Chemistry of Heterocyclic Compounds, Vol. 40, No. 8, 2004

REACTIONS OF 1,3-SUBSTITUTED BENZOTHIENO[2,3-*c*]PYRYLIUM SALTS WITH PRIMARY AMINES

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We have studied the reactions of benzothieno[2,3-c]pyrylium salts with primary amines. We have shown that recyclization occurs in two directions, and whether benzothieno[2,3-c]pyridinium salts or 1-aminodibenzothiophenes are formed is determined by the nature of the primary amine.

Keywords: 1-aminodibenzothiophenes, benzothieno[2,3-*c*]pyridinium perchlorates, benzothieno[2,3-*c*]-pyrylium perchlorates, recyclization.

Recyclization of alkyl-substituted pyrylium salts by primary amines can occur both with participation of the α-alkyl substituents (leading to alkylanilines) or without involvement of the substituents (forming N-pyridinium salts). The reaction of monocyclic pyrylium salts and 1,3-dialkyl-substituted benzo[*c*]pyrylium salts with primary amines leads to pyridinium and isoquinolinium salts [1, 2]. On the other hand, 1-alkyl-3-aryl- and 1-alkyl-3,4-diaryl-substituted benzo[*c*]pyrylium salts reacted with primary amines yield only substituted naphthylamines [3]. Reactions between primary amines and pyrylium salts annelated with heterocycles have not been studied.

We have studied the reaction of 1,3-disubstituted benzothieno[2,3-*c*]pyrylium salts **1, 2** with primary amines. It has been hypothesized that recyclization of pyrylium salts by primary amines occurs according to an ANRORC scheme, and includes addition of the nucleophile at the position 1 of the pyrylium ring [4]. Further opening of the pyran ring leads to intermediate formation of ketimines **A**, which exist in equilibrium with the tautomeric enamine form **B**. Formation of the end products (benzothieno[2,3-*c*]pyridinium salts **3-5** and 1-aminodibenzothiophenes **6**) obviously is determined by the ratio of forms **A** and **B**, and depends on the nature of amine.

So reaction of pyrylium salts **1a,b** with anilines leads to pyridinium salts **3b,c** and **4a,b**, while recyclization of pyrylium salts **2a,b** by methylamine and monoethanolamine leads exclusively to the 1-R^4-aminobenzothiophenes **6b-d**. Reactions of the salts **1a** and **2c,b** with benzylamine and furfurylamine lead to a mixture of pyridinium salts **3a, 5a,b** and 1-R^4-aminodibenzothiophenes **6a,d,e**.

The structure of 1-R^4-aminobenzothiophenes **6a-e**, established from the ^{1}H NMR spectra, confirms that addition of primary amines to pyrylium salts **1, 2** occurs at the position 1. The presence of an arylamino group at the position 3 of the pyrylium ring should signify that the product of ring opening after addition of amine at $C_{(1)}$ occurs to be not able to undergo further recyclizations. In fact, in studying the reaction of 1,6-dimethyl-3-(4'-tolylamino)benzothieno[2,3-*c*]pyrylium perchlorate (**7**) with benzylamine, we isolated for the first time the

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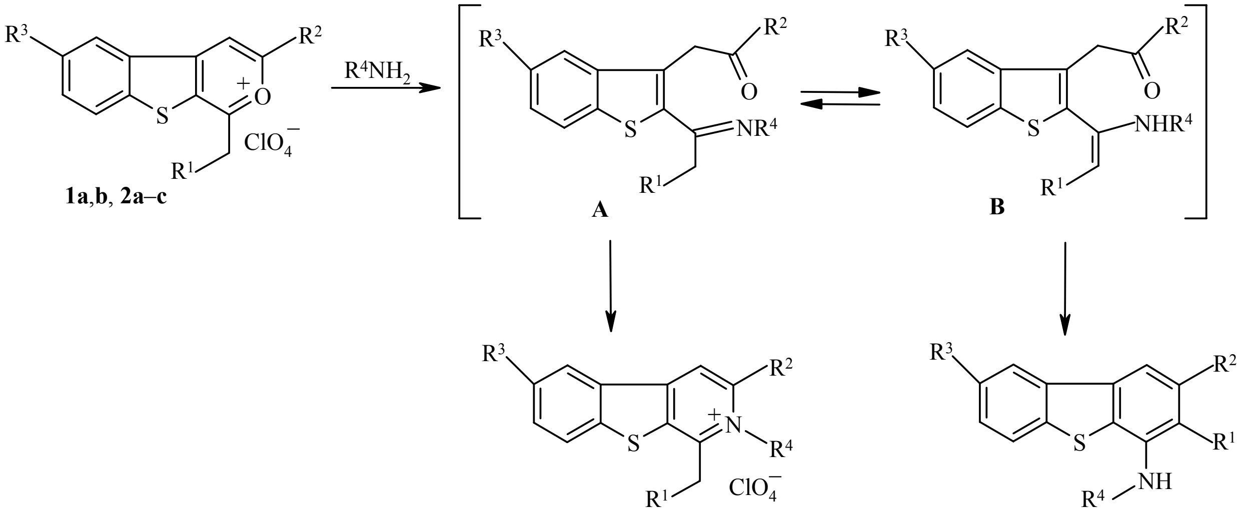

