CYCLIZATION OF ALLYLTHIOPHENETHIOLS

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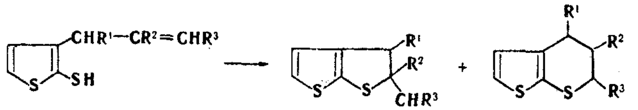
Investigation of the chemical properties of allylthiophenols is complicated by their high reactivity, which results in their high rate of cyclization to compounds of the dihydrobenzothiophene and thiochroman series [1]. In the present work we investigated the cyclization of allylthiophenethiols, which are formed with high yields during the rearrangement of the isomeric allyl thienyl sulfides [2] and are fairly stable when heated up to 120°C.

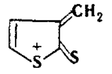
In all cases cyclization of allylthiophenethiols (I) leads to the formation of compounds of the 2,3-dihydrothienothiophene series (II) and thienodihydrothiopyran (III), for example:



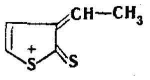
Ia-d IIa-d IIIa-d

I–III a $R^1=R^2=R^3=H$; b $R^1=R^3=H$, $R^2=CH_3$; c $R^1=CH_3$, $R^2=R^3=H$; d $R^1=R^2=H$, $R^3=CH_3$

The structure of the products from the cyclization of allylthiophenethiols was established by PMR spectroscopy and by chromatomass spectrometry (Table 1). The main direction in the mass-spectrometric decomposition of compounds (IIa-d) is the elimination of a hydrogen atom, the alkyl radical, and the SH radical, characteristic also of alkyldihydrobenzothiophenes. Under electron impact, compounds (IIIa-d) undergo retrodiene decomposition to form the common ion A in addition to elimination of a methyl radical (for IIIb, d), and fragmentation of compound (IIIc) gives the ion B with m/e 142, having a similar structure:



A



B

The ratio of the isomers (II) and (III) in the reaction products is affected significantly by the experimental conditions and by the structure of the initial thiol. Realization of the cyclization of compounds (Ia-d) in such a low-polarity solvent as m-xylene and also in the absence of a solvent promotes the preferential formation of compounds (IIIa-d) (Table 2). In more polar nitrogen bases and hexamethylphosphorotriamide, compounds (IIa-d) are mainly formed during cyclization of the allylthiophenethiols (Ia-d) (Table 2).

It is known that the cyclization of o-allylphenols can occur both with heterolytic and with homolytic cleavage of the O–H bond, and compounds with only a five-membered or only a six-membered heterocycle are formed in each case [3]. During the cyclization of allylthiophenethiols only the heterolytic path of intramolecular addition of the S–H group at the double bond of the allyl chain is evidently realized. This is favored by the absence of di(3-allyl-2-thienyl) disulfide in the products from the transformation of compound (Ia) and by the identical isomeric compositions of the product from its cyclization both in the presence of an inhibitor of radical reactions (hydroquinone) and in its absence (Table 2).

According to the classification proposed by Baldwin [4], the formation of 2,3-dihydrothieno[2,3-b]thiophenes (IIa-d) can be regarded as 5-exocyclization, and that of thienodihydrothiopyrans (IIIa-d) can be regarded as 6-endocyclization. The preferential occurrence of cyclization of the thiols (Ia-d) by one or the other type in each case is determined by

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TABLE 1. PMR Spectra of the Products from Cyclization of the Allylthiophenethiols

Compound	Chemical shifts, δ, ppm				
	2-H, 2-R	3-H, 3-R		4-H	5-H
IIa	4,0—4,5 (CH, 1H, (sext) 1,4 (CH_3, 3H, d)	2,34—3,2 (CH_2, 2H, (two q)		6,74	6,46
IIb	1,53 (CH_3, 6H, s)	3,0 (CH_2, 2H, s)		7,10	6,97
IIc	1,15 (CH_3, 3H, d) 2,8 (CH, 1H, q)	1,4 (CH_3, 3H, d) 3,8 (CH, 1H, q)		6,50	6,79
2-Methyl-2,3-dihydrothieno-[3,2-b]thiophene (VII)	4,28 (1H, sext) 1,42 (CH_3, 3H, d)	2,8—3,66 (CH_2, 2H, two q)		6,48	6,99
				5-H	6-H
	2-H 2-R	3-H 3-R	4-H 4-R		
IIIa	1,6—2,03 (CH_2, 2H, m)	2,36—2,84 (CH_2, 4H, m)		6,45	6,70
IIIc	1,5 (CH_2, 2H, m)	2,6 (CH_2, 2H, m)	1,0 (CH_3, 3H, d); 2,85—3—35 (CH, 1H, m)	6,60	6,70
VI	1,83—2,23 (CH_2, 2H, m)	2,4—3,04 (CH_2, 4H, m)		6,44	6,90
X	1,7 (CH_2, 2H, d)	2,4—2,9 (CH, CH_2, 3H, m); 1,0 (CH_3, 3H, d)		6,43	6,85

