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Synthesis of Monoazacrown Ethers under Phase-Transfer Catalysis

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Abstract—A procedure has been proposed for the synthesis of monoazacrown ethers by reaction of *N*-benzyldiethanolamine with oligo(ethylene glycol) bis-*p*-toluenesulfonates in a two-phase system aromatic hydrocarbon–50% aqueous alkali, followed by removal of the benzyl group by catalytic hydrogenolysis. The maximal yields of *N*-benzylaza-12-crown-4, -18-crown-6, and -21-crown-7 were achieved by adding 4–10 equiv of LiCl, $BaBr_2$, and CsCl, respectively, to the reaction mixture, which probably indicated template effect.

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Persistent interest in azacrown ethers over past decades [1] is related primarily to their unusual complexing properties which may be regarded as intermediate between the properties of crown ethers that firmly bind alkali and alkaline-earth metal cations and cyclic polyamines that form stable complexes with heavy and transition metal ions. In addition, azacrown ethers attract attention as convenient starting compounds for the synthesis of various lariat crown ethers, including those containing chromogenic, fluorescent, photochromic, and other fragments, bis-crown ethers, and biologically active substances based thereon.

Monoazacrown ethers are generally prepared by alkylation of unsubstituted or N-protected diethanolamine with the corresponding oligo(ethylene glycol) bis-*p*-toluenesulfonates or dichlorides in the presence of alkali metal *tert*-butoxides or sodium hydride in anhydrous solvents (*t*-BuOH, dioxane, THF, DMSO, or DMFA) and subsequent removal of the protecting group [2–4]. Intramolecular cyclization of *N*,*N*-bis(oligooxyethylene)amines in the presence of an equimolar amount of arenesulfonyl chloride or excess alkali metal hydroxide in dioxane [5] and reaction of *p*-toluenesulfonamide with oligo(ethylene glycol) bis-*p*-toluenesulfonates [6] were used more rarely. As protecting groups, *p*-toluenesulfonyl [7], triphenylmethyl [8], benzyl [9], and cyano groups [10] were reported. 1-Benzyl-1-aza-12-crown-4 is generally synthesized from benzylamine and diiodide derived from tetraethylene glycol [11].

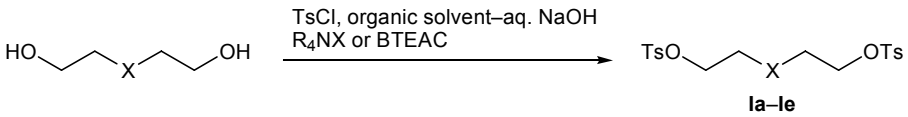
The above listed procedures require large volumes of anhydrous solvents and large amounts of alkali metal hydrides or *tert*-butoxides as bases and ensure relatively low yields of monoazacrown ethers, which strongly restricts the scope of their practical application. In some cases, additional purification of the target products by column chromatography [3] or by transformation into complexes with alkali metal thiocyanates [2] is necessary.

We previously showed [12] that di- and polyazacrown ethers and cryptands can be synthesized under conditions of phase-transfer catalysis. Taking into account that the described procedure is free from the above disadvantages, in the present work we developed a convenient method for the synthesis of monoazacrown ethers via macrocyclization of *N*-benzyldiethanolamine with oligo(ethylene glycol) bis-*p*-toluenesulfonates in a two-phase system, followed by removal of the benzyl group from intermediate *N*-benzylmonoazacrown ethers.

Initial oligo(ethylene glycol) bis-*p*-toluenesulfonates **Ia**–**Ie** were synthesized by acylation of the corresponding glycols with *p*-toluenesulfonyl chloride in a two-phase system consisting of an organic solvent and aqueous sodium hydroxide in the presence of

† Deceased.

Scheme 1.



Ia–Ie

X = O (**a**), OCH_2CH_2O (**b**), $O(CH_2CH_2O)_2$ (**c**), $O(CH_2CH_2O)_3$ (**d**), *o*-OC_6H_4O (**e**).

