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SYNTHESIS AND EXTRACTION PROPERTIES OF NEW BIS-CROWN ETHERS DERIVED FROM STEREOISOMER OF 1,2-CYCLOHEXANE-DIOLS FOR ALKALI AND ALKALINE EARTH METAL CATIONS

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Abstract – Stereoisomers of new bis(benzo-15-crown-5) derivatives were synthesized from *cis*- and *trans*-1,2-cyclohexanediols. The complexing ability of these bis-crown ethers toward sodium, potassium, lithium, calcium, and magnesium cations has been measured by the solvent extraction method. The extraction data show that the extractabilities of these cations are increased due to the formation of “sandwich – type” complexes by the *cis*-isomer. The results also show that steric hindrance of substituent on the benzene rings does not have any interference with the formation of a sandwich-type complex in the *cis*-form.

INTRODUCTION

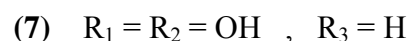
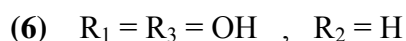
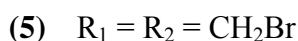
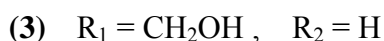
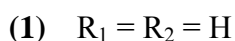
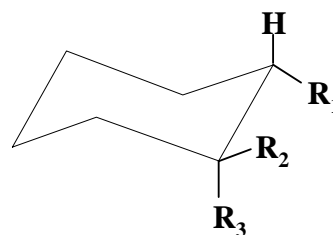
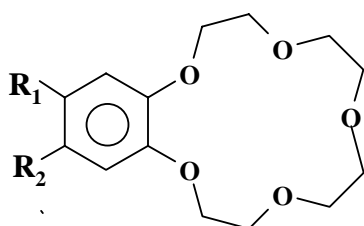
Bis-crown ethers containing benzo-15-crown-5 moieties at the end of a short bridge chain have received considerable attention because of their attractive cation-binding properties.¹⁻⁵ They can form stable “sandwich – type” 2:1 crown ether ring to cation complexes intramolecularly, which results in high selectivity of cation on binding with alkali and alkaline earth metal cations.^{4,6} Among these, bis (benzo15-crown-5) derivatives which are capable of adopting the *trans* – and *cis* – geometries compose a versatile class of bis-crowns that can control the complexation of metal cation by their geometries.⁷⁻¹³ More recently, Odashima and co-workers¹³ have synthesized some *cis*-and *trans*-azobis(benzo-15-crown-5) derivatives and have made extensive studies on their extraction properties for alkali metal cations.

However, no report on complexing properties of *cis*- and *trans*-bis(benzo-15-crown-5) which are derived from *cis*-1,2- and *trans*-1,2-cyclohexanediols has appeared except one in which the K^+ -selectivities of the bis(benzo-crown-5) derived from *cis*-1,2- and *trans*-1,2-cyclohexanedicarboxylic acids are investigated by measuring the electrochemical selectivity of coated-wire ion-selective electrodes.⁸

In this paper, we describe the synthesis and extraction properties of the stereoisomeric of *cis*- and *trans*-bis(benzo-15-crown-5) ethers (**8-11**) for alkali and alkaline earth metal cations. The effect of substituent on both benzene rings in complexation behavior of these compounds also is investigated.

RESULT AND DISCUSSION

Both benzo-15-crown-5 (**1**) and 4-formylbenzo-15-crown-5 (**2**) were prepared from catechole and 3,4-dihydroxybenzaldehyde respectively by Pedersen's procedure.¹⁵ Reduction of **2** by sodium borohydride was afforded 4-hydroxymethyl benzo-15-crown-5 (**3**).⁹ Treatment of the alcohol (**3**) with thionyl chloride afforded the crystalline chloromethyl compound (**4**).⁹ 4,5-Bis(bromomethyl)benzo-15-crown-5 (**5**) was prepared from benzo-15-crown-5 (**1**) by reaction with paraformaldehyde and 33% solution of HBr in acetic acid.¹⁶ *cis*-1,2-, and *trans*-1,2-cyclohexanediols (**6**) and (**7**) were obtained by oxidation of cyclohexene with potassium permanganate¹⁷ and formic acid / hydrogen peroxide,¹⁸ respectively. Reaction of chloromethyl compound (**4**) with *cis*-diol (**6**) and *trans*-diol (**7**) in the presence of sodium hydride and tetra-*n*-butylammonium iodide in 1,2-dimethoxyethane afforded *cis*-bis-ether (**8**) and *trans*-bis-ether (**10**), respectively.⁹ Similarly, reaction of 4,5-bis-bromomethyl compound (**5**) with diols (**6**) and (**7**) afforded *cis*-bis-ether (**9**) and *trans*-bis-ether (**11**), respectively⁹ (Figure 1).



