SYNTHESIS AND REACTIONS OF BENZO[b]THIENO[2,3-c]PYRYLIUM PAIRS

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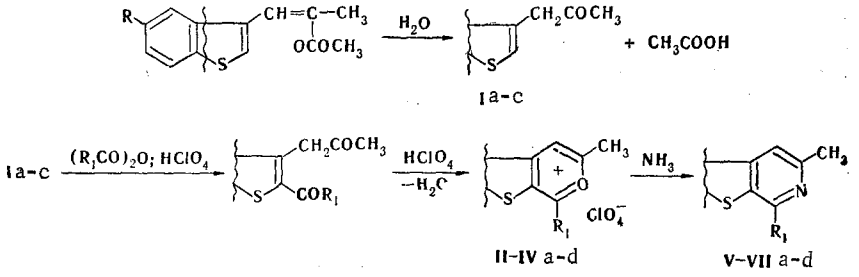
Benzo[b]thieno[2,3-c]pyrylium perchlorates were obtained in high yields in the acylation of benzo[b]thien-3-ylacetone with aliphatic acid anhydrides in the presence of 70% perchloric acid. Treatment of the products with ammonia converts them to benzo[b]thieno[2,3-c]pyridines (in yields higher than 90%), whereas hydroxy and dialkylamino derivatives of dibenzothiophene were obtained in up to 50% yields by treatment of the products with alkalis or secondary amines, respectively.

The preparation of benzo[b]thieno[2,3-c]pyrylium salts [1] by heterocyclization [2] has been previously reported. In the present paper we describe the synthesis of substituted benzo[b]thieno[2,3-c]pyrylium salts by acylation of benzo[b]thiophene derivatives Ia-c with carboxylic acid anhydrides in the presence of perchlorid acid. Substituted 3-acetonylbenzo-[b]thiophenes Ia-c are obtained in satisfactory yields by the Dakin–West reaction (by heating in excess acetic anhydride in the presence of sodium acetate) from benzo[b]thien-3-ylacetic acids [3].

The latter became accessible after the research of Sauter, who used the intramolecular cyclization of γ-arylmercaptoacetoacetic esters in polyphosphric acid (PPA) for their synthesis [4-6].

In the synthesis of Ia-c it was established by gas-liquid chromatography (GLC) and PMR and IR spectroscopy that some of the ketone is converted to its enol acetate, and 3-acetonylbenzo[b]thiophenes Ia-c were therefore purified by subjecting them to treatment with an aqueous alcohol solution of alkali.



I a R=H; b R=CH_3; c R=Cl; II, V a, b, c, d, R=H; III, VI a, b, c, d R=CH_3; IV, VII a, b, c, d R=Cl; II–VII a R_1=CH_3; b R_1=C_2H_5; c R_1=C_3H_7; d R_1=C_4H_9

Regardless of the substituent in the benzene ring of Ia-c, perchloric acid-catalyzed acylacylation takes place in the 2 position, i.e., in the thiophene ring. The yields of perchlorates II-IV are almost quantitative. However, the presence of a chlorine atom in the 5 position lowers the reactivity of I significantly. Whereas pyrylium salts IIa-d and IIIa-d are formed in high yields in the acylation of Ia, b even when the reagents are mixed at 20°C, brief heating to 70-80°C is required for Ic.

The IR spectra of II-IV contain two strong absorption bands at 1620 and 1530 cm^{-1}, which correspond to the stretching vibrations of the pyrylium ring. A characteristic very strong band of a ClO_4^- ion appears at 1085-1095 cm^{-1}. Signals of methyl (alkyl) groups, the chemical shift of which depends on their position in the benzo[b]thieno[2,3-c]pyrylium II-IV molecules, are observed in the PMR spectra. Thus the protons of the methyl groups of 1,3-dimethylbenzo[b]-thieno[2,3-c]pyrylium salt IIa are observed at 3.25 and 3.06 ppm, whereas an addi-

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TABLE 1. Benzo[b]thieno[2,3-c]pyrylium Perchlorates (II-IV)