Table 1. Reaction of oligo(ethylene glycols) with *p*-toluenesulfonyl chloride

Compound no.	Base	Concentration of NaOH, %	Organic solvent	Temperature, °C	Catalyst	Yield, %
Ia	Et_3N	–	Dioxane	5	–	80
	NaOH	15	CH_2Cl_2	5	BTEAC	46
	NaOH	20	CH_2Cl_2	5	BTEAC	61
	NaOH	30	CH_2Cl_2	5	BTEAC	84
	NaOH	35	CH_2Cl_2	5	BTEAC	86
	NaOH	45	CH_2Cl_2	5	BTEAC	78
	NaOH	30	THF	5	BTEAC	76
	NaOH	20	THF	5	BTEAC	77
	NaOH	30	CH_2Cl_2	5	Bu_4NBr	69
	NaOH	30	CH_2Cl_2	5	Bu_4NI	65
	NaOH	30	CH_2Cl_2	5	–	65
	NaOH	30	CH_2Cl_2	5–10	BTEAC	83
	NaOH	30	CH_2Cl_2	8–20	BTEAC	82
	NaOH	30	CH_2Cl_2	8–20	–	68
Ib	Et_3N	–	Dioxane	5	–	85
	NaOH	17.5	Dioxane	5	BTEAC	74
	NaOH	17.5	Dioxane	8–21	–	76
	NaOH	30	CH_2Cl_2	5	BTEAC	86
	NaOH	30	CH_2Cl_2	8–20	BTEAC	86
	NaOH	30	CH_2Cl_2	10–15	Bu_4NBr	67
Ic	Et_3N	–	Dioxane	5	–	90
	NaOH	30	CH_2Cl_2	5–15	BTEAC	96
Id	Et_3N	–	Dioxane	5	–	84
	NaOH	30	CH_2Cl_2	5–15	BTEAC	94
Ie	Et_3N	–	Dioxane	5	–	80
	NaOH	17.5	THF	5	–	87
	NaOH	17.5	Dioxane	5	–	85
	NaOH	30	Chloroform	5	BTEAC	52
	NaOH	30	CH_2Cl_2	5	BTEAC	82
	NaOH	30	CH_2Cl_2	10–15	BTEAC	90
	NaOH	30	CH_2Cl_2	16–20	BTEAC	90

Table 2. Yields of *N*-benzylazacrown ethers **IIa**–**IIe**, depending on the nature and amount of phase-transfer catalyst and temperature[a]

Comp. no.	Catalyst	Amount of catalyst, mol	Temperature, °C	Yield, %	Comp. no.	Catalyst	Amount of catalyst, mol	Temperature, °C	Yield, %
IIa	Bu_4NBr	0.25	55	39	**IIc**	Bu_4NI	0.25	65	69
	Bu_4NI	0.25	60	63		Bu_4NBr	0.25	70	73
	Bu_4NI	0.25	65	70		Bu_4NBr	0.25	75	58
	Bu_4NBr	0.25	70	71		Bu_4NBr	0.25	85	46
	Bu_4NI	0.25	75	65		Bu_4NBr	0.15	70	65
	Bu_4NBr	0.25	85	48		Bu_4NBr	0.1	70	41
	Bu_4NI	0.15	65	64		Bu_4NCl	0.25	70	48
	Bu_4NI	0.1	65	38		Et_4NBr	0.25	70	17
	Bu_4NI	0.3	65	70	**IId**	Bu_4NI	0.25	55	26
	BTEAC	0.25	70	47		Bu_4NI	0.25	65	56
	Bu_4NCl	0.25	70	56		Bu_4NBr	0.25	70	58
IIb	Bu_4NBr	0.25	55	30		Bu_4NI	0.25	85	32
	Bu_4NBr	0.25	60	63		Bu_4NBr	0.1	70	27
	Bu_4NI	0.25	65	78		BTEAC	0.25	65	27
	Bu_4NBr	0.25	70	75		Et_4NBr	0.25	65	21
	Bu_4NBr	0.25	75	66	**IIe**	Bu_4NBr	0.25	55	31
	Bu_4NBr	0.25	85	50		Bu_4NBr	0.25	60	67
	Bu_4NBr	0.15	70	67		Bu_4NBr	0.25	65	42
	Bu_4NBr	0.1	70	47		Bu_4NBr	0.25	70	70
	Bu_4NBr	0.3	70	74		Bu_4NBr	0.25	75	63
	Bu_4NHSO_4	0.025	70	43		Bu_4NBr	0.25	85	40
	Et_4NBr	0.25	70	22		Bu_4NBr	0.1	65	38
IIc	Bu_4NBr	0.25	55	33		Bu_4NCl	0.25	65	33
	Bu_4NBr	0.25	60	60		Et_4NI	0.25	65	12

