



ORIGINAL ARTICLE

Synthesis of New Lariat Diaza Crown-ether as Receiver Heavy Cations in Environment

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ABSTRACT

Some functionalized *N*-pivot lariat diaza crown ethers were synthesized as cationic and molecular acceptors. Lariat diaza crown ethers 7 was prepared by mannich reaction of macrocyclic diamide 5 and phenole compounds in the presence of paraformaldehyde by refluxing in dry toluene. The structures were characterized by FT-IR, ¹H NMR, ¹³C NMR spectrometric analyses.

Keywords: Macrocyclic diamides, Mannich condensation, *N*-Pivot lariat ether diaza crown ether, Liquid membrane transport.

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INTRODUCTION

Macrocycles as diamide derivatives are macrocyclic compounds. Their properties are similar to those of crown ethers. Following Pedersen's report that these macrocyclic ethers were able to bind alkali metal cations, considerable amounts of these compounds have been synthesized. Macrocyclic diamides are formed during the formation of aza-crown compounds, and they are viewed as very valuable intermediates. Furthermore, in terms of effective complexation with various transition and heavy metals, molecular ions, and neutral molecules, they show a very high capability. Nowadays, since they are widely needed and used in chemistry, biology, industry, medicine, molecular recognition, and agriculture, macrocyclic diamides and their related aza-crown compounds have received a lot of significance in the mentioned fields [1].

Macrocyclic diamides are prepared through Mannich condensation. They are also used as a heteronuclear metal ion receptor. Such a receptor is designed to simultaneously bind soft-transition and hard-alkali or alkaline earth metal ions, which results in one molecule or a supramolecular mass. Since the important function of heteronuclear metal ion receptors in binding two metal ions influences the redox properties of the cation of the complexed transition metal, heteronuclear metal ion receptors have become significantly important [2].

Reducing the size of devices and machines and making them as light as possible is the general trend of the present time—which sometimes bears with itself the name of "knowledge age." The goal of this trend is to facilitate the use of devices and machines and prevent extravagance and waste. In recent years, and with the rapid growth of supramolecular chemistry, the supramolecular bottom-up approach provides an endless number of possible designs and ways of constructing artificial molecular devices and machines. Such machines feasibly perform a wide variety of functions. They can be employed in signal transfer (in the form of energy, electrons, protons, etc.), energy conversion (e.g. conversion of light into an electrochemical potential), and a wide variety of mechanical aspects (e.g. transportation of a cargo through a membrane). So far, efforts for constructing molecular components which are to be used in information processing have been able to develop chemicals at nanoscale which have the capability of operating as wires, switches, memories, sensors, antennas, plug socket and extension cable systems, and logic gates [3].

Through the use of Mannich condensation of phenols and secondary diamines, studies have found a viable method to synthesize mono- and polycyclic aza-crown macrocycles—which hold aromatic fragments [4]. In order to functionalize aza-crown ethers with more ligating units, the Mannich reaction is widely regarded as an effective method [5].

The complexes formed by macrocyclic polyethers with side groups which contain donor atoms (lariat crown ethers) are in a three dimensional coordination sphere shape because the coordination is achieved by the two chains—side and macroring. This feature increases the unusual complexing properties. These properties have no direct correspondence with the extent of size matching between the cation and macroring cavity; instead, they are influenced by the structure of the side substituents [6].

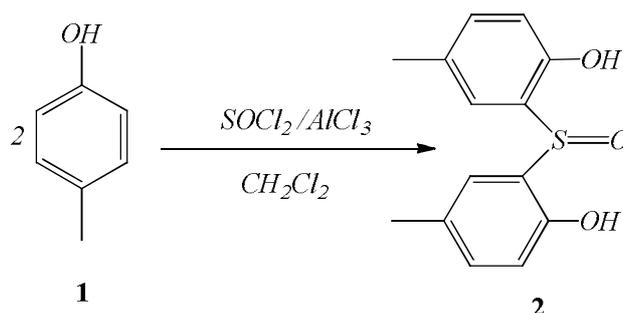
There have been a considerable number of studies concerning methods of transporting cations across an organic liquid membrane separating two water phases. Studies have found that certain natural antibiotic macrocycles are able to change the degree to which a biological membrane is permeable for certain cations to pass through; therefore, to mimic this function, macrocyclic compounds, such as crown ethers, are synthesized and used as model carriers. The complexes which are formed through the reaction between nitrogen-oxygen mixed donor macrocycles and alkali or transition metal cations are stable; consequently, these macrocycles are regarded as desirable receptors for a certain group of cations [7].

Macrocyclic diamides along with lariat ether compounds are widely used in such fields as chemistry, medicine, environmental sciences, nanotechnology, biology, metal separation and transport, industry, and atomic energy. Aza crown ethers together with functional donor groups in the side chain are capable of forming complexes with metal cations, which are stronger than those formed with their unsubstituted analogs. Also, in this case, they show very selective complex formation [8].

