

Novel Functionalized Symmetrical Dibenzosulfoxo-Crown Ethers with High Selectivity for Pb^{2+} , K^+ , and Ba^{2+}

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ABSTRACT: A new series of crown ether-based macrocycles bearing two hydroxyl groups and a dibenzosulfoxide moiety was synthesized. These symmetrical dibenzosulfoxo- (aza)-crown ethers were synthesized by the reaction of an active symmetrical bisepoxide pod and with diol reagents in the presence of sodium hydride as a strong base and dry tetrahydrofuran as the solvent. In fact, the reaction begins with the opening of the epoxide rings via the nucleophilic attack (S_N2) of dialkoxide and ends with the formation of a macrocyclic ring. The final compounds were characterized by FT-IR, 1H NMR, ^{13}C NMR, and FAB-MS spectroscopic methods. They were evaluated for their extraction ability and selectivity for various metallic cations in the form of picrate salt in dichloromethane solvent at room temperature. The new macrocycles showed good extraction ability especially for Pb^{2+} (72%), K^+ (66%), and Ba^{2+} (56%) among the used cations, for **3b**, **3c**, and **3a** respectively. Compound **3b** (dibenzosulfoxo-20-aza-crown-4-ether) showed the excellent selectivity for Pb^{2+} (72%).

KEYWORDS: Symmetrical macrocycle; Dibenzosulfoxo-crown ethers; Cation selectivity; Dibenzosulfoxide.

INTRODUCTION

A cyclic structure containing at least 12 atoms is called a macrocycle. These molecules are important ligands in host-guest interactions in supramolecular chemistry [1-3]. Cyclic polyethers, called crown ethers, are the first molecular structures in the history of organic chemistry that are classified by Pedersen into macrocyclic class [4]. To date, due to the presence of electron-donating oxygen atoms in the structures of crown ethers, they have been continuously used for metal ions recognitions [1]. Pedersen showed that one or some of the oxygen atoms in the structure of the crown ethers can be replaced by other electron-donating atoms, such as sulfur and nitrogen, to form thia- and aza-crown ethers, respectively [4]. In the synthesis of macrocycles, the cyclization reaction

should be able to compete with polycondensation reactions [5]. The main factors involving in the cyclization reaction are chain length, nature of the atoms, type of cyclization, and ring closure methods [1]. Various factors are involved in the selectivity of a macrocycle for different ions, including: the cavity size and shape, substituent effects, conformational flexibility/rigidity, and the type of heteroatom [6]. Considering the cation selectivity of macrocycles and taking into account the biological disadvantages of some heavy metal cations, the importance of the synthesis of new macrocyclic compounds can be found [7,8].

The above-mentioned properties of the macrocyclic compounds led us to synthesize new functionalized (aza)-crown ethers with properties of cation selectivity.

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These macrocycles with two hydroxyl groups are very important intermediates in the synthesis of aza-crown ethers, lariat ethers, cryptands, bis-crowns, and other similar compounds. In addition, due to the importance of metal cations in biological systems, the selectivity of these macrocycles for special metal cations can pave the way for their use in biological systems.

EXPERIMENTAL SECTION

Material and instrumentation

The melting points of all compounds were recorded on Electrothermal engineering LTD 9100 apparatus without calibration. IR spectra were recorded on Perkin-Elmer model 543 spectrometer and ^1H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra measured with Bruker AM-300 spectrometer in CDCl_3 using TMS as the internal reference. Mass spectra were recorded on a JEOL-JMS 600 (FAB MS) instrument. Thin-layer chromatography (TLC) analyses were carried out on silica gel plates. All chemicals were purchased from Merck (Germany) and used as received by standard procedures. All of the instruments, chemicals, and solvents were dried according to standard methods. Open chained molecule, compound **1** as a dibenzosulfoxide bisepoxide was prepared according to previously published method as colorless crystals [5].

