MACROHETEROCYCLES.

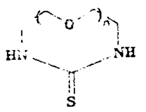
25.* CONVENIENT SYNTHESIS OF CROWN-COMPOUNDS WITH THIOCARBAMIDE GROUPS

N. G. Luk'yanenko, T. A. Kirichenko,
V. V. Limich, and A. V. Bogatskii†

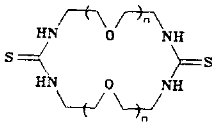
UDC 547.898.07

The reaction of polyoxyethylene diamines with polyoxyethylene diisothiocyanates leads to new crowns with thiocarbamide groups having 13- to 34-membered rings. Binuclear crown compounds with thiocarbamide groups are prepared by the reaction of polyoxyethylene diisothiocyanates with aza-15-crown-5.

In previous papers [2-4] we have described the preparation of crown compounds by the reaction of polyoxyethylene diamines with carbon disulfide in ethanol at high dilution. The reaction leads to the simultaneous formation of compounds of types A and B which can be separated from the reaction mixture by liquid chromatography in overall yield of 35-59% [3].



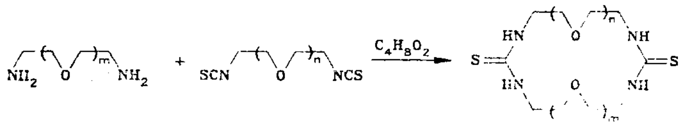
A



B

The ratio of the products A and B varies with the concentration of the reactants but it is not possible to find conditions such that only one of the compounds is formed. By this method only symmetrical crown compounds with two thiocarbamide groups of type B can be prepared.

The reaction of polyoxyethylene diisothiocyanates with diamines [5] provides a promising route to the synthesis of crown compounds with thiocarbamide groups, and we have employed it for the preparation of the crown compounds I-XIV.



I–XIV

I–IV n=0, V–VIII n=1, IX–XI n=2, XII, XIII n=3, XIV n=4; I, V m=1, II, VI, IX m=2, III, VII, X, XII m=3, IV, VIII, XI, XIII, XIV m=4

The reaction is carried out in dioxane (or in any other inert solvent) at high dilution of the reactants which are fed into the reaction vessel in equimolecular quantities by micropumps. The crown compounds with thio-carbamide groups were in most cases purified by crystallization from an appropriate solvent; in a few cases recourse chromatography was used. In spite of what has been stated previously [2,3] this method enables one to prepare both symmetrical (n = m) and unsymmetrical (n ≠ m) crown compounds having two thiocarbamide groups. It should be noted that as the size of the ring increases from 13 to 34 members, the yields fall from 86 to 40%.

---

*For communication 24, see [1].
†Deceased.

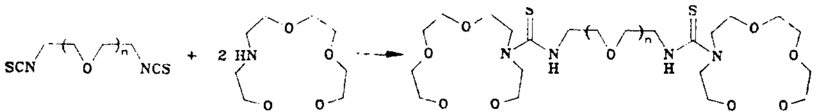
A. V. Bogatskii Physicochemical Institute, Academy of Sciences of the Ukrainian SSR, Odessa 270080. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 263-266, February, 1987. Original article submitted July 15, 1985.