Our aim was attempt to developing the aza crown ether improvement through the connection of aromatic fragments (phenolic fragments) into the aza crown macrocyclic structures. These phenolic units make it easier to modify the macrocyclic host with U.V. and/or fluorescent active groups, proton ionizable fragments and functional groups.

MATERIALS AND METHODS

The drawing of chemical formula structure were proceeded ChemBioDraw Version Ultra 12.0. The melting points were measured with an Electrothermal engineering LTD 9100 apparatus. The IR spectra were recorded on Perkin- Elmer model 843 using KBr pellets in the region of 4000-400 cm^{-1} . ^1H NMR spectra were recorded a Bruker Avance Drx 500 MHz spectrometer in CDCl_3 . ^{13}C NMR spectra were recorded a Bruker Avance Drx 125 MHz spectrometer in CDCl_3 . All commercially available chemicals were of analytical grade and were used without further purification. All the materials purchased from Merck and Fluka. The reactions were carried out in an efficient hood. Dichloromethan was dried over P_2O_5 and then distilled from CaH_2 . Toluene was dried over P_2O_5 and then distilled.



Preparation of compound 7

Treatment of bisphenole (**3**) with methyl chloroacetate in the presence of K_2CO_3 and KI by refluxed in dry acetone gave dimethyl ester (**4**) in 98% yield. IR (KBr, cm^{-1}): 2960, 2940, 1760, 1480, 1440, 1280, 1250, 1200, 1150, 1080, 990, 800. ^1H NMR(400 MHz, CDCl_3) δ : 2.2 (s, 6H), 3.7 (s, 6H), 4.65 (s, 4H), 6.8-7.2 (m, 6H).

Macrocyclic diamide (**5**) was prepared by amidation dimethyl ester (**4**) and diethylene triamine in 75%. IR(KBr, cm^{-1}): 3420, 3360, 3040, 2940, 2880, 1680, 1570, 1490, 1280, 1250, 1210, 1080, 1050, 830, 800, 770, 680, 590, 560, 438. ^1H NMR (400 MHz, CDCl_3) δ : 2.21(s, 6H), 2.73-2.76 (m, 3H), 3.33-

3.37 (m, 4H), 4.55 (s, 4H), 6.77-6.79 (d, 2H), 6.87 (s, 2H), 7.04-7.06 (d, 2H), 7.43 (s, 2H). ^{13}C NMR(100 MHz, CDCl_3) δ : 20.97, 39.25, 49.33, 67.88, 112.29, 122.19, 129.7, 132.51, 132.61, 153.58, 168.27.

The new lariat ether compound is prepared according to the literature [2,8]. Preparation of the compound 7: 11-(5-bromo-2-hydroxybenzyl)-2,20-dimethyl-9,10,11,12,13,14-hexahydro-6H-dibenzo[b,e][1,7,4,10,13,16]dioxathiatriazacyclooctadecine-7,15(8H,16H)-dione (**7**): To a solution of 1.35 g (45 mmol) of paraformaldehyde in 50 mL of CH_3OH was added 14.51g (33.8 mmol) of macrocycle compound **5**. After standing for 45 min., CH_3OH was removed and to the residue was added 4.89g (40mmol) of 4-bromophenol and solved in 150 ml of toluene. The mixture was stirred under reflux at 110 °C for 36 h. The solvent was evaporated by rotatory evaporation, and the yellow crystals of (**1**) were formed. The colorless crystals of (**1**) were obtained by recrystallization of compound from methanol. The resulting crystals were collected by filtration and dried. Yield 52%, mp. 169-172 °C. IR (KBr, cm^{-1}): 3735, 3470, 3398, 3036, 2927, 2856, 2080, 1672, 1659, 1533, 1498, 1484, 1451, 1235, 1142, 1055, 873, 797, 665, 560. ^1H NMR (500 MHz, CDCl_3) δ : 2.2 (s, 3H), 2.24 (s, 3H), 2.26(s,2H), 2.34 (s, 3H), 2.79-2.85 (m, 4H), 3.4-3.58 (m,4H), 4.49 (s, 2H), 4.57(s, 2H), 4.6(s, 4H), 6.81-6.82 (d, 2H), 6.92(s, 2 H), 7.09- 7.1 (d,2H), 6.65-7.21 (m,8H), 7.49 (b,7H). ^{13}C NMR (125 MHz, CDCl_3) δ : 16.2, 26.58, 20.91, 20.98, 21.0, 38.8, 39.3, 44.8, 49.3, 67.6, 67.9, 68.3, 112.35, 115.1, 122.3, 127.6, 128.4, 129.7, 131.4, 132.0, 132.6, 132.7, 136.3, 153.6, 165.9, 168.4.

