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SYNTHESIS AND COMPLEXATION PROPERTIES OF (TROPON-2-YL)MONOAZA-18-CROWN-6 ETHERS

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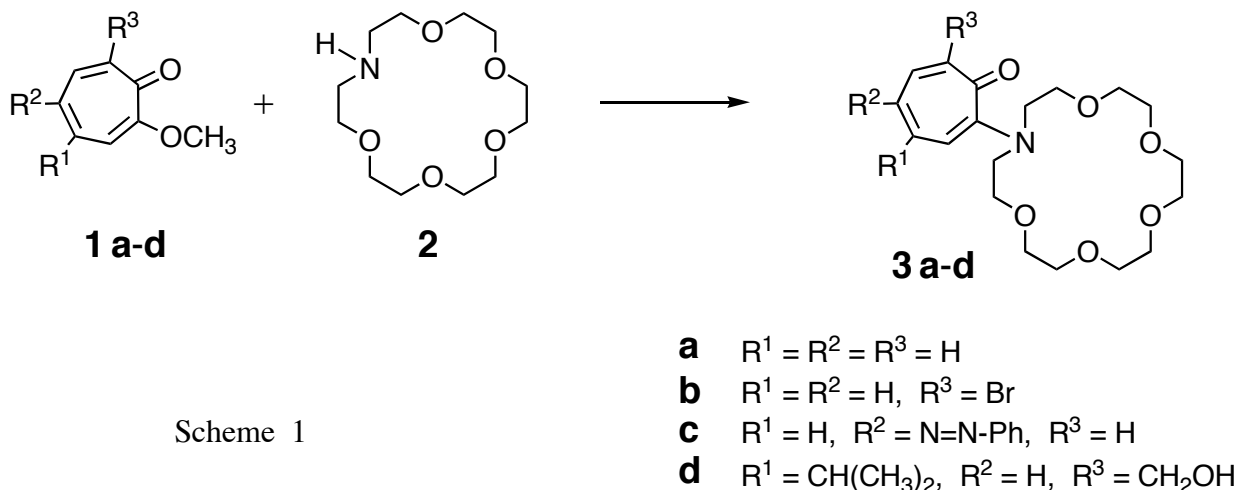
Abstract – Four (tropon-2-yl)monoaza-18-crown-6 ethers (**3a-d**) were prepared by the reactions of 2-methoxytropone (**1a-d**) with monoaza-18-crown-6 (**2**) in moderate yields. The UV-VIS spectra of these monoazacrown ethers (**3a-d**) were dramatically changed by adding metal salts. The complexations with moderately hard cations (Ba^{2+} and Pb^{2+}) were more effectively occurred than those with hard cations (Ca^{2+} , Na^+ , K^+ , and Cs^+) and with soft cations (Hg^{2+} and Cd^{2+}).

Chromogenic crown ethers have been received considerable attention as spectrophotometric analytical reagents for the detection of particular metal cations because of the specific spectral change upon selective complexation.¹ Recently, Mori *et al.* reported the synthesis and complexation behaviors of thiocrown ethers^{2,3} and azacrown ether derivatives^{4,5} having tropone chromophore. It was found that complexation gave rise to deconjugation between the tropone ring and the nonbonding electron pair of the nitrogen atom. In the present paper, we report the synthesis and complexation properties of monoaza-18-crown-6 derivatives bearing a variety of tropone chromophores.

RESULTS AND DISCUSSION

When a solution of 2-methoxytropone (**1a-d**) and monoaza-18-crown-6 (**2**) in benzene (chloroform for **3c** and toluene for **3d**) was refluxed for 20 h in the base-free condition, (tropon-2-yl)monoaza-18-crown-6 ethers (**3a-d**) were obtained in moderate yields (46-84%) (Scheme 1). (Tropon-2-yl)monoaza-18-

crown-6 ethers (**3a,b**) are soluble in water and in organic solvents, but **3c,d** is less soluble in water.