General Procedure for the Synthesis of symmetrical 3a–c

NaH (24 mg, 1mmol) and compound **2a-c** (1 mmol) in dry THF (10 mL) were placed together in a condenser-equipped round bottom flask. The reaction mixture was placed in an ice bath under the argon atmosphere. The compound **1** (0.2 g, 0.535 mol) in dry THF (5 mL) was drop-wisely then added to the reaction mixture in the reflux condition for 24 h. The solvent was evaporated under reduced pressure. The residue was purified by thin-layer chromatography.

Dibenzosulfoxo-18-crown-4-ether (3a):

yield, 89%; m.p., 214-217 °C; IR (KBr, v, cm^{-1}): 3412 (OH), 2950, 2866, 1563 (C=C), 1406, 1149 (C-O), 1060 (S=O), 914, 869, 758 (C-H). ^1H NMR (300 MHz; CDCl_3 ; δ , ppm): 0.92-0.94 (m, 2H), 2.23 (s, 6H), 3.12-3.34 (m, 4H), 4.23 (s, 2H, OH), 4.36-4.37 (d, 4H, J = 4.19 Hz), 5.12-5.16 (d, 4H, J = 11.39 Hz), 5.61-5.70 (m, 2H), 6.74-6.76 (d, 2H, J = 8.39 Hz), 7.53-7.71 (m, 2H), 8.0 (s, 2H); ^{13}C NMR (75 MHz; CDCl_3 ; δ , ppm): 19.3, 28.7, 61.8, 66.5,

67.1, 68.7, 112.4, 116.8, 130.6 (2C), 131.2, 134.0; FAB-MS (m/z): 450.54 (M+).

Dibenzosulfoxo-20-aza-crown-4-ether (3b)

yield, 72%; m.p., 222-225 °C; IR (KBr, v, cm^{-1}): 3158 (OH), 3013 (NH), 2920, 2867, 1660, 1600 (C=C), 1469, 1396, 1133 (C-O), 1100(S=O), 1060, 961, 881, 748 (C-H). ^1H NMR (300 MHz; CDCl_3 ; δ , ppm): 2.46 (s, 6H), 2.63-2.96 (m, 4H), 3.45-3.50 (m, 4H), 3.74 (s, 2H, OH), 4.24-4.25 (d, 4H, J = 3.96 Hz), 4.81-4.82 (d, 4H, J = 1.94 Hz), 5.12-5.15 (m, 2H), 5.78 (s, 1H, NH), 6.54-6.60 (m, 2H), 7.34-7.36 (m, 2H), 7.83 (s, 2H); ^{13}C NMR (75 MHz; CDCl_3 ; δ , ppm): 19.6, 39.5, 42.5, 48.7, 64.3, 67.7, 112.0, 117.6, 128.7, 130.7, 133.9, 153.1; FAB-MS (m/z): 479.91 (M+).

Dibenzosulfoxo-21-crown-4-ether (3c)

