CH_2), 1.1–1.4 (m, 22 H, $CH_3(CH_2)_{11}$), 2.76 (s, 2 H, $PhCH_2$), 3.1–3.4 (m, 12 H, OCH_2), 3.44 (s, 6 H, OCH_3), 6.8–8.0 (m, 3 H, Ar H), 11.08 (s, 1 H, OH); MS, *m/e* 511 (M^+). Anal. Calcd for $C_{28}H_{49}NO_7$: the same as for **19**. Found: C, 65.55; H, 9.68; N, 2.84. **21**: deep yellow liquid (13%); IR (neat) 3080, 1540, 1270, 1110 cm^{-1}; ^1H NMR δ 0.89 (t, 3 H, CH_3CH_2), 1.2–1.5 (m, 22 H, $CH_3(CH_2)_{11}$), 2.89 (s, 2 H, $PhCH_2$), 3.2–3.4 (m, 12 H, OCH_2), 3.44 (s, 6 H, OCH_3), 8.4–8.8 (m, 2 H, Ar H), 11.49 (s, 1 H, OH); MS, *m/e* 557 (M^+). Anal. Calcd for $C_{28}H_{48}N_2O_9$: C, 60.41; H, 8.69; N, 5.03. Found: C, 60.68; H, 8.79; N, 4.92.

12-Dodecyl-12-(2-hydroxy-3,5-dinitrobenzyl)-1,4,7,10-tetraoxacyclotridecane (22) was prepared by the nitration of **40** with fuming HNO_3 and isolated as a yellow solid (43%): mp 76.5 °C (from MeOH); IR (KBr) 3180, 1540, 1245, 1122 cm^{-1}; ^1H NMR δ 0.88 (t, 3 H, CH_3), 1.1–1.5 (m, 22 H, $CH_3(CH_2)_{11}$), 2.72 (s, 2 H, $PhCH_2$), 3.1–3.7 (m, 16 H, OCH_2), 8.4–8.9 (m, 2 H, Ar H), 11.47 (s, 1 H, OH); MS, *m/e* 555 (M^+). Anal. Calcd for $C_{28}H_{46}N_2O_9$: C, 60.63; H, 8.36; N, 5.05. Found: C, 60.70; H, 8.37; N, 4.75.

15-Dodecyl-15-(2-hydroxy-5-nitrobenzyl)-, 15-dodecyl-15-(2-hydroxy-3-nitrobenzyl)-, and 15-dodecyl-15-(2-hydroxy-3,5-dinitrobenzyl)-1,4,7,10,13-pentaoxacyclohexadecane (23, 24, and 25) were obtained concurrently by the concentrated HNO_3 nitration of **41**. **23**: red liquid (13%); IR (neat) 3145, 1518, 1240, 1118 cm^{-1}; ^1H NMR δ 0.89 (t, 3 H, CH_3), 1.1–1.5 (m, 22 H, $CH_3(CH_2)_{11}$), 2.58 (s, 2 H, $PhCH_2$), 3.2–3.8 (m, 20 H, OCH_2), 6.8–8.1 (m, 3 H, Ar H), 8.95 (s, 1 H, OH); MS, *m/e* 554 (M^+). Anal. Calcd for $C_{30}H_{51}NO_8$: C, 65.07; H, 9.28; N, 2.53. Found: C, 64.98; H, 9.26; N, 2.39. **24**: red liquid (12%); IR (neat) 3160, 1540, 1258, 1130 cm^{-1}; ^1H NMR δ 0.88 (t, 3 H, CH_3), 1.1–1.4 (m, 22 H, $CH_3(CH_2)_{11}$), 2.72 (s, 2 H, $PhCH_2$), 3.2–3.7 (m, 20 H, OCH_2), 6.7–8.0 (m, 3 H, Ar H), 11.08 (s, 1 H, OH); MS, *m/e* 554 (M^+). Anal. Calcd for $C_{30}H_{51}NO_8$: the same as for **23**. Found: C, 64.94; H, 9.28; N, 2.53. **25**: yellow solid (41%): mp 67 °C (from MeOH); IR (KBr) 3200, 1540, 1270, 1122 cm^{-1}; ^1H NMR δ 0.88 (t, 3 H, CH_3), 1.2–1.4 (m, 22 H, $cH_3(CH_2)_{11}$), 2.84 (s, 2 H, $PhCH_2$), 3.2–3.6 (m, 20 H, OCH_2), 8.4–8.8 (m, 2 H, Ar H), 11.46 (s, 1 H, OH); MS, *m/e* 599 (M^+). Anal. Calcd for $C_{30}H_{50}N_2O_{10}$: C, 60.18; H, 8.42; N, 4.68. Found: C, 60.19; H, 8.36; N, 4.50.