Scheme 1

The UV-VIS spectra of (tropon-2-yl)monoaza-18-crown-6 ethers (**3a,b,d**) in methanol are similar to those of 2-aminotropones and exhibited two absorption bands at λ 350-360 and 410-440 nm, while the spectrum of (4-phenylazotropon-2-yl)monoaza-18-crown-6 (**3c**) showed a strong absorption band at λ 453 nm and is very similar to that of 2-amino-4-phenylazotropone. By addition of a variety of metal salts (LiSCN, NaSCN, KSCN, CsSCN, NH_4SCN , $Ca(SCN)_2$, $Ba(SCN)_2$, CdI_2 , $Pb(ClO_4)_2$, $Hg(SCN)_2$), the UV-VIS spectra were dramatically changed. These observations were attributed to the complex formation of monoaza-18-crown-6 ethers (**3a-d**) with guest cations. It is known that the complexations of (tropon-2-yl)monoaza-15-crown-5 ethers caused deconjugation between the tropone ring and the nonbonding electron pair of the nitrogen atom. The complexation behaviors of (tropon-2-yl)monoaza-18-crown-6 (**3a-d**) were examined spectrophotometrically, as shown in Fig. 1. When a 5×10^{-3} M $Pb(ClO_4)_2$ solution was added to a 5×10^{-5} M solution of (tropon-2-yl)monoaza-18-crown-6 (**3a**), two absorption bands at λ 354 and 416 nm disappeared and a new absorption band appeared around λ 330 nm. This new band is similar to that of tropone. Monoaza-18-crown-6 ethers (**3b-d**) exhibited similar behaviors. The guest cation-induced absorption shifts ($\Delta\lambda = |\lambda_{\text{complex}} - \lambda_{\text{free}}|$), where λ_{complex} and λ_{free} are absorption bands for a complex and a longer absorption band of free monoazacrowns, decreased in the following: **3a**: Ca^{2+} (99.5 nm) > Pb^{2+} (92) > K^+ (70) > Cd^{2+} (3.5) > Cs^+ (3) > Na^+ (2) > Li^+ (1.5) > Hg^{2+} (0.5) > NH_4^+ (0); **3b**: Ba^{2+} (110) > Ca^{2+} (100) > Pb^{2+} (95) > K^+ (81.5) > Cd^{2+} (1.5) > Li^+ (1) > Na^+ = Hg^{2+} = NH_4^+ (~ 0); **3c**: Ba^{2+} (97), > K^+ (85) > Ca^{2+} (83) > Pb^{2+} (73) > Hg^{2+} (70) > Na^+ (60) > Cd^{2+} (7) > NH_4^+ (3); **3d**: Pb^{2+} (130) > Ba^{2+} (71) > K^+ (8) > Ca^{2+} (4.5) > Na^+ (2) > Cs^+ (1.0) > Ca^{2+} = Hg^{2+} = NH_4^+ (0).

The association constants of azacrown ethers (**3a-d**) with a variety of guest cations in methanol were determined by a nonlinear curve-fitting method.⁶ The results are listed in Table 1.

