Synthesis and Crystal Structure of A New Armed-tetraazacrown Ether and Its Liquid Membrane Transport of Alkali Metal Cations

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A new tetra-*N*-substituted tetraazacrown ether derivative　4　7　13　16-tetra 2-cyanobenzyl -1 10-dioxa-4 7 13 16-tetraazacy-clooctadecane　$C_{44}H_{48}N_8O_2$　has been synthesized and structurally characterized．It crystallizes in the monoclinic system space group $P2_1/c$ with $a = 1.1176\ 3$　nm　$b = 2.1906\ 7$　nm $c = 0.8430\ 3$　nm　$V = 2.0132\ 10$　nm^3　$\beta = 102.740\ 5$ ° $Z = 4$　$D_c = 1.189$ g/cm^3　final $R_1 = 0.0460$　$wR_2 = 0.0803$. The liquid membrane transports of alkali metal cations using the new macrocycle as the ion-carrier were also studied．Compared with some macrocyclic ligands　our newly synthesized ligand showed a good selectivity ratio for Na$^+$/Li$^+$．

Keywords　　　　tetraazacrown ether　crystal structure　liquid membrane transport

Introduction

　　Transport of cations across an organic liquid membrane which separates two water phases has been extensively investigated.[1] The synthetic macrocyclic ligands such as crown ethers　are usually used as model carriers to mimic the naturally occurring antibiotic macrocycles which have been shown to alter the permeability of biological membranes to certain cations.[2,3] Thus　they have important applications in both chemistry and biology to selective complexation of various metal cations.[4,5] It was reported that the divalent transition-metal complexes of tetraaza-macrocyclic ligand with four 2-cyanoethyl pendent groups exhibited antitumor activity.[6] Nitrogen-oxygen mixed donor macrocycles can form stable complexes with both alkali and transition metal ions　therefore　they have received much attention as receptors for a range of metal ions and other cations.[7,8] It has been clearly documented that the coordination properties of such ligands often span those of the well studied crown polyethers and polyaza categories of macrocycle．These macrocycles chosen as membrane carriers should have limited water solubility to prevent loss of carrier to water phases.[9] In recent years　many macrocyclic azacrown ethers have been synthesized and their liquid membrane transport have been studied.[10-13] In our pre-vious work　we have synthesized the nitrogen-oxygen donor macrocycle　1 10-dioxo-4 7 13 16-tetraazacyclooctadecane　and its complexes with lanthanum III　ion[14] and transition metal ions.[15] Because 1 10-dioxo-4 7 13 16-tetraazacyclooctadecane is an amphiphile which can be soluble both in aqueous solution and organic solvent　it is not an suitable carrier in liquid membrane transport．In addition　the pendent cyano groups could hydrolyze to be a co-ordinating carboxyl groups which will have enhanced coordination property compared with the unsubstituted parent macrocycles.[16,17] Aiming at the hydrolysis and enhancing the lipophilic property of the azacrown ether　we synthesized the new azacrown ether compound which contain the hydrolysable cyanobenzyl groups．Herein we report the crystal structure of the new compound and the liquid membrane transports of alkali metal actions with it as the ion-carrier．

Experimental

Materials and methods

　　All commercially available chemicals were of analytical grade and were used without further purification．C　H and N were determined using a Elementar vario EL elemental analyzer．UV-vis spectra in aqueous solution were recorded on a GBC Cintra 10e UV-Visible spectrophotometer．IR spectra were recorded on a Nicolet-AVATAR 360 FT-IR spectrometer using KBr pellets in the region of 4000—400 cm^{-1}．^{1}H NMR spectra were recorded on a Varian 500 Bruker spectrometer in CDCl$_3$．

　　The following crown ethers **1** and **2** were prepared according to the reported method[18] with minor modification．
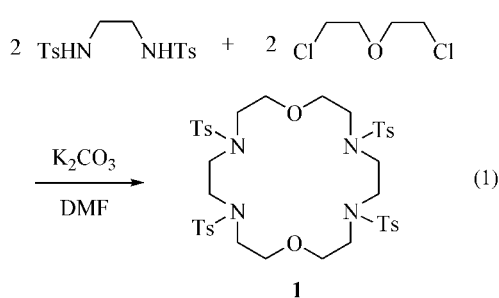
Preparation of 4 7 13 16-tetra 4-methylphenylsulfonyl -1 10-dioxo-4 7 13 16-tetraazacyclooctadecane **1**