General Procedure for Diazo Coupling to Crown Azophenol. An appropriate aniline derivative (4.2 mmol) was suspended in THF–water (25/25 mL) containing concentrated HCl (1 mL), and the mixture was then cooled in an ice bath. To the mixture was added $NaNO_2$ (4.2 mmol) while stirring. The stirring was continued until the mixture turned clear. To the resulted

diazonium salt solution was quickly added a precooled THF–water (25/25 mL) solution of a crown phenol (or crown *o*-nitrophenol) (1.04 mmol) and $NaHCO_3$ (12 mmol) while stirring. The stirring was continued for 3 h while the mixture was cooled in an ice bath. After the reaction the THF was removed by rotary evaporator. The residue was extracted with $CHCl_3$ (100 mL × 3). The $CHCl_3$ solution was washed successively by 10% K_2CO_3 and 0.2% CH_3CO_2H aqueous solutions. Evaporation of the solvent afforded crude products, which were separated and purified by reversed-phase liquid chromatography (MeOH/$CHCl_3$ (10/1) for **6–9** and MeOH/H_2O (10/1) for **14**). The retention time of the isomers on the chromatography was increased in the order para < ortho < bis(phenylazo) isomers. The solid products can be further purified by recrystallization.

6-Dodecyl-6-[2-hydroxy-5-[(4-(*N*,*N*-dimethylsulfamoyl)-phenyl)azo]benzyl]-1,4,8,11-tetraoxacyclotetradecane (5) was prepared as described in the general procedure for the diazo coupling using *p*-(*N*,*N*-dimethylsulfamoyl)aniline and crown phenol **31** ($R_2 = C_{12}H_{25}$) and isolated as a deep red solid (43%): mp 79.5 °C (from MeOH); IR (KBr) 3150, 1582, 1348, 1272, 1268, 1112 cm^{-1}; ^1H NMR δ 0.86 (t, 3 H, CH_3CH_2), 1.0–1.4 (m, 22 H, $CH_3(CH_2)_{11}$), 1.5–1.8 (m, 2 H, $(OCH_2)_2CH_2$), 2.48 (s, 2 H, $PhCH_2$), 2.68 (s, 6 H, NCH_3), 3.2–3.7 (m, 16 H, OCH_2), 6.8–8.0 (m, 7 H, Ar H), 8.68 (s, 1 H, OH); MS, *m/e* 689 (M^+). Anal. Calcd for $C_{37}H_{59}N_3O_7S$: C, 64.41; H, 8.62; N, 6.09. Found: C, 64.64; H, 8.72; N, 5.79.

