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A series of double armed diaza-15-crown-5 ethers (**9a** – **16a**) and diaza-18-crown-6 ethers (**9b** – **16b**) have been prepared by the Mannich reaction of 2,6-disubstituted phenols with the corresponding *N,N'*-dimethoxymethyldiaza-crown ethers in benzene. The crystal structures of the diaza-18-crown-6 ethers having *iso*-propyl (**10b**), *tert*-butyl (**11b**), and mixed methyl and *tert*-butyl groups (**12b**) at positions 3' and 5' of the phenolic side arms were determined using X-ray diffraction methods. Competitive transport by these ligands for sodium, potassium and cesium cations were measured under basic-source phase and acidic-receiving phase conditions.

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Many armed macrocycles possessing appended hydroxybenzyl groups as additional binding sites have been prepared using the Mannich reaction [1-8]. The Mannich reaction is suited for armed macrocycles, because aminomethylation on a phenol occurs at the *ortho*-positions of the phenolic OH group. When armed macrocycles are designed so that the binding site of the side arm does not coordinate to a guest cation incorporated in the macrocycle, the side arm could bind guest cations incorporated in another macrocycle forming a polymer-like with the metal cations. Recently, we reported synthesis and molecular structures of polymer-like complexes with armed monoaza-15-crown-5 and armed monoaza-12-crown-4 ethers having a 4'-hydroxy-3',5'-disubstitutedbenzyl group as a side arm (**1a** – **8b**) [9-12]. In order to further investigate the steric and/or electronic effects of the substituents next to the OH group, we have reported a series of double armed azacrown ethers having hydroxybenzyl groups with various substituents at the 3'- and 5'-positions on the side arm. This paper reports the synthesis of double-armed diaza-15-crown-5 ethers (**9a** – **16a**) and diaza-18-crown-6 ethers (**9b** – **16b**), X-ray crystal structures of diaza-18-crown-6 derivatives (**10b**, **11b** and **12b**), and transport abilities of some of these double armed macrocycles for the alkali-metal cations.

The double-armed azacrown ethers were prepared by treating various 2,6-disubstituted phenols with the appropriate *N,N'*-dimethoxymethyldiazacrown ethers in absolute benzene (Scheme 1). Armed azacrown ethers with alkyl groups at positions 3' and 5' of the side arms were obtained in relative good yields (49 - 86%). Some compounds having methoxy, allyl, phenyl and fluorine groups in the side arms were obtained in lower yields (21 - 48%) because they decomposed during purification by column chromatography.

The structures of all ligands were confirmed by ¹H nmr, ei-ms and elemental analyses. Ligands **10b**, **11b** and **12b** were obtained as single crystals, and their structures were

determined by X-ray crystallography. Figure 1 shows the ORTEP views of ligands **10b**, **11b** and **12b**. The crown ether rings of ligands **11b** and **12b** adopt chair

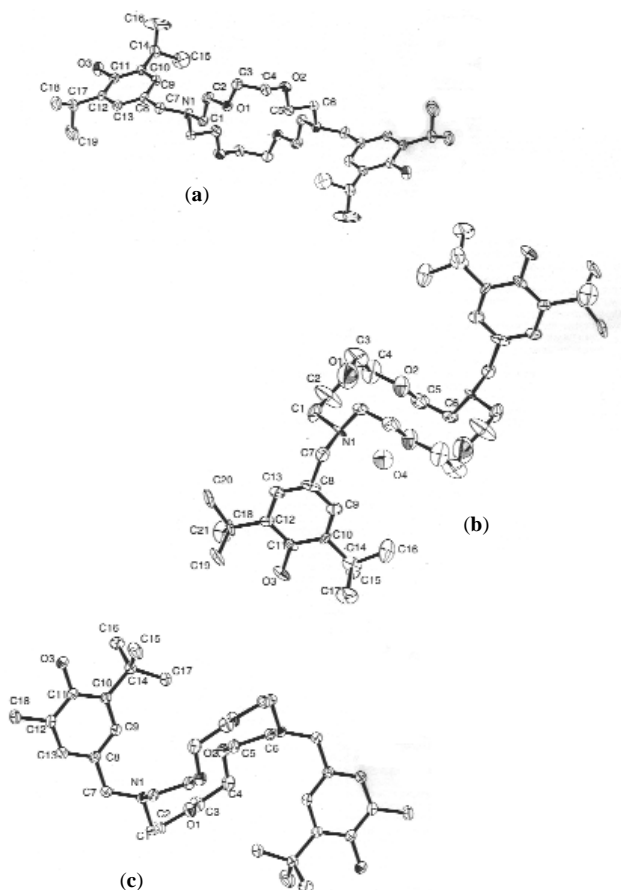


Figure 1. ORTEP diagrams (hydrogen atoms omitted) of (a) **10b**, (b) **11b** and (c) **12b**.

Table 1
Competitive Transport of Alkali Metal Cations with Double
Armed-Diaza-15-crown-5 and Diaza-18-crown-6 Ethers

Carrier	Transport rate ($\mu\text{mole/h}$) [a]		Cs ⁺
	Na ⁺	K ⁺	
9a	35	< 1	< 1
10a	30	2	< 1
12a	42	< 1	< 1
15a	160	< 1	< 1
9b	4	27	2
10b	6	37	2
11b	8	31	< 1
12b	< 1	31	2
15b	26	130	9

[a] Reproducibility is $\pm 10\%$ or better.

conformations, and the *tert*-butyl groups of the side arms in these ligands are located on the top and bottom of the rings. On the other hand, the crown ring of ligand **10b** does not adopt a chair conformation and the side arms are located along the side of the crown ether ring.