　　The crown ether **1** was prepared following Eq．1．

A mixture of ditosyl ethylenediamine[19] 33.3 g 0.09 mol K_2CO_3 18 g 0.13 mol and 2-chloroethyl ether 11.9 mL in dimethylformamide 40 mL was heated on an oil bath at 170 ℃ for 10 h. After cooling to room temperature water 100 mL was added to the reaction mixture. The resulting precipitate was washed thoroughly several times with water then washed with acetone 100 mL . The crude product was recrystallized from DMF to give the crown ether **1** as white prism-shape solid. Yield 20% m.p. 245—247 ℃ lit.[18] 245 ℃ .

Preparation of 1 10-*dioxo-*4 7 13 16-*tetraazacycloocta-decane* **2**

The crown ether **2** was prepared following Eq. 2 .
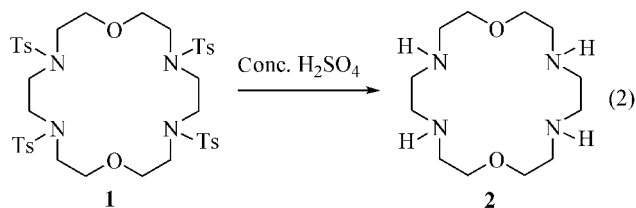

A solution of tetra 4-methylphenylsulfonyl tetraazacrown **1** 15 g in conc. H_2SO_4 40 mL was heated at 100 ℃ for 3 d. The reaction mixture was treated with excess sodium hydroxide solution and the pH of the resultant mixed solution was adjusted to 11—12 then extracted with chloroform dried with anhydrous sodium sulfate and evaporated. The residual oil was recrystallized from *n*-heptane to yield the tetraazacrown ether **2** as colorless needles. Yield 40% m.p. 59—60 ℃ lit.[18] 58—60 ℃ . Anal. calcd for C_{12}H_{28}N_4O_2 C 54.46 H 10.62 N 20.92 found C 54.36 H 10.76 N 21.12.

Preparation of 4 7 13 16-*tetra* 2-*cyanobenzyl* -1 10-*dioxa-*4 7 13 16-*tetraazacyclooctadecan* **3**

A mixture of **2** 0.26 g 1 mmol and anhydrous K_2CO_3 1.10 g 8 mmol was refluxed in 15 mL of acetonitrile for 4 h then 15 mL of acetonitrile solution of 2-bromomethylbenzonitrile 0.78 g 4 mmol was added. The mixture was refluxed for another 20 h. The precipitate was filtered out and the mother liquor was cooled slowly to room temperature. The crystals were collected and recystallized from dichloromethane/acetonitrile 1∶5 V∶V

mixture to give the compound **3** as plate colourless crystals suitable for X-ray diffraction analysis. Yield 70% m.p. 119—121 ℃ ^{1}H NMR CDCl_3 500 MHz δ 2.79—2.83 m 16H NCH_2 3.56—3.58 t J = 5.5 Hz 8H OCH_2 3.80 s 8H CH_2 7.31—7.34 t J = 7.7 Hz 4H ArH 7.49—7.53 m 4H ArH 7.59—7.61 d J = 7.7 Hz 8H ArH IR KBr ν 2223 1596 1447 1364 1350 1310 1121 1064 1051 937 772 561 cm^{-1}. Anal. calcd for C_{44}H_{48}N_8O_2 C 73.29 H 6.66 N 14.89 found C 72.69 H 5.99 N 14.89.
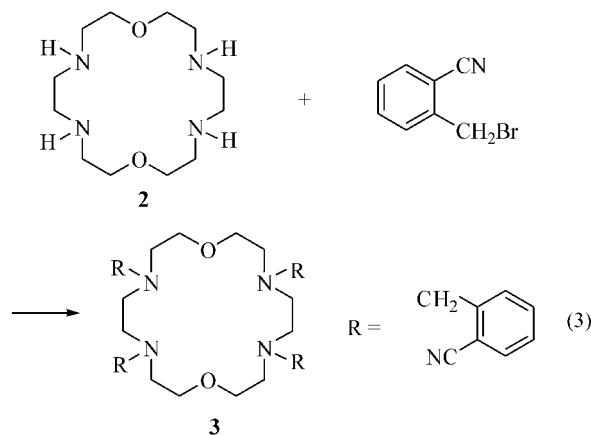
X-*Ray crystallography*