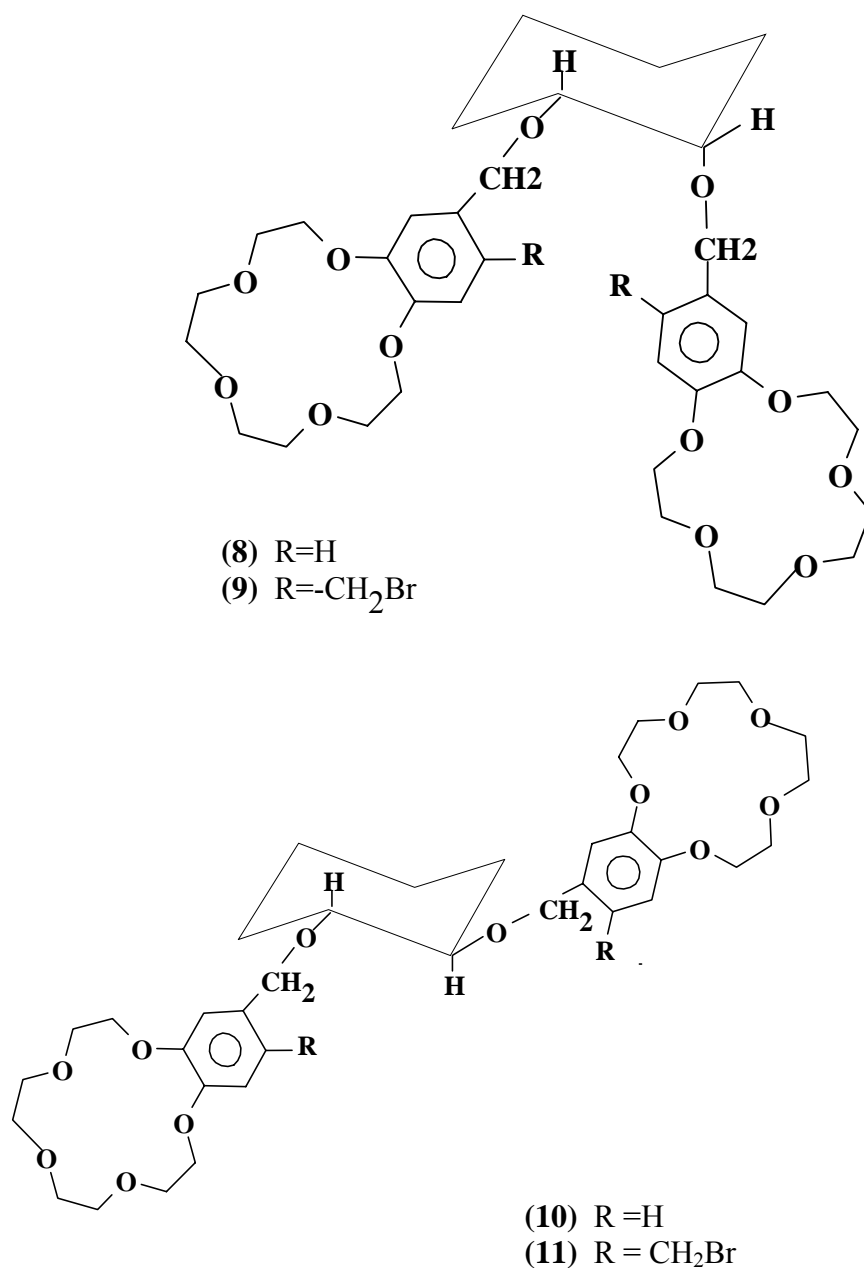


Figure 1. Schematic representation of compounds.

Alkali Metal and Alkaline Earth Metal Picrate Extractions. The alkali metal cation complexing abilities of *cis*-bis-crown ethers (**8**) and (**9**), *trans*-bis-crown ethers (**10**) and (**11**), and two model compounds (**2**) and (**5**) were assessed by solvent extraction of alkali metal picrate from aqueous solution into dichloromethane according to Haines's procedure.⁹ The picrate extraction results are presented in Table 1. Whereas selective extraction of Na⁺ normally would be anticipated on the basis of the 15-crown-5 ring size,^{19,20} the data in Table 1 indicate that the *cis*-bis-crown compound (**8**), when compared with the *trans*-bis-compound (**10**), exhibits selectivity toward K⁺ which suggests the formation of a 2:1 host-guest sandwich complex.^{13,20} The observed extraction selectivity order for **8** is K⁺>Na⁺>Li⁺.²⁰