TABLE 2. Cyclization of Allylthiophenethiols (length of experiment 2 h, temperature 120°C)

Thiol	Solvent	Yield of cyclic products, %	Composition of cyclic products, %	
			II	III
Ia	N,N-Dimethylaniline (DMA)	20	74	26
	Quinoline	62	95	5
	HMPT	50	100	—
	Tri-n-butylamine	51	99	1
	m-Xylene	30	28	72
	Without solvent	21	23	77
	N,N-DMA*	89	19	81
	N,N-DMA with hydroquinone*	91	17	83
Ib	Quinoline	Not. det.	89	11
Ic	Quinoline	71	85 (cis + trans)	15
	HMPT	68	85 (cis + trans)	15
Id	Without solvent	70†	37	63
	m-Xylene	16†	31	69
	N,N-DMA	45	34	66
	Quinoline	47	45	55
			VII	VI
V	Without solvent	60	10	90
	m-Xylene	30	6	94
	N,N-DMA	15	32	68
	HMPT	40	11	89

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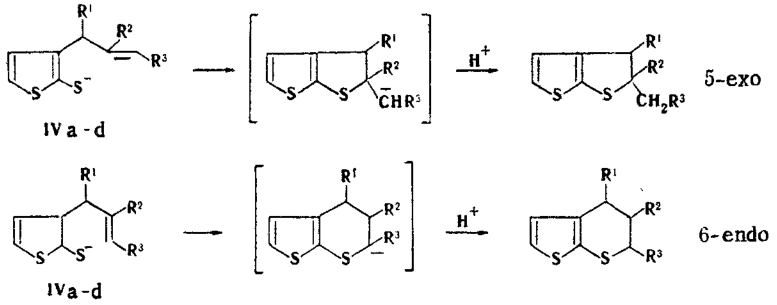
*The experiments were carried out at 160°C.

†The length of the experiment was 3 h.

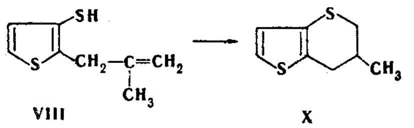
the possibility of the attainment of the geometry of the transition state.

When the reaction is realized in nitrogen bases or in dipolar aprotic solvents, the S—H bond in the allylthiophenethiols is strongly polarized, and it is even possible that the thiol dissociates to form an anion (IVa-d) [5]. It can be supposed that the mutual repulsion of the p electrons of the sulfur atom and the π electrons of the double bond in the allyl group has the main effect on the cyclization path of the anion (IVa-d). Increase in the cyclization temperature from 120°C, where 5-exocyclization is preferred (Table 2), to 160°C leads to an increase in the freedom of rotation about the single bond between the $C_{(\alpha)}$ and $C_{(\beta)}$ atoms in the allyl group, and 6-endocyclization is consequently facilitated:



The mutual repulsion of the p electrons of the sulfur atom and the π electrons of the double bond has a smaller effect on the cyclization of the thiols (Ia-d) without a solvent and in the low-polarity m-xylene, where dissociation is less likely, and 6-endocyclization to form thienodihydrothiopyrans is preferred (Table 2).

The cyclization of 2-allyl-3-thiophenethiol (V) with the S—H group at the β position of the thiophene ring occurs with the preferential formation of thieno[3,2-b]dihydrothiopyran (VI) (Table 2). The cyclization of 2-(β-methylallyl)-3-thiophenethiol (VIII) [formed during rearrangement of (β-methylallyl)-3-thienyl sulfide (IX)], in which the methyl group at the β-carbon atom in the allyl chain can create additional steric hindrances to 5-exocyclization, the only product is 3-methylthieno[3,2-b]dihydrothiopyran (X), i.e., the process occurs exclusively as 6-endocyclization:



The cyclization of 3-(α-methylallyl)-2-thiophenethiol (Ic) leads to the formation of cis- and trans-2,3-dimethyl-2,3-dihydrothieno[2,3-b]thiophene (IIc) in a ratio of 1:5, according to GLC, and 4-methylthieno[2,3-b]dihydrothiopyran (IIIc). The preferential formation of trans-(IIc) compared with cis-(IIc) becomes understandable if account is taken of the fact that the mutual repulsion of the methyl groups is considerably stronger in cis-(IIc) than in trans-(IIc), and on account of the almost planar structure of the dihydrothiophene ring no rotation about the $C_{(2)}—C_{(3)}$ bond can reduce this repulsion.