6-Dodecyl-6-[2-hydroxy-5-((4-nitrophenyl)azo)benzyl]-, 6-dodecyl-6-[2-hydroxy-3-((4-nitrophenyl)azo)benzyl]-, and 6-dodecyl-6-[2-hydroxy-3,5-bis((4-nitrophenyl)azo)-benzyl]-1,4,8,11-tetraoxacyclotetradecane (6, 7, and 8) were obtained concurrently by the diazo coupling of *p*-nitroaniline and **31** ($R_2 = C_{12}H_{25}$). **6**: reddish orange solid (32%); mp 80.5 °C (from MeOH/$CHCl_3$ (10/1)); IR (KBr) 3100, 1586, 1520, 1280, 1132, 1095 cm^{-1}; ^1H NMR δ 0.88 (t, 3 H, CH_3), 1.1–1.5 (m, 22 H, $CH_3(CH_2)_{11}$), 1.6–1.8 (m, 2 H, $(OCH_2)_2CH_2$), 2.52 (s, 2 H, $PhCH_2$), 3.2–3.7 (m, 16 H, OCH_2), 6.8–8.4 (m, 7 H, Ar H), 8.76 (s, 1 H, OH); MS, *m/e* 627 (M^+). Anal. Calcd for $C_{35}H_{53}N_3O_7$: C, 66.96; H, 8.51; N, 6.69. Found: C, 66.73; H, 8.49; N, 6.66. **7**: deep red liquid (14%); IR (neat) 3100, 1590, 1520, 1278, 1120 cm^{-1}; ^1H NMR δ 0.88 (t, 3 H, CH_3), 1.1–1.4 (m, 22 H, $CH_3(CH_2)_{11}$), 1.5–1.8 (m, 2 H, $(OCH_2)_2CH_2$), 2.64 (s, 2 H, $PhCH_2$), 3.32 (s, 4 H, $(OCH_2)_2C$), 3.5–3.7 (m, 12 H, OCH_2CH_2O and $(OCH_2)_2CH_2$), 6.9–8.4 (m, 7 H, Ar H), 12.86 (s, 1 H, OH); MS, *m/e* 627 (M^+). Anal. Calcd for $C_{35}H_{53}N_3O_7$: the same as for **6**. Found: C, 67.11; H, 8.59; N, 6.72. **8**: reddish orange solid (10%); mp 105.5 °C (from MeOH/$CHCl_3$ (10/1)); IR (neat) 3380, 1595, 1520, 1240, 1136, 1120 cm^{-1}; ^1H NMR δ 0.85 (t, 3 H, CH_3), 1.1–1.5 (m, 22 H, $CH_3(CH_2)_{11}$), 1.5–1.8 (m, 2 H, $(OCH_2)_2CH_2$), 2.72 (s, 2 H, $PhCH_2$), 3.2–3.7 (m, 16 H, OCH_2), 7.8–8.5 (m, 10 H, Ar H), 13.32 (s, 1 H, OH); MS, *m/e* 776 (M^+). Anal. Calcd for $C_{41}H_{56}N_6O_9$: C, 63.38; H, 7.27; N, 10.82. Found: C, 63.54; H, 7.27; N, 10.68.

6-Dodecyl-6-[2-hydroxy-3-nitro-5-((4-nitrophenyl)azo)-benzyl]-1,4,8,11-tetraoxacyclotetradecane (9) was produced by the diazo coupling of *p*-nitroaniline and crown *o*-nitrophenol **2** and isolated as a red solid (30%): mp 87.5 °C (from MeOH/$CHCl_3$ (10/1)); IR (KBr) 3180, 1610, 1520, 1260, 1130, 1112 cm^{-1}; ^1H NMR δ 0.88 (t, 3 H, CH_3), 1.1–1.4 (m, 22 H, $CH_3(CH_2)_{11}$), 1.5–1.8 (m, 2 H, $(OCH_2)_2CH_2$), 2.76 (s, 2 H, $PhCH_2$), 3.2–3.7 (m, 16 H, OCH_2), 7.8–8.6 (m, 6 H, Ar H), 11.40 (s, 1 H, OH); MS, *m/e* 672 (M^+). Anal. Calcd for $C_{35}H_{52}N_4O_9$: C, 62.48; H, 7.79; N, 8.33. Found: C, 62.45; H, 7.81; N, 8.19.

6-[2-Hydroxy-3-nitro-5-((4-nitrophenyl)azo)benzyl]-6-methyl-1,4,8,11-tetraoxacyclotetradecane (14) was prepared by the diazo coupling of *p*-nitroaniline and crown *o*-nitrophenol **12** and isolated as a red solid (52%): mp 149 °C (from MeOH/$CHCl_3$ (10/1)); IR (KBr) 3200, 1605, 1520, 1260, 1130, 1115 cm^{-1}; ^1H NMR δ 0.87 (s, 3 H, CH_3), 1.7–1.9 (m, 2 H, $(OCH_2)_2CH_2$), 2.84 (s, 2 H, $PhCH_2$), 3.43 (s, 4 H, $(OCH_2)_2C$), 3.6–3.8 (m, 12 H, $(OCH_2)_2CH_2$ and OCH_2CH_2O), 7.9–8.7 (m, 6 H, Ar H), 11.34 (s, 1 H, OH); MS, *m/e* 518 (M^+). Anal. Calcd for $C_{24}H_{30}N_4O_9$: C, 55.59; H, 5.83; N, 10.81. Found: C, 55.67; H, 5.79; N, 10.69.

