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RECYCLIZATION OF 1,3-DIMETHYLBENZO[*b*]FURO[2,3-*c*]- AND 1,3-DIMETHYLBENZO[*b*]THIENO[2,3-*c*]PYRYLIUM WHEN TREATED WITH SECONDARY AMINES. SYNTHESIS OF 3-DIALKYLAMINO DERIVATIVES OF DIBENZOFURAN AND DIBENZOTHIOPHENE

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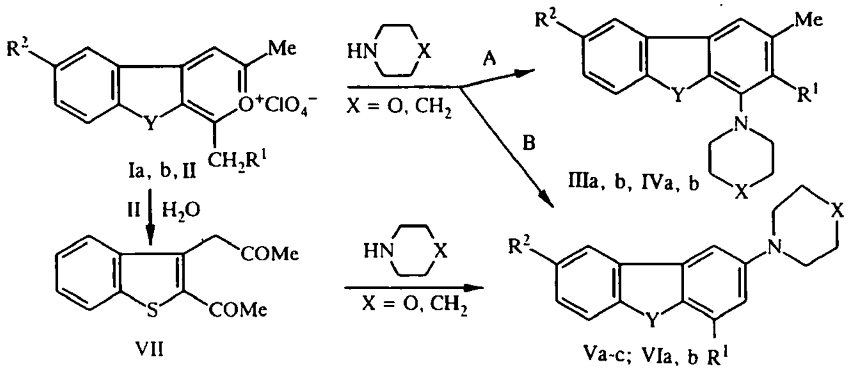
We have established that 2,4-dimethylbenzo[b]furo[3,2-c]pyrylium and 2,4-dimethylbenzo[b]thieno[3,2-c]-pyrylium salts can undergo recyclization to 3-dialkylamino derivatives of dibenzofuran and dibenzothiophene when treated with secondary amines. We compare the physicochemical and spectral characteristics of the compounds obtained with the recyclization products of 1,3-dimethylbenzo[b]furo[2,3-c]- and 1,3-dimethylbenzo[b]thieno[2,3-c]pyrylium salts.

Recyclization of alkyl-substituted pyrylium salts when treated with secondary amines occurs with participation of α-alkyl substituents and leads to formation of dialkylanilines [1, 2]. Benzo[*c*]pyrylium cations and pyrylium cations condensed with heterocyclic compounds behave similarly [3-6]. The structure of the recyclization products formed in the case of benzo[*c*]pyrylium salts and their hetero analogs depends on the site of initial addition of the secondary amine, and occurs according to an ANRORC scheme. We showed earlier that the reaction of 1-ethyl-3-methylbenzo[*b*]furo[2,3-*c*]- and 1-ethyl-3-methylbenzo[*b*]thieno[2,3-*c*]pyrylium salts with secondary amines occurs along route *A* with formation of 1-dialkylaminodibenzofurans and 1-dialkylaminodibenzothiophenes [5, 6]. The structure of the recyclization products was established from their ^{1}H NMR spectra (route A, $R^1 = CH^3$), while the question of the structure of the amino derivatives IIIa, IVa (R^1 = H) obtained from 1,3-dimethyl-substituted salts has remained unanswered because in this case it is difficult to determine the structure of the reaction product by ^{1}H NMR spectroscopy, and the method of analogy (transfer of the results of recyclization of a model compound having 1-ethyl-3-methyl substituents to the corresponding 1,3-dimethyl substituents) may lead to error.



