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Chromogenic Proton-Dissociable Azocrown Ether Reagents for Lithium Ions

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Abstract: Synthesis of new proton-dissociable chromogenic azocrown ethers bearing phenol and two azo groups as parts of macrocycle has been developed. Color reactions of the modified crown ethers with metal cations are described. High selectivity of lithium complex formation was found by spectrophotometry.
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Chromoionophores discovered by J.P. Dix and F. Vögtle[1] present valuable dye reagents changing color or causing fluorescence upon interaction with ions.[2] Proton-dissociable chromogenic crown ethers[3] in general could be used for determination of metal cations by spectrophotometric methods. However, a problem exists with regard to the spectral behavior of anionic forms of chromophores in homogeneous, water-containing solvents. Similarly to many conventional metallochromic reagents, electronic spectra of anionic chromophores, typically phenolate derivatives, are not sensitive to the difference between the metal species in coordination as the shifts (10-30 nm) are small. In addition, spectral separations between the hydrated "free" anions and the "coordinated" anions are usually very small when "coordination" with alkali metal ions is concerned. These situations make spectrophotometric study of anionic chromoionophores difficult in essentially aqueous media.[3]

The inconvenience related to troublesome spectroscopic properties of the so far described chromoionophores could be overcome by inserting the chromophores directly into the macrocyclic moiety of crown ether. This paper describes new proton-dissociable crown compounds (**1** - **3**). The azo groups form parts of the macrocycle; inside the cavity the phenolic OH forms strong intramolecular hydrogen bond with one of these groups. By structural features the compounds resemble mordant azo-dyes. It was expected, that cations forming complexes will coordinate to phenolate anion and to electron donating atoms of the macrocycle, including one of the nitrogen atoms of each azo group.[4] This, in turn, should cause large spectral differences between the anion and its cation complex. The predicted participation of -N=N- chromophore in cation capture inside the crown ether cavity should increase stability of the formed complex and selectivity of the chromoionophore towards cations of different size.

Synthesis of the desired compounds **1** - **3** was achieved as shown in the scheme. Bis(*o*-aminophenoxy)-3-oxapentane or bis(*o*-aminophenoxy)-3,6-dioxaoctane[5,6] were diazotized and the bis-diazonium salts coupled with phenols. The phenols were *p*-substituted to force coupling in the required *o*-position. Coupling of bis(diazonium) salt under high dilution conditions using different salts as templates affords moderate yields of macrocyclic compounds.[7]

A procedure leading to relevant compounds, derivatives of resorcinol was described;[5] the products,

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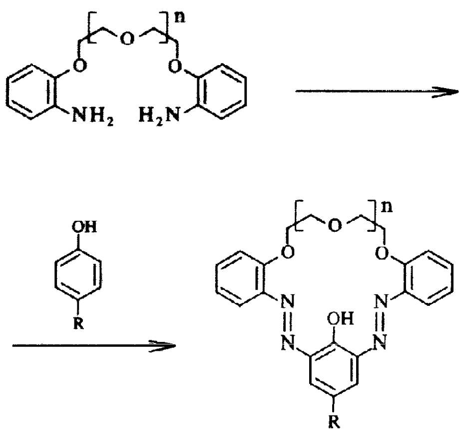

1. R = CH₃ ; n = 1
2. R = C(CH₃)₃ ; n = 1
3. R = CH₃ ; n = 2

however, were not studied as chromogenic reagents.

The chromogenic azocrown ethers are unstable in many solvents; the most stable solutions are in dioxane. They may be stored for a long time without significant spectral changes. The chromogenic crown ethers form complexes with different cations. Many of them could be distinguished by TLC; often their Rf values differ from the free ligand. Their colors also differ. Magnesium, calcium and barium complexes are green, whereas sodium and potassium complexes are brown.

The most interesting reaction of **1** is with lithium salts. A solution of the compound in dioxane is brownish. Upon adding even small amounts of lithium acetate the color turned to pink. This reaction could be used to identify small amounts of this element. For spectrophotometric determination of lithium better conditions were found in alkaline water-dioxane solutions. Under these conditions many metal cations do not interfere because of insolubility of their hydroxides.