Acidity Constant. The constants for chromogenic crown ethers and their noncyclic analogues were evaluated spectrophotometrically at room temperature. As the solvent was chosen water–dioxane (1/1) since most of the crown ethers employed are practically insoluble in pure water. The initial solution (50 mL) contained 7×10^{-5} M crown ether (1.75×10^{-5} M for **6**, **7**, and **9**, 3.5×10^{-6} M for **8**), 1×10^{-3} M HCl, and 9.9×10^{-2} M tetramethylammonium chloride. Titration was made with 10% TMAOH aqueous solution and then electronic spectrum was measured at each pH. The acidity constant, defined as $K_a = ([H^+][L^-])/[HL]$, was determined graphically by using eq 4, where

$$[H^+]A = -K_aA + \epsilon_{L^-}K_a[HL]_t \quad (4)$$

A and ϵ_{L^-} denote absorbance and molar absorptivity, respectively, for the proton-dissociated crown ethers at a wavelength where the undissociated species does not absorb. Plots of $[H^+]A$ against A gave straight lines, and the K_a values were computed from the slopes.

Cation Extraction. Extraction experiments for the qualitative comparison of cation extractabilities were done as follows: In a stoppered centrifuge tube were placed a 1,2-dichloroethane solution (5 mL) of 7×10^{-5} M crown ether and a basic aqueous solution of 1 M metal chloride. The mixture was shaken vigorously for 30 s at room temperature. After centrifugation 4 mL of the organic phase was taken which was then subjected to spectrophotometry. The pH in the aqueous phase was controlled by TMAOH and buffers of 3-[*N*-(tris(hydroxymethyl)methyl)-amino]propanesulfonic acid (TAPS) or 3-morpholinopropanesulfonic acid (MOPS) and TMAOH. For the K_{ex} determination, extractions were carried out at 25 °C, by varying the metal ion concentration and keeping the crown ether concentration constant. The constant crown ether concentrations ranged from 1.75×10^{-3} to 7×10^{-5} M, being dependent on the cation extractability and molar absorbtivity of the crown ethers. The metal chloride concentrations were (1×10^{-2})–(7×10^{-1}) M for Li^+, (1×10^{-2})–2 M for Na^+, and (2×10^{-2})–1 M for K^+. The pH in the aqueous phase was adjusted to 12.0 for **1**, **2**, **5–8**, **10**, **12**, **15**, **16**, **19**, **20**, **23**, and **24** with TMAOH, 9.12 for **9** and **14** with a TAPS/TMAOH buffer, and 8.23 for **3**, **21**, **22**, and **25** with MOPS/TMAOH buffers. Equal volumes (3 mL) of the dichloroethane and aqueous solutions were placed into a stoppered tube connected with a 1-cm quartz cell. The tube was vigorously shaken for 30 s and then was allowed to stand for 12 h in a thermostated bath of 25 °C. Electronic spectrum of the organic phase, which was at lower level of the two phases, was in situ measured in a cell holder thermostated at 25 °C. The plots for eq 2 or 3 afforded straight lines with coefficients of correlation of better than 0.999 in any of the extraction systems where the K_{ex} value was obtainable.