When the alkali metal picrate extraction capability of **8** is compared with **2**, it is observed that **8** extracts all three alkali metal picrates more efficiently than does an equivalent concentration of the model compound (**2**). This result, is consistent with the efficacious juxtaposition of pairs of crown ether moieties which is present in **8** and results in the formation of host-guest sandwich complexes with K^+ and the larger alkali metal cations.²⁰

The data in Table 1 also indicate that the *cis*-bis-crown compound (**9**), when compared with the *trans*-bis-compound (**11**), exhibits selectivity toward K^+ which shows the formation of a 2:1 host-guest sandwich complex.^{13,20} When extraction capability of **9** is compared with **5**, it is also observed that **9** extracts the three alkali metal picrates more efficiently than does an equivalent concentration of the model compound (**5**). Furthermore, these results contrast that steric hindrance by the $-CH_2Br$ group of **9** does not interfere with the formation of sandwich-type complex in the *cis*-form.¹³

The data obtained for alkaline earth metal picrate extractions by *cis*-bis-crown ethers (**8**) and (**10**) and the corresponding model compound (**2**) are presented in Table 2. Extraction efficiencies are observed to be low in all cases, and display the same picrate extraction selectivity, i. e., $Mg^{2+} > Ca^{2+}$. Although the extraction efficiency for Mg^{2+} and Ca^{2+} which is observed with bis-crown ethers (**8**) and (**10**) is higher than that for model compound (**2**), the overall results show that there is no appreciable difference in the alkaline earth metal cation complexation.²⁰ Therefore, it seems that even the enhanced charge-dipole interactions anticipated for divalent metal ions are insufficient to produce cooperativity between the crown ether units in bis-crown ethers (**8**) and (**10**).

EXPERIMENTAL

The IR spectra were recorded with a Shimadzu Fourier transform infrared spectrophotometer model 4300. Proton NMR spectra were obtained by using a Bruker 100 Fourier transform spectrometer. Chemical shifts are reported in ppm (δ) downfield from tetramethylsilane (TMS) as an internal standard. A Beckman model DU6 UV-visible spectrophotometer was used to measure absorbance at 354 nm in connection with the picrate extraction experiments described below. MS spectra were recorded on Varian-CH7 Mass spectrometer. Microanalytical data were measured by personnel at chemistry department, University of Tarbiat Modarres, Tehran, Iran. Benzo-15-crown-5 (**1**),¹⁵ 4-formylbenzo-15-crown-5 (**2**),²¹ 4-hydroxymethylbenzo-15-crown-5 (**3**),⁹ 4-chloromethyl benzo-15-crown-5 (**4**),⁹ 3,4-bis(bromomethyl)benzo-15-crown-5 (**5**),¹⁶ *cis*-1,2-cyclohexandiol (**6**),¹⁷ and *trans*-1,2-cyclohexandiol (**7**),¹⁸ were prepared by literature procedure. All of these compounds showed satisfactory mp, MS, ¹HNMR and IR spectral data.

General procedure for the synthesis of *cis*- and *trans*-bis-crown ethers (8-11**).**⁹ To a stirred solution of the cyclohexanediol (5 mmol) in 1,2-dimethoxyethane (25 mL) was added sodium hydride (*ca.* 5 g)

followed by tetra-n-butylammonium iodide (*ca.* 0.02 g). After 20 min, the chloro compound (**4**), or bis-bromo compound (**5**) (10 mmol) was added and the reaction mixture was stirred overnight at rt. Methanol (2 mL) was added to the stirred solution. Concentration of the solution gave a residue which was taken up in water and extracted with dichloromethane (3*25 mL). The combined organic extracts were dried over sodium sulfate and then concentrated to give an oily yellow chromatographically (column, ethyl acetate) pure product. The following bis-crown ethers were prepared.

The *cis*-bis-benzocrown (8). (67%), IR 1610, 1500 (ν C=C aromatic), 1120 cm^{-1} (ν COC aryl ether). $^1\text{HNMR}$ (CDCl_3) δ 0.8-1.8 (8H, m, cyclohexane), 3.2-3.4 (2H, m, H-1 and H-2 of cyclohexane), 3.5-4.0 (32H, m, crown ring), 4.2 (4H, s, $\text{ArCH}_2\text{-O}$), 6.8-6.9 (6H, m, ArH). *Anal.* Calcd for $\text{C}_{36}\text{H}_{52}\text{O}_{12}$: C, 63.9; H, 7.7. Found; C, 63.4; H, 8.1.