I Y = O, a $R^1 = R^2$ = H; b R^1 = H, R^2 = Me; II Y = S, $R^1 = R^2$ = H; III Y = O, X = O, a $R^1 = R^2$ = H; b R^1 = H, R^2 = Me; IV Y = S, $R^1 = R^2$ = H; a X = O, b X = CH_2; V Y = O, a R^1 = Me, R^2 = H, X = O; b $R^1 = R^2$ = Me, X = O; c $R^1 = R^2$ = Me, X = CH_2; VI Y = S, a R^1 = Me, R^2 = H, X = O; b R^1 = Me, R^2 = H, X = CH_2

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TABLE 1. Characteristics of Synthesized Compounds III-VI

Compound	Empirical formula	Found % / Calculated % C	H	S(Cl)	N	mp°C	Yield, %
III a	$C_{17}H_{17}NO_2$	$\frac{76{,}6}{76{,}4}$	$\frac{6{,}2}{6{,}4}$	—	$\frac{5{,}2}{5{,}2}$	103 - 104	56
III b	$C_{18}H_{19}NO_2$	$\frac{76{,}8}{76{,}9}$	$\frac{6{,}6}{6{,}8}$	—	$\frac{5{,}1}{5{,}0}$	117 - 118	53
IV a	$C_{17}H_{17}NO_2$	$\frac{76{,}5}{76{,}4}$	$\frac{6{,}2}{6{,}4}$	—	$\frac{5{,}0}{5{,}2}$	151 - 152	56
V b	$C_{18}H_{19}NO_2$	$\frac{77{,}0}{76{,}9}$	$\frac{6{,}6}{6{,}8}$	—	$\frac{5{,}1}{5{,}0}$	117 - 118	54
V c	$C_{19}H_{22}ClNO$*	$\frac{69{,}0}{68{,}8}$	$\frac{6{,}7}{6{,}6}$	$\frac{(10{,}5)}{(10{,}7)}$	$\frac{4{,}0}{4{,}2}$	264 - 265	42
V d	$C_{22}H_{19}NO_2$	$\frac{80{,}0}{80{,}2}$	$\frac{5{,}1}{5{,}2}$	—	$\frac{4{,}1}{4{,}3}$	125 - 126	68
VI a	$C_{17}H_{17}NOS$	$\frac{71{,}9}{72{,}1}$	$\frac{6{,}1}{6{,}0}$	$\frac{11{,}2}{11{,}3}$	$\frac{5{,}2}{5{,}0}$	143 - 144	56
VI b	$C_{18}H_{20}ClNS$*	$\frac{68{,}3}{68{,}1}$	$\frac{6{,}4}{6{,}3}$	$\frac{9{,}9\ (11{,}4)}{10{,}1\ (11{,}2)}$	$\frac{4{,}2}{4{,}4}$	233 - 234	42
VI c	$C_{22}H_{19}NOS$	$\frac{76{,}3}{76{,}5}$	$\frac{5{,}3}{5{,}5}$	$\frac{9{,}0}{9{,}3}$	$\frac{4{,}0}{4{,}1}$	158 -159	90

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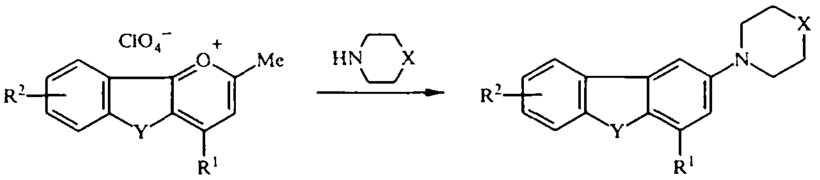
*Hydrochloride.

We must note that in all preceding papers on recyclization of benzo[*c*]pyrylium salts and their hetero analogs with secondary amines, no rigorous proof has been provided for the structure of the compounds formed, and only in [7] is the structure established using x-ray diffraction.

Accordingly, we studied the reaction of perchlorates of 2,4-dimethylbenzo[*b*]furo[3,2-*b*]- and 2,4-dimethylbenzo[*b*]thieno[3,2-*b*]pyrylium VIIIa-e with secondary amines. The 2,4-dimethylbenzo[*b*]furo[3,2-*b*]- and 2,4-dimethylbenzo[*b*]thieno[3,2-*b*]pyrylium salts represent one of the four possible isomeric forms of pyrylium salts condensed with the heterocyclic moiety of benzo[*b*]thiophene and benzo[*b*]furan. Their reactions have been inadequately studied, probably because of the formal similarity with benzo[*b*]pyrylium salts, for which recyclization reactions are not typical. Our interest in reactions of salts VIIIa-e with secondary amines is connected with the possibility of obtaining 3-dialkylaminodibenzofurans V and 3-dialkylaminodibenzothiophenes VI, which are some of the possible recyclization products of salts Ia and II via route B.