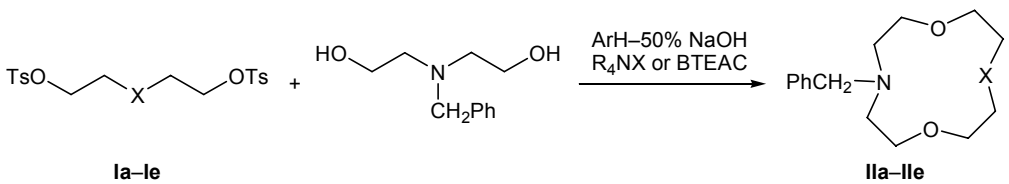
[a] Molar ratio *N*-benzyldiethanolamine–**I** 1 : 1.

quaternary ammonium salts (Scheme 1). Unlike known methods [13–15], this procedure requires neither low temperature conditions nor additional purification of oily tetra- and pentaethylene glycol bis-*p*-toluenesulfonates by column chromatography.

The data in Table 1 show that, among the examined solvents, methylene chloride and THF ensured the best results, regardless of the concentration of alkali and catalyst nature. The optimal concentration of alkali was 30–35%, and the most efficient phase-transfer catalyst was benzyltriethylammonium chloride (BTEAC) (as compared to Bu_4NBr and Bu_4NI). The yield of **Ia**–**Ie** almost did not depend on the temperature in the range from 0 to 20°C.

Bis-*p*-toluenesulfonates **Ia**–**Ie** were brought into reaction with *N*-benzyldiethanolamine in a two-phase system aromatic hydrocarbon–50% aqueous alkali in the presence of a quaternary ammonium salt. As aromatic solvent we used benzene, toluene, or xylene (Scheme 2). Decrease of the alkali concentration below

Scheme 2.



Ia–Ie **IIa–IIe**

Table 3. Effect of the ratio of the aqueous and organic phases on the yield of *N*-benzylazacrown ethers **IIa**–**IIe**

Compound no.	Volume ratio 50% NaOH–benzene, ml	Yield, %
IIa[a]	50:650 (1:13)	33
	65:635 (1:9.8)	41
	87.5:612.5 (1:7)	61
	100:600 (1:6)	71
	350:350 (1:1)	72
	400:300 (1:0.75)	71
IIb	50:650 (1:13)	34
	87.5:612.5 (1:7)	65
	100:600 (1:6)	75
	400:300 (1:0.75)	71
IIc[b]	65:635 (1:9.8)	55
	82.5:612.5 (1:7)	68
	100:600 (1:6)	73
IId[c]	50:650 (1:13)	29
	82.5:612.5 (1:7)	49
	100:600 (1:6)	58
IIe	65:635 (1:9.8)	32
	82.5:612.5 (1:7)	63
	100:600 (1:6)	70

[a] In the presence of LiCl,
[b] In the presence of KBr,
[c] In the presence of CsCl.

