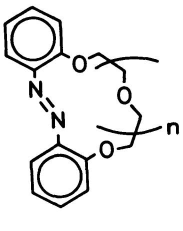
© 1984 The Chemical Society of Japan Bull. Chem. Soc. Jpn., 57, 412—415 (1984) [Vol. 57, No. 2

Synthesis of Azobenzo-crown Ethers and Their Complexation Behavior with Metal Ions

Masanobu Shiga, Hiroshi Nakamura, Makoto Takagi,* and Keihei Ueno†
Department of Organic Synthesis, Faculty of Engineering, Kyushu University, Hakozaki, Higashi-ku, Fukuoka 812
†Department of Industrial Chemistry, Kumamoto Institute of Technology, 4-22-1 Ikeda, Kumamoto 860
(Received September 1, 1983)

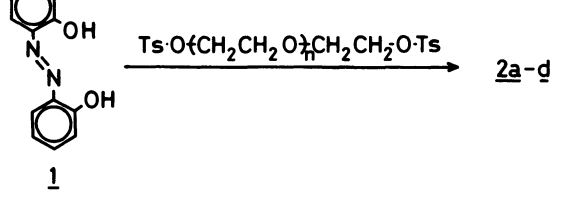
New crown ethers which have a benzeneazo group as a building block of a macrocyclic polyether ring. The complexation properties of these new azobenzo-crown ethers with alkali and alkaline earth metal iodide salts were investigated in acetonitrile solution spectrophotometrically. The complex formation constants were evaluated for alkali metal salts. The azo group is not particularly a favorable component of a crown ether macrocycle for stabilizing the metal complexes.

During the course of our investigation to develop the chromogenic crown ether reagents for the photometric determination of alkali and alkaline earth metal ions, a series of new crown ethers have been synthesized, in which 2,2′-positions of azobenzene were bridged by oligoethylene glycol to form a skeletal structure of crown ether. The crown ethers synthesized in this study are shown in structure **2**. They are conveniently named as azobenzo-crown ether or azobenzo-13-crown-4 for **2a** as an example, because the structure and hole size of **2a** is comparable with that of 13-crown-4 when azobenzene moiety takes trans-conformation.



2a n = 1
b n = 2
c n = 3
d n = 4

In our previous communication,[1] we reported the photoisomerization of azobenzo-crown ethers. The trans-isomer was more favorable for metal ion complexation. The complexation behavior of azobenzo-crown ethers was also evaluated semiquantitatively by the ion-pair extraction of metal complex with tetrabromophenolphthalein ethyl ester. Lithium was not extracted by any of these crown ethers, but sodium was extracted by **2a** preferentially over potassium. **2b** preferred the extraction of potassium. Recently, Shinkai, Manabe and co-workers described the 4,4′-(oligoethylene glycol-linked) azobenzene, which showed a marked photo-responsive metal extraction properties in relation to their trans-cis isomerization of azo linkage.[2]



Scheme 1.

As we have found that considerable spectral change was observed for these azobenzo-crown ethers upon complexation with metal ion in aprotic solvents such as acetonitrile, a detailed photometric investigation has been done to evaluate the interaction quantitatively.

Experimental

Synthesis of Azobenzo-crown Ethers. The synthetic reaction is shown below, and the procedure for azobenzo-13-crown-4 is described below as an example.

*Azobenzo-13-crown-4 (**2a**).* To a 200 ml round bottomed flask containing 1.0 g (4.7 mmol) of 2,2′-dihydroxyazobenzene (**1**)[3] was added 1.1 g (9.8 mmol) of potassium *t*-butoxide in 50 ml THF under a nitrogen atmosphere at room temperature, and the mixture was stirred for 30 min. To this mixture, 2.0 g (4.8 mmol) of diethylene glycol ditosylate was added dropwise in 1 h, and refluxed for 16 h. After cooling, the precipitate in the reaction mixture was filtered off, and the filtrate was evaporated under a reduced pressure. The residue was taken into chloroform, and washed with water. After evaporation, the residual mass was applied on a silica-gel column (WAKO-gel C-200, 20×100 mm), and eluted with benzene, followed by chloroform. The red colored fraction was collected, and evaporated to obtain crystalline mass, which was recrystallized from heptane. Yield 0.36 g (27%). Mp 69.5—71 °C. IR (KBr disk) 2920 (CH), 1590 cm^{-1} (N=N). ^{1}H NMR (δ ppm from TMS; $CDCl_3$); δ=3.8—4.0 (4H, m, $-CH_2OCH_2-$), 4.12—4.35 (4H, m, $ArOCH_2-$), 6.63—7.50 (8H, m, Ar-H). Ms (m/z); 284 (M^+). Found: C, 67.36; H, 5.82; N, 9.56%. Calcd for $C_{16}H_{16}N_2O_3$: C, 67.59; H, 5.67; N, 9.85%.