We have established that when salts VIIIa-e are boiled with secondary amines, their recyclization to 3-dialkylaminodibenzofurans Va-c and 3-dialkylaminobenzothiophenes VIa-c occurs.



VIIIa-e Va-e, VIa-c

V Y = O, a R^1 = Me, R^2 = H, X = O; b R^1 = R^2 = Me, X = O; c R^1 = R^2 = Me, X = CH_2;
d R^1 = Ph, R^2 = H, X = O; VI Y = S, a R^1 = Me, R^2 = H, X = O; b R^1 = Me, R^2 = H, X = CH_2;
c R^1 = Ph, R^2 = H, X = O; VIIIa,b,c Y = O,d, e Y = S; a R^1 = Me, R^2 = H; b R^1 = R^2 = Me;
c R^1 = Ph, R^2 = H; d R^1 = Me, R^2 = H; e R^1 = Ph, R^2 = H

Investigating the composition of the recyclization products of salts Ia and II by HPLC using compounds Va and VIa, b as markers, we observed that the major reaction products are compounds IIIa and IVa (95% of the mixture) with a small impurity of the corresponding isomeric compounds Va and VIa (no more than 5% of the mixture). Formation of the isomeric structures Va and VIa from salts Ia and II can be explained not only by addition of a secondary amine at the 3 position of the pyrylium cations I and II, but also by the possibility of opening of the pyrylium ring formed during the reaction with water to a 1,5-dicarbonyl compound, which may form first of all 1-hydroxy derivatives of dibenzothiophene and dibenzofuran and

TABLE 2. ^1H NMR Spectral Data for Compounds III-VI

Compound	^1H NMR Spectrum, ppm; spin–spin coupling constant (J), Hz								
	1-CH_3 (3-CH_3)	6-CH_3	2-H	4-H	5-H	6-H	7-H	8-H	Other protons
IIIa	(2,42)	—	6,82	7,48	7,78 d, J - 8,4	7,28 t	7,28 t	7,6 d, J - 8,4	3,36 and 3,94 (8H, m, CH_2- morpholine)
IIIb	(2,42)	2,47	6,82	7,48	7,81	—	7,25 d, J - 8,4	7,61 d, J - 8,4	3,36 and 3,94 (8H, m, CH_2- morpholine)
Va	2,49	—	6,80	7,46	7,80 d, J - 8,4	7,30 t	7,30 t	7,60 d, J - 8,4	3,36 and 3,94 (8H, m, CH_2- morpholine)
Vb	2,50	2,47	6,82	7,48	7,80	—	7,25 d, J - 8,4	7,61 d, J - 8,4	1,50, 1,67, 3,20 (9H, m, CH_2- piperidine)
VIa	2,50	—	7,15	7,84	8,36, J - 9,2	7,50	7,50	8,0 d, J - 9,2	3,40 and 400 (8H, m, CH_2- morpholine)
VIb	2,50	—	7,15	7,84	8,36, J - 9,2	7,48 t	7,48 t	8,0 d, J - 9,2	1,50, 1,67, 3,20 (9H, m, CH_2- piperidine)

secondly the already known amino derivatives. Indirect confirmation of the hypothesis that 1,5-dicarbonyl compounds are formed in the reaction mixture is the fact that in most cases, upon reaction with secondary amines the corresponding hydroxy derivatives were isolated [5, 6]. This hypothesis was tested by reacting 2-acetyl-3-acetonylbenzo[*b*]thiophene VII (obtained from the perchlorate II) with morpholine (in this case, we isolated the amine Vb and 1-hydroxy-3-methyldibenzothiophene).

