Synthesis and Complexing Ability of New Type of Macrobicyclic Compounds

Yohji NAKATSUJI, Takashi KIKUI, Isao IKEDA, and Mitsuo OKAHARA*
Department of Applied Chemistry, Faculty of Engineering, Osaka University,
Yamada-oka, Suita, Osaka 565
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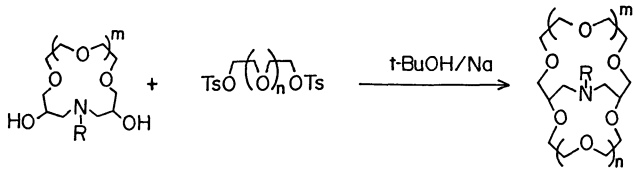
Synopsis. New types of macrobicyclic compounds were synthesized from monoaza crown ethers bearing two hydroxyl groups and their complexing abilities regarding alkali metal cations were investigated.

Lipophilic monoaza crown ethers are good synthetic ionophores for the active transport of cations since they have a basic nitrogen atom as a constituent of the ring.[1] In order to improve selectivity toward a specific cation, it is necessary to design the structure of ionophores. From this viewpoint, we are reporting on the syntheses of new monoaza cryptands.[2,3]

Monoaza crown ethers (**1**)[4] bearing two hydroxyl groups, which were prepared by reactions between oligoethylene glycol diglycidyl ether and ammonia (or an appropriate primary amine), were treated with tri- or tetraethylene glycol ditosylate (**2**) in the presence of *t*-BuONa to give cryptands (**3**), generally as pale-yellow oils in fair yields (Scheme). As another route to lipophilic cryptands, *N*-unsubstituted derivatives **3a** (m=1, n=2) and **3b** (m=n=2) were easily alkylated by 1-bromodecane to afford **3h** and **3d**, respectively.

It is noteworthy that the new "Shell-shaped" cryptands **3** showed fairly good complexing abilities and selectivities in comparison with the starting crowns **1**. Derivatives with 15—17 (**3d** and **3g**) and 18—17 (**3e**) membered rings possessed selectivities



Scheme 1.

regarding Na^+ and K^+, respectively (Table 1). A comparison of the stability constants of **3g** with those of **3d** seems to show a contribution of the electron-donating side arm to complexation.[5] Although these compounds were mixtures of stereoisomers and their separations have, so far, not been successful, the ease of preparation should be useful when they are practically used as complexing agents or carriers for a variety of cations.

Experimental

The ^{1}H-NMR spectra were taken at 100 MHz on a JEOL JNM-PS-100 spectrometer using tetramethylsilane as the internal standard. The infrared spectra were obtained on a Hitachi 260-10 spectrometer. The mass spectra were measured with a Hitachi RMU-6E mass spectrometer at an ionization potential of 70 eV.

2,5,8,11,14,17,20-Heptaoxa-23-azabicyclo[10.9.3]-tetracosane (3a): To a solution of sodium *t*-butoxide (Na: 1.0 g, 0.0435 mol) in *t*-butyl alcohol (160 ml), 1,4,7-trioxa-11-azacyclotetradecane-9,13-diol[4] (**1a**) (R=H, m=1, 4.71 g, 0.02 mol) was added and the mixture was then refluxed for 1 h. Triethylene glycol ditosylate (**2b**) (n=2, 9.17 g, 0.02 mol) in dioxane (40 ml) was added dropwise to the resulting mixture at 40 °C over a 2-h period and the mixture was further stirred for another 12 h. Insoluble matter was removed by filtration and the solvent was evaporated. The crude product was distilled in a Kugelrohr apparatus under reduced pressure (150—155 °C/0.01 Torr: 1 Torr=133.3 Pa) to give **3a** as a pale-yellow oil (2.61 g, 37%); ^{1}H-NMR ($CDCl_3$) δ=2.19 (s, 1H), 2.6—3.3 (m, 4H), 3.3—4.0 (m, 26H); MS, m/z (rel intensity) 349 (M^+, 10), 320 (9), 244 (20), 218 (20), 118 (36), 87 (58), 45 (100); IR (neat) 3320, 2855, 1455, 1350, 1245, 1100 cm^{-1}.