The *cis*-bis-benzocrown (9). (65.5%). IR 1610, 1520 (ν C=C aromatic), 1120 (ν COC aryl ether), 590 cm^{-1} (ν $-\text{CH}_2\text{Br}$). $^1\text{HNMR}$ (CDCl_3) δ 1.0-2.0 (8H, m, cyclohexane), 3.0 (2H, m, H-1 and H-2 of cyclohexane), 3.6 (4H, s, $-\text{CH}_2\text{Br}$), 3.8-4.4 (32H, m, crown ring), 4.6 (4H, s, $\text{ArCH}_2\text{-O}$), 7.2 (4H, s, ArH). *Anal.* Calcd for $\text{C}_{38}\text{H}_{54}\text{O}_{12}\text{Br}_2$: C, 52.9; H, 6.3. Found; C, 53.4; H, 6.1.

The *trans*-bis-benzocrown (10). (65%). IR 1610, 1450 (ν C=C aromatic), 1125 cm^{-1} (ν COC aryl ether). $^1\text{HNMR}$ (CDCl_3) δ 0.8-1.25 (8H, m, cyclohexane), 3.3-4.0 (34H, m, H-1 and H-2 of cyclohexane and crown ring), 4.1(4H, s, $\text{ArCH}_2\text{-O}$), 6.75-6.9 (6H, s, ArH). *Anal.* Calcd for $\text{C}_{36}\text{H}_{52}\text{O}_{12}$: C, 63.9; H, 7.7. Found; C, 63.5; H, 7.8.

The *trans*-bis-benzocrown (11). (62.7%). IR 1610, 1515 (ν C=C aromatic), 1130 (ν COC aryl ether), 590 cm^{-1} (ν $-\text{CH}_2\text{Br}$). $^1\text{HNMR}$ (CDCl_3) δ 0.8-1.6 (8H, m, cyclohexane), 2.7 (2H, m, H-1 and H-2 of cyclohexane), 3.4 (4H, s, $-\text{CH}_2\text{Br}$), 3.5-4.2 (32H, m, crown ring), 4.3 (4H, s, $\text{ArCH}_2\text{-O}$), 7.0 (4H, s, ArH). *Anal.* Calcd for $\text{C}_{38}\text{H}_{54}\text{O}_{12}\text{Br}_2$: C, 52.9; H, 6.3; O, 22.2. Found; C, 53.2; H, 6.6; O, 21.8.

Extraction Measurement. Aqueous solution (15 mL) containing picric acid (7.00×10^{-6} M or 7.00×10^{-5} M), alkali metal chloride (1.00×10^{-3} M) and alkali metal hydroxide (1.00×10^{-2} M) was vigorously shaken with equal volume of dichloromethane containing crowns (7.00×10^{-6} M or 7.00×10^{-4} M) for 15 min. The absorbance, *A*, of the aqueous layer before and after the extraction experiment, *A*₀ and *A*_e, respectively,

was measured at the position of maximum absorption band at 354 nm and the percentage of extraction of alkali-metal picrates into the organic layer was calculated by the expression $100 (A_o - A_e)/A_o$. Results are given in Tables 1 and 2.

Table 1. Alkali metal picrate extraction data from aqueous solution into dichloromethane by using **2**, **5** and **8-11**.

compound	percent of picrate extracted (%) ^a		
	Li ⁺	Na ⁺	K ⁺
2 ^b	0	4.93	10.29
5 ^c	4.8	11.3	14.5
8 ^b	1	16.63	28.26
9 ^c	27.5	35.8	88.7
10 ^b	0.53	14.52	22.24
11 ^c	22.4	29.7	82.9

^aAverage for three samples

^bOrganic phase [dichloromethane]: [**2** and bis-crown] = 7.00×10^{-6} M. Aqueous phase: [picric acid] = 7.00×10^{-6} . [alkali metal chloride] = 1.00×10^{-3} M.

^cOrganic phase [dichloromethane]: [**5** and bis-crown] = 7.00×10^{-4} M. Aqueous phase: [picric acid] = 7.00×10^{-5} M. [alkali metal hydroxide] = 1.00×10^{-2} M.

Table 2. Alkaline earth metal picrate extraction data from aqueous solution into dichloromethane by using **2**, **8** and **10**.

compound	percent of picrate extracted (%) ^a	
	Ca ²⁺	Mg ²⁺
2	0.91	2.01
8	5.21	8.86
10	4.66	5.10

^aOrganic phase [dichloromethane]: [**2** and bis-crown] = 7.00×10^{-6} M. Aqueous phase: [picric acid] = 7.00×10^{-6} . [alkali metal chloride] = 1.00×10^{-3} M.

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