1a,**b**, **2a–c**

3a–c, **4a**,**b**, **5a**,**b**

6a–e

1 a, b R^1 = H, R^2 = Me, **a** R^3 = H, **b** R^3 = Cl; **2 a**, **c** R^1 = H, **b** R^1 = Me, **a-c** R^2 = Ph,
a, **b** R^3 = H, **c** R^3 = Me; **3 a-c** R^1 = R^3 = H, R^2 = Me, **a** R^4 = Bn, **b** R^4 = *p*-MeC_6H_4,
c R^4 = *p*-ClC_6H_4; **4 a**,**b** R^1 = H, R^2 = Me, R^3 = Cl, **a** R^4 = Ph, **b** R^4 = *p*-ClC_6H_4;
5 a R^1 = H, **b** R^1 = Me, **a**, **b** R^2 = Ph, **a** R^3 = Me, **b** R^3 = H, **a**, **b** R^4 = furfuryl;
6 a-c, **e** R^1 = H, **d** R^1 = Me, **a** R^2 = Me, **b-e** R^2 = Ph, **a-d** R^3 = H, **e** R^3 = Me;
a R^4 = Bn, **b** R^4 = Me, **c** R^4 = CH_2CH_2OH, **d**, **e** R^4 = furfuryl

TABLE 1. Characteristics of Synthesized Compounds

Compound	Empirical formula	Found, % Calculated, %					mp, °C	Yield, %
		C	H	Cl	N	S		
3a	$C_{20}H_{18}ClNO_4S$	59.61 59.48	4.33 4.46	8.65 8.80	3.31 3.47	7.80 7.93	270	14
3b	$C_{20}H_{18}ClNO_4S$	59.36 59.48	4.31 4.46	8.94 8.80	3.33 3.47	7.85 7.93	243-244	78
3c	$C_{19}H_{15}Cl_2NO_4S$	53.61 53.77	3.41 3.54	16.88 16.75	3.45 3.30	7.61 7.55	267-268	74
4a	$C_{19}H_{15}Cl_2NO_4S$	53.95 53.77	3.41 3.54	16.86 16.75	3.47 3.30	7.60 7.55	283	58
4b	$C_{19}H_{14}Cl_3NO_4S$	49.91 49.73	3.17 3.05	23.35 23.23	3.12 3.05	7.12 6.98	273-274	50
5a	$C_{24}H_{20}ClNO_5S$	61.52 61.34	4.39 4.26	7.34 7.56	2.73 2.98	6.69 6.82	248	12
5b	$C_{24}H_{20}ClNO_5S$	61.52 61.34	4.18 4.26	7.73 7.56	2.81 2.98	6.77 6.82	173	18
6a*	$C_{20}H_{18}ClNS$	70.57 70.69	5.44 5.30	10.21 10.46	4.23 4.12	9.35 9.43	171-172	23
6b	$C_{19}H_{15}NS$	79.02 78.89	5.31 5.19	—	4.71 4.85	11.16 11.07	94-95	86
6c	$C_{20}H_{17}NOS$	75.17 75.24	5.47 5.33	—	4.28 4.39	10.21 10.03	148-149	90
6d*	$C_{24}H_{20}ClNOS$	71.15 71.02	4.87 4.93	8.61 8.75	3.60 3.45	7.67 7.89	175-177	57
6e	$C_{24}H_{19}NOS$	78.22 78.05	5.37 5.15	—	3.65 3.79	8.82 8.67	116	78
8	$C_{27}H_{26}N_2OS$	75.87 76.02	6.25 6.14	—	6.44 6.57	7.60 7.52	150-152	91

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* Hydrochlorides.