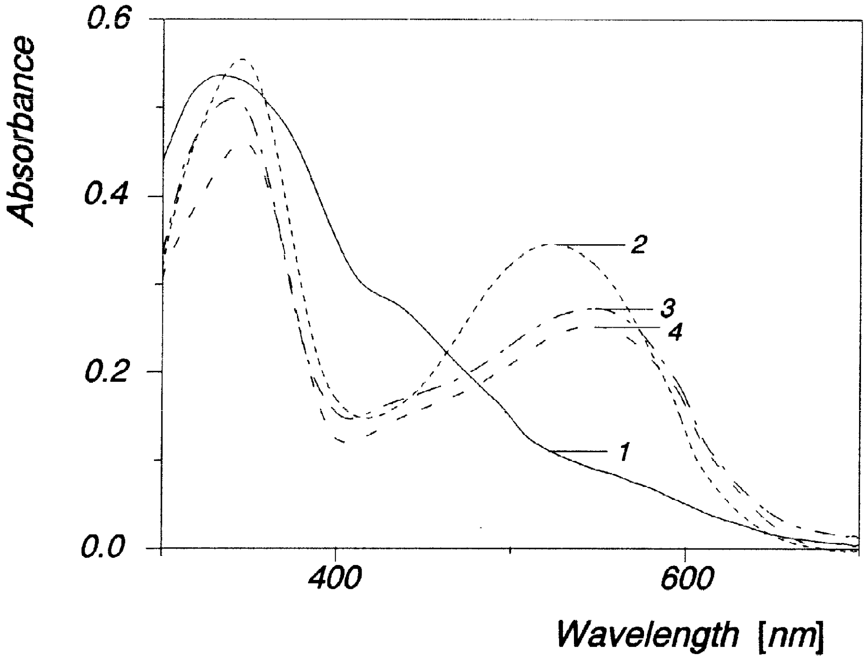

Figure 1. Absorption spectra of azocrown ether **1** - metal salt systems in dioxane -water (1:1 v/v) at pH ≈ 12. Crown ether concentration 2.5×10^{-5} M. (1) Pure anionic form of crown; (2) spectrum in the presence of LiCl (0.05 M); (3) KCl (0.2 M) and (4) NaCl (0.2 M).

Absorption spectra of azocrown ether **1** (Figure 1) in dioxane-water (1:1 v/v; crown concentration 2.5×10^{-5} M; pH adjusted to about 12 with tetraethylammonium hydroxide) showed no absorption maximum in the region about 500 nm. In the presence of lithium chloride new band appears at $\lambda_{max} = 525$ nm. A well-pronounced isosbestic point ($\lambda = 463$ nm) for the system containing lithium suggests two absorbing species under equilibrium. The number of absorbing species was also checked by the factor analysis;[8] the presence of only two species was confirmed. The complex has 1:1 stoichiometry. The association constant for this complex K_{Li} is 880 M^{-1}. This value was obtained in good agreement by factor analysis and by calculations using Benesi-Hildebrand method.[9]

For stability constants of lithium complexes with azocrown ethers and determination of lithium with the use of different chromogenic crown ethers see.[10]

Both sodium and potassium chlorides form complexes with compound **1**, however their stability constants are lower. A new band $\lambda_{max} = 549$ nm appears for systems containing sodium or potassium chloride (Figure 1). Again a well-pronounced isosbestic point ($\lambda = 481$ nm) for sodium system suggests two absorbing species under equilibrium. Calculations performed using both mentioned methods gives ($K_{Na} = 326$ M^{-1}).

The potassium complex ($K_K = 82$ M^{-1}, calculated by Benesi-Hildebrand method) is even weaker. In this case the isosbestic point is less pronounced. The complexes of stoichiometry different from 1:1 (metal : ligand) may also be formed.

Complex formation was also observed using ^{1}H NMR spectroscopy. One of the triplets (at 4.50 ppm) characteristic for polyether chain of the free ligand is replaced by multiplet for LiI complex in acetone. Similarly, the pattern of aromatic protons are more complicated for complex. It could be concluded, that lithium ion is coordinated by all oxygen atoms and by one nitrogen atom of azo groups. Participation of azo group in lithium complex formation with dibenzo-13-azocrown-5 ether was demonstrated by X-ray analysis.[11]

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REFERENCES AND NOTES

1. Dix J.P.; Vögtle F. *Chem. Ber.* **1981**, *114*, 638.
2. Loehr H.G.; Vögtle F. *Acc. Chem. Res.* **1985**, *18*, 65.
3. Takagi M. *Complexation by Chromoionophores* in: *Cation Binding by Macrocycles. Complexation of Cationic Species by Crown Ethers* Inoue Y.; Gokel G.W. [Eds.], Marcel Dekker, Inc., New York and Basel 1990, p. 465; Takagi M.; Ueno K. *Topics in Current Chem.* **1984**, *121*, 39; Takagi M.; Nakamura H. *J. Coord. Chem.* **1986**, *15*, 53; Kaneda T. *J. Synth. Org. Chem. Jap.* **46**, 96 (1988); Hayashita T. *Chromoionophores Based on Crown Ethers and Related Structures* in: *Comprehensive Supramolecular Chemistry* J.L. Atwood, J.E.D. Davies, D.D. MacNicol, F. Vögtle, J.-M. Lehn [Eds.], Pergamon 1996, Vol. 1 [G.W. Gokel, Volume Ed.], p. 635.
4. Skwierawska A.; Luboch E.; Biernat J.F.; Kravtsov V.Ch.; Simonov Yu.A.; Dvorkin A.A.; Bel'skii V.K. *J. Incl. Phenom.*, accepted

5. Sultanov A.V.; Savvin S.B. *Khimia Geterocycl. Soed. Russ.* **1988**, 126.

6. Biernat J.F.; Jereczek E.; Bujewski A. *Pol. J. Chem.* **1979**, *53*, 2367; Bradshaw J.S.; Koyama H.; Dalley N.K.; Izatt R.M.; Biernat J.F.; Bocheńska M. *J. Heterocyclic Chem.* **1987**, *24*, 1077.