RESULTS AND DISCUSSION

This paper describes the synthesis of the substituted lariat diaza crown ethers. The macrocycle diamid compound 2,20-dimethyl-9,10,11,12,13,14-hexahydro-6H-dibenzo[b,e][1,7,4,10,13,16]dioxathiatriazacyclooctadecine-7,15(8H,16H)-dione (**5**) was prepared according to the literature [9,10,11,12] (Figure 1). In this work, in continuation, the reaction of **5** with phenol derivatives **6** was afforded new substituted aza crown ether (**7**) (Figure 2). In fact, the Mannich reaction of secondary amine in **5** with formalin (formaldehyde) in methanol and then reacted with phenol derivative, was obtained **7**.

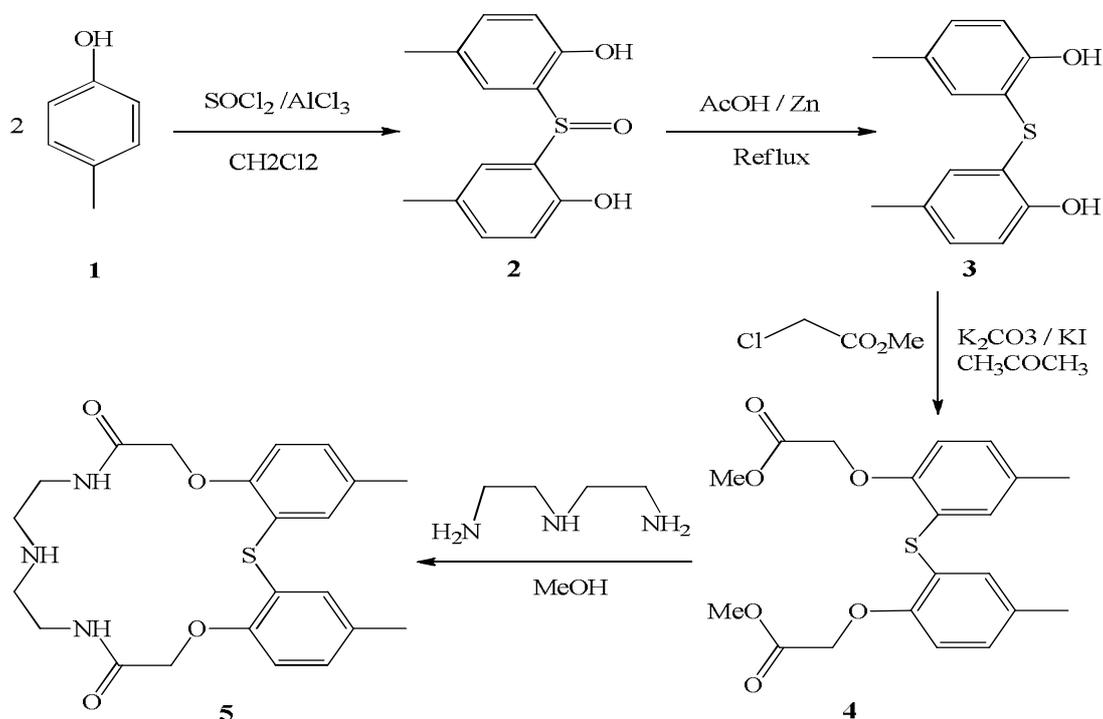


Figure 1. The synthetic route of macrocycle diamide compounds **5** [9,10,11,12].