Found: C, 55.04; H, 9.07; N. 3.94. Calcd for $C_{16}H_{31}NO_7$: C, 55.00; H, 8.94; N, 4.01.

3,6,9,12,15,18,21,24-Octaoxa-26-azabicyclo[12.10.3]-heptacosane (3b): Bp 165—170 °C/0.006 Torr (Kugelrohr); ^{1}H-NMR ($CDCl_3$) δ=2.3—3.2 (m, 6H), 3.3—4.1 (m, 29H); MS, m/z (rel intensity) 393 (M^+, 8), 364 (7), 288 (13), 202 (15), 88 (39), 45 (100); IR (neat) 3320, 2875, 1460, 1355, 1255,

Table 1. Complexing Ability of Macrobicyclic Compounds

	Macrobicyclic Compound R	m	n	ring size	log K'[6,a] Na^+	log K'[6,a] K^+	Extraction Data[7,b] Li^+	Na^+	K^+	Rb^+	Cs^+
3d	n-$C_{10}H_{21}$	2	2	(15—17)	2.57	2.44	13	25	13	7	7
3e	n-$C_{10}H_{21}$	2	3	(18—17)	2.84	3.66	6	19	45	29	24
3f	n-$C_4H_9(OCH_2CH_2)_2$	1	2	(15—14)	3.33	2.98	27	38	18	8	8
3g	n-$C_4H_9(OCH_2CH_2)_2$	2	2	(15—17)	3.40	3.14	27	45	29	15	12
(1b)	n-$C_4H_9(OCH_2CH_2)_2$	1	—	(14)	1.26	<1	2	0	1	0	3
(1e)	n-$C_{10}H_{21}$	2	—	(17)	1.34	1.91	10	7	9	6	9

a) In MeOH, at 25 °C. b) Picrate, CH_2Cl_2/H_2O, 22 °C.

1155 cm^{-1}.

Found: C, 54.69; H, 9.10; N, 3.50. Calcd for $C_{18}H_{35}NO_8$: C, 54.94; H, 8.97; N, 3.56.

26-Ethyl-3,6,9,12,15,18,21,24-octaoxa-26-azabicyclo-[12.10.3]-heptacosane (3c): Bp 160—165 °C/0.004 Torr (Kugelrohr); ^{1}H-NMR ($CDCl_3$) δ=0.98+1.02 (t+t, 3H), 2.3—2.8 (m, 6H), 3.3—4.1 (m, 30H); MS, *m/z* (rel intensity) 421 (M^+, 5), 232 (40), 216 (36), 72 (100), 58 (54); IR (neat) 2880, 1455, 1355, 1255, 1125 cm^{-1}.

Found: C, 56.95; H, 9.48; N, 3.39. Calcd for $C_{20}H_{39}NO_8$: C, 56.99; H, 9.33; N, 3.32.

26-Decyl-3,6,9,12,15,18,21,24-octaoxa-26-azabicyclo-[12.10.3]-heptacosane (3d): Bp 175—180 °C/0.005 Torr (Kugelrohr); ^{1}H-NMR ($CDCl_3$) δ=0.87 (t, 3H), 1.0—1.6 (m, 16H), 2.1—3.1 (m, 6H), 3.4—4.1 (m, 30H), MS, *m/z* (rel intensity) 533 (M^+, 11), 406 (100), 376 (25), 344 (16), 328 (19), 184 (35), 170 (28), 144 (26); IR (neat) 2925, 2810, 1465, 1350, 1250, 1115 cm^{-1}.

Found: C, 62.67; H, 10.73; N, 2.69. Calcd for $C_{28}H_{55}NO_8$: C, 63.01; H, 10.39; N, 2.62.