A crystal with dimensions 0.3 mm × 0.25 mm × 0.20 mm was selected for X-ray diffraction experiment. The measurements were performed on a SMART 1000 CCD diffractometer at 293 K with graphite monochromatized Mo Kα radiation λ = 0.071073 nm . The structure was solved by direct methods and refined by full-matrix least-squares on F^2 using the SHELX-97 program. All nonhydrogen atoms were refined anisotropically. The hydrogen atoms were located by difference Fourier synthesis and refined isotropically. A summary of the crystallographic data and details of the structure refinements are listed in Table 1.

Transport of cations across a liquid membrane

The apparatus used for the liquid membrane transport was made consulting the literature[20] as shown in Fig. 1. The transport experiment was performed at 25 ± 0.5 ℃ in a thermostatic water bath magnetic bar 20 mm in length and 6 mm in diameter 160 r/min. Dichloromethane of reagent grade was shaken with deionized water four times and to saturate the solvent with water.[21] Phase 1 the source phase 20 mL of the mixed solution of alkali-metal nitrate or metal hydroxide[22] 0.1 mol/L and picric acid 2 × 10^{-3} mol/L .[23] Phase 2 receiving phase deionized water 20 mL . Phase 3 liquid membrane 50 mL of dichloromethane solution of the macrocycle to be studied 4 × 10^{-4} or 7 × 10^{-4} mol/L . The concentration of the metal picrate in the receiving phase was monitored

Table 1 Crystal data and structure refinement of the title compound

Empirical formula	$C_{44}H_{48}N_8O_2$
Formula weight	720.90
Temperature	293 2 K
Wavelength	0.071073 nm
Crystal system space group	Monoclinic $P2_1/c$
Unit cell dimensions	$a = 1.1176$ 3 nm $\alpha = 90°$
	$b = 2.1906$ 7 nm $\beta = 102.740$ 5 °
	$c = 0.8430$ 3 nm $\gamma = 90°$
Volume	2.0132 10 nm^3
Z Calculated density	4 1.189 g/cm^3
Absorption coefficient	0.075 mm^{-1}
F 000	768
Crystal size	0.30 mm × 0.25 mm × 0.20 mm
θ range for data collection	1.86°—25.35°
Limiting indices	$-13 \leqslant h \leqslant 13$ $-26 \leqslant k \leqslant 24$ $-7 \leqslant l \leqslant 10$
Reflections collected/unique	8491/3690 $R_{int} = 0.0532$
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9851 and 0.9778
Refinement method	Full-matrix least-squares on F^2
Goodness-of-fit on F^2	0.964
Final R indices $I > 2\sigma$ I	$R_1 = 0.0460$ $wR_2 = 0.0803$
R indices all data	$R_1 = 0.1180$ $wR_2 = 0.0945$

by the UV-vis absorption of the picrate at 355.0 nm. Standard curves were obtained from the solution with known concentrations.
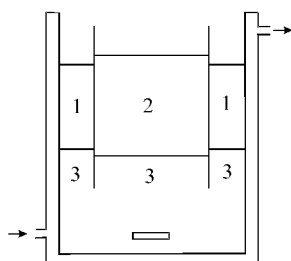

Fig. 1 Liquid membrane cell. 1 The source phase 2 receiving phase 3 liquid membrane.