EXPERIMENTAL

Chromatographic analysis was realized on an LKhM8-MD chromatograph (model No. 1) with a thermal conductivity detector (column length 3 m, diameter 0.4 cm, 5% SE-30 on silylated Chromaton N, 0.2-0.3 mm, column temperature 150°C, helium). The PMR spectra were recorded on a Varian T-60 spectrometer in carbon tetrachloride with HMDS as internal standard.

TABLE 3. Physicochemical Constants and PMR Spectra of Allylthiophenethiols

Compound	bp, °C (mm Hg)	n_D^{20}	Chemical shifts, δ, ppm							
			5-H	4-H	S—H	$-CH_2-$	$=CH_2$	$=CH-$	$-CH_3$	$-CH$
Ia	68—71 (3)	1,5895	6,96 (d)	6,66 (d)	3,03 (s)	3,26 (d)	4,70—5,00 (m)	5,46—6,10 (m)		
Ib	69—71 (3)	—	6,96 (d)	6,66 (d)	3,10 (s)	3,20 (s)	4,60 (d)		1,47 (s)	
Ic	97—98 (3)	1,5690	6,94 (d)	6,64 (d)	2,94 (s)		4,60—4,94 (m)	6,00 (m)	1,20 (d)	3.67 (m)
Id	98—100 (3)	—	7,00 (d)	6,66 (d)	3,00 (s)	3,23 (m)		5,34 (m)	1,60 (m)	
V	72—74 (3)	1,5885	7,00 (d)	6,80 (d)	2,90 (s)	3,50 (d)	5,20 (m)	5,50—6,20 (m)		

Chromatomass-spectrometric analysis was performed on a Varian MAT-111 (Gnom) instrument with an ionizing energy of 80 eV and an emission current of 270 mA (column length 1.5 m, internal diameter 0.4 cm, 10% OV-1, temperature programing 80-220°C, 10 deg/min, helium, 20 ml/min).

The initial allylthiophenethiols were obtained by rearrangement of the isomeric allyl thienyl sulfides in m-xylene at 120°C with reaction times of 30-60 min. The physicochemical constants and PMR spectra are given in Table 3.

β-Methylallyl 3-Thienyl Sulfide (IX). Compound (IX) was obtained by the reaction of 3-thiophenethiol with β-methylallyl chloride in an aqueous alkaline solution. The yield was 54%; bp 61-62°C (2 mm Hg), n_D^{20} 1.5769. PMR spectrum, δ: 1.76 (CH_3, 3H, s), 3.23 ($-CH_2-$, 2H, s), 4.57 ($=CH_2$, 2H, m), 6.8-7.2 ppm (3H, m). The rearrangement of compound (IX) was realized at 120°C in an atmosphere of nitrogen, and 3-methylthieno[3,2-b]dihydrothiopyran (X) was isolated from the reaction products by vacuum distillation.

Cyclization of Allylthiophenethiols. The reaction was carried out in a thermostated flask with a stirrer and a reflux condenser in an atmosphere of nitrogen. At the end of the experiment the reaction mixture was dissolved in ether, washed three times with a 10% solution of potassium hydroxide and then to a neutral reaction with water, and dried with magnesium sulfate. The ether was distilled, and the residue was analyzed by GLC, PMR spectroscopy, and chromatomass spectrometry.

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MESOIONIC COMPOUNDS WITH A BRIDGING NITROGEN ATOM

1. INVESTIGATION OF THE PRODUCT FROM DEHYDRATING CYCLIZATION OF (2-PYRIDYLTHIO)ACETIC ACID

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It has been considered [1, 2] that the product first obtained in 1924 by Koenigs [3] by heating (2-pyridylthio)acetic acid in acetic anhydride solution has the structure of thiazolo-[3,2-a]pyridinio-3-oxide (IIa), as proposed in 1951 by Duffin and Kendall [4].

In a development of investigations into polymethine dyes (derivatives of condensed heterocycles [5]), we decided to undertake the synthesis of compounds (IIb, c) in order to obtain the dyes (IId-f) from them. However, the elemental composition of the compound obtained by condensation of the substance with the supposed structure (IIb) with 1-ethyl-2-sulfo-6-methylquinolinium betaine differed greatly from that required for the structure (IIe). This prompted us to investigate the structure of the mesoionic compound formed from (2-pyridylthio)acetic acids [4, 6].

The molecular weight of the product with the supposed structure (IIa) was determined and was found to be twice the calculated value.

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