29-Decyl-2,5,8,11,14,17,20,23,26-nonaoxa-29-azabicyclo-[13.12.3]triacontane (3e): Bp 185—190 °C/0.002 Torr (Kugelrohr); ^{1}H-NMR ($CDCl_3$) δ=0.87 (t, 3H), 1.0—1.6 (m, 16H), 2.3—3.1 (m, 6H), 3.2—4.1 (m, 34H); MS, *m/z* (rel intensity) 576 (M^+—1, 7), 450 (100), 420 (17), 328 (16), 184 (31), 170 (21), 144 (21); IR (neat) 2910, 2855, 1470, 1350, 1250, 1120 cm^{-1}.

Found: C, 62.08; H, 10.38; N, 2.49. Calcd for $C_{30}H_{59}NO_9$: C, 62.36; H, 10.29; N, 2.42.

23-[2-(2-Butoxyethoxy)ethyl]-2,5,8,11,14,17,20-heptaoxa-23-azabicyclo[10.9.3]tetracosane (3f): Bp 165—170 °C/0.005 Torr (Kugelrohr); ^{1}H-NMR ($CDCl_3$) δ=0.90 (t, 3H), 1.2—1.8 (m, 4H), 2.6—3.1 (m, 6H), 3.4—4.1 (m, 34H); MS, *m/z* (rel intensity) 493 (M^+, 1), 450 (100), 332 (21), 248 (23), 230 (16), 188 (19); IR (neat) 2880, 1465, 1355, 1255, 1120 cm^{-1}.

Found: C, 58.38; H, 9.81; N, 3.23. Calcd for $C_{24}H_{47}NO_9$: C, 58.39; H, 9.60; N, 2.84.

26-[2-(2-Butoxyethoxy)ethyl]-3,6,9,12,15,18,21,24-octaoxa-26-azabicyclo[12.10.3]heptacosane (3g): Bp 175—180 °C/0.005 Torr; ^{1}H-NMR ($CDCl_3$) δ=0.89 (t, 3H), 1.1—1.7 (m, 4H), 2.5—3.1 (m, 6H), 3.4—4.1 (m, 38H); MS, *m/z* (rel intensity) 536 (M^+—1, 1), 406 (100), 376 (11), 349 (8), 274 (18), 188 (17); IR (neat) 2880, 1460, 1350, 1255, 1120 cm^{-1}.

Found: C, 57.82; H, 9.68; N, 2.64. Calcd for $C_{26}H_{51}NO_{10}$: C, 58.08; H, 9.56; N, 2.61.

Alkylation of Unsubstituted Cryptands (3a and 3b): A mixture of cryptand **3b** (1.0 g, 0.0025 mol), 1-bromodecane (0.60 g, 0.0027 mol), and powdered sodium carbonate (0.20 g, 0.0019 mol) in dioxane (10 ml) was stirred for 12 h at 80 °C. Insoluble matter was removed by filtration and the solvent was concentrated. The residue was dissolved in hexane (50 ml). The hexane-soluble part was concentrated and distilled in a Kugelrohr apparatus (175—180 °C/0.005 Torr) to give **3d** in 63% yield. All analytical data regarding this compound were coincident with those described above. Compound **3h** was prepared by a reaction of **3a** with 1-bromodecane using the same procedure with a 64% yield; bp 160—165 °C/0.003 Torr (Kugelrohr); ^{1}H-NMR ($CDCl_3$) δ=0.87 (t, 3H), 1.1—1.5 (m, 16H), 2.1—3.1 (m, 6H), 3.4—4.3 (m, 26H) MS, *m/z* (rel intensity) 489 (M^+, 14), 362 (100), 248 (30), 184 (36), 170 (34), 100 (95), 45 (73); IR (neat) 2915, 2850, 1465, 1350, 1250, 1120 cm^{-1}.

Found: C, 63.47; H, 10.54; N, 2.84. Calcd for $C_{26}H_{51}NO_7$: C, 63.77; H, 10.50; N, 2.86.

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