Competitive alkali-metal ion transport by these ligands was carried out using a double tube transport apparatus. Results of the transport experiments are summarized in Table 1. When diaza-15-crown-5 derivatives (**9a**, **10a**, **12a** and **15a**) and diaza-18-crown-6 derivatives (**9b**, **10b**, **11b**, **12b** and **15b**) were used as carriers in bulk liquid membrane transport under basic-source phase/acidic-receiving phase conditions (using alkali-metal hydroxides), sodium and potassium cations were selectively transported, respectively. Thus, the transport experiments showed that these ligands transport size-matched alkali-metal cations under the conditions studied. In addition, the most lipophilic ligands **15a** and **15b** with phenyl groups at side arm positions 3' and 5' gave the highest transport rates. Ligands with one or two methoxy groups in the side arm (**13a**, **13b**, **14a** and **14b**) decomposed during the transport experiments. Transport by ligands **16a** and **16b** having fluorine atoms in the side arm could not be carried out because of their low solubility in chloroform.

Table 2
Crystal and Selected Experimental Data for **10b**, **11b** and **12b**.

	10b	11b	12b
Formula	C ₃₈ H ₆₂ N ₂ O ₆	C ₄₂ H ₇₀ N ₂ O ₈	C ₃₆ H ₅₈ N ₂ O ₆
<i>M</i>	642.92	731.02	614.86
Crystal system	monoclinic	monoclinic	monoclinic
Space group	P2 ₁ /n	C2/c	P2 ₁ /n
<i>a</i> /Å	9.788(5)	19.80(1)	11.366(2)
<i>b</i> /Å	19.788(9)	11.67(2)	10.430(3)
<i>c</i> /Å	10.620(6)	20.49(2)	15.208(2)
β /°	113.23(3)	113.82(5)	93.62(1)
<i>U</i> /Å ³	1890(1)	4331(8)	1799.2(6)
<i>Z</i>	2	4	2
Dc/g cm ⁻³	1.130	1.121	1.135
<i>F</i> (000)	704.00	1600.00	672
μ (Mo-K α)/cm ⁻¹	0.75	0.76	0.76
Crystal dimensions/mm	0.50x0.50x0.10	0.20x0.30x0.30	0.50x0.25x0.70
No. of reflections for unit cell determination (2 θ range) ^o	25 (20.0-23.7)	21 (20.2-22.6)	25 (28.0-29.9)
Scan width ^o	1.05+0.30tan θ	1.37+0.30tan θ	1.47+0.30 tan θ
Limiting indices	0 \leq h \leq 12 0 \leq k \leq 25 -13 \leq l \leq 12	-19 \leq h \leq 18 0 \leq k \leq 12 -22 \leq l \leq 0	0 \leq h \leq 14 -13 \leq k \leq 0 -19 \leq l \leq 19
No. reflections measured	4730	2831	4570
unique (R _{int})	4482 (0.031)	2676 (0.096)	4291 (0.047)
used[all data], <i>N_o</i>	4344	2673	4326
R	0.124	0.327	0.122
R _w	0.220	0.276	0.217
R1 [<i>I</i> > 2.0 σ (<i>I</i>)]	0.066	0.093	0.065
Goodness of fit	1.33	1.17	1.40
No. parameters, <i>N_p</i>	208	235	199
Maximum shift/error in final cycle	0.003	0.002	0.001
Maximum, minimum peaks in final difference map/e Å ⁻³	0.30, -0.27	0.88, -0.95	0.61, -0.46

* Details in common: ω -2 θ scan; scan range 2 θ 0-55°; $R_w = [\sum w(|F_o| - |F_c|)^2 / \sum w F_o^2]^{1/2}$, $R_1 = \sum ||F_o| - |F_c|| / \sum |F_o|$, goodness of fit $[\sum w(|F_o| - |F_c|)^2 / (N_o - N_p)]^{1/2}$.

