MACROHETEROCYCLES.

24.* SYNTHESIS OF NEW DERIVATIVES OF DIAZA-18-CROWN-6

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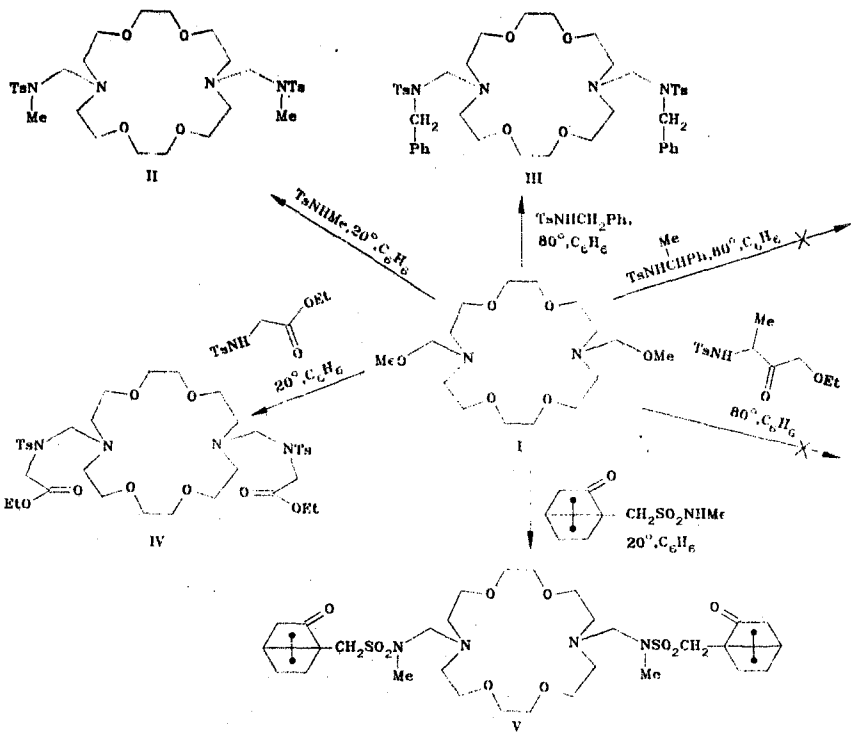
New derivatives of diaza-18-crown-6 have been prepared by the aminomethylation of N-alkylsulfonamides under the action of N,N'-bismethoxymethyldiaza-18-crown-6.

It is known that the complex-forming and ion-selective properties of crown ethers are determined by their topology and by the nature of the reactive centers situated both in the ring and in the side chains [2, 3]. Hence, modification of a macrocycle by the introduction of functional substituents allows considerable variation in the complex-forming properties to be achieved and is one of the major directions of the development of the chemistry of macroheterocycles.

It has been shown previously that aza-crown ethers containing reactive secondary amino groups enter readily into aminomethylation reactions on C, O, and N atoms [4, 5]. The present paper reports the results of a study of the aminomethylation of N-alkylsulfonamides by the action of N,N'-bismethoxymethyldiaza-18-crown-6 (I).



It has been established that as the size of the substituent on the nitrogen atom in the sulfonamides increases, reaction becomes noticeably more difficult. Thus, whereas aminomethylation of N-methyl-p-toluenesulfonamide by I proceeds at 20°C and of N-benzyl-p-toluenesulfonamide at 80°C, reaction of N-tosyl-S-(−)-α-phenylethylamine does not take place even in benzene at boiling point.

*For Communication 23, see [1].
†Deceased.

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TABLE 1. Characteristics of Aza-Crown ethers II-V

Compound	mp. °C	Found, %			Empirical formula	Calc. %			Yield, %
		C	H	N		C	H	N	
II	oil	54,9	9,6	8,6	$C_{30}H_{48}N_4O_8S_2$	54,8	7,4	8,5	98
III	oil	62,1	6,7	7,0	$C_{42}H_{56}N_4O_8S_2$	62,3	7,0	6,9	95
IV	70—72	53,7	7,1	6,9	$C_{36}H_{56}N_4O_{12}S_2$	54,0	7,0	7,0	87
V	90	55,4	8,3	7,2	$C_{36}H_{64}N_4O_{10}S_2$	56,6	8,3	7,2	87