Compound	mp, °C	Found, %				Empirical formula	Calc., %				Yield, %
		C	H	Cl	S		C	H	Cl	S	
IIa	194—195	49,7	3,4	11,1	10,1	$C_{13}H_{11}ClO_5S$	49,5	3,5	11,3	10,2	88
IIb	199—200	51,4	4,1	10,5	9,9	$C_{14}H_{13}ClO_5S$	51,2	4,0	10,8	9,8	89
IIc	158—160	52,8	4,5	10,2	9,1	$C_{15}H_{15}ClO_5S$	52,6	4,4	10,4	9,4	83
IId	167—168	53,9	4,9	10,0	9,1	$C_{16}H_{17}ClO_5S$	53,8	4,8	9,9	9,0	80
IIIa	202—203	51,4	3,8	10,6	9,6	$C_{14}H_{13}ClO_5S$	51,2	4,0	10,8	9,9	93
IIIb	195—196	52,7	4,5	10,6	9,2	$C_{15}H_{15}ClO_5S$	52,6	4,4	10,4	9,4	87
IIIc	218- 219	53,9	4,9	10,1	9,1	$C_{16}H_{17}ClO_5S$	53,8	4,8	9,9	9,0	85
IIId	226—227	55,4	5,1	9,3	8,7	$C_{17}H_{19}ClO_5S$	55,1	5,2	9,6	8,6	85
IVa	227—228	44,8	3,0	20,5	9,2	$C_{13}H_{10}Cl_2O_5S$	44,7	2,9	20,3	9,2	85
IVb	210—211	46,5	3,5	19,7	8,6	$C_{14}H_{12}Cl_2O_5S$	46,3	3,3	19,5	8,8	81
IVc	223—224	47,8	3,8	18,9	8,5	$C_{15}H_{14}Cl_2O_5S$	47,7	3,7	18,8	8,5	80
IVd	204—205	49,2	4,3	18,1	8,3	$C_{16}H_{16}Cl_2O_5S$	49,1	4,1	18,2	8,2	80

TABLE 2. Benzo[b]thieno[2,3-c]pyridines (V-VII)

Compound	mp, °C	Found, %					Empirical formula	Calc., %					Yield, %	mp of the picrate, °C
		C	H	Cl	N	S		C	H	Cl	N	S		
Va	94—95	73,4	5,3	—	6,7	15,0	$C_{13}H_{11}NS$	73,2	5,2	—	6,6	15,1	94	260—261
Vb	98—99	74,1	5,8	—	6,3	14,0	$C_{14}H_{13}NS$	74,0	5,7	—	6,2	14,1	95	257—258
Vc	—	74,9	6,4	—	5,9	13,2	$C_{15}H_{15}NS$	74,7	6,2	—	5,8	13,3	93	233—235
Vd	40	75,3	7,1	—	5,8	12,7	$C_{16}H_{17}NS$	75,2	6,8	—	5,5	12,6	93	202—203
VIa	115	74,2	5,8	—	6,4	14,2	$C_{14}H_{13}NS$	74,0	5,7	—	6,2	14,1	94	267—268
VIb	55—56	74,8	6,5	—	5,9	13,2	$C_{15}H_{15}NS$	74,7	6,2	—	5,8	13,3	93	262—263
VIc	46—47	75,3	6,8	—	5,7	12,5	$C_{16}H_{17}NS$	75,2	6,8	—	5,5	12,5	92	238—239
VId	62—63	75,9	7,2	—	5,3	12,1	$C_{17}H_{19}NS$	75,8	7,0	—	5,2	11,9	90	195—196
VIIa	121—122	63,2	4,1	14,2	5,5	12,8	$C_{13}H_{10}ClNS$	63,1	4,0	14,4	5,7	12,9	92	257—258
VIIb	91—92	64,5	4,6	13,4	5,2	12,3	$C_{14}H_{12}ClNS$	64,2	4,6	13,6	5,4	12,2	90	246—247
VIIc	67—68	65,5	5,2	12,6	5,0	11,5	$C_{15}H_{14}ClNS$	65,3	5,1	12,9	5,1	11,6	90	222—223

TABLE 3. 1-Hydroxy- and 1-Amino Derivatives of Dibenzothiophene (VIII-XII)