Registry No. **1**, 98506-68-4; **1**$^-$, 106419-48-1; **1**·Li^+, 106420-07-9; **1**·Na^+, 106420-24-0; **2**, 98506-69-5; **2**$^-$, 106419-49-2; **2**·Li^+, 106420-08-0; **3**, 98506-70-8; **3**$^-$, 106419-50-5; **3**·Li^+, 106420-09-1; **3**·Na^+, 106420-25-1; **4**, 106419-28-7; **4**$^-$, 106419-51-6; **5**, 98786-85-7; **5**$^-$, 106419-52-7; **5**·Li^+, 106420-10-4; **6**, 106419-29-8; **6**$^-$, 106419-53-8; **6**·Li^+, 106420-11-5; **7**, 106419-30-1; **7**$^-$, 106419-54-9; **7**·Li^+, 106420-12-6; **8**, 106419-31-2; **8**$^-$, 106419-55-0; **8**·Li^+, 106420-13-7; **8**·Na^+, 106420-26-2; **9**, 106419-32-3; **9**$^-$, 106419-56-1; **9**·Li^+, 106420-14-8; **9**·Na^+, 106420-27-3; **10**, 106419-33-4; **10**$^-$, 106419-57-2; **10**·Li^+, 106420-15-9; **11**·Na^+, 106420-28-4; **11**, 106434-35-9; **11**$^-$, 106419-58-3; **11**·Li^+, 106420-16-0; **12**, 106419-34-5; **12**$^-$, 106419-59-4; **12**·Li^+, 106420-17-1; **13**, 106419-35-6; **13**$^-$, 106419-60-7; **13**·Li^+, 106420-18-2; **13**·Na^+, 106420-29-5; **14**, 106419-36-7; **14**$^-$, 106419-61-8; **14**·Li^+, 106420-19-3; **14**·Na^+, 106420-30-8; **15**, 106419-37-8; **15**$^-$, 106419-62-9; **15**·Li^+, 106420-20-6; **15**·Na^+, 106420-06-8; **16**, 106419-38-9; **16**$^-$, 106419-63-0; **16**·Li^+, 106420-21-7; **17**, 106419-39-0; **17**$^-$, 106419-64-1; **17**·Li^+, 106420-22-8; **17**·Na^+, 106434-38-2; *o*-**18**, 106419-40-3; *p*-**18**, 106420-04-6; *o*-**18**$^-$, 106419-65-2; *p*-**18**$^-$, 106420-05-7; *o*-**18**·Li^+, 106420-23-9; *p*-**18**·Li^+, 106420-04-6; **19**, 106419-41-4; **19**$^-$, 106419-66-3; **20**, 106419-42-5; **20**$^-$, 106419-67-4; **21**, 106419-43-6; **21**$^-$, 106419-68-5; **22**, 106419-44-7; **22**$^-$, 106419-69-6; **23**, 106419-45-8; **23**$^-$, 106419-70-9; **23**·Li^+, 106420-33-1; **23**·Na^+, 106420-31-9; **24**, 106419-46-9; **24**$^-$, 106419-71-0; **24**·Na^+, 106434-39-3; **25**, 106419-47-0; **25**$^-$, 106419-72-1; **25**·Li^+, 106420-34-2; **25**·Na^+, 106420-32-0; *o*-**26** ($R_2 = C_{12}H_{25}$), 106419-73-2; *p*-**26** ($R^2 = C_{12}H_{25}$), 106419-76-5; **26** ($R_2 = CH_2Ph$), 106419-74-3; **26** ($R_2 = H$), 77738-20-6; **27** ($R^2 = C_{12}H_{25}$), 98506-66-2; **27** ($R_2 = CH_2Ph$), 106434-36-0; **27** ($R_2 = H$), 106419-77-6; **27** ($R_2 = CH_3$), 106419-78-7; **29** ($R_2 = C_{12}H_{25}$), 98514-81-9; **29** ($R_2 = CH_2Ph$), 106419-80-1; **29** ($R_2 = H$), 106419-81-2; **29** ($R_2 = CH_3$), 106419-82-3; **30** ($R_2 = C_{12}H_{25}$), 106419-83-4; **31** ($R_2 = C_{12}H_{25}$), 106419-84-5; **31** ($R_2 =$

$PhCH_2$), 106419-85-6; **31** (R_2 = H), 106419-84-5; **31** (R_2 = CH_3), 106419-86-7; **32** (R_2 = $C_{12}H_{25}$), 98506-67-3; **33** (R_2 = $C_{12}H_{25}$), 106419-87-8; **33** (R_2 = $PhCH_2$), 106434-37-1; **33** (R_2 = H), 106419-88-9; **33** (R_2 = CH_3), 106419-89-0; **34** (R_2 = $C_{12}H_{25}$), 106419-90-3; **34** (R_2 = $PhCH_2$), 106419-91-4; **34** (R_2 = H), 106419-92-5; **34** (R_2 = CH_3), 106419-93-6; **35** (R_2 = $C_{12}H_{25}$), 106419-94-7; **35** (R_2 = $PhCH_2$), 106419-95-8; **35** (R_2 = H), 106419-96-9; **35** (R_2 = CH_3), 106419-97-0; **36**, 106419-98-1; **37**, 106419-99-2; **38**, 106420-00-2; **39**, 106420-01-3; **40**, 106420-02-4; **41**, 106420-03-5; $CH_3(CH_2)_{11}CH(COOEt)_2$, 7252-87-1; $PhCH_2CH(COOEt)_2$, 607-81-8; $CH_2(COOEt)_2$, 105-53-3; $CH_3CH(COOEt)_2$, 609-08-5; *o*-$CH_3OC_6H_4CH_2Br$, 52289-93-7; *p*-$CH_3OC_6H_4CH_2Br$, 2746-25-0; *o*-$CH_3OC_6H_4CH_2C(COOEt)_2CH_3$, 106419-75-4; *p*-$CH_3OC_6H_4CH_2C(CH_2OH)_2(CH_2)_{11}CH_3$, 106419-79-8; (*p*-$CH_3C_6H_4SO_2O(CH_2)_2O)_2(CH_2)_3$, 92144-75-7; *o*-$BrCH_2C_6H_4OCH_2Ph$, 103633-30-3; *p*-$CH_3C_6H_4SO_2O(CH_2)_2OCH_3$, 17178-10-8; (*p*-$CH_3C_6H_4SO_2O(CH_2)_2O)_2(CH_2)_2$, 19249-03-7; (*p*-$CH_3C_6H_4SO_2O(CH_2)_2O(CH_2)_2)_2O$, 37860-51-8; $(CH_3)_2NSO_2C_6H_4NH_2$, 1709-59-7; *p*-$O_2NC_6H_4NH_2$, 100-01-6; Li^+, 17341-24-1; Na^+, 17341-25-2; K^+, 24203-36-9; Rb^+, 22537-38-8; Cs^+, 18459-37-5; Mg^{2+}, 22537-22-0; Ca^{2+}, 14127-61-8; Sr^{2+}, 22537-39-9; Ba^{2+}, 22541-12-4; *o*-salicylaldehyde, 90-02-8; *p*-salicylaldehyde, 123-08-0.