Table 3
Atomic Coordinates and B_{iso}/B_{eq} for **10b**

Atom	x	y	z	B_{eq}
O(1)	1.0668(2)	-0.1107(1)	0.7251(2)	3.65(6)
O(2)	1.3545(3)	-0.1012(1)	0.6818(2)	4.16(6)
O(3)	0.4953(3)	0.2566(1)	0.8911(3)	4.51(7)
N(1)	0.7874(3)	0.0225(1)	0.6591(3)	2.98(6)
C(1)	0.8553(4)	-0.0410(2)	0.6431(4)	3.50(8)
C(2)	0.9945(4)	-0.0582(2)	0.7645(4)	4.37(10)
C(3)	1.2138(4)	-0.1244(2)	0.8227(4)	4.11(9)
C(4)	1.3099(4)	-0.1509(2)	0.7541(4)	3.59(9)
C(5)	1.2487(4)	-0.0883(2)	0.5476(4)	4.10(9)
C(6)	1.3220(4)	-0.0454(2)	0.4750(3)	3.24(8)
C(7)	0.7200(4)	0.0148(2)	0.7594(4)	3.46(9)
C(8)	0.6607(4)	0.0809(2)	0.7901(3)	3.05(8)
C(9)	0.7362(4)	0.1416(2)	0.8012(3)	3.23(8)
C(10)	0.6844(4)	0.2018(2)	0.8319(3)	3.00(8)
C(11)	0.5529(4)	0.2002(2)	0.8543(3)	2.97(8)
C(12)	0.4732(4)	0.1406(2)	0.8441(3)	3.00(8)
C(13)	0.5297(4)	0.0814(2)	0.8113(3)	3.16(8)
C(14)	0.7698(4)	0.2667(2)	0.8432(5)	4.4(1)
C(15)	0.8108(8)	0.2804(3)	0.7272(6)	10.5(2)
C(16)	0.9036(9)	0.2693(4)	0.9698(7)	14.3(3)
C(17)	0.3269(4)	0.1400(2)	0.8640(4)	4.14(10)
C(18)	0.3181(5)	0.0847(2)	0.9589(5)	5.7(1)
C(19)	0.1956(5)	0.1379(3)	0.7288(5)	8.0(2)
H(1)	0.7855	-0.0777	0.6300	4.4450
H(2)	0.8783	-0.0390	0.5639	4.4450
H(3)	0.9723	-0.0718	0.8416	5.5490
H(4)	1.0581	-0.0188	0.7932	5.5490
H(5)	1.2580	-0.0833	0.8698	4.9866
H(6)	1.2099	-0.1559	0.8897	4.9866
H(7)	1.2522	-0.1857	0.6890	4.3499
H(8)	1.3945	-0.1731	0.8198	4.3499
H(9)	1.2129	-0.1304	0.4994	4.9962
H(10)	1.1627	-0.0655	0.5511	4.9962
H(13)	1.3995	-0.0712	0.4622	3.9713
H(14)	1.3692	-0.0071	0.5312	3.9713
H(15)	0.6386	-0.0176	0.7251	4.3259
H(16)	0.7921	-0.0043	0.8428	4.3259
H(19)	0.8286	0.1416	0.7874	3.8185
H(22)	0.4767	0.0393	0.8042	3.9342
H(24)	0.7085	0.3041	0.8508	5.6867
H(25)	0.8759	0.2472	0.7198	11.9820
H(26)	0.7229	0.2815	0.6428	11.9820
H(27)	0.8578	0.3242	0.7360	11.9820
H(31)	0.8867	0.2595	1.0475	15.4489
H(32)	0.9740	0.2341	0.9625	15.4489
H(33)	0.9559	0.3111	0.9795	15.4489
H(38)	0.3203	0.1828	0.9062	5.0461
H(39)	0.2316	0.0875	0.9770	6.8683
H(40)	0.3230	0.0411	0.9214	6.8683
H(41)	0.4038	0.0872	1.0471	6.8683
H(45)	0.1040	0.1359	0.7405	9.4516
H(46)	0.1945	0.1737	0.6710	9.4516
H(47)	0.2008	0.0955	0.6812	9.4516
H(48)	0.5297	0.2968	0.8760	6.2361

$$B_{eq} = 8/3\pi^2(U_{11}(aa^*)^2 + U_{22}(bb^*)^2 + U_{33}(cc^*)^2 + 2U_{12}aa^*bb^* \cos\gamma + 2U_{13}aa^*cc^* \cos\beta + 2U_{23}bb^*cc^* \cos\alpha)$$

Table 4
Atomic Coordinates and B_{iso}/B_{eq} for **11b**

Atom	x	y	z	B_{eq}
O(1)	1.056(1)	0.495(2)	0.1497(8)	13.7(7)
O(2)	0.9779(6)	0.6679(9)	0.0541(7)	7.0(4)
O(3)	0.7199(5)	-0.0163(7)	0.0095(5)	5.0(3)
O(4)	0.8987(5)	0.4066(8)	-0.0170(5)	7.8(3)
N(1)	1.0252(5)	0.255(1)	0.0803(7)	4.6(4)
C(1)	1.0322(9)	0.294(2)	0.1519(9)	8.1(6)
C(2)	1.016(2)	0.429(2)	0.158(2)	13(1)
C(3)	1.050(1)	0.614(2)	0.166(1)	9.5(8)
C(4)	0.988(1)	0.677(2)	0.128(1)	8.2(7)
C(5)	0.9168(9)	0.732(2)	0.008(1)	6.8(6)
C(6)	0.9093(7)	0.716(1)	-0.0676(8)	6.1(5)
C(7)	1.0137(7)	0.127(1)	0.0747(7)	4.5(4)
C(8)	0.9349(8)	0.089(1)	0.059(1)	4.6(5)
C(9)	0.8798(9)	0.111(1)	-0.0082(8)	4.4(5)
C(10)	0.8095(8)	0.075(1)	-0.0257(7)	3.8(4)
C(11)	0.7903(8)	0.020(1)	0.0268(9)	3.7(4)
C(12)	0.8444(8)	0.002(1)	0.0962(8)	3.5(4)
C(13)	0.9155(8)	0.037(1)	0.1106(8)	4.9(5)
C(14)	0.7515(8)	0.088(1)	-0.1031(9)	5.0(5)
C(15)	0.6885(9)	0.171(1)	-0.1031(7)	7.4(5)
C(16)	0.7841(9)	0.153(1)	-0.1484(8)	7.9(6)
C(17)	0.7191(9)	-0.020(1)	-0.1383(9)	7.7(5)
C(18)	0.8258(8)	-0.057(1)	0.1523(8)	4.5(5)
C(19)	0.7983(7)	-0.179(1)	0.1337(8)	6.6(5)
C(20)	0.8949(9)	-0.067(1)	0.2245(8)	7.2(5)
C(21)	0.7682(9)	0.012(1)	0.1700(8)	7.9(6)
H(1)	1.0074	0.2566	0.1786 0	10.7933
H(2)	1.0875	0.2936	0.1933	10.7933
H(3)	0.9925	0.4657	0.1845	8.9261
H(4)	0.9715	0.4546	0.1032	8.9261
H(5)	1.0662	0.6178	0.2274	18.5728
H(6)	1.1018	0.6618	0.1771	18.5728
H(7)	0.9907	0.7610	0.1449	10.2768
H(8)	0.9475	0.6479	0.1394	10.2768
H(9)	0.9204	0.8168	0.0121	8.9406
H(10)	0.8677	0.7157	0.0074	8.9406
H(11)	0.8618	0.7582	-0.1057	8.3272
H(12)	0.8924	0.6351	-0.0843	8.3272
H(13)	1.0349	0.0966	0.0403	5.7997
H(14)	1.0492	0.0867	0.1203	5.7997
H(15)	0.8888	0.1532	-0.0480	6.8603
H(16)	0.9540	0.0331	0.1572	5.4576
H(17)	0.6671	0.1389	-0.0767	7.7207
H(18)	0.7113	0.2435	-0.0852	7.7207
H(19)	0.6491	0.1902	-0.1517	7.7207
H(20)	0.7913	0.2336	-0.13900	9.8423
H(21)	0.7502	0.1608	-0.2069	9.8423
H(22)	0.8286	0.1254	-0.1535	9.8423
H(23)	0.6892	-0.0268	-0.1929	9.4589
H(24)	0.7618	-0.0800	-0.1382	9.4589
H(25)	0.6952	-0.0614	-0.1177	9.4589
H(26)	0.7561	-0.1933	0.0889	7.9927
H(27)	0.8368	-0.2298	0.1347	7.9927
H(28)	0.7797	-0.2246	0.1687	7.9927
H(29)	0.9253	-0.1170	0.2135	5.7962
H(30)	0.8836	-0.1021	0.2628	5.7962
H(31)	0.9133	0.0045	0.2376	5.7962
H(32)	0.7512	-0.0265	0.2089	9.6194
H(33)	0.7873	0.0835	0.1950	9.6194
H(34)	0.7211	0.0274	0.1333	9.6194
H(35)	0.7325	-0.1044	0.0294	4.2143