50% led to sharp reduction of the yield of target azacrown ethers **IIa**–**IIe**, presumably as a result of increase of the rate of hydrolysis of both initial bis-*p*-toluenesulfonates and diethanolamine salt. The yield of **IIa**–**IIe** strongly depended on the nature and amount of phase-transfer catalyst and on the temperature. The optimal ratio catalyst–*N*-benzyldiethanolamine–**I** was 0.25:1:1 (Table 2); this ratio ensured the best yields of the cyclic products. Reduction of the amount of the catalyst resulted in a lower yield of azacrown ethers, whereas increase of the catalyst concentration did not affect the yield of **II** to an appreciable extent, but hampered isolation of the products, so that the use of a larger amount of the catalyst is undesirable. Change of the reactant ratio to non-equimolar also strongly reduced the yield and favored formation of a large amount of polymeric products.

Among the examined catalysts (Bu_4NI, Bu_4NBr, Bu_4NCl, Et_3BnNCl, Bu_4NHSO_4, Et_4NI, and Et_4NBr), tetrabutylammonium bromide and iodide showed the best results. The optimal temperature was 70±2°C in the reaction catalyzed by tetrabutylammonium bromide and 65±2°C in the reaction with Bu_4NI. Lower yields of *N*-benzylazacrown ethers at lower or higher temperature (Table 2) may be rationalized by reduction of the rate of macrocyclization or formation of a considerable amount of oligomeric products due to increased rate of polycondensation.

The reactant concentration also appreciably affected the yield of the cyclization products. The maximal yields were obtained at a concentration of 0.01–0.11 M. Increase in their concentration was accompanied by reduction of the yield and strong tarring, whereas insignificant increase of the yield at lower concentration (<0.01 M) cannot be regarded as profitable because of considerable reduction of the yield per unit volume of the reaction mixture.

In addition, an important factor was the volume ratio of the aqueous and organic phases, the optimal value being 1:6. Raising the fraction of the organic solvent resulted in reduced yield, whereas increase in the fraction of aqueous alkali did not affect the yield, but led to inefficient consumption of NaOH (Table 3). One more important factor determining the yield of *N*-benzylazacrown ethers was the nature of alkali. The maximal yield of 15-membered azacrown ethers was obtained with the use of NaOH, while KOH and CsOH were the most efficient in the synthesis of 1-benzyl-1-aza-18-crown-6 (**IIc**) and 1-benzyl-1-aza-21-crown-7 (**IId**), respectively. Taking into account that a 50% solution of LiOH cannot be prepared and that the reaction at lower concentration of alkali gives unsatisfactory results, 1-benzyl-1-aza-12-crown-4 (**IIa**) was synthesized in 45% yield using a 50% solution of NaOH containing 5–10 equiv of LiOH (with respect to **Ia**).

These findings indicated template effect of metal cation, which is well known in the synthesis of macrocyclic polyethers but still remains questionable as applied to azacrown ethers [9, 16]. Some authors [17] presumed dual template effect of metal cation in the synthesis of azacrown ethers. We examined the effect of addition of alkali and alkaline-earth metal salts on the yield of *N*-benzylazacrown ethers. The reactions were carried out under the same conditions as above, but 2–10 equiv of the corresponding metal salt was added to the aqueous phase (Table 4). The yield of **IIa** considerably increased in the presence of lithium salts and attained its maximal value upon addition of 4–10 equiv of LiHlg. In the synthesis of 1-benzyl-1-aza-15-crown-5 (**IIb**), addition of metal salts did not produce an appreciable effect on the yield if aqueous

Table 4. Effect of the nature and amount of added salt on the yield of *N*-benzylazacrown ethers **IIa**–**IIe**