*Azobenzo-16-crown-5 (**2b**), -19-crown-6 (**2c**), and -22-crown-7 (**2d**).* The procedures were almost the same as that of **2a**, except for the use of tri-, tetra- and pentaethylene glycol ditosylates for **2b**, **2c**, and **2d**, respectively, in place of diethylene glycol ditopsylate.

2b. Yield 11% (red crystal). Mp 67.5—68.0 °C. IR (KBr disk) 2900 (CH), 1590 cm^{-1}(N=N). ^{1}H NMR ($CDCl_3$); δ=3.62—4.00 (8H, m, $-CH_2OCH_2-$), 4.10—4.32 (4H, m, $ArOCH_2-$), 6.71—7.75 (8H, m, Ar-H). MS (m/z); 328 (M^+). Found: C, 65.84; H, 6.18; N, 8.49%. Calcd for $C_{18}H_{20}N_2O_4$: C, 65.84; H, 6.04; N, 8.53%

2c. Yield 23% (red plates). Mp 111.0—113.5 °C. IR (KBr disk) 2960 (CH), 1580 cm^{-1} (N=N). ^{1}H NMR ($CDCl_3$); δ=3.32—3.95 (12H, m, $-CH_2OCH_2-$), 4.10—4.42 (4H, m, $ArOCH_2-$), 6.71—7.45 (8H, m, Ar-H). MS (m/z); 372 (M^+). Found: C, 64.52; H, 6.45; N, 7.53%. Calcd for $C_{20}H_{24}N_2O_5$: C, 64.50; H, 6.50; N, 7.52%.

2d. Yield 31% (red syrup). IR (neat) 2900 (CH), 1590 cm^{-1} (N=N). ^{1}H NMR ($CDCl_3$); δ=3.51—4.00 (16H, m,

-CH_2OCH_2-), 4.15—4.48 (4H, m, $ArOCH_2$-), 6.75—7.60 (8H, m, Ar-H). MS (m/z); 416 (M^+). Found: C, 63.45; H, 6.78; N, 6.73%. Calcd for $C_{22}H_{18}N_2O_6$: C, 64.21; H, 6.63; N, 7.35%.

Reagents. Other reagents were of analytical grade.

Apparatus. Absorption spectra were recorded using a Hitachi-556 double wavelength spectrophotometer. ^1H NMR and IR spectra were obtained by Hitachi R-24B ^1H NMR spectrometer and JASCO DS 403GR infrared spectrophotometer, respectively.

Measurement of Complex Formation Constants. To a 1.0×10^{-4} M (1 M=1 mol dm^{-3}) acetonitrile solution of azobenzo-crown ether, various amount of alkali iodide, was added to give a final concentration of $(0—1.0)\times10^{-2}$ M, and the resulting spectral change was measured using a standard 1 cm quartz cell. The optical absorbances were treated in a standard manner, and the complexation constants were calculated according to the Marquardt's nonlinear least square method.[4]

Results and Discussion

Synthesis. The syntheses of azobezo-crown ethers proceeded in a usual manner[5] and proposed structures of azobenzo-crown ethers were fully supported by the elemental analyses and the spectral informations.

Spectral Change and Complexation Behavior. Absorption spectra of azobenzo-13-crown-4, -16-crown-5, -19-crown-6, and -22-crown-7 in acetonitrile in the absence and in the presence of metal iodide are shown in Figs. 1, 2, 3, and 4, respectively. Acetonitrile was chosen as a common solvent for azobenzo-crown ethers and metal iodides. Since no spectral change was observed in a system of 2,2'-dimethoxyazobenzene and metal iodide in acetonitrile under comparable reaction conditions, such spectral change was understood to be due to the complexation of metal ions with the crown ether rings.