$$B_{eq} = 8/3\pi^2(U_{11}(aa^*)^2 + U_{22}(bb^*)^2 + U_{33}(cc^*)^2 + 2U_{12}aa^*bb^* \cos\gamma + 2U_{13}aa^*cc^* \cos\beta + 2U_{23}bb^*cc^* \cos\alpha)$$

Scheme 1

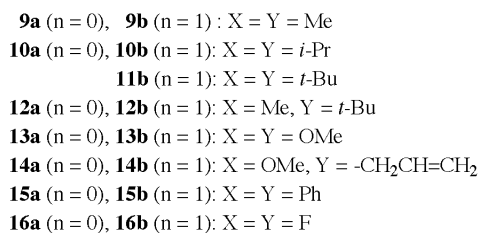
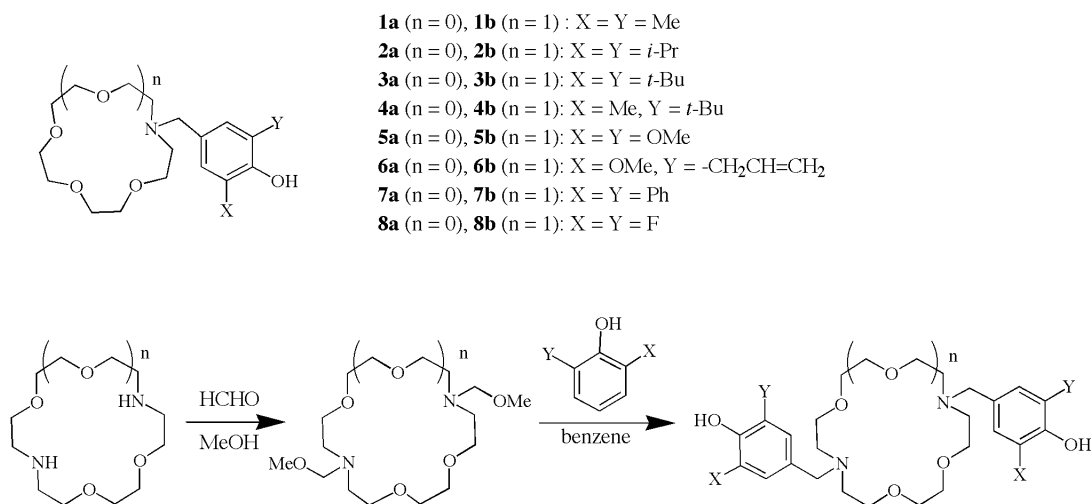