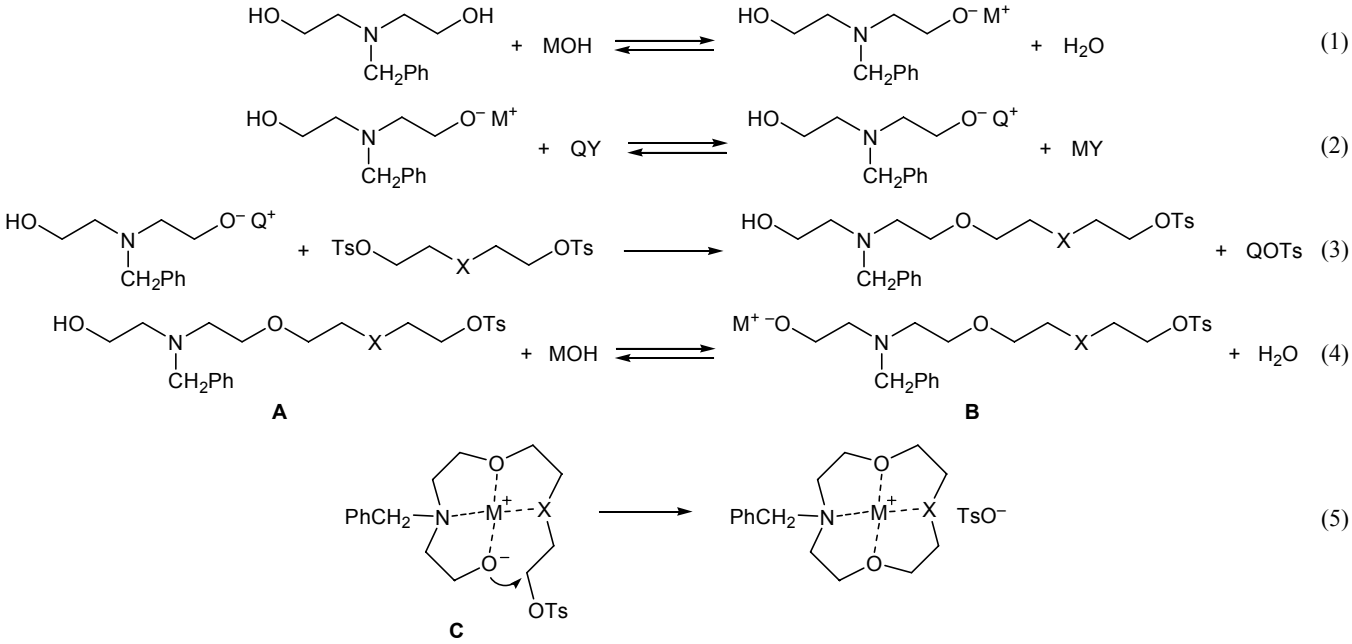
Compound no.	Base	Salt	Amount of salt, mol	Yield, %	Compound no.	Base	Salt	Amount of salt, mol	Yield, %
IIa	NaOH	–	0	42	**IIc**	NaOH	CsCl	4	71
	NaOH	$LiClO_4$	2	25		NaOH	RbCl	4	48
	NaOH	LiCl	1	54		NaOH	$SrCl_2$	4	65
	NaOH	LiCl	2	56		NaOH	$BaBr_2$	4	74
	NaOH	LiCl	4	71		KOH	–	0	59
	NaOH	LiCl	8	71		KOH	$BaBr_2$	4	72
	NaOH	LiCl	10	72	**IId**	NaOH	–	0	36
	NaOH	LiBr	4	71		NaOH	$CsClO_4$	2	36
	NaOH	LiBr	10	72		NaOH	CsCl	3.3	37
	NaOH	NaBr	4	48		NaOH	CsCl	4.7	49
	KOH	LiCl	4	58		NaOH	CsCl	10	58
IIb	NaOH	–	0	72		NaOH	$BaBr_2$	10	47
	NaOH	LiCl	4	70		KOH	–	0	42
	NaOH	NaBr	4	68		KOH	$CsClO_4$	4	41
	NaOH	$BaBr_2$	2.7	58		KOH	RbCl	4	46
	KOH	–	0	61	**IId**	KOH	$BaBr_2$	4	50
IIc	KOH	NaBr	4	72		CsOH	–	0	48
	CsOH	–	0	44	**IIe**	NaOH	–	0	70
	CsOH	NaBr	4	69		NaOH	LiBr	4	65
	NaOH	–	0	51		NaOH	NaCl	6	63
	NaOH	$KClO_4$	2	45		NaOH	$SrCl_2$	4	67
	NaOH	KCl	6	69		KOH	–	0	58
	NaOH	KBr	5	56		KOH	NaBr	4	66
	NaOH	KBr	7	63		CsOH	–	0	39
	NaOH	KBr	10	73		CsOH	NaCl	4	68