Results and discussion

Description of the crystal structure

Fig. 2 shows the molecular structure of the title compound **3**. The selected bond lengths and angles are listed in Table 2. The macrocycle has a crystallographic center of symmetry. In the solid state the structure could be described as a pre-organized three-dimensional host. Four cyanobenzyl groups in the molecule are roughly in a 1 2-alternate conformation with two cyanobenzyl groups being above the tetraazacrown ring and the other two below it. This is similar to the structure of 4 7 13 16-tetrathenoyl-1 10-dioxa-4 7 13 16-tetraazacyclooctadecane [24] in contrast to the structure of tetra *N*-substituted cyclanes where four functional groups oriented on the same side of the ring. [25]
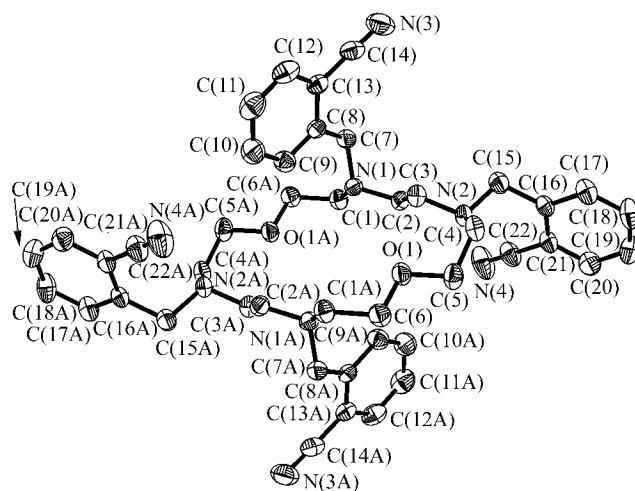

Fig. 2 Molecular structure of the title compound **3**.

The six donor atoms of crown ring N 1 N 2 N 1A N 2A O 1 and O 1A are not coplanar and adopt a chair conformation. The deviations from the mean plane defined by N 1 N 2 N 1A N 2A O 1 and O 1A are -0.03160 0.02351 0.03159 -0.02350 -0.03126 and 0.03125 nm respectively. The N 2 and N 2A atoms reside 0.10504 nm above and below the N_2O_2 plane N 1 N 1A O 1 and O 1A and both are 0.3930 nm far from the symmetry center. The dihedral angles of 0° demonstrate that the ring C 8 —C 13 is parallel to the ring C 8A —C 13A as the ring C 16 —C 21 with the ring C 16A —C 21A . The dihedral angle between the ring C 8 —C 13 or C 8A —C 13A and the N_4 plane defined by N 1 N 2 N 1A and N 2A is 88.0°. The dihedral angle

Table 2   Selected bond lengths   nm   and bond angles   °   of the title compound **3**[a]

bond length			
N 1 —C 2	0.1461 2	C 1 —C 6 #1	0.1502 3
N 1 —C 7	0.1461 2	C 2 —C 3	0.1510 2
N 1 —C 1	0.1465 2	C 4 —C 5	0.1498 3
N 2 —C 4	0.1466 2	C 6 —C 1 #1	0.1502 3
N 2 —C 15	0.1466 2	C 8 —C 13	0.1391 3
N 2 —C 3	0.1468 2	C 13 —C 14	0.1438 3
N 3 —C 14	0.1136 3	C 15 —C 16	0.1499 3
N 4 —C 22	0.1137 3	C 16 —C 21	0.1383 3
O 1 —C 6	0.1411 2	C 21 —C 22	0.1447 3
O 1 —C 5	0.1417 2		
bond angle			
C 2 -N 1 -C 7	112.67 16	N 1 -C 7 -C 8	113.46 17
C 2 -N 1 -C 1	110.77 15	N 3 -C 14 -C 13	177.3 3
C 7 -N 1 -C 1	112.70 16	N 3 -C 14 -C 13	177.3 3
C 4 -N 2 -C 15	109.85 16	N 2 -C 15 -C 16	111.48 17
C 4 -N 2 -C 3	111.38 15	N 4 -C 22 -C 21	176.1 3
C 15 -N 2 -C 3	110.75 16	C 12 -C 13 -C 14	118.7 2
C 6 -O 1 -C 5	113.03 16	C 7 -C 8 -C 13	120.8 2
N 1 -C 1 -C 6 #1	113.65 17	C 8 -C 13 -C 14	120.2 2
N 1 -C 2 -C 3	111.80 16	C 21 -C 16 -C 17	116.8 2
N 2 -C 3 -C 2	111.82 16	C 21 -C 16 -C 15	121.03 19
N 2 -C 4 -C 5	114.46 17	C 16 -C 21 -C 22	120.1 2
O 1 -C 5 -C 4	111.57 18	C 20 -C 21 -C 22	118.1 2
O 1 -C 6 -C 1 #1	108.84 17		

[a] Symmetry transformations used to generate equivalent atoms   #1   − x + 1   − y   − z + 1.

between the ring C 16 —C 21   or C 16A —C 21A and the above N₄ plane is 79.5°. All these data demonstrate that these four aromatic rings are nearly vertical to the N_4 plane of the crown ring. The dihedral angles between two adjacent aromatic rings are all 61.2°   indicating a high symmetry of the molecule.