Table 5

Atomic Coordinates and $B_{\text{iso}}/B_{\text{eq}}$ for **12b**

Atom	x	y	z	B_{eq}
O(1)	0.3393(2)	-0.1977(2)	0.4370(1)	3.80(4)
O(2)	0.5502(2)	-0.2893(2)	0.5319(1)	3.85(4)
O(3)	0.8605(1)	0.1405(2)	0.1292(1)	3.94(4)
N(1)	0.3822(2)	0.0188(2)	0.3161(1)	2.75(4)
C(1)	0.2693(2)	-0.0382(3)	0.3368(2)	3.56(6)
C(2)	0.2767(2)	-0.1779(3)	0.3550(2)	3.82(6)
C(3)	0.3593(3)	-0.3287(3)	0.4561(2)	4.12(6)
C(4)	0.4351(3)	-0.3392(3)	0.5405(2)	4.06(6)
C(5)	0.5649(2)	-0.1589(3)	0.5604(2)	3.37(6)
C(6)	0.6086(2)	-0.1528(2)	0.6562(2)	2.95(5)
C(7)	0.4035(2)	-0.0003(2)	0.2232(1)	3.02(5)
C(8)	0.5253(2)	0.0402(2)	0.1986(1)	2.71(5)
C(9)	0.6227(2)	0.0279(2)	0.2581(1)	2.66(5)
C(10)	0.7357(2)	0.0625(2)	0.2371(1)	2.57(5)
C(11)	0.7491(2)	0.1074(2)	0.1507(1)	2.72(5)
C(12)	0.6531(2)	0.1189(2)	0.0896(1)	2.83(5)
C(13)	0.5419(2)	0.0860(2)	0.1148(2)	2.88(5)
C(14)	0.8412(2)	0.0505(3)	0.3059(2)	3.25(5)
C(15)	0.9013(3)	0.1802(3)	0.3212(2)	5.73(9)
C(16)	0.9290(2)	-0.0489(3)	0.2750(2)	4.91(7)
C(17)	0.8027(2)	0.0028(3)	0.3945(2)	4.37(7)
C(18)	0.6678(2)	0.1671(3)	-0.0027(2)	3.80(6)
H(1)	0.2425	0.0039	0.3881	4.4460
H(2)	0.2126	-0.0226	0.2888	4.4460
H(3)	0.3194	-0.2191	0.3091	4.8127
H(4)	0.2009	-0.2156	0.3544	4.8127

Table 5 (continued)

Atom	x	y	z	B_{eq}
H(5)	0.2856	-0.3721	0.4610	5.1775
H(6)	0.3988	-0.3681	0.4091	5.1775
H(7)	0.4403	-0.4276	0.5580	4.9262
H(8)	0.3972	-0.2933	0.5857	4.9262
H(9)	0.6199	-0.1156	0.5252	4.2293
H(10)	0.4907	-0.1143	0.5525	4.2293
H(11)	0.6836	-0.1948	0.6638	3.7679
H(12)	0.5544	-0.1982	0.6912	3.7679
H(13)	0.3929	-0.0900	0.2087	3.8009
H(14)	0.3458	0.0469	0.1876	3.8009
H(15)	0.6129	-0.0060	0.3154	3.2909
H(16)	0.4741	0.0960	0.0727	3.5896
H(17)	0.9675	0.1732	0.3630	7.2794
H(18)	0.9269	0.2150	0.2680	7.2794
H(19)	0.8469	0.2411	0.3450	7.2794
H(20)	0.8919	-0.1326	0.2691	6.0666
H(21)	0.9576	-0.0267	0.2200	6.0666
H(22)	0.9948	-0.0580	0.3175	6.0666
H(23)	0.7461	0.0621	0.4176	5.5654
H(24)	0.7654	-0.0788	0.3892	5.5654
H(25)	0.8679	-0.0026	0.4369	5.5654
H(26)	0.7481	0.1874	-0.0103	4.8662
H(27)	0.6405	0.1065	-0.0451	4.8662
H(28)	0.6223	0.2455	-0.0124	4.8662
H(29)	0.8660	0.1551	0.0680	6.2215

$$B_{\text{eq}} = 8/3\pi^2(U_{11}(\text{aa}^*)^2 + U_{22}(\text{bb}^*)^2 + U_{33}(\text{cc}^*)^2 + 2U_{12}\text{aa}^*\text{bb}^*\cos\gamma + 2U_{13}\text{aa}^*\text{cc}^*\cos\beta + 2U_{23}\text{bb}^*\text{cc}^*\cos\alpha)$$

EXPERIMENTAL

N,N'-Dimethoxymethyldiazacrown ethers were prepared as reported [1,9]. 2,6-Disubstituted phenols were used without further purification. The ^1H nmr spectra were measured in deuteriochloroform on a Bruker AC-250 (250 MHz) spectrometer. The ei-ms were performed using a Hitachi M-80 spectrometer. Melting points were taken on a Mel-Temp melting point apparatus and are uncorrected.

General Procedure for the Reaction of 2,6-Disubstituted Phenols with *N,N'*-Dimethoxymethyldiazacrown Ethers.

A mixture of *N,N'*-dimethoxymethyldiaza-15-crown-5 (1.0 mmole) and 2,6-disubstituted phenol (2.0 mmoles) in absolute benzene (20 ml) was refluxed under a nitrogen atmosphere for 24 hours. The reaction mixture was cooled and then concentrated under reduced pressure. The residual oil was separated and purified by silicagel and then gel-permeation column chromatography to give the following products.

N,N'-Bis(4'-hydroxy-3',5'-dimethylbenzyl)-1,4,10-trioxa-7,13-diazacyclopentadecane (**9a**).

This compound was isolated in a 49% yield as a pale yellow hygroscopic oil; ^1H nmr: δ 6.93 (s, 4H), 4.56 (s, 2H), 3.75-3.43 (m, 16H), 2.82-2.72 (m, 8H), 2.22 (s, 12H); ms: ei (m/z) 487 (M^+ , 100%).

Anal. Calcd. for $\text{C}_{28}\text{H}_{42}\text{N}_2\text{O}_5$: C, 69.11, H, 8.70. Found: C, 69.33; H, 8.88.

N,N'-Bis(4'-hydroxy-3',5'-di-*iso*-propylbenzyl)-1,4,10-trioxa-7,13-diazacyclopentadecane (**10a**).

This compound was isolated in a 74% yield as white crystals; mp 122-123.5° (from acetonitrile); ^1H nmr: δ 6.99 (s, 4H), 4.71 (s, 2H), 3.64-3.60 (m, 16H), 3.13 (7, 4H, $J = 6.9$ Hz), 2.81 (t, 4H, $J = 6.0$ Hz), 2.76 (t, 4H, $J = 5.2$ Hz); ms: ei (m/z) 599 (M^+ , 0.46%), 191 ($[\text{HOC}_6\text{H}_2(\text{CH}(\text{CH}_3)_2)_2\text{CH}_2]^+$, 100%).