[a] Molar ratio *N*-benzyldiethanolamine–**I** 1 : 1.

sodium hydroxide was used. However, the yield of **IIb** increased upon addition of sodium salts when the reaction was carried out using aqueous KOH or CsOH. Higher yield of 1-benzyl-1-aza-18-crown-6 (**IIc**) was favored by the presence of potassium, cesium, or barium salts, and addition of 10 equiv of CsCl ensured the best yield of 1-benzyl-1-aza-21-crown-7 (**IId**). These findings allowed us to presume template effect in the synthesis of *N*-benzylazacrown ethers under phase-transfer catalysis.

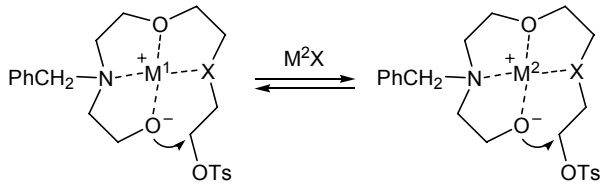
On the basis of general relations holding in nucleophilic reactions occurring in two-phase systems [18], the formation of *N*-benzylazacrown ethers may be illustrated by Scheme 3. Obviously, the first step is generation of alkoxide ion in the aqueous phase or at the phase boundary [reaction (1)]. Next follows exchange reaction (2) with quaternary ammonium salt, and lipophilic ion pair $RO^- Q^+$ thus formed is transferred to the organic phase where the alkoxide ion undergoes alkylation with the corresponding bis-*p*-toluenesulfonate [reaction (3)]. Deprotonation of intermediate **A** yields anion **B** [reaction (4)] which is converted into cation-associated structure **C** as precursor of azacrown ether. The process is completed by intramolecular cyclization (5). Obviously, the formation of associate **C** is the key step determining the yield of cyclization products. By analogy with crown ethers [19], we believe that the stability of intermediate **C** is directly related to the stability of the complex formed by the cyclization product with one or another metal cation. Presumably, in the presence of metal salts the metal ion in intermediate **C** is replaced by a metal ion

Scheme 3.



which fits better the macroring cavity (Scheme 4). As a result, the yield of *N*-benzylazacrown ethers depends on the nature of metal cations present in the reaction mixture.

Scheme 4.



Thus the optimal conditions for the synthesis of *N*-benzylazacrown ethers in a two-phase system are as follows: (1) volume ratio benzene–50% aqueous NaOH 1:6, (2) reactant concentration 0.01–0.11 M, (3) tetrabutylammonium iodide or bromide (25 mol %) as catalyst, and (4) temperature 65–70°C. In the syntheses of 1-benzyl-1-aza-12-crown-4, 1-benzyl-1-aza-18-crown-6, and 1-benzyl-1-aza-21-crown-7, 4 to 10 equiv of LiCl, $BaBr_2$, or CsCl, respectively, should be added to the aqueous phase.