TABLE 1. Characteristics of Crown Compounds I-XVII

Compound	T_{mp}, deg C	Found, %			Empirical formula	Calculated, %			Yield, %
		C	H	N		C	H	N	
I	216—217	38,5	6,5	22,0	$C_8H_{16}N_4OS_2$	38,7	6,5	22,6	86
II	222	41,2	6,9	19,3	$C_{10}H_{20}N_4O_2S_2$	41,1	6,9	19,2	80
III	192	42,8	7,2	16,5	$C_{12}H_{24}N_4O_3S_2$	42,8	7,2	16,6	75
IV	162	44,3	7,6	14,9	$C_{14}H_{28}N_4O_4S_2$	44,2	7,4	14,7	65
V	233	41,3	6,7	19,0	$C_{10}H_{20}N_4O_2S_2$	41,1	6,9	19,2	75
VI	131	42,7	7,3	16,8	$C_{12}H_{24}N_4O_3S_2$	42,8	7,2	16,6	75
VII	67	44,3	7,5	14,9	$C_{14}H_{28}N_4O_4S_2$	44,2	7,4	14,7	68
VIII	55	45,2	7,7	13,4	$C_{16}H_{32}N_4O_5S_2$	45,3	7,6	13,2	70
IX	194	44,3	7,5	14,5	$C_{14}H_{28}N_4O_4S_2$	44,2	7,4	14,7	66
X	103—104	45,4	7,8	13,4	$C_{16}H_{32}N_4O_5S_2$	45,3	7,6	13,2	69
XI	Oil	46,4	7,9	11,8	$C_{18}H_{36}N_4O_6S_2$	46,1	7,7	11,9	47
XII	117	46,2	7,9	11,8	$C_{18}H_{36}N_4O_6S_2$	46,1	7,7	11,9	49
XIII	Oil	46,6	7,9	10,7	$C_{20}H_{40}N_4O_7S_2$	46,8	7,8	10,9	55
XIV	119—120	47,3	8,0	10,2	$C_{22}H_{44}N_4O_8S_2$	47,5	7,9	10,1	40
XV	Oil	49,7	8,1	9,2	$C_{26}H_{50}N_4O_9S_2$	49,8	8,0	8,9	98
XVI	Oil	50,5	8,2	7,6	$C_{30}H_{58}N_4O_{11}S_2$	50,4	8,2	7,8	98
XVII	Oil	50,5	8,1	7,4	$C_{32}H_{62}N_4O_{12}S_2$	50,6	8,2	7,4	98

The prepared compounds I-XIV were in general white crystalline substances whose solubility in most organic solvents increased with increase in ring size. It is characteristic that the melting points of both symmetrical (V, IX, XII, XIV) and unsymmetrical (I-VI, VI-VIII, X, XI, XII) compounds fall with increase in ring size. However, the melting point of the symmetrical compounds is always higher than that of the unsymmetrical compounds with the same ring size: for example V & II, IX & VII, XII & XI (Table 1).

In recent years, binuclear crown ethers have come in for a great deal of attention [6, 7]. Compounds of this type can be easily prepared in almost quantitative yield in the form of light yellow oils by the reaction of polyoxyethylene diisothiocyanates with aza-crown ethers in alcohols, ethers, or benzene.



XV-XVII

XV n=1, XVI n=3, XVII n=4

The aza-15-crown-5 starting material is prepared by reaction of diethanol-amine with the ditosylate of triethylene glycol in the presence of sodium tert-butoxide in a manner similar to that of [8].

The structure of the prepared compounds I-XVII was confirmed by IR, UV, NMR, and mass spectra (see Table 2).

EXPERIMENTAL

Infrared spectra were obtained on a Perkin-ELmer 580B instrument in KBr discs and UV spectra on a Specord-M-40 UV-Vis. A Tesla BS 467 (60 MHz) spectrometer was used to obtain NMR spectra using 5-10% solutions and TMS internal standard. Mass spectra were run on a Variar MAT-12 with direct introduction of sample, 40 eV ionization energy and a temperature of 100-200°C. TLC was carried out on plates with a fixed layer of Silufol UV-254 silica gel, eluents being introduced as required by the properties of the individual compounds; development was with iodine vapor. Silica gel L 100/250 was used for liquid chromatography.

The starting materials, polyoxyethylene diamides and polyoxyethylene diisothiocyanates, were prepared as described previously [3, 9].

Crown Compounds with Thiocarbamide Groups (I-XIV). Using previously calibrated metering pumps, solution of 0.05 mole diisothiocyanate and polyoxyethylene diamide each in 500 ml dioxane were added to 500 ml dioxane at boiling point with vigorous stirring over a period of 7 h. The mixture was cooled and the dioxane distilled off under reduced pressure. Compounds I and IX were purified by recrystallization from DMSO, II from glacial acetic acid, III and IV from DMF, VI from tert-butanol, and VIII from benzene. Compounds V, X, XI, XIII were