Anal. Calcd. for $\text{C}_{36}\text{H}_{58}\text{N}_2\text{O}_5$: C, 72.20; H, 9.76. Found: C, 72.13; H, 10.12.

N,N'-Bis(4'-hydroxy-3'-*tert*-butyl-5'-methylbenzyl)-1,4,10-trioxa-7,13-diazacyclopentadecane (**12a**).

This compound was isolated in a 59% yield as a pale yellow hygroscopic oil; ^1H nmr: δ 7.04 (s, 2H), 6.97 (s, 2H), 4.67 (s, 2H), 3.63-3.56 (m, 16H), 2.83-2.73 (m, 8H), 2.22 (s, 6H), 1.40 (s, 18H); ms: ei (m/z) 571 (M^+ , 100%).

Anal. Calcd. for $\text{C}_{36}\text{H}_{58}\text{N}_2\text{O}_5 \cdot 1/2\text{H}_2\text{O}$: C, 71.13, H, 9.78. Found: C, 71.25; H, 9.59.

N,N'-Bis(4'-hydroxy-3',5'-dimethoxybenzyl)-1,4,10-trioxa-7,13-diazacyclopentadecane (**13a**).

This compound was isolated in a 25% yield as a pale yellow hygroscopic oil; ^1H nmr: δ 6.59 (s, 4H), 5.43 (s, 2H), 3.88 (s, 2H), 3.65-3.58 (m, 16H), 2.82 (t, 4H, $J = 6.0$ Hz), 2.75 (t, 4H, $J = 5.0$ Hz); ms: ei (m/z) 551 (M^+ , 0.31%), 167 ($[\text{HOC}_6\text{H}_2(\text{OCH}_3)_2\text{CH}_2]^+$, 100%).

Anal. Calcd. for $\text{C}_{28}\text{H}_{42}\text{N}_2\text{O}_9 \cdot 1/2\text{H}_2\text{O}$: C, 60.09; H, 7.74. Found: C, 60.33; H, 8.02.

N,N'-Bis(4'-hydroxy-3'-allyl-5'-methylbenzyl)-1,4,10-trioxa-7,13-diazacyclopentadecane (**14a**).

This compound was isolated in a 20% yield as a pale yellow hygroscopic oil; ^1H nmr: δ 6.81 (s, 2H), 6.66 (s, 2H), 6.07-5.92 (m, 2H), 5.58 (broad-s, OH), 5.12-4.99 (m, 4H), 3.86 (s, 6H),

3.72-3.51 (m, 16H), 3.38 (d, 4H, $J = 6.6$ Hz), 2.80 (t, 4H, $J = 6.0$ Hz), 2.74 (t, 4H, $J = 5.4$ Hz); ms: ei (m/z) 571 (M^+ , 6.70%), 177 ($[\text{HOC}_6\text{H}_2(\text{OCH}_3)(\text{CH}_2\text{-CH}=\text{CH}_2)\text{CH}_2]^+$, 100%).

Anal. Calcd. for $\text{C}_{32}\text{H}_{46}\text{N}_2\text{O}_7 \cdot 3/4\text{H}_2\text{O}$: C, 65.79; H, 8.19. Found: C, 65.99; N, 8.21.

N,N'-Bis(4'-hydroxy-3',5'-diphenylbenzyl)-1,4,10-trioxa-7,13-diazacyclopentadecane (**15a**).

This compound was isolated in a 21% yield as a pale yellow hygroscopic oil; ^1H nmr: δ 7.57-7.32 (m, 20H), 7.23 (s, 4H), 5.33 (s, 2H), 3.65-3.42 (m, 16H), 2.84-2.72 (m, 8H); ms: ei (m/z) 736 (M^+ +1, 0.23%), 219 ($[(\text{CH}_2\text{OCH}_2\text{CH}_2\text{NCH}_2\text{CH}_2\text{OCH}_2)_2]^+$, 2, 100%).

Anal. Calcd. for $\text{C}_{48}\text{H}_{50}\text{N}_2\text{O}_5$: C, 78.45; H, 6.86. Found: C, 78.46; H, 7.08.

N,N'-Bis(4'-hydroxy-3',5'-difluorobenzyl)-1,4,10-trioxa-7,13-diazacyclopentadecane (**16a**).

This compound was isolated in a 30% yield as a pale yellow hygroscopic oil; ^1H nmr: δ 6.93 (d, 4H, $J = 7.6$ Hz), 3.65-3.55 (m, 18H), 2.80-2.64 (m, 8H); ms: ei (m/z) 503 (M^+ , 0.23%), 133 ($[\text{HOC}_6\text{H}_2\text{F}_2]^+$ +2, 100%).

Anal. Calcd. for $\text{C}_{24}\text{H}_{30}\text{F}_4\text{N}_2\text{O}_5 \cdot 1/2\text{H}_2\text{O}$: C, 56.36; H, 6.11. Found: C, 56.51; H, 5.89.

N,N'-Bis(4'-hydroxy-3',5'-di-*iso*-propylbenzyl)-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane (**10b**).

This compound was isolated in a 86% yield as white crystals; mp 125.5-127° (from acetonitrile); ^1H nmr: δ 6.99 (s, 4H), 4.72 (s, 2H), 3.72-3.53 (m, 20H), 3.13 (hept, 4H, $J = 6.8$ Hz), 2.81 (t, 8H, $J = 5.9$ Hz), 1.26 (d, 24H, $J = 6.8$ Hz); ms: ei (m/z) 644 (M^+ +1, 1.2%), 191 ($[\text{HOC}_6\text{H}_2(\text{CH}(\text{CH}_3)_2)_2\text{CH}_2]^+$, 100%). The single crystal used for X-ray analysis was obtained by recrystallization from a mixture of acetonitrile and methanol.