Deprotection of *N*-benzylazacrown ethers is generally performed by catalytic hydrogenation over palladium catalyst (10% Pd/C) in anhydrous ethanol or acetic acid under a hydrogen pressure of 3–5 atm (reaction time 15–25 h) [1, 12, 13]. We found that benzyl group can be removed from compounds **IIa**–**IId** by the action of hydrogen over 10% Pd/C under atmospheric pressure in reagent-grade methanol (reaction time 7–8 h). Addition of a catalytic amount of acetic or concentrated hydrochloric acid made it possible to shorten the reaction time to 3–5 h. Addition of a larger amount of acid almost did not accelerate the process but hindered isolation of the products.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on a Varian VXR-300 spectrometer operating at 300 MHz. The mass spectra (electron impact, 70 eV) were obtained on an MKh-1321 instrument with direct sample admission into the ion source heated to 200°C. The purity of the isolated compounds was checked by TLC (Silufol UV-254) and GLC (Chrom-5 chromatograph equipped with a flame-ionization detector; stationary phase 5–10% of SE-30, OV-17, or SP-2100 on Chromaton N-AW-HMDS or Inerton; carrier has helium; the carrier gas flow rate and oven temperature depended on the properties of compounds being analyzed).

Oligo(ethylene glycol) bis-*p*-toluenesulfonates Ia–Ie (*general procedure*). A solution of 63 g (0.33 mol) of *p*-toluenesulfonyl chloride in 75 ml of methylene chloride was added over a period of 0.5 h under vigorous stirring to a mixture of 0.15 mol of the corresponding oligo(ethylene glycol), 150 ml of methylene chloride, 1.35 g (6 mmol) of benzyltriethylammonium chloride, and 115 ml of 30% aqueous sodium hydroxide. The mixture was stirred for 6 h, the organic phase was separated, washed with water (3 × 75 ml),

dried over anhydrous sodium sulfate, and evaporated under reduced pressure, and the residue was recrystallized from ethanol or methanol (oily products were used without additional purification).

Diethylene glycol bis-*p*-toluenesulfonate (Ia). Yield 83%, mp 89°C; published data [14, 15]: mp 88–89°C.

Triethylene glycol bis-*p*-toluenesulfonate (Ib). Yield 86%, mp 80–81°C [14, 15].

Tatraethylene glycol bis-*p*-toluenesulfonate (Ic). Yield 96%, oily substance.

Pentaethylene glycol bis-*p*-toluenesulfonate (Id). Yield 94%, oily substance.

Benzene-1,2-diylbis(oxyethane-2,1-diyl) bis-*p*-toluenesulfonate (Ie). Yield 90%, mp 98–100°C; published data [9]: mp 95–96°C.

***N*-Benzylazacrown ethers IIa–IIe (*general procedure*).** A solution of 0.05 mol of compound **Ia**–**Ie** in 600 ml of benzene was added to a mixture of 9.75 g (0.05 mol) of *N*-benzyldiethanolamine, 4.025 g (0.0125 mol) of tetrabutylammonium bromide, and 100 ml of 50% aqueous NaOH, and the mixture was stirred for 7–25 h at 70±2°C. The mixture was cooled, the organic phase was separated, washed with water (3×100 ml), and evaporated under reduced pressure, the residue was treated with boiling hexane (3×150 ml), the extract was evaporated under reduced pressure, and the residue was distilled in a vacuum.

1-Benzyl-1-aza-12-crown-4 (IIa). Lithium chloride, 8.5 g (0.2 mol), was added to the aqueous phase; reaction time 25 h. Yield 71%, bp 140–142°C (0.05 mm). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.60 t (4H, CH_2N), 3.42 m (14H, CH_2O, C**H**$_2$Ph), 7.07 s (5H, C_6H_5). Mass spectrum: *m*/*z* 265 $[M]^+$.

1-Benzyl-1-aza-15-crown-5 (IIb). Reaction time 10 h. Yield 72%, bp 148–153°C (0.05 mm). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.62 t (4H, CH_2N), 3.45 m (18H, CH_2O, C**H**$_2$Ph), 7.08 s (5H, C_6H_5). Mass spectrum: *m*/*z* 309 $[M]^+$.