TABLE 2. Spectral Characteristics of Crown Ethers II-V

Compound	NMR in $CDCl_3$, δ, ppm (J, Hz)	IR (CCl_4), ν, cm^{-1}	Mass spec. M+
II	2,30 (6H, s), $ArCH_3$; 2,63 (6H, s), NCH_2; 2,80 (8H, t[6,0]), NCH_2; 3,48 (16H, m), OCH_2; 3,86 (4H, s), NCH_2N; 6,88 (4H, d [11,0]), ArH; 7,05 (4H, d [11,0]), ArH	1165 1350 (SO_2), 1600 (C=C), 3040—3080 (=C—H)	657
III	2,33 (6H, s), $ArCH_3$; 2,63 (8H, t[5,8]), NCH_2; 3,38 (16H, m), OCH_2; 4,03 (4H, s), $ArCH_2$; 4,36 (4H, s), NCH_2N; 6,90 (14H, m), ArH; 6,94 (4H, d [10,0]), ArH	1165, 1350 (SO_2), 1600 (C=C), 3040—3080 (=C—H)	809
IV	0,90 (6H, t [7,5]), CH_2CH_3; 2,17 (6H, s), $ArCH_3$; 2,60 (8H, t[5,7]), NCH_2; 3,33 (16H, m), OCH_2; 3,78 (4H, q [7,5]), OCH_2CH_3; 3,93 (4H, s $COCH_2$; 3,97 (4H, s), NCH_2N; 7,03 (4H, s [10,0]), ArH; 7,46 (4H, s [10,0]), ArH	1165, 1350 (SO_2), 1600 (C=C), 1700 (C=O), 3030—3080 (=C—H)	801
V*	0,85 (6H, s), CH_3; 1,13 (6H, s), CH_3; 1,63 (14H, m), $(CH_2)_2CHCH_2$; 2,52 (2H d[13,3]), CH; 2,83 (8H, t [6,0]), NCH_2; 2,88 (6H, s), NCH_3; 3,22 (2H, d [13,3]), CH; 3,53 (16H, m), OCH_2; 4,03 (4H, d), NCH_2N	1165, 1340 (SO_2), 1750 (C=O)	777

*$[\alpha]_D$ = + 23.48° (C 4.6, C_2H_5OH).

Analogous results were observed for the aminomethylation of ethyl esters of N-tosylglycine and n-tosyl-α-alanine. This lends support to a hypothesis which we put forward earlier, that spatial factors play an important part in the course of aminomethylation reactions based on macrocyclic N-methoxymethylamines [4, 5].

Aminomethylation of D-(+)-N-methyl-camphor-10-sulfonamide occurs in high yield. The identity of the compounds prepared, II-V, was monitored by TLC and their composition and structure were determined from the results of elemental analysis (Table 1), and from their NMR, IR, and mass spectra (Table 2).

EXPERIMENTAL

Plates coated with Silufol UV-254 were used for TLC, the eluant being selected according to the properties of the compound under examination; iodine vapor was used for development. NMR spectra were run in 5-10% (by vol.) solution in $CDCl_3$ on a Tesla BS 467 (Czechoslovakia) instrument (60 MHz) using hexamethyldisiloxane as internal standard. Infrared spectra were run on a Perkin-Elmer 580B (USA) instrument and the mass spectra on a Varian MAT-112 spectrometer with direct introduction of the sample and 70 eV ionizing electron energy.

N,N'-Bis(N-methyl-p-toluenesulfonamidomethyl)diaza-18-crown-6 (II). A mixture of 1.37 g (3.9 mmoles) crown ether I [4], 1.45 g (7.8 mmoles) N-methyl-p-toluenesulfonamide and 10 ml dry benzene was held at 20°C for 2 h. The solution was filtered and the filtrate evaporated yielding 2.52 g of compound II.

N,N'-Bis(n-benzyl-p-toluenesulfonamidomethyl)diaza-18-crown-6 (III) was prepared in a similar way from 0.87 g (25 mmoles) crown ether I and 1.33 g (5 mmoles) N-benzyl-p-toluenesulfonamide at 80°C, yielding 1.92 g of compound III.

N,N'-Bis(N-tosylethoxycarbonylmethylaminomethyl)diaza-18-crown-6 (IV) was prepared in a similar way from 1.47 g (4.2 mmoles) crown ether I and 2.17 g (8.4 mmoles) ethyl ester of N-tosylglycine at 20°C; the yield was 2.94 g of compound IV.

N,N'-Bis-D-(+)-(N-methylcamphor-10-sulfonamidomethyl)diaza-18-crown-6 (V) was similarly prepared from 0.94 g (2.7 mmoles) crown ether I and 1.34 g (5.4 mmoles) D-(+)-N-methylcamphor-10-sulfonamide to yield 1.85 g of compound V.

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