It is seen from Figs. 1 and 2 that the spectral changes occurred mainly in the increase of absorption intensity, but not much in the shift of absorption maxi-

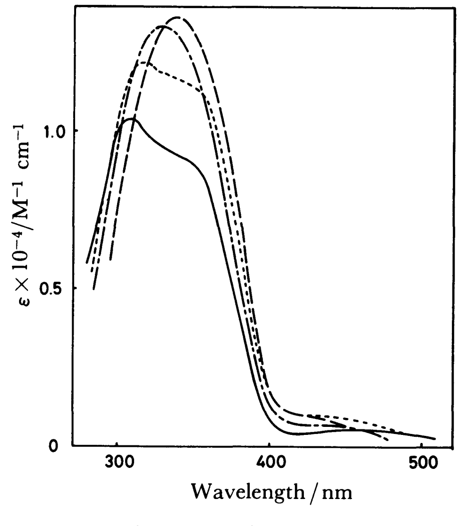


Fig. 1. Spectral change of azobenzo-13-crown-4 on the addition of metal salts. [L]=1×10^{-4} M, [MI]=1×10^{-3} M, [MI_2]=1×10^{-3} M, acetonitrile: ——, without salt; ----, LiI; — —, CaI_2; —·—·-, BaI_2.

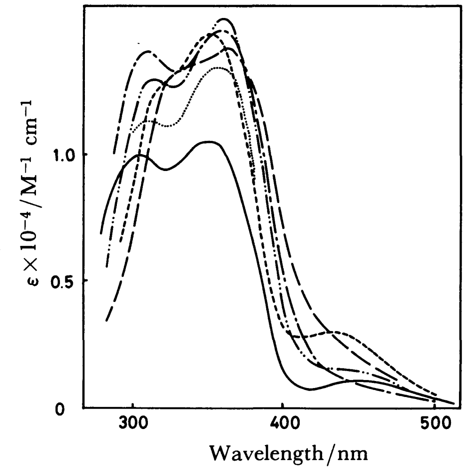


Fig. 2. Spectral change of azobenzo-16-crown-5 on the addition of metal salts. [L]=1×10^{-4} M, [MI]=1×10^{-3} M, [MI_2]=1×10^{-3} M, acetonitrile: ——, without salt; -----, LiI; —··—··-, NaI; ·····, KI; — —, CaI_2; —·—·—, BaI_2.

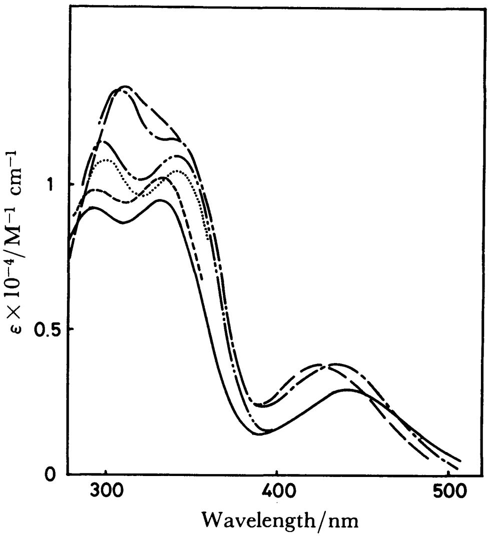


Fig. 3. Spectral change of azobenzo-19-crown-6 on the addition of metal salts. [L]=1×10^{-4} M, [MI]=1×10^{-3} M, [MI_2]=1×10^{-3} M, acetonitrile: ——, without salt; -----, LiI; —··—··-, NaI; ·····, KI; — —, CaI_2; —·—·—, BaI_2.

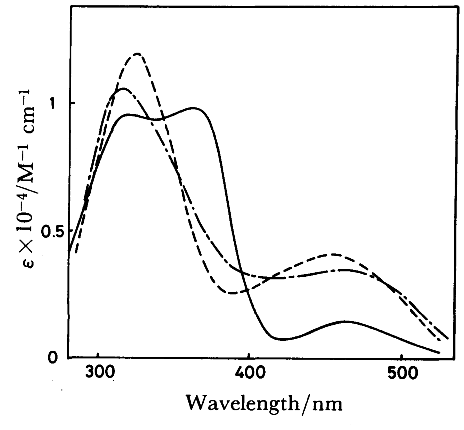


Fig. 4. Spectral change of azobenzo-22-crown-7 on the addition of metal salts. [L]=1×10^{-4} M, [MI]=1×10^{-3} M, acetonitrile: ——, without salt; — —, CaI_2; —·—·-, BaI_2.