Compound	mp, °C	Chemical shifts of the protons and methyl groups, ppm			Found, %				Empirical formula	Calc., %				Yield, %
		CH_3	R	R_2	C	H	N	S		C	H	N	S	
VIIIa	174—175	2,40	—	—	73,1	4,7	—	14,8	$C_{13}H_{10}OS$	72,9	4,6	—	14,9	50
VIIIb	167—169	2,44	—	2,30	73,8	5,2	—	14,0	$C_{14}H_{12}OS$	73,6	5,3	—	14,1	55
IXa	151—152	2,40	2,27	—	73,9	5,5	—	14,3	$C_{14}H_{12}OS$	73,6	5,3	—	14,1	53
IXb	180—181	2,43	2,20	2,33	74,7	5,9	—	13,0	$C_{15}H_{14}OS$	74,4	5,8	—	13,2	54
X*	225—226	2,43	—	2,3	64,3	4,4	—	12,5	$C_{14}H_{11}ClOS$	64,0	4,2	—	12,2	52
XIa	99—100	2,42	—	—	77,0	6,9	5,1	11,2	$C_{18}H_{19}NS$	76,8	6,7	5,0	11,4	41
XIb	73—74	2,40	—	2,35	76,9	7,3	5,0	10,6	$C_{19}H_{21}NS$	77,3	7,1	4,7	10,9	43
XIc	129—130	2,46	—	—	72,4	6,3	4,8	11,0	$C_{17}H_{17}NOS$	72,1	6,0	5,0	11,3	45
XId	143—144	2,44	—	2,4	72,4	6,6	4,9	11,1	$C_{18}H_{19}NOS$	72,7	6,4	4,7	10,8	43
XII†	123—124	—	—	—	68,8	5,5	4,7	10,5	$C_{18}H_{18}ClNS$	68,4	5,7	4,4	10,2	43

*Found: Cl. 13.6%. Calculated: Cl 13.4%.

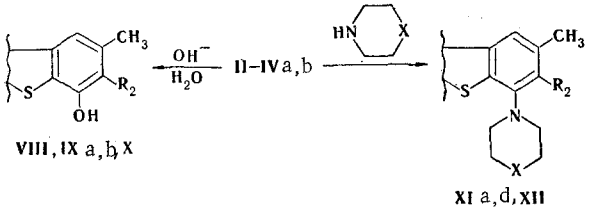
†Found: Cl 11.6%; Calculated: Cl 11.3%.

tional signal of a methyl group in the 6 position appears in the spectrum of IIIa at 2.66 ppm. The weak-field shift of the signals of the methyl groups is due to their deshielding by the positively charged heteroatom of the pyrylium ring. The aromatic protons are observed in the form of a multiplet at 7.8-8.4 ppm.

In order to synthesize new condensed derivatives of benzo[b]thiophene we studied the recyclization of II-IV under the influence of nucleophilic reagents (ammonia, secondary amines, and sodium hydroxide). Under the influence of ammonia, pyrylium salts II-IV are converted to benzo[b]thieno[2,3-c]pyridines V-VII in yields that are close to quantitative (Table 2). The latter are sulfur analogs of β-carbolines, and a study of their biological activity may prove to be of interest. The method for the preparation of pyridines V-VII from benzo[b]-

thieno[2,3-c]pyrylium salts differs favorably from the known methods based on the Bischler–Napieralski [7] and Pictet–Gams [8] reactions, since it makes it possible to vary the substituents in the benzo[b]thieno[2,3-c]pyridine molecule.

In our study of the reaction of pyrylium perchlorates with alkalis and secondary amines we developed methods for the synthesis of functional derivatives of dibenzothiophene that contain hydroxy and dialkylamino groups. The recyclization of II-IV in an alkaline medium leads to the formation of 1-hydroxydibenzothiophenes. The position of the hydroxy group was proved by means of the PMR spectra in the case of the products of the recyclization of 1-ethyl-substituted pyrylium perchlorates as in [9]. The presence in the PMR spectra of singlets of methyl groups indicates unambiguously the formation of 1-hydroxy derivatives of



VIII a,b R=H; a R_2=H; b R_2=CH_3; IX a,b R=CH_3; a R_2=H, b R_2=CH_3; X R=Cl; R_2=CH_3; XI a, b, c, d R=H; a,c R_2=H; b,d R_2=CH_3; a,b X=CH_2; c,d X=O; XII R=Cl; R_2=H; X=CH_2

dibenzothiophene (Table 3). The IR spectra contain an absorption band at 3620 cm^{-1}, which is characteristic for a phenolic group. Upon reaction with secondary amines (piperidine and morpholine), II-IV form 1-(N-piperidino)- and 1-(N-morpholino)dibenzothiophenes (Table 3). The structures of the latter were proved by their PMR spectra, as in the proof of the structure of the hydroxy derivatives of dibenzothiophene adduced above.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds obtained were recorded with a Perkin-Elmer 180 spectrometer. The PMR spectra were recorded with a Tesla BS-467 spectrometer (60 MHz) with tetramethylsilane as the standard; the spectra of the pyrylium salts were recorded in CF_3COOH, while the spectra of the hydroxy and dialkylamino derivatifes of dibenzothiophene were recorded in CCl_4.