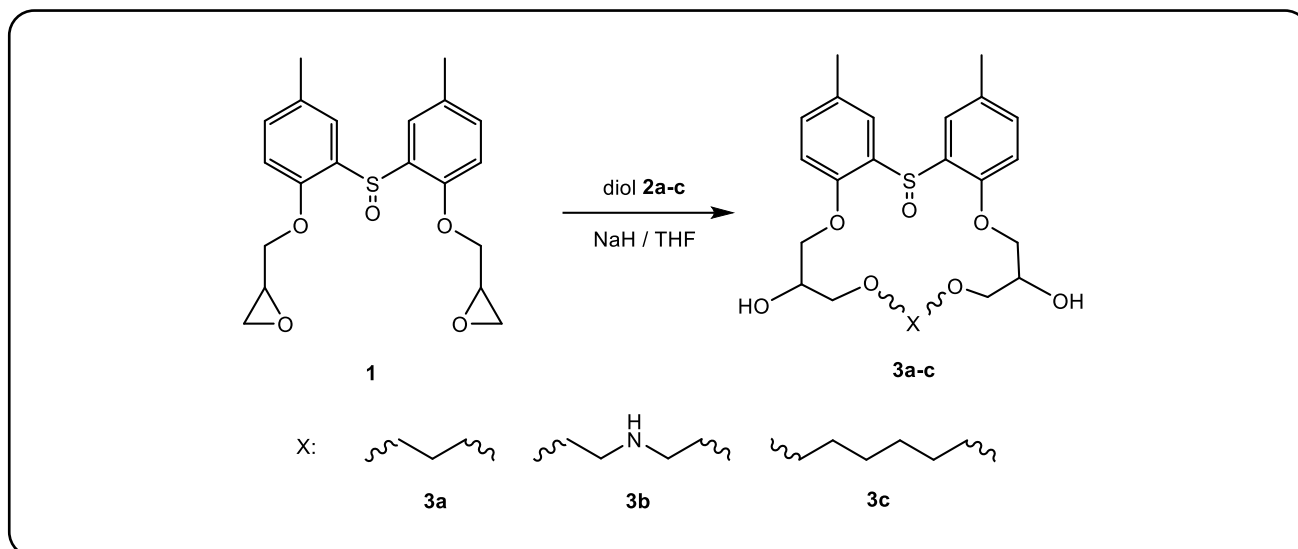
yield, 78%; m.p., 202-205 °C; IR (KBr, v, cm^{-1}): 3344 (OH), 2939, 2862, 1590 (C=C), 1482, 1468, 1431, 1299, 1282, 1211, 1164 (C-O), 1115, 1057(S=O), 935, 852. ^1H NMR (300 MHz; CDCl_3 ; δ , ppm): 1.24-1.28 (t, 4H, J = 7.1 Hz), 1.32-1.41 (m, 4H), 2.05 (s, 6H), 2.28-2.38(m, 4H), 3.15-3.21 (m, 4H), 4.03-4.15 (m, 4H), 4.31-5.15 (m, 4H), 4.78 (s, 2H, OH), 6.71-6.74 (d, 2H, J = 8.34 Hz), 7.32-7.36 (m, 2H), 8.03 (s, 2H); ^{13}C NMR (75 MHz; CDCl_3 ; δ , ppm): 7.5, 13.2, 19.3, 20.1, 44.1, 59.4, 68.6, 112.2, 116.8, 127.0, 130.6, 131.1, 134.0; FAB-MS (m/z): 492.27 (M+).

Analytical Procedure

The analytical procedure of the extraction of some of the metal ions was performed based on the previously published method with some modifications [9]. In detail, the organic phase (5 mL of CH_2Cl_2), containing macrocyclic compound **3a-c** (2.50 mM), and the aqueous phase (5 mL), containing $\text{M}^+ \text{Pic}^-$ (0.25 mM), NaOH (0.10 M), and NaCl (0.50 M), were mixed and shaken overnight at room temperature. Extraction percentage values were determined spectrophotometrically at 357 nm. Blank experiments showed that no picrate extraction occurred in the absence of a macrocycle.

RESULTS AND DISCUSSION

The synthetic route to symmetrical macrocycles **3a-c** is depicted in Scheme 1. The synthetic strategy involves the reaction of diol compounds (1,3-propanediol (**2a**), diethanolamine (**2b**), and 1,6-hexanediol (**2c**)) with



Scheme 1: Synthetic pathway to symmetrical dibenzosulfoxo-crown ethers 3a-c

a symmetrical dibenzosulfoxide bearing two epoxide arms as an active open-chain molecule (podand) in the presence of sodium hydride in dry tetrahydrofuran (THF) under reflux condition for 24 h. The ring closure method is based on the attack of dialkoxide (formed via the reaction of a diol with NaH) as a nucleophile at the lower steric hindrance side of epoxide rings of podand (S_N2), and followed by the ring-opening of epoxides and the formation of hydroxyl groups. The template effect of a sodium cation (from the used base) deals directly with this issue. Sodium cation causes the open-chain podand to assemble itself around the positive ion in a circle or semicircle form via negative charges of oxygen atoms itself. Thus, the two reactive ends will be close together. The structure of the obtained macrocycles was characterized by NMR, FT-IR, and FAB-MS spectroscopic methods. The presence of sulfoxide groups was confirmed by the bands at about 1060 cm^{-1} in FT-IR spectra of **3a-c**. In addition, there is one signal for hydroxyl groups in $^1\text{H-NMR}$ spectra of **3a-c**, including 4.23, 3.74, 4.78 ppm, respectively. The presence of N-H bond in compound **3b** was confirmed by a broad peak at about $3100\text{-}3200\text{ cm}^{-1}$ in FT-IR spectrum [10] and a single peak at 5.78 ppm in $^1\text{H-NMR}$ spectrum (Fig. 1 and Fig. 2).