mum. The change is more pronounced with divalent metal ions than with monovalent ions, indicating the importance of ion-dipole interaction between the metal and the chromophore group. Similar spectral changes have been also reported by Dix and Vögtle on monoaza-crown ethers with a pendent *p*-arylazophenyl group on the crown ether nitrogen.[6)]

The extent of spectral changes depends on the nature of azobenzo-crown ethers and metal salts. It also depends on their concentrations. The association equilibrium constants of azobenzo-crown ethers with metal salts can be evaluated from these changes in absorption spectra. It should be recalled in the passing that the spectral shift widths on the rate of absorption enhancement can not be a measure of the energy of association between the crown ether and the metal salts. These may reflect the extent of interaction between the azo group and the metal, but not represent that between the crown ether entity and metal.

Spectrophotometrically, we have no way to differentiate metal ion (M^+) from metal iodide (MI), nor metal ion-crown ether complex (ML^+) from its iodide complex (MLI) in acetonitrile solution. Therefore the conditional association constant (K_{ML}) as defined by Eq. 1 was used to evaluate the extent of interaction between azobenzo-crown ether and metal iodide.

$$K_{ML}=\frac{[(MLI)_t]}{[L][(MI)_t]}, \tag{1}$$

where

$$[(MLI)_t]=[ML^+]+[MLI], \tag{2}$$

and

$$[(MI)_t]=[M^+]+[MI]. \tag{3}$$

The optical absorbance of the solution of this system can be expressed by Eq. 4,

$$A=\varepsilon_{MLI}[(MLI)_t]+\varepsilon_L[L], \tag{4}$$

where, ε_{MLI} and ε_L are molar absorption coefficients of metal complex and crown ether, respectively. The total concentrations of metal salt and crown ether are defined as follows:

$$C_M=[(MI)_t]+[(MLI)_t], \tag{5}$$

$$C_L=[L]+[(MLI)_t]. \tag{6}$$

By combining Eqs. 1—6, the mean molar absorption coefficient ε is derived as in Eq. 7.

$$\varepsilon = A/C_L = \{(\varepsilon_{MLI}-\varepsilon_L)((K_{ML}(C_M+C_L)+1) - \sqrt{(K_{ML}(C_M+C_L)+1)^2-4K_{ML}{}^2C_MC_L})\}/(2K_{ML}\cdot C_L) + \varepsilon_L. \tag{7}$$

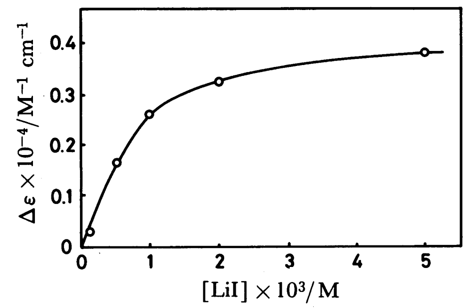


Fig. 5. Change of absorbance on the addition of lithium iodide to azobenzo-13-crown-4. 350 nm, [L]=1×10^{-3} M.

Experimentally, the value of $\varepsilon-\varepsilon_L$ ($\simeq\Delta\varepsilon$) is measured as a function of metal salt concentration as illustrated in Fig. 5. The values of K_{ML} and ε_{MLI} are then simultaneously determined from Eq. 7 by using Marquardt's non-linear least-squares method.

The constants obtained are summarized in Table 1. The spectral changes of **2a** on interaction with sodium iodide and potassium iodide and those of **2d** with alkali metal iodides were so small that the meaningful values of K_{ML} could not be obtained. As to the complexation with alkaline earth metal salts, the calculated values scattered and dependented on the wave lengths adopted for calculation. This indicates that the reactions can not be formulated in a simple manner as in Eqs. 1—6.