Benzo[b]thieno[2,3-c]pyrilium Perchlorates (IIa-d to IVa-d). An acylating mixture consisting of 0.05 mole of the corresponding anhydride and 0.01 mole of 70% perchloric acid was added with stirring at 0°C to 0.01 mole of Ia-c, during which the reaction mixture warmed up and then solidified after a certain time. After 10 min, 50 ml of ether was added to the reaction mixture, and the precipitate was removed by filtration, washed with cold alcohol and ether, dried, and crystallized from glacial acetic acid. Data on IIa-d to IVa-d are presented in Table 1.

Benzo[b]thieno[2,3-c]pyridines (Va-d to VIIa-d). Ammonia gas was passed into a suspension of 0.01 mole of IIa-d to IVa-d in 30 ml of alcohol at 20°C for 20 min, after which the solution was refluxed for 10 min and poured into a mixture of water and ice. The reaction product was extracted with ether and dried over sodium hydroxide. The ether was evaporated, and the residue was crystallized from hexane. Data on Va-d to VIIa-d are presented in Table 2.

1-Hydroxy Derivatives of Dibenzothiophene (VIIIa, b, IXa, b, and X). A solution of 0.07 mole of sodium hydroxide in 6 ml of water was added to 0.01 mole of IIa, b, to IVa, b in 30 ml of alcohol, and the reaction mixture was refluxed for 6 h. It was then cooled and poured into 100 ml of water, and aqueous mixture was extracted with ether. The aqueous layer was separated and acidified with hydrochloric acid. The precipitate was removed by filtration and crystallized from aqueous alcohol. Data on VIIIa, b, IXa, b, and X are presented in Table 3.

1-Dialkylamino Derivatives of Dibenzothiophene (XIa-d, XII). A mixture of 0.01 mole of IIa-d or IVa and 15 ml of the secondary amine was refluxed for 5 h, after which the excess amine was removed by vacuum distillation, and the residue was dissolved in ether. The ether solution was washed thoroughly with an alkaline solution to remove the hydroxy compound, and the ether layer was dried over sodium hydroxide. The ether was removed, and the residue was crystallized from hexane. Data on XIa-d andXII are presented in Table 3.

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RING-CHAIN TAUTOMERISM OF SUBSTITUTED HYDRAZONES. 18.* SYNTHESIS OF 2-HYDRAZINO-1-PROPANETHIOL AND STRUCTURE OF ITS ALKYLIDENE DERIVATIVES

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1-Aminoaziridines react with hydrogen sulfide with ring opening to give vic-hydrazino thiols. In the case of 1-amino-2-methylaziridine the reaction proceeds regioselectively with the formation of 2-hydrazino-1-propanethiol. The products of condensation of the latter with carbonyl compounds exist in solution, depending on their structure, in the form of the corresponding perhydro-1,3,4-thiadiazines, (2-mercapto-1-methylethyl)hydrazones, or tautomeric mixtures of these compounds. The thermodynamic parameters of the tautomeric equilibria were determined for several systems from the ^{1}H NMR spectra.

In connection with the study of the ring-chain tautomerism of perhydro-1,3,4-thiadiazines, compounds that are not substituted in the 4 position are of special interest, since 4-alkylperhydrothiadiazines exist exclusively in the cyclic form in solutions in most cases [1]. The simplest method for the synthesis of such compounds consists in the condensation of aldehydes or ketones with hydrazino thiols. However, up until recently, the first representatives of the homologous series of vicinal hydrazino thiols were unknown. It was only recently that we described 2-hydrazinoethanethiol, which was isolated in low yield as a side product in the reaction of acetone hydrazone with thiirane [2]. N-Alkylhydrazino thiols are obtained by mercaptoalkylation of alkylhydrazines with thiiranes in nonpolar solvents [3] or in several steps under severe conditions with the aid of an S-benzyl protective group [4]. The latter method, which is extremely laborious, is hardly suitable for the preparative synthesis of the more labile N-unsubstituted hydrazino thiols. As regards the first method, our attempts to subject hydrazine hydrate or anhydrous hydrazine to the reaction with lower thiiranes with the use of a large number of solvents led to the formation of only products of the polymerization of the thiirane.

In order to develop a general preparative method for the production of vicinal hydrazino thiols with an unsubstituted hydrazo group we checked out the reaction of 1-aminoaziridines with hydrogen sulfide. It is known that hydrogen sulfide reacts smoothly with 1-alkyl- and 1-acylaziridines at low temperatures to give the corresponding amino thiols [5, p. 19].

Aminoaziridines I were synthesized by cyclization of β-hydrazinoalkyl sulfates under the conditions of the Wenker reaction [6]. We found that the use of pure aminoaziridines, which

*See [1] for Communication 17.

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