Reactions of (Benzothiazol-2-ylthio)(trimethylsilyl)methane. A General Method for α-Mercaptoalkylation by Alkylation and Alkylative Desilylation

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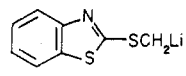
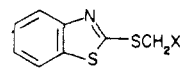
Readily available (benzothiazol-2-ylthio)(trimethylsilyl)methane (**2a**) provides a convenient synthon for $HSCH^{2-}$ and enables the general conversions RR'CO → RR'C(OH)CH(SH)R'' and RBr → $RCH(SH)SiMe_3$. The lithium derivative of **2a** reacts with aldehydes and ketones to give Peterson olefination products which are protected vinyl mercaptans converted into vinyl mercaptans by reaction with methyllithium. This overall conversion is RR'CO → RR'C:CHSH.

We have recently developed[1] a convenient two-step procedure for the mercaptomethylation of alkyl halides, and of aromatic aldehydes and ketones, which involved (i) their treatment with 2-[(lithiomethyl)thio]benzothiazole (**1**) and (ii) subsequent reaction with *n*-butyllithium (nucleophilic attack at the benzothiazole 2-position). This procedure was limited to mercaptomethylation, since carbanions analogous to **1** could not readily be prepared by deprotonation of 2-(ethylthio)benzothiazole (**2b**) or of higher homologues. Although there are alternative



(1)



(2)

a X = $SiMe_3$
b X = Me
c X = H
d X = $PhCH_2$

methods to effect mercaptomethylation,[2-4] no general method for α-mercaptoalkylation, i.e., for the introduction of the group CHRSH, is available. As other results in our laboratories[5] suggest that the second step of our mercaptomethylation sequence could be of general application, we have therefore sought a system **2** where the group X would enhance the acidity of the α-methylene protons and could be easily removed with concomitant introduction of functionality: trimethylsilyl (as in **2a**) suited both these purposes. Carbanions adjacent to both sulfur and silicon have found extensive synthetic applications.[6-9] Furthermore, the reaction of α-heterosubstituted silyl derivatives with aldehydes has yielded the alcohols deriving from the addition of the C–Si bond to the carbonyl group in recent nucleophilic amino- and hydroxymethylations of carbonyl compounds.[10,11]

Table I. Products and Yields from the Reaction of 2a with LDA and Electrophiles

R^1	R^2	product	yield, %
$(CH_2)_3$		**5g**	86
H	Me	**5h**	32
$PhCH_2$		**6a**	90
Me		**6b**	91
n-Hex		**6c**	93
p-MeC_6H_4	H	**11d**	98
$CH_3CH_2CH_2$	H	**11e**	98
$(CH_2)_5$		**11f**	77

We now report the application of **2a** as a synthon for $HSCH^{2-}$, by successive (i) deprotonation with LDA and reaction with electrophiles, (ii) fluoride anion promoted desilylation, followed by reaction with a carbonyl compound, and (iii) nucleophilic attack by alkyllithiums at the benzothiazole 2-position. This sequence provides a general method for the mercaptoalkylation of carbonyl compounds and also opens up a variety of other useful synthetic transformations.

Results and Discussion

Reactions of 2a with LDA and Electrophiles. The trimethylsilyl derivative **2a** was previously prepared by the

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