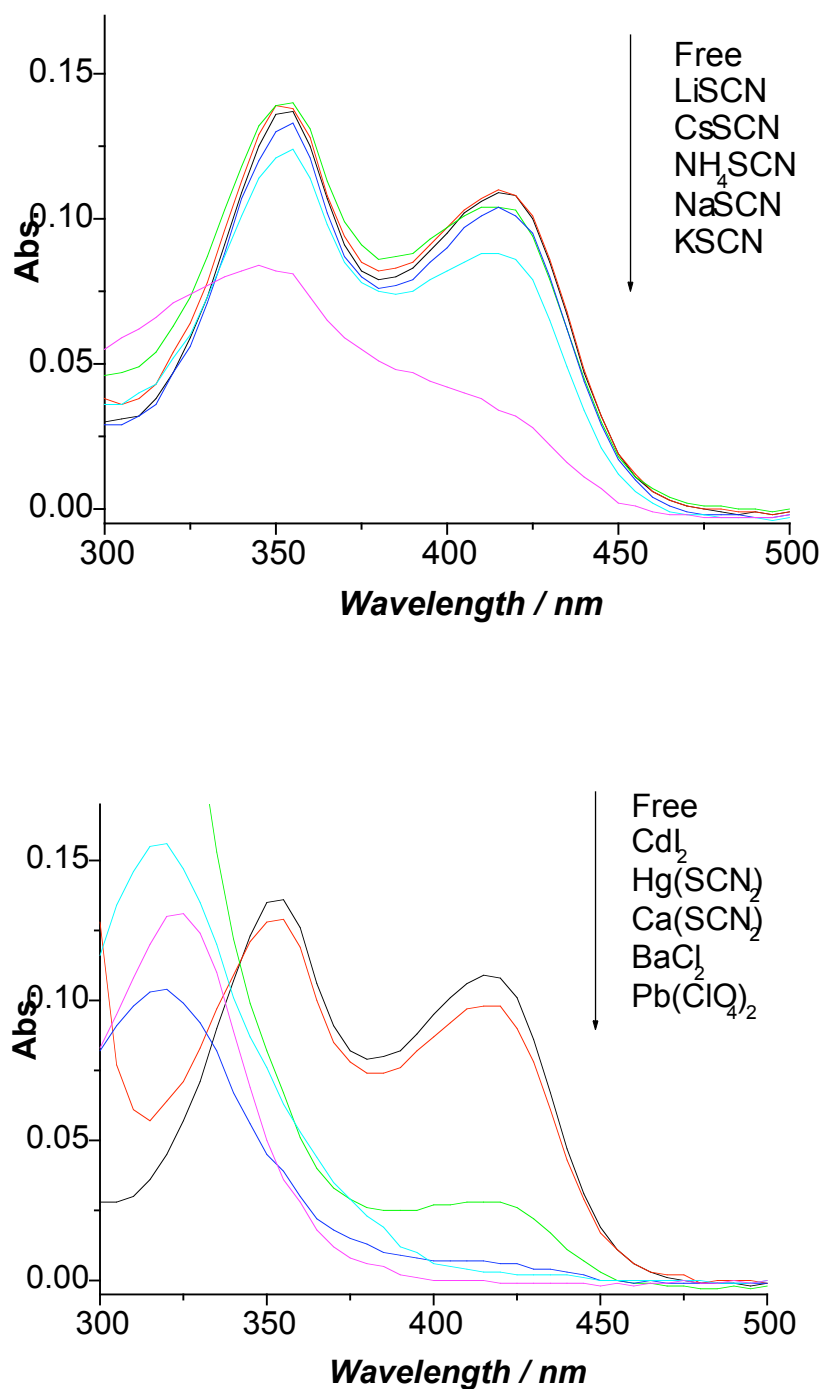


Fig. 1. Absorption spectra of **3a** (5.0×10^{-5} M) with and without guest salts (5.0×10^{-3} M) in methanol

As compared with tropone-functionalized monoaza-15-crown-5 series, the monoaza-18-crown-6 ethers (**3a-d**) showed the highest complexation with potassium cation in alkaline cations. Additionally, association constants of monoazacrown ethers (**3a-d**) with alkali metal cations decreased in the order of $K^+ > Na^+ > Cs^+ > Li^+$ and these behaviors are similar to that of unfunctionalized monoaza-18-crown-6 (K^+

Table 1. Association Constants ($\log K/M^{-1}$) of **3a-d** for Various Cations in Methanol