Anal. Calcd. for $\text{C}_{38}\text{H}_{62}\text{N}_2\text{O}_6 \cdot 1/4\text{H}_2\text{O}$: C, 70.50; H, 9.73. Found: C, 70.57; H, 9.64.

N,N'-Bis(4'-hydroxy-3',5'-di-*tert*-butylbenzyl)-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane (**11b**).

This compound was isolated in a 68% yield as white crystals; mp 135-136° (from acetonitrile); ^1H nmr: δ 7.10 (s, 4H), 5.09 (s, 2H), 3.75-3.53 (m, 20H), 2.81 (t, 8H, $J = 5.9$ Hz), 1.43 (s, 36H); ms: ei (m/z) 700 (M^+ +1, 1.50%), 161 ($[\text{O}=\text{C}_6\text{H}_2(\text{C}(\text{CH}_3)_3)\text{CH}_2]^+$ +1, 100%). The single crystal used for X-ray analysis was obtained by recrystallization from a mixture of acetonitrile and methanol.

Anal. Calcd. for $\text{C}_{42}\text{H}_{70}\text{N}_2\text{O}_6 \cdot 1/4\text{H}_2\text{O}$: C, 71.70; H, 10.10. Found: C, 71.79; H, 10.34.

N,N'-Bis(4'-hydroxy-3'-*tert*-butyl-5'-methylbenzyl)-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane (**12b**).

This compound was isolated in a 79% yield as white crystals; mp 99-100.5° (from acetonitrile); ^1H nmr: δ 7.04 (s, 2H), 6.95 (s, 2H), 4.74 (s, 2H), 3.69-3.45 (m, 20H), 2.80 (t, 8H, $J = 6.7$ Hz), 2.21 (s, 6H), 1.40 (s, 18H); ms: ei (m/z) 615 (M^+ , 0.26%), 161 ($[\text{O}=\text{C}_6\text{H}_2(\text{CH}_3)(=\text{C}(\text{CH}_3)_2)\text{CH}_2]^+$, 100%).

Anal. Calcd. for $\text{C}_{36}\text{H}_{58}\text{N}_2\text{O}_6$: C, 70.32; H, 9.51. Found: C, 70.10; H, 9.53.

N,N'-Bis(4'-hydroxy-3',5'-dimethoxybenzyl)-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane (**13b**).

This compound was isolated in a 48% yield as a pale yellow hygroscopic oil; ^1H nmr: δ 6.58 (s, 4H), 5.43 (s, 2H), 3.88 (s, 12H), 3.64-3.60 (m, 20H), 2.82 (t, 8H, $J = 5.9$ Hz); ms: ei (m/z) 594 (M^+ , 3.00%), 428 ($[\text{M-CH}_2\text{C}_6\text{H}_2(\text{OCH}_3)_2\text{OH}]^+$, 100%).

Anal. Calcd. for $C_{30}H_{46}N_2O_{10} \cdot 1/2H_2O$: C, 59.69; H, 7.85. Found; C, 59.73; H, 8.09.

N,N'-Bis(4'-hydroxy-3'-allyl-5'-methoxybenzyl)-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane (**14b**).

This compound was isolated in a 31% yield as white crystals; mp 80-81.5° (from acetonitrile); 1H nmr: δ 6.78 (s, 2H), 6.66 (s, 2H), 6.08-5.91 (m, 2H), 5.61 (s, 2H), 5.09-5.02 (m, 4H), 3.87 (s, 6H), 3.64-3.52 (m, 20H), 3.38 (d, 4H, $J = 6.5$ Hz), 2.80 (t, 8H, $J = 5.8$ Hz); ms: ei (m/z) 615 (M^+ , 7.58%), 218 ($[(CH_2OCH_2CH_2NCH_2CH_2OCH_2)_2-OCH_2CH]^+ + 1$, 100%).

Anal. Calcd. for $C_{34}H_{50}N_2O_8$: C, 66.43; H, 8.20. Found: C, 66.50; H, 8.34.

N,N'-Bis(4'-hydroxy-3',5'-diphenylbenzyl)-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane (**15b**).

This compound was isolated in a 29% yield as white crystals; mp 133-134.5° (from acetonitrile); 1H nmr: δ 7.56-7.32 (m, 20H), 7.23 (s, 4H), 5.31 (s, 2H), 3.66-3.57 (m, 20H), 2.82 (t, 8H, $J = 6.0$ Hz); ms: ei (m/z) 259 ($[HOC_6H_2(C_6H_5)_2CH_2]^+$, 100%), 519 ($[M-CH_2C_6H_2(C_6H_5)_2OH]^+ - 1$, 11.58%).

Anal. Calcd. for $C_{50}H_{54}N_2O_6 \cdot 1/4H_2O$: C, 76.65; H, 7.01. Found: C, 76.77; H, 7.01.

N,N'-Bis(4'-hydroxy-3',5'-difluorobenzyl)-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane (**16b**).

This compound was isolated in a 29% yield as white crystals; mp 135-135.5° (from acetonitrile); 1H nmr: δ 6.89 (d, 4H, $J = 8.5$ Hz), 3.65-3.50 (m, 22H), 2.80 (t, 8H, $J = 5.6$ Hz); ms: ei (m/z) 547 ($M^+ + 1$, 0.19%), 132 ($[HOC_6H_3F_2]^+ + 1$, 100%).