TABLE 2. Spectroscopic Characteristics of Crown Compounds

Compound	IR spectra, cm^{-1}			UV spectra (in C_2H_5OH), λ_{max}, nm (lg ε)	Proton NMR spectra (in $CDCl_3$), δ, ppm	Mass spectra M^+
	ν_{NH}	$\nu_{N-C=S}$, δ_{NH}	ν_{C-O-C}			
I	3340, 3230, 3020	1570, 1520	1100, 1090	210 (4,49)^a; 245,9 (4,25)	3,85 (12H, m, CH_2O, CH_2N)^b; 8,08 (4H, m, NH)	248
II	3300, 3210, 3120, 3030	1580	1120, 1100	210 (4,65)^a; 244,3 (4,42)	3,71 (16H, m., CH_2O, CH_2N)^b; 8,83 (4H, m, NH)	292
III	3335, 3310, 3100	1560, 1540	1105, 1085	210 (4,76)^{a,c}; 243,8 (4,45)	3,83 (20H, m, CH_2O, CH_2N)^b; 9,33 (4H, m, NH)	336
IV	3370, 3340, 3080	1550	1105, 1095	210 (4,94)^{a,c}; 243,6 (4,68)	3,87 (24H, m. CH_2O, CH_2N)^b; 9,16 (4H, m, NH)	380
V	3310, 3210	1570, 1530	1095	209 (4,44)^a; 244,3 (4,43)	3,34 (16H, m., CH_2O, CH_2N)^b; 7,83 (4H, m, NH)	292
VI	3280, 3230, 3130, 3020	1570, 1530	1100, 1080	210 (4,54)^{a,c}; 241,7 (4,36)	3,80 (20H, m, CH_2O, CH_2N)^b, 8,66 (4H, m, NH)	336
VII	3360, 3280, 3080	1560	1115, 1080	205,8 (4,37)^c; 241,5 (4,40)	3,63 (24H, m, CH_2O, CH_2N); 7,17 (4H, m, NH)	380
VIII	3370, 3300, 3060	1550	1120, 1090	206,3 (4,26)^c; 242,5 (4,31)	3,63 (28H, m, CH_2O, CH_2N); 7,17 (4H, m, NH)	424
IX	3370, 3340, 3300, 3075	1550	1090, 1070	210,3 (4,28); 247,8 (4,32)	3,35 (24H, m, CH_2O, CH_2N)^b; 8,48 (4H, m, NH)	380
X	3290, 3070	1550	1080	206,8 (4,25)^c; 242,5 (4,29)	3,63 (28H, m, CH_2O, CH_2N); 7,17 (4H, m, NH)	424
XI	3300^d	1555	1115, 1095	206,1 (4,29)^c; 242,5 (4,30)	3,63 (32H, m, CH_2O, CH_2N); 7,17 (4H, m, NH)	468
XII	3380, 3080	1555	1110	207,0 (4,32)^c; 242,7 (4,36)	3,67 (32H, m, CH_2O, CH_2N); 7,17 (4H, m NH)	468
XIII	3340^d, 3080	1555	1120, 1095	200,0 (4,44)^c; 241,1 (4,40)	3,57 (36H, m., CH_2O, CH_2N); 7,17 (4H, m, NH)	512
XIV	3380, 3325, 3070	1555	1140, 1095	206,3 (4,40)^c; 241,8 (4,42)	3,63 (40H, m, CH_2O, CH_2N); 7,17 (4H, m, NH)	556
XV	3300^d, 3100	1570, 1535	1120, 1095	211,3 (4,29); 247,3 (4,37)	3,63 (48H, m, CH_2O, CH_2N); 7,73 (2H, m, NH)	626
XVI	3300^d, 3100	1565, 1535	1120	211,3 (4,28); 247,8 (4,35)	3,73 (56H, m, CH_2O, CH_2N); 7,70 (2H, m, NH)	714
XVII	3300^d	1565, 1530	1120, 1095	210,3 (4,28); 247,8 (4,32)	3,70 (60H, m., CH_2O, CH_2N); 7,67 (2H, m., NH)	758

---

[a] in CH_3OH; b) in CF_3COOH; c) Broad peak, maximum not accurately localized; d) in $CHCl_3$.

separated on a chromatography column packed with silica gel using a 5:1 mixture of chloroform and methanol as eluent (for compound V) and 8:1 for compounds X, XI, XIII. The crown compounds XII and XIV were separated from the residue remaining after distilling off the dioxane by extraction with hot benzene (3 × 100 ml); compound VII was extracted with hot ethyl acetate (3 × 100 ml). Purification of compounds VII, XII, and XIV was effected by recrystallization from acetonitrile, benzene, and methanol respectively.