The availability of benzo[*b*]thieno[3,2-*b*]- and benzo[*b*]furo[3,2-*b*]pyrylium salts and their facile conversion to the corresponding amino derivatives of dibenzothiophene and dibenzofuran makes this reaction convenient for obtaining the latter. In Table 1, we present data on the results of recyclization of salts VIIIa-e (which have different substituents on the pyrylium and benzene rings) with secondary amines.

EXPERIMENTAL

The IR spectra were recorded on a Perkin-Elmer 180 spectrometer in Vaseline oil. The ^1H NMR spectra were recorded on a Gemini-200 in pyridine-D_5, internal standard TMS. Analysis of the reaction products was done by HPLC, on a chromatograph made by Laboratory Pristroje [Instrument] (Prague); the detector was an RIDK-102 differential refractometer, 3 × 150 mm, Separon C_{18} as the stationary phase, 7:3 methanol–water as the mobile phase. The characteristics of the synthesized compounds are presented in Table 1.

The starting compounds Ia, b and II were synthesized by the procedures in [5, 6]; the compounds VIIIa, c-e were synthesized as in [8, 9].

The 2,4,8-trimethylbenzo-[*b*]furo[3,2-*b*]pyrylium perchlorate VIIIb was obtained by the method previously described in [9] in 83% yield, mp 220-221°C.

General Procedure for Obtaining Compounds III-VI. A mixture of 5 mmoles of the appropriate perchlorate I, II, or VIII, 3 ml of the secondary amine, and 15 ml of isopropyl alcohol was boiled for 3 h. The solvent was driven off at reduced pressure. The residue was dissolved in benzene. This was washed with water and a 10% solute of base to remove hydroxy compounds. The benzene layer was dried with $MgSO_4$. The benzene was driven off, and the residue was crystallized from heptane. Compounds Vc and VIb were isolated as the hydrochlorides. They were crystallized from alcohol. The data on compounds III-VI are presented in Table 1.

2-Acetyl-3-acetonylbenzo[*b*]thiophene VII. A total of 50 ml of a 10% $NaHCO_3$ solution was added with shaking to a suspension of 3.15 g (0.01 moles) salt II in 100 ml benzene. The shaking was continued until complete disappearance of the suspension of perchlorate II. The benzene layer was separated, washed with water, and dried with $MgSO_4$. The benzene was driven off under vacuum. Yield, 2.5 g (91%). mp 67-68°C (from heptane). IR spectrum: 1705, 1655, 1580, 1550, 1430, 1360, 1320, 1240, 1170, 970, 770, 740 cm^{-1}. Found, %: C 67.5; H 5.5; S 13.6. $C_{13}H_{12}O_2S$. Calculated, %: C 67.3; H 5.4; S 13.8.

1-Methyl-3-morpholinodibenzothiophene VIa. A mixture of 2.3 g (10 mmoles) compound VII and 10 ml morpholine was boiled for 4 h. The excess amine was distilled off under vacuum. The residue was dissolved in benzene and washed with 10% HCl. The benzene layer was separated and the water layer was made alkaline. The separated amine was extracted with ether. The ether layer was dried with $MgSO_4$ and evaporated down. The residue was crystallized from heptane. Yield, 0.56 g (20%) of dibenzothiophene VIa. The IR spectrum and the NMR spectrum of the material were identical to the spectra of 1-methyl-3-morpholinodibenzothiophene obtained from the perchlorate VIIId (Table 1). A mixed sample of these compounds did not give a depression of the melting point. IR spectrum: 1590, 1580, 1565, 1420, 1390, 1300, 1260, 1250, 1200, 1120, 980, 900, 860, 775, 750 cm^{-1}.

1-Hydroxy-3-methyldibenzothiophene with characteristics identical to the literature data in [5] was isolated from the benzene layer. Yield, 11%. Using the same procedure, 1-methyl-3-morpholinodibenzothiophene (VIb), which was identical to the compound obtained from the perchlorate VIIId (Table 1), was obtained in 23% yield using the same procedure from compounds VII and piperidine. IR spectrum: 1590, 1575, 1500, 1420, 1300, 1200, 1160, 1060, 1040, 875, 770, 740, 725 cm^{-1}.

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