Guest cation	3a	3b	3c	3d
Li ⁺	ND	ND	ND	ND
Na ⁺	2.58 $\pm$ 0.01	2.42 $\pm$ 0.09	2.17 $\pm$ 0.32	2.91 $\pm$ 0.07
K ⁺	2.96 $\pm$ 0.01	2.68 $\pm$ 0.30	2.37 $\pm$ 0.02	3.70 $\pm$ 0.03
Cs ⁺	2.11 $\pm$ 0.02	< 1	< 1	2.39 $\pm$ 0.05
NH ₄ ⁺	2.07 $\pm$ 0.40	1.73 $\pm$ 0.17	1.01 $\pm$ 0.34	2.75 $\pm$ 0.08
Ca ²⁺	3.77 $\pm$ 0.05	3.23 $\pm$ 0.01	2.46 $\pm$ 0.04	4.33 $\pm$ 0.09
Ba ²⁺	5.61 $\pm$ 0.02	5.25 $\pm$ 0.09	3.80 $\pm$ 0.01	5.83 $\pm$ 0.00
Cd ²⁺	2.60 $\pm$ 0.21	2.68 $\pm$ 0.29	1.00 $\pm$ 0.30	2.93 $\pm$ 0.07
Hg ²⁺	2.34 $\pm$ 0.20	1.64 $\pm$ 0.12	1.68 $\pm$ 0.60	3.48 $\pm$ 0.05
Pb ²⁺	5.71 $\pm$ 0.05	4.81 $\pm$ 0.02	4.66 $\pm$ 0.08	5.64 $\pm$ 0.05

> Na⁺).⁷ It was found that the complexation with moderately hard metal cations, Ba²⁺ and Pb²⁺, are occurred more effectively than those with hard cations, Ca²⁺, K⁺, Na⁺ and Cs⁺, and soft cations, Hg²⁺ and Cd²⁺. It is interesting that introduction of isopropyl and hydroxymethyl group into the 4- and 7-position of tropone ring, respectively, enhanced complexation ability. It might be thought that the oxygen atom in the hydroxymethyl group gives additional direct complex forming effect, besides the electron-donating effects of the isopropyl and hydroxymethyl group.

In conclusion, the tropon-2-yl-substituted monoaza-18-crown-6 ethers (**3a-d**) were prepared by means of condensation of a variety of 2-methoxytropone (**1a-d**) with monoaza-18-crown-6 ether (**2**) in moderate yields. These monoaza-18-crown-6 ethers (**3a-d**) displayed unique absorption spectral changes in the presence of guest cations. The association constants were evaluated.

EXPERIMENTAL

The ¹H NMR spectra were recorded with a Bruker AV-300 spectrometer (300 MHz). The UV-VIS spectra were taken on a Hitachi U-3010 spectrophotometer. The MS data were obtained by a Hewlett Packard 1100-HPCL/MSD and a JEOL JMS SX 102A apparatus. A Qingtao Gel (100-200 mesh) was used for column chromatography.

Preparation of (Tropon-2-yl)monoaza-18-crown-6 Ethers (3a-d): General Procedure. A solution of monoaza-18-crown-6 (**2**) (289 mg, 1.1 mmol) and 2-methoxytropone (**1a-d**) (1.0 mmol) in an appropriate solvent (5 mL) was refluxed for 20 h. After the solvent was removed under reduced pressure, the residue was purified by using a silica gel column to give the corresponding (tropon-2-yl)monoaza-18-crown-6 ethers (**3a-d**).

N-(Tropon-2-yl)monoaza-18-crown-6 (3a). The preparation was carried out in benzene and chromatographed with ethyl acetate-chloroform-methanol as the eluent to give **3a** as brown oil, yield 170 mg (46%); ^1H NMR (CDCl_3) δ 3.58-3.85 (24H, m), 6.54 (1H, dd, $J = 9.6, 8.8$ Hz, 4-H), 6.69 (1H, d, $J = 9.6$ Hz, 3-H), 6.87 (1H, d, $J = 11.5$ Hz, 7-H), 7.01 (1H, dd, $J = 11.5, 10.7$ Hz, 6-H), 7.07 (1H, dd, $J = 10.7, 8.8$ Hz, 5-H); UV (CH_3OH) $\lambda_{\text{max}}/\text{nm}$ (ϵ) 254 (4600), 354 (2780), 416 (2180); MS (APCI) m/z 368 (M+1). HRMS (FAB) Found: m/z 367.1972. Calcd for $\text{C}_{19}\text{H}_{29}\text{NO}_6$: M 367.1995.