1-Benzyl-1-aza-18-crown-6 (IIc). Barium bromide, 59 g (0.2 mol), was added to the aqueous phase; reaction time 15 h. Yield 74%, bp 190–193°C (0.05 mm). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.59 t (4H, CH_2N), 3.51 m (22H, CH_2O, C**H**$_2$Ph), 7.08 s (5H, C_6H_5). Mass spectrum: *m*/*z* 353 $[M]^+$.

1-Benzyl-1-aza-21-crown-7 (IId). Cesium chloride, 84 g (0.5 mol), was added to the aqueous phase; reaction time 15 h. Yield 58%, bp 205–208°C (0.05 mm). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.63 t (4H, CH_2N), 3.50 m (26H, CH_2O, C**H**$_2$Ph), 7.08 s (5H, C_6H_5). Mass spectrum: *m*/*z* 397 $[M]^+$.

8,9-Benzo-1-benzyl-1-aza-15-crown-5 (IIe). Reaction time 7 h. Yield 70%, oily substance (the product was not subjected to additional purification). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.63 t (4H, CH_2N), 3.52 s (2H, C**H**$_2$Ph), 3.56 m (8H, CH_2O), 3.62 m (4H, C_6H_4OC**H**$_2$), 6.78 m (4H, C_6H_4), 7.00 s (5H, C_6H_5). Mass spectrum: *m*/*z* 357 $[M]^+$.

Removal of benzyl protection (*general procedure*). A mixture of 2 g of 10% Pd/C and 50 ml of methanol was saturated with hydrogen over a period of 1 h under stirring on a magnetic stirrer, a solution of 0.1 mol of azacrown ether **IIa**–**IIe** and 1 ml of acetic acid in 200 ml of methanol was added, and the mixture was stirred for 4–5 h in a stream of hydrogen. The catalyst was filtered off and washed with methanol (3×20 ml), the filtrate was combined with the washings and evaporated to dryness under reduced pressure, the residue was dissolved in 60–70 ml of water, and the solution was extracted with benzene (3×50 ml). The benzene extracts were discarded, the aqueous phase was made alkaline by adding NaOH to pH 9–10 and extracted with methylene chloride or chloroform (7×50 ml). The solvent was distilled off, the residue was treated with boiling hexane (3×100 ml), the extract was evaporated to dryness under reduced pressure, and the residue was distilled under reduced pressure.

1-Aza-12-crown-4. bp 85–91°C (0.05 mm); mp 59–60°C [11]. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.48 m (1H, NH), 2.62 t (4H, CH_2N), 3.59 t (12H, CH_2O). Mass spectrum: *m*/*z* 175 $[M]^+$.

1-Aza-15-crown-5. bp 98–100°C (0.05 mm), mp 30–32°C [10]. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.50 m (1H, NH), 2.75 t (4H, CH_2N), 3.55 m (16H, CH_2O). Mass spectrum: *m*/*z* 219 $[M]^+$.

1-Aza-18-crown-6. bp 110–112°C (0.05 mm), mp 49–51°C [19]. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.52 m (1H, NH), 2.81 t (4H, CH_2N), 3.60 m (20H, CH_2O). Mass spectrum: *m*/*z* 263 $[M]^+$.

1-Aza-21-crown-7. bp 125–134°C (0.05 mm). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.39 m (1H, NH), 2.59 t (4H, CH_2N), 3.56 m (24H, CH_2O). Mass spectrum: *m*/*z* 307 $[M]^+$.

8,9-Benzo-1-aza-15-crown-5. mp 148–149°C; published data [6]: mp 142–143°C. ^{1}H NMR spectrum

($CDCl_3$), δ, ppm: 2.73 m (5H, NH, CH_2N), 3.80 t (12H, CH_2O), 6.80 s (4H, C_6H_4). Mass spectrum: *m*/*z* 267 $[M]^+$.

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