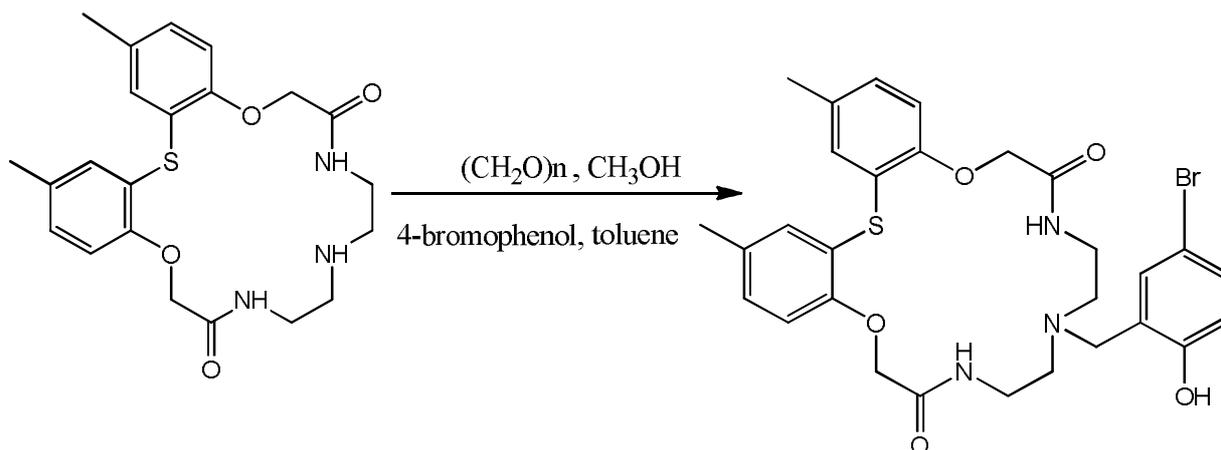


Figure 2. The synthetic route of substituted lariat diaza crown ethers **7**

The best evidence for the substitution of phenyl methylene on secondary amine in diaza crown ether **5a-5b** is the appearance of phenolic hydroxyl group in IR spectra and a peak for methylene group on phenolic ring in ^1H NMR spectra.

It seems that these compounds (phenolic substituted cyclic diaza crown ether **7**) are existed in two tautomeric forms of lactam-lactim forms due to the appearance of nonequivalency in chemical shifts of the methyl substituents on phenyl rings and methylene groups on crown ether cycle (Figure 3). On the other hand, the different in chemical shifts presumably depends to the rigidity and flexibility affect on the diastereotopic character of the protons in the cavity. In comparison with the flexibility of *N*-pivot lariat crown ethers such as 4,13-bis(benzotriazolymethyl)-4,13-diaza-1,7,10,16-tetraoxacyclooctadecane [13], the crown ethers **7** expects to have rigidity due to the existence of two phenyl rings in the diaza crown ether skeleton.

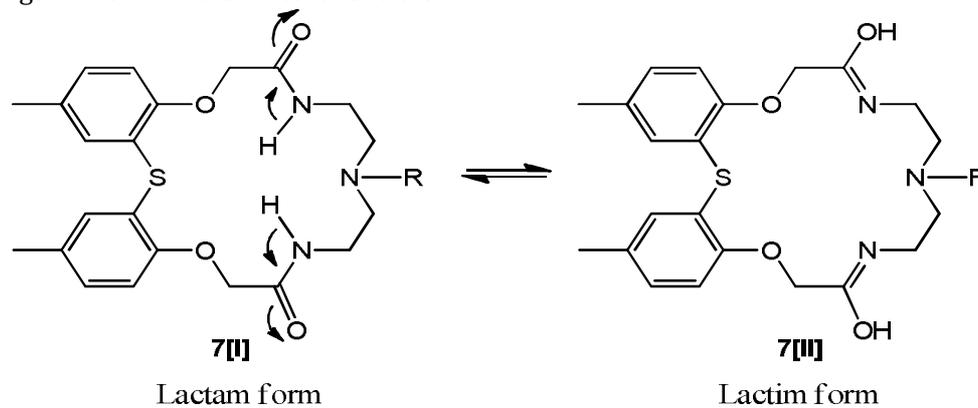


figure 3. Possible lactam-lactim tautomeric forms of **7**.

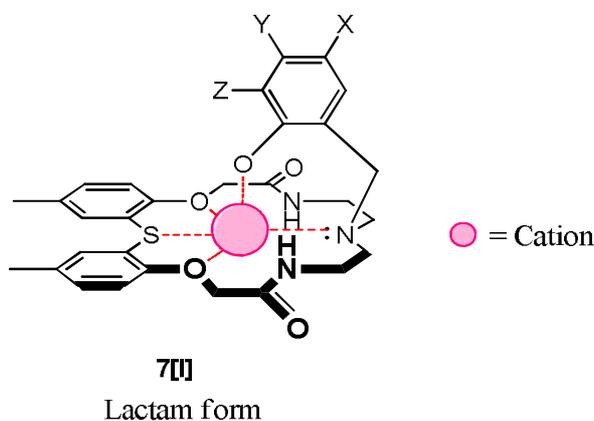


Figure 1. Multidendate behavior of **7** (● is representation of a suitable cation).

CONCLUSION

In summary this method is a very simple, convenient and proper technique the preparation of macrocyclic diamides in moderate to good yields and can be take place in quantitative scales (for example 1-10 gr). Based on ¹H NMR analysis of these macrocycles compared to dibenzosulfoxide macrocycles series in our previous work, these series of macrocycles are more flexible.¹HN MR analysis of these series proved that they are also relatively more flexible compared to smaller macrocycles. As a general result, the smaller the cavity, the more reduction in flexibility was observed. The important point found in this analysis is the rigidity and flexibility affect on the diastereotopic character of the protons in the cavity. The more rigid the cavity due to the more diastereotopic protons. For example there is no diastereotopicity for the protons in the cavity of macrocycle.

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