7. Syntheses: A suspension of 1,5-bis(2-aminophenoxy)-3-oxapentane[5,6] in water was cooled, acidified with conc. hydrochloric acid and diazotized with sodium nitrite. Solution of the above bisdiazonium salt and an alkaline solution of *p*-cresol were gradually added to large volume of ice-cooled 2% solution of strontium nitrate (template) in water. The reaction mixture was left to stand for 3 hours in an ice bath and for 0.5 hour more at room temperature. The solid product was collected, dissolved in methylene chloride and purified by column chromatography using a mixture of methylene chloride : acetic acid (8 : 1) as an eluent. The dark brown fraction was collected and the solvent was evaporated. The residue was purified once again in the same way. After crystallization from toluene the macrocyclic compound **1** was obtained with 27% yield, m.p. 178-179°C; MS: for $C_{23}H_{22}N_4O_4$ calcd. m.w. 418.46; m/z = 418. ^{1}H NMR, $CDCl_3$ (δ ppm): 2.49 (s, 3H); 4.01 (t, 4H; J=5.13 Hz); 4.50 (t, 4H, J=4.16 Hz); 7.03-7.11 (m, 4H); 7.37-7.46 (m, 2H); 7.79-7.84 (m, 4H).

   Compound **2** was obtained analogously by coupling *p-tert*-butylphenol with the above diazonium salt. Magnesium nitrate was used as a template. Yield 10%; m.p. 164-166°. MS: for $C_{26}H_{28}N_4O_4$ calculated m.w. 460.54; m/z = 460. ^{1}H NMR, $CDCl_3$ (δ ppm): 1.47 (s, 9H); 4.03 (t, 4H, J=5.12 Hz); 4.53 (t, 4H, J=5.17 Hz); 7.06-7.13 (m, 4H); 7.40-7.44 (m, 2H); 7.85 (dd, 2H, J_1=7.86 Hz, J_2=8.05 Hz); 8.02 (s, 2H).

   Compound **3** was obtained from *p*-cresol and bis-diazonium salt (n=2) in the presence of strontium nitrate as a template. Yield 20%; m.p. 149-150°. MS: for $C_{25}H_{26}N_4O_5$ calculated m.w. 462.51; m/z = 462. ^{1}H NMR, $CDCl_3$ (δ ppm): 2.46 (s, 3H); 3.93 (s, 4H); 4.0 (t, 4H, J=4.07 Hz); 4.32 (t, 4H, J=3.95 Hz); 7.05-7.12 (m, 4H); 7.37-7.46 (m, 2H); 7.77-7.84 (m, 4H).

8. Malinowski E.R.; Howery D.G. *Factor Analysis in Chemistry*, Wiley-Interscience, New York, 1980; Gamp H.; Maeder M.; Meyer C.J.; Zuberbuehler A.D. *Comments Inorg. Chem* **1987**, *6*, 41.

9. Benesi H.A.; Hildebrand J.H. *J. Am. Chem. Soc.* **1949**, *71*, 2703; Ketelaar J.A.A.; van de Stolpe C.; Goudsmit A.; Dzoubas W. *Rec. Trav. Chim. Pays-Bas Belg.* **1952**, *71*, 1104.

10. Nakashima K.; Nakatsuji S.; Akiyama S.; Kaneda T.; Misumi S. *Chem. Pharm. Bull.* **1986**, *34*, 168; Shiga M.; Nakamura H.; Takagi M.; Ueno K. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 412; Nakashima K.; Nakatsuji S.; Akiyama S.; Kaneda T.; Misumi S. *Chem. Lett.* **1982**, 1781; Kaneda T.; Umeda S.; Tanigawa H.; Misumi S. *J. Am. Chem. Soc.* **1985**, *107*, 4802; Bartsch R.A.; Czech B.P.; Kang S.I.; Stewart D.E.; Walkowiak W.; Charewicz W.A.; Heo G.S.; Son B. *J. Am. Chem. Soc.* **1985**, *107*, 4997.

11. Luboch E.; Biernat J.F.; Kravtsov V.Ch.; Simonov Yu.A. *J. Incl. Phenom.*, accepted