TABLE 2 ^1H NMR Spectral Characteristics of Benzothieno[2,3-*c*]pyridinium perchlorates **3-5** and 1-R^4-aminodibenzothiophenes **6a-e**

Com-pound	Chemical shifts, δ, ppm (*J*, Hz)			
	Aliphatic protons			Aromatic protons
	$1-CH_3$ ($1-C_2H_5$) [$4'-CH_3$]	$3-CH_3$ ($6-CH_3$) [$2-CH_3$]	NR^4, NHR^4	
3a	3.03	2.84	6.03 (CH_2)	7.10 (2H, m, 2'-, 6'-H); 7.40 (3H, m, 3'-, 4'-, 5'-H); 7.78 (1H, t, 7-H); 7.90 (1H, t, 6-H); 8.35 (1H, d, J_{56} = 8.4, 5-H); 8.65 (1H, d, J_{78} = 8.4, 8-H); 8.94 (1H, s, 4-H)
3b	3.70 [2.28]	2.55	—	7.44 (2H, d, J_{32} = 8.2, 3'-, 5'-H); 7.69 (2H, d, J_{23} = 8.2, 2'-, 6'-H,); 7.76 (1H, t, 7-H); 7.88 (1H, t, 6-H); 8.40 (1H, d, J_{87} = 8.0, 8-H); 8.75 (1H, d, J_{56} = 8.0, 5-H); 9.05 (1H, s, 4-H)
3c	2.69	2.50	—	7.76-8.00 (2H, m, 6-, 7-H); 7.79 (2H, d, J_{32} = 8.2, 3'-, 5'-H); 7.90 (2H, d, J_{23} = 8.2, 2'-, 6'-H); 8.40 (1H, d, J_{87} = 8.0, 8-H); 8.75 (1H, d, J_{56} = 8.0, 5-H); 9.05 (1H, s, 4-H)
4a	2.68	2.48	—	7.69-7.84 (5H, m, 2'-, 3'-, 4'-, 5'-, 6'-H); 7.97 (1H, dd, J_{78} = 8.8, J_{75} = 2.1, 7-H); 8.44 (1H, d, J_{87} = 8.8, 8-H); 8.90 (1H, d, J_{57} = 2.1, 5-H); 9.05 (1H, s, 4-H)
4b	2.70	2.49	—	7.77 (2H, d, J_{32} = 8.1, 3'-, 5'-H); 7.89 (2H, d, J_{23} = 8.1, 2'-, 6'-H); 7.97 (1H, d, J_{78} = 8.7, 7-H); 8.45 (1H, d, J_{87} = 8.7, 8-H); 8.91 (1H, s, 5-H); 9.09 (1H, s, 4-H)
5a	2.55	(2.35)	4.43 (CH_2)	7.08 (12H, m)
5b	(1.00, 2.98, *J* = 7.1)	—	5.05 (CH_2)	7.50-7.25 (13H)
6a*	—	2.31	4.51 (CH_2); 6.56 (NH)	7.20-7.48 (9H, m); 7.51 (1H, s, 4-H); 8.00 (1H, d, *J* = 8.4, 8-H); 8.20 (1H, d, *J* = 8.4, 5-H)
6b	—	—	3.80 (d, *J* = 5.4, CH_3); 5.65 (q, NH)	6.85 (1H, s, 2-H); 7.27-7.54 (5H, m); 7.80-7.82 (2H, m, 6-, 7-H); 7.85 (1H, s, 4-H); 8.10 (1H, d, J_{87} = 8.4, 8-H); 8.36 (1H, d, J_{56} = 8.4, 5-H)
6c	—	—	3.45 (2H, m, $C\underline{H}_2NH$); 3.68 (2H, m, $C\underline{H}_2OH$); 4.95 (t, *J* = 5.6, OH); 5.49 (t, *J* = 5.5, NH)	6.96 (1H, s, 2-H); 7.30-7.60 (5H, m); 7.75-7.86 (2H, m, 6-, 7-H); 7.90 (1H, s, 4-H); 8.10 (1H, d, J_{87} = 8.4, 8-H); 8.38 (1H, d, J_{56} = 8.4, 5-H)
6d	–	[2.15]	4.55 (2H, d, *J* = 6.3, CH_2); 6.25 (t, NH)	6.15 (1H, s, 4-H_{furan}); 6.25 (1H, s, 3-H_{furan}); 7.30-7.59 (7H, m, H_{phenyl}); 7.59 (1H, s, 5-H_{furan}); 7.79 (1H, s, 4-H); 7.90 (1H, d, J_{87} = 8.4, 8-H); 8.22 (1H, d, J_{56} = 8.4, 5-H)
6e	–	(2.49)	4.57 (2H, d, *J* = 6.3, CH_2); 6.25 (t, NH)	6.38 (2H, m, 3-, 4-H_{furan}); 7.03 (1H, s, 2-H); 7.31-7.49 (5H, m, H_{phenyl}); 7.59 (1H, s, 5-H_{furan}); 7.74 (1H, s, 4-H); 7.76 (1H, d, J_{78} = 7.4, 7-H); 7.88 (1H, d, J_{87} = 7.4, 8-H); 8.22 (1H, s, 5-H)