Anal. Calcd. for $C_{26}H_{34}F_4N_2O_6$: C, 57.14; H, 6.27. Found: C, 56.92; H, 6.26.

Crystallography.

The crystallographic and experimental data are listed in Table 2. Each of the single crystals was mounted in a glass capillary. All measurements were made at 298 K on a Rigaku AFC5S four-circle diffractometer with graphite-monochromated Mo $K\alpha$ radiation (0.71069 Å) and a 12kW rotating-anode generator. Cell contacts and an orientation matrix for data collection were obtained from a least-squares refinement. The data were collected using the ω - 2θ scan technique to an above maximum 2θ value of 55.0°. All intensities were corrected for Lorentz and polarization effects. The structure was solved by direct methods (SIR 92) [13]. The non-hydrogen atoms were refined anisotropically. The coordinates of all hydrogen atoms except the hydrogen atoms of the phenolic OH group were calculated at ideal positions and were refined (Tables 3, 4 and 5). Neutral atom scattering factors were taken from Cromer and Weber [14]. Anomalous dispersion effects were included in Fc [15]; the values for $\Delta f'$ and $\Delta f''$ were those of Creagh and McAuley [16]. The values for the mass attenuation coefficients are those of Creagh and Hubbel [17]. All calculations were made using the teXsan™ crystallographic software package of Molecular Structure Corporation [18].

Metal Ion Transport Experiments.

The transport experiments were carried out using a double tube (diameter of the inner and outer tubes are 10 mm and 20 mm, respectively) at $25 \pm 2^\circ$. Initial conditions of the competitive transport were as follows; [basic source phase] = aqueous

solution containing a mixture of 0.1 mole/l of sodium hydroxide, potassium hydroxide and cesium hydroxide (4 ml): [membrane phase] = 2 mmoles/l of crown ether in chloroform (4 ml): [acidic receiving phase] = 0.1 mole/l of hydrochloric acid (1 ml). The concentration of the receiving phase was determined by ion chromatography. The transport rate was calculated from the amounts of alkali-metal cations in the receiving phase. The aqueous and organic phases were stirred by a stirring bar (10 mm) at 500 rpm by a synchronous motor in order to avoid a stirring error. The amounts of metal ions in the receiving phases were measured by ion chromatography. The initial transport rate was calculated from the increase of the cation concentration in the receiving phase after a period of 6 hours.

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REFERENCES AND NOTES

- [*] E-mail: habata@chem.sci.toho-u.ac.jp; Int. Phone/Fax: +81-47-472-4322.
- [1] A. V. Bogatsky, N. G. Lukyanenko, V. N. Pastushok, and R. G. Kostyanovsky, *Synthesis*, 992 (1983).
 - [2] A. V. Bordunov, J. S. Bradshaw, V. N. Pastushok, and R. M. Izatt, *Synlett*, 933 (1996) and references cited therein.
 - [3] J. Wang, *Yingyong Huaxue*, **13**, 69 (1996).
 - [4] K. Chi, H. Wei, T. Kottke, and R. Lagow, *J. Org. Chem.*, **61**, 5684 (1996).
 - [5] M. M. Yang, J. Q. Zhang, and Z. Shen, *Chin. Chem. Lett.*, **8**, 845 (1997).
 - [6] J. S. Bradshaw, A. V. Bordunov, X. X. Zhang, V. N. Pastushok, and R. M. Izatt, *ACS Symp. Ser.*, **716**, 133 (1999).
 - [7] Y. Habata, S. Akabori, R. M. Izatt, and J. S. Bradshaw, *Ind. Eng. Chem. Res.*, **39**, 3465 (2000).
 - [8] Y. Habata, T. Saeki, S. Akabori, X. X. Zhang, and J. S. Bradshaw, *J. Heterocyclic Chem.*, **38**, 253 (2001).
 - [9] Y. Habata and S. Akabori, *J. Chem. Soc., Dalton Trans.*, 3871 (1996).
 - [10] Y. Habata, T. Saeki, S. Akabori, and J. S. Bradshaw, *J. Heterocyclic Chem.*, **36**, 355 (1999).
 - [11] Y. Habata, T. Saeki, S. Akabori, X. X. Zhang, and J. S. Bradshaw, *J. Chem. Soc., Chem. Comm.*, 1469 (2000).
 - [12] Y. Habata, A. Watanabe, and S. Akabori, *Supramol. Chem.*, in press.
 - [13] A. Altomare, M. C. Burla, M. Camalli, M. Cascarano, C. Giacovazzo, A. Guagliardi, and G. Polidori, *J. Appl. Cryst.*, **27**, 435 (1994).
 - [14] D. T. Cromer and J. T. Waber, *International Tables for X-ray Crystallography*, Vol **IV**, The Kynoch Press, Birmingham, England, 1974, Table 2.2A.
 - [15] J. A. Ibers and W. C. Hamilton, *Acta Crystallogr.*, **17**, 781 (1964).
 - [16] D. C. Creagh and W. J. McAuley, *International Tables for Crystallography*, Vol **C**, (Wilson, A. J. C. Ed.), Kluwer Academic Publishers, Boston, 1992, Table 4.2.6.8, pp 219-222.
 - [17] D. C. Creagh and J. H. Hubbell, *International Tables for Crystallography*, Vol **C**, (Wilson, A. J. C. Ed.), Kluwer Academic Publishers, Boston, 1992, Table 4.2.4.3, pp 200-226.
 - [18] TeXsan™: Crystal Structure Analysis Package, Molecular Structure Corporation (1985 & 1999).