Due to the difference in the number of atoms in the used diols, the ring cavity size of the formed symmetrical macrocycles is different. In this way, the number of atoms in the macrocyclic cavity in compounds **3a-c** is 18, 20, and 21,

respectively. Hence, according to the size-fitting hypothesis in host-guest interactions [11], the hosting behavior of these macrocyclic cavities against different metal cations will be different from each other.

A previous study on the ligand-cation interaction of dibenzosulfoxide moiety in the presence of similar macrocycles indicates that this part is interesting in interacting with heavy metal cations such as Pb^{2+} [12]. On the other hand, the presence of additional oxygen atom considerably increases its hydrogen binding capacity and these properties can improve the biological and complexation characteristics of these compounds [13]. In addition, replacing oxygen atoms with sulfur and nitrogen in the structure of the crown ether cavity changes the selectivity of macrocycle toward different cations. Sulfur and nitrogen, due to their less electronegativity in comparison to oxygen are softer bases, and thus prefer the softer acids such as heavy metal ions (e.g., silver) [14].

In order to evaluate the potential cation selectivity of the synthesized macrocycles, solvent extraction of metal picrate salts from water into an organic solvent CH_2Cl_2 was performed at room temperature following a modified version of Pedersen's procedure [4]. This was done according to a liquid-liquid ion-pair extraction method. The principle of the method is to transfer an inorganic reagent from one phase (especially water) to an organic phase that does not mix with water (e.g., chloroform, dichloromethane). According Equation 1, the extraction process causes ion-pair formation between a cation-ligand

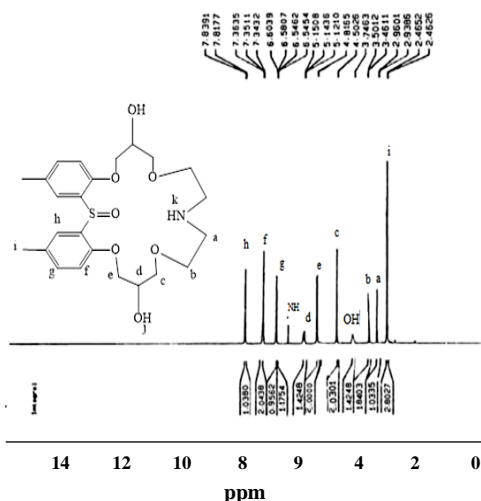


Fig. 1: $^1\text{H-NMR}$ Spectrum of compound **3b** in CDCl_3 .

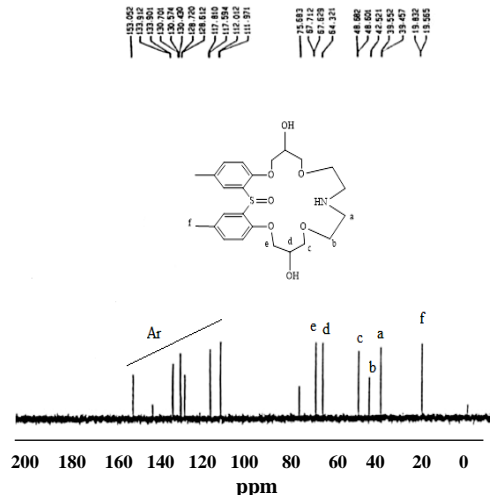


Fig. 2: $^{13}\text{C-NMR}$ Spectrum of compound **3b** in CDCl_3 .