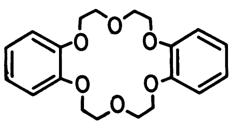
It is seen from the table that the association constant for lithium is highest with **2a** and decreases with increasing hole size of crown ether, indicating that (the trans form of) azobenzo-13-crown-4 (**2a**), whose hole size is approximately comparable with that of 12-crown-4, fits most well lithium ion. It is interesting to note that, among the alkali metal iodides investigated in this study, lithium ion forms about the most stable complexes with azobenzo-crown ethers, regardless of the hole size of crown ethers. Sodium then follows. This result does not agree with the generally accepted ion-cavity size fitness concept, suggesting that the energy of metal salt-crown ether interaction is primarily governed by a simple ion-dipole interaction (enthalpy contribution) rather than a macrocyclic encapsulating interaction (entropy contribution). The smallest lithium ion thus exercises the highest effective interaction with the crown ethers.

The complexation constants of **2b** and **2c** with sodium iodide or potassium iodide are unanimously lower than those of dibenzo-18-crown-6 (**3**) and "dicyclohexyl-18-crown-6" (**4**).[7)] Even though **2c** has

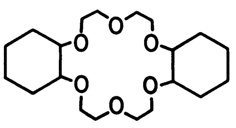
Table 1. Complex formation constants in acetonitrile

Crown ether	LiI			NaI			KI				
	log K_{MLI}	$\frac{\varepsilon_{MLI}\times10^{-4}}{M^{-1}\,cm^{-1}}$	$\left(\frac{\lambda_{max}}{nm}\right)$	log K_{MLI}	$\frac{\varepsilon_{MLI}\times10^{-4}}{M^{-1}\,cm^{-1}}$	$\left(\frac{\lambda_{max}}{nm}\right)$	log K_{MLI}	$\frac{\varepsilon_{MLI}\times10^{-4}}{M^{-1}\,cm^{-1}}$	$\left(\frac{\lambda_{max}}{nm}\right)$	$\frac{\varepsilon_L\times10^{-4}}{M^{-1}\,cm^{-1}}$	$\left(\frac{\lambda_{max}}{nm}\right)$
2a	4.10	1.58	(327)	—	—		—	—		1.08	(310)
2b	4.00	1.28	(355)	3.69	1.40	(365)	3.15	1.37	(355)	0.99	(350)
2c	3.41	1.08	(320)	3.43	1.06	(295)	3.37	1.00	(300)	0.84	(331)
3	—			5.04[a)]			4.83[a)]				
4	—			5.20[a)]			5.63[a)]				

a) K_{ML} refers to the equilibrium, $M^++L\rightleftharpoons ML^+$. Ref. 7.



3



4

almost the same hole size as **3**, the K_{ML} value of **2c** is 40 times lower than that of **3**. A relatively low complexation ability of azobenzo-crown ethers as compared with normal crown ethers has been previously noticed.[1] The conformational structure of azobenzo-crown ether is suggested from CPK model considerations to be slightly distorted and disordered from that of standard crown ethers, and it is likely that the azo group does not contribute much to the stabilization of complexes. In the case of the azobenzo-crown ether having larger ether ring such as **2c** and **2d**, metal ion should be readily accomodated in the crown ether ring, but the spectral change upon metal complexation is less than that of **2a** and **2b**.

Dix and Vögtle synthesized a variety of crown ether dyes and described the spectral change upon interaction with metal salts in acetonitrile.[6] Some of the crown ethers showed a drastic spectral shift as large as 100 nm. Unfortunately, they did not treat the data in terms of the association equilibrium constants; however, the spectral pictures they showed suggest that the association constants are in the similar order of magnitude to the present study.

References

1) M. Shiga, M. Takagi, and K. Ueno, *Chem. Lett.*, **1980**, 1021.

2) S. Shinkai, T. Minami, Y. Kusano, and O. Manabe, *J. Am. Chem. Soc.*, **105**, 1851 (1983).

3) D. C. Freeman and C. E. White, *J. Am. Chem. Soc.*, **78**, 2678 (1956).

4) D. W. Marquardt, *J. Soc. Ind. Appl. Math.*, **11**, 431 (1963).

5) F. de Jong, M. G. Siegel, and D. J. Cram, *J. Chem. Soc., Chem. Commun.*, **1975**, 552.

6) J. P. Dix and F. Vögtle, *Angew. Chem., Int. Ed. Engl.*, **17**, 857 (1978); *Chem. Ber.*, **113**, 459 (1980); **114**, 638 (1981).

7) D. F. Evans, S. L. Wellington, J. A. Nadis, and E. L. Cussler, *J. Solution Chem.*, **1**, 499 (1972).