Transport of alkali metal cations

The title compound can form 1:1 type complex with alkali metal picrate   so it can be used as cation carrier. The experiment was performed through a dichloromethane membrane separating two aqueous solutions. The alkali metal picrates were transported with the aid of the ligand from an aqueous phase   phase 1   to another aqueous phase   phase 2 . The picrate concentration was found to increase in phase 2   detected by UV-vis spectrophotometry.

The transport of Li^+ Na^+ and K^+ cations was studied individually from an aqueous solution which contained a mixture of metal nitrate   or metal hydroxide   and picrate. The transported co-anion should be the picrate because of its lipophilic property. In the control experiment it was shown that no transport was detectable in the absence of the carrier. In addition   the transport experiments with the standard dibenzo-18-crown-6 were also carried out and established that our apparatus gave the results in fair good agreement with those reported in the literatures.[23 26] The transport rates were calculated from the linear part of the

transport curves. The transport rates and selectivity ratios are given in Table 3.

From the investigation it is established that the nature of the species   the ring size   the kind of donor and substituting group   and concentration of the crown ether have an important effect on cation transport.[9 27 28] The 18-crown-6 systems preferentially transport the size-matched K^+ ion. Although a direct comparison is difficult to make with different individual experiments   the dibenzo-18-crown-6 however   transports metal ions much more efficiently under the same experimental conditions. The transport rate of the new macrocycle here prepared seems not very high. According to the hard-soft acid-base theory   the rather soft nitrogen donors can not coordinate as well to hard alkali-metal cations as hard oxygen donors. The steric inhibition of the four cyanobenzyl groups also affect the coordination ability. In addition   from the molecular structure of the title compound   it can be seen that the crown ether ring is twisted to result in a decrease of its efficient cavity size. From the results of the transport experiment   several conclusions can be drawn as following   1 Along with the increase of the carrier concentration   the transport rates for Li^+ Na^+ and K^+ all become larger   but the selectivity ratios for Na^+/Li^+ K^+/Li^+ and K^+/Na^+ did not vary.   2 In the source phase   the nature of counter anions   nitrate or hydroxide   hardly affected the transport rates for Li^+ Na^+ and K^+.   3   The transport rate of K^+ by the new ligand is superior to that of the other two alkali metal cations and the selectivity order is $K^+ > Na^+ \gg Li^+$.   4

Table 3 Transport rates and selectivity ratios of alkali metal picrates through a liquid membrane

Carrier concentration mol/L	Cation	Transport rate 10^{-8} mol/h	Selectivity ratio		
			Na^+/Li^+	K^+/Li^+	K^+/Na^+
4×10^{-4} [a]	Li^+	0.20			
	Na^+	5.9	29.5	43.5	1.5
	K^+	8.7			
4×10^{-4} [b]	Li^+	0.18			
	Na^+	5.5	30.5	45.5	1.5
	K^+	8.2			
7×10^{-4} [a]	Li^+	0.24			
	Na^+	7.4	30.8	44.1	1.4
	K^+	10.6			
7×10^{-4} [b]	Li^+	0.22			
	Na^+	7.0	31.8	44.5	1.4
	K^+	9.8			

[a] The source phase 20 mL of the mixed solution of alkali-metal nitrate 0.1 mol/L and picrate 2×10^{-3} mol/L [b] the source phase 20 mL of the mixed solution of alkali-metal hydroxide 0.1 mol/L and picrate 2×10^{-3} mol/L .

The average transport selectivity ratios for Na^+/Li^+ K^+/Li^+ and K^+/Na^+ are 30.6 44.4 and 1.4 respectively.

Though variations in the stirring speed and other factors do not permit precise comparisons of the transport efficiency with other carriers to our ligand the absolute rate of transport is 10—8 mol/h which is in fair good agreement with those obtained in other laboratories.[10 12 22 23 26] Compared with some macrocyclic ligands our newly synthesized ligand may decrease the selectivity ratio for K^+/Na^+ and K^+/Li^+ but increase that for Na^+/Li^+ therefore providing a new efficient carrier for Na^+/Li^+ separation.[11 23 26]

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