N-(7-Bromotropon-2-yl)monoaza-18-crown-6 (3b). The preparation was carried out in benzene and chromatographed with ethyl acetate as the eluent to give **3b** as red oil, yield 308 mg (69%); ^1H NMR (CDCl_3) δ 3.64-3.97 (24H, m), 6.39 (1H, dd, $J = 10.7, 9.7$ Hz, 5-H), 6.96 (1H, d, $J = 9.6$ Hz, 3-H), 7.10 (1H, dd, $J = 10.2, 9.6$ Hz, 4-H), 7.92 (1H, d, $J = 9.7$ Hz, 6-H); UV (CH_3OH) $\lambda_{\text{max}}/\text{nm}$ (ϵ) 268 (11860), 360 (9400), 439 (7620); MS (APCI) m/z 446 (M+1). HRMS (FAB) Found: m/z 445.1124. Calcd for $\text{C}_{19}\text{H}_{28}\text{NO}_6\text{Br}$: M 445.1100.

N-(5-Phenylazotropon-2-yl)monoaza-18-crown-6 (3c). The preparation was carried out in chloroform and chromatographed with ethyl acetate as the eluent to give **3c** as red oil, yield 396 mg (84%); ^1H NMR (CDCl_3) δ 3.65-3.98 (24H, m), 6.80 (1H, d, $J = 11.4$ Hz, 3-H), 6.88 (1H, d, $J = 12.5$ Hz, 7-H), 7.41-7.52 (3H, m), 7.82-7.85 (3H, m), 7.97 (1H, dd, $J = 12.5, 2.0$ Hz, 6-H); UV (CH_3OH) $\lambda_{\text{max}}/\text{nm}$ (ϵ) 246 (10780), 294 (7260), 453 (22320); MS (APCI) m/z 472 (M+1). HRMS (FAB) Found: m/z 471.2358. Calcd for $\text{C}_{25}\text{H}_{33}\text{N}_3\text{O}_6$: 471.2369.

N-(7-Hydroxymethyl-4-isopropyltropon-2-yl)monoaza-18-crown-6 (3d). The preparation was carried out in toluene and chromatographed with ethyl acetate-methanol (5 : 1) as the eluent to give **3d** as red oil, yield 202 mg (46%); ^1H NMR (CDCl_3) δ 1.27 (6H, d, $J = 6.8$ Hz, $\text{CH}_3 \times 2$), 2.81 (1H, sept, $J = 6.8$ Hz, $-\text{CH}<$), 3.64-3.82 (24H, m), 4.58 (2H, s, CH_2), 6.53 (1H, d, $J = 9.2$ Hz, 6-H), 6.78 (1H, s, 3-H), 7.20 (1H, d, $J = 9.2$ Hz, 5-H); UV (CH_3OH) $\lambda_{\text{max}}/\text{nm}$ (ϵ) 264 (13360), 353 (7700), 412 (5500); MS (APCI) m/z 440 (M+1). HRMS (FAB) Found: m/z 439.2558. Calcd for $\text{C}_{23}\text{H}_{37}\text{NO}_7$: M 439.2570.

Determination of Association Constants. The titrations were conducted by adding a metal salt

solution (1.0×10^{-2} M) progressively monoiazacrown solution (5.0×10^{-5} M) in methanol in the range from 0.5 to 50 equivalents. The spectrum was recorded after each addition. A self-written nonlinear curve-fitting computer program was used to fit the experimental titration curves. The association constants were determined from the absorption intensity change around 420 nm.

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