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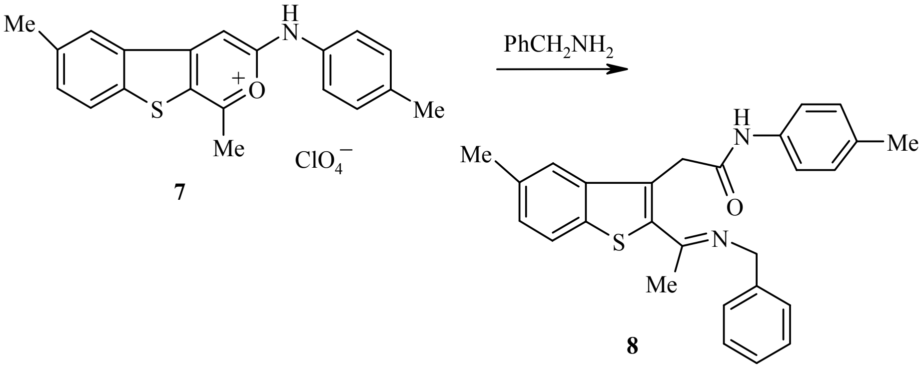
* Spectra of hydrochlorides.

product of addition of amine at the position 1 of N-(*p*-tolyl)amide of 2-[(1-benzylimino)ethyl]-5-methylbenzothiophene-3-acetic acid (**8**). Formation of such intermediate ketimines was postulated earlier by Dimroth and other researchers [1, 4-6].



EXPERIMENTAL

The ^{1}H NMR spectra were taken on a Gemini-200 (200 MHz) spectrometer in DMSO-d_6, internal standard TMS. The characteristics of the synthesized compounds are given in Tables 1 and 2.

1,3-Disubstituted benzothieno[2,3-*c*]pyrylium perchlorates **1a,b, 2a-c** were obtained by the procedures in [7, 8].

Synthesis of N-Aryl-1,3-dimethylbenzothieno[2,3-*c*]pyridinium Perchlorates (3) (General Procedure). The corresponding pyrylium perchlorates **1a,b** (5 mmol) were added to solution of arylamine (5 mmol) in acetic acid. The mixture was heated on a water bath for 1 h. The mixture was cooled down; the precipitate was filtered off and washed with alcohol and then ether, and then dried. Compounds **3b,c, 4a,b** were obtained. They were crystallized from methanol.

Reaction of Benzothieno[2,3-*c*]pyrylium Perchlorates with Aliphatic Amines. The corresponding primary amine (5.1 mmol) was added to suspension of the substituted pyrylium perchlorates (5 mmol) in alcohol and then heated for 1 h and cooled down. The precipitate of pyridinium perchlorates **3a, 5a,b** formed was filtered off, washed with acetone and then ether, and then dried. The obtained products were crystallized from methanol. The filtrate was evaporated down and then diluted with water; the precipitate of 1-R^4-aminodibenzothiophenes **6a-e** was filtered off and then crystallized from isopropyl alcohol.

N-(*p*-Tolyl)amide of 2-[(1-Benzylimino)ethyl]-5-methylbenzothiophene-3-acetic Acid (8). Benzylamine (2.5 ml) was added to suspension of 1,6-dimethyl-3-(4'-tolylamino)benzothieno[2,3-*c*]pyrylium perchlorate **7** (5 mmol) in isopropyl alcohol (25 ml). The reaction mixture was cooled down and water (25 ml) was added. The precipitate was filtered off and washed with water, and then crystallized from a mixture of benzene–hexane, 1:3. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.15 (3H, s, 4'-CH_3); 2.42 (3H, s, 5-CH_3); 2.49 (3H, s, $CH_3C=N$); 4.13 (2H, s, CH_2CO); 4.79 (2H, s, CH_2N); 6.91 (2H, d, *J* = 8.0, 3'-, 5'-H); 7.03 (2H, d, *J* = 8.0, 2'-, 6'-H); 7.24-7.31 (5H, m, H); 7.46 (1H, d, *J* = 8.2, 6-H); 7.80 (1H, d, *J* = 8.2, 7-H); 7.86 (1H, s, 4-H); 10.48 (1H, s, NH).

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