1-Aza-4,7,10,13-tetraoxacyclopentadecane (Aza-15-crown-5) [8]. Sodium metal (0.09 mole) was dissolved in 250 ml dry tert-butanol and 0.03 diethanolamine added. To this solution, a solution of 0.03 mole triethylene glycol ditosylate in 150 ml dioxane was added dropwise over a period of 3 h at 40°C. The mixture was stirred 1 h at the same temperature and then filtered. The filtrate was evaporated under reduced pressure. To the residue was added 25 ml water and the solution washed once with hexane. The aqueous solution was extracted with methylene chloride and the methylene chloride evaporated under reduced pressure. The residue was distilled in vacuum to give a fraction with bp 8085°C (0.02 mm), mp 23-26°C. Yield 45%.

Binuclear Crown-Ethers (XV-XVII). Solutions of 0.01 mole aza-15-crown-5 and 0.005 mole of the corresponding polyoxyethylene diisothiocyanate in 5 ml methanol were mixed with stirring. The reaction mixture was warmed to 40-45°C. After stirring for 15 min, the methanol was extracted under reduced pressure. The product was obtained in the form of an oil which did not require further purification.

LITERATURE CITED

1. N. G. Luk'yanenko, R. G. Kostyanovskii, V. N. Pastushok, and A. V. Bogatskii, Khim. Geterotsikl. Soedin., No. 3, 413 (1986).
2. A. V. Bogatskii, N. G. Luk'yanenko, and T. I. Kirichenko, Tetrahedron Lett., 21, 313 (1980).
3. A. V. Bogatskii, N. G. Luk'yanenko, and T. I. Kirichenko, Zh. Org. Khim., 16, 1301 (1980).
4. A. V. Bogatskii, K. S. Zakharov, N. G. Luk'yanenko, and T. I. Kirichenko, Zh. Org. Khim., 18, No. 5, 1101-1106 (1982).
5. B. Dietrich, T. M. Fyles, J. M. Lehn, L. G. Pease, and D. L. Fyles, J. Chem. Soc., Chem. Commun., No. 21, 934 (1978).
6. K. H. Wong and H. L. Ng, Synth. Commun., 10, 385 (1980).
7. Eur. Pat. 97 960; Chem. Abstr., 101, 23517 (1984).
8. H. Maeda, Y. Nakatsuji, and M. Okahara, J. Chem. Soc., Chem. Commun., No. 10, 471 (1981).
9. N. G. Luk'yanenko, V. V. Limich, S. V. Shcherbakov, and T. I. Kirichenko, Zh. Obshch. Khim., 55, 2100 (1985).

BASICITY AND MECHANISM OF TRANSMISSION OF ELECTRONIC EFFECTS OF SUBSTITUENTS IN THE SERIES OF 2-AMINO-5-ARYL-1,3,4-THIADIAZOLES

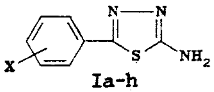
I. V. Zubets, S. N. Vergizov, S. I. Yakovlev,
and K. A. V'yunov

UDC 547.794.3.04:548.422.6

The basicity of 2-amino-5-aryl-1,3,4-thiadiazoles was studied. A correlation was obtained between the pK_{BH^+} values of the compounds and the σ constants of the substituents. It was shown that the electronic effects of the substituents in the phenyl ring are transmitted both on account of conjugation and by an induction mechanism.

2-Amino-5-aryl-1,3,4-thiadiazoles (I) are potential biologically active substances [1]. In order to predict the behavior in acid-catalyzed reactions and to assess the transmission of the effects of the substituents through the thiadiazole ring we investigated their basicity. For this purpose we studied the IR spectra of compounds (I) in aqueous solutions with various acidities.

The electronic spectra of aqueous solutions of compounds (I) are characterized by an absorption maximum in the region of 275-300 nm [with the exception of (Ih)].



Ia-h

I a X=H; b X=p-OCH_3; c X=m-Br; d X=p-Br; e X=p-Cl; f X=p-F; g X=m-NO_2; h X=p-NO_2

Lensovet Leningrad Technological Institute. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 267-270, February, 1987. Original article submitted July 25, 1985.