complex and a counter ion, where M^{m+} is the metal ion, A^- is the counter ion, L is the ligand.

$$\text{M}_{(w)}^m + m\text{A}_{(w)}^- + \text{L}_{(w)}\text{MLA}_m(\text{org.}) \quad (1)$$

The extractability (Ex%) of the metal cations is expressed by means of the following equation.

$$\text{Ex}\% = \left(\frac{A_0 - A}{A_0}\right) \times 100 \quad (\lambda_{\max} = 357\text{nm}) \quad (2)$$

where A_0 and A are the absorbances in the absence and the presence of ligands, respectively.

The results for the extraction ability of **3a-c** are summarized in Table 1 for picrate salt of Li^+ , Co^{2+} , Fe^{3+} , Cd^{2+} , Ag^+ , Pb^{2+} , K^+ , and Ba^{2+} .

Considering the size-fitting hypothesis [11], soft/hard rules in acid-base interaction [14], and bare ionic radius of the used metal cations (Table 2) [15] in this study, the values of extraction percentages for these cations can be explained easily.

Due to the high ratio in the number of the oxygen atoms to the other heteroatoms (S and N) in the ring cavity of **3a-c**, it can be concluded that the present crowns are more likely to have complexes with hard to intermediate acids such as K^+ and Pb^{2+} . On the other hand, raising ring cavities among ligands **3a-c** enhances their extraction ability for cations with a higher radius. In the case of **3b** as a dibenzosulfoxo-20-aza-crown-4-ether, the presence of the nitrogen in its ring cavity has led to a greater tendency of the ligand to form a stable

complex with lead cation and ultimately increase its extraction rate to 72%. So, ligand **3b**, possessing a NH and a S=O group, has an excellent affinity towards heavy metal cation Pb^{2+} as an intermediate acid. On the other hand, in comparison with K^+ , Pb^{2+} , and Ba^{2+} cations, the Li^+ , Co^{2+} , Fe^{3+} ions with hard to intermediate acid characters also form relatively weaker complexes with the ligands **3a-c**, due to their smaller sizes than the ligands' ring cavity. Finally, the K^+ and Pb^{2+} ions with more appropriate sizes and harder acid characters than the other used cations in this study, form the most stable complexes with the dibenzosulfoxo-crown ethers **3a-c**.

CONCLUSIONS

Briefly, in this study, we demonstrated the syntheses and metal cation extraction ability of three new symmetrical dibenzosulfoxo-(aza)-crown ethers bearing two hydroxyl groups. These macrocycles were synthesized by epoxide ring-opening $\text{S}_{\text{N}}2$ reaction and then followed by the macrocycle ring formation. They showed different extraction ability for some metal cations (hard to soft acid characters) by liquid-liquid ion-pair extraction method. The best results are belonged to extraction of Pb^{2+} (72%), K^+ (66%), and Ba^{2+} (56%). These macrocycles have two major advantages that are due to the bearing of free hydroxyl groups, and special selectivities for various metal cations. Therefore, considering the importance of free hydroxyl groups and metal cations in the living systems,

Table 1: The percentage extraction value (Ex %) of ligand 3a-c for picrate salts.

	Li ⁺	Co ²⁺	Fe ³⁺	Cd ²⁺	Ag ⁺	Pb ²⁺	K ⁺	Ba ²⁺
3a	4	27	33	29	18	42	51	56
3b	2	39	37	23	22	72	49	41
3c	0	15	24	18	17	54	66	33

Table 2: Radius [15] and acidity type of used metal cations.

Cation	Radius (Å ^o)	Acidity Type*	Cation	Radius (Å ^o)	Acidity Type*
Li ⁺	0.6	H	Ag ⁺	1.15	S
Co ²⁺	0.75	I	Pb ²⁺	1.20	I
Fe ³⁺	0.80	H	K ⁺	1.35	H
Cd ²⁺	1.00	S	Ba ²⁺	1.45	H

the importance of these molecules in biological systems can be pointed out.

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