Reactions of sulfur ylides with α,β-unsaturated thioamides: synthesis of dihydrothiophenes and cyclopropanes

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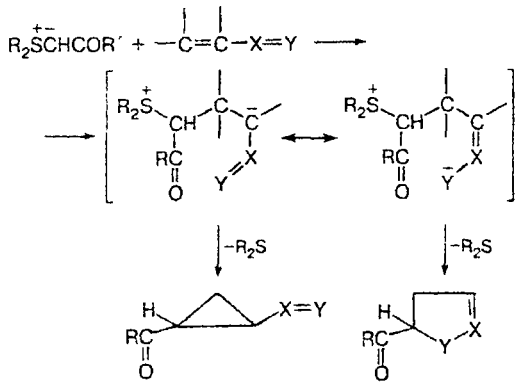
The reactions of stabilized sulfonium ylides with arylmethylenecyanothioacetamides proceed stereoselectively to yield 2-amino-4,5-dihydrothiophenes and cyclopropanethiocarboxamides. The structures of the latter compounds were confirmed by X-ray diffraction analysis.

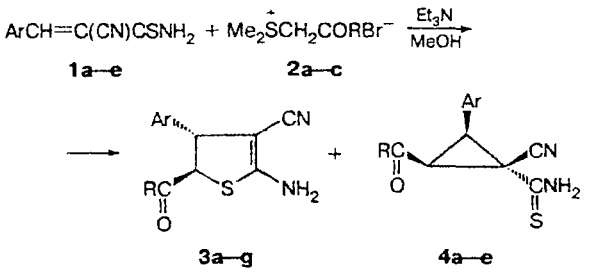
Key words: sulfur ylides; α,β-unsaturated thioamides; 2-amino-4,5-dihydrothiophenes; cyclopropanethiocarboxamides, X-ray diffraction analysis.

The reactions of stabilized sulfonium ylides with electron-deficient $-\overset{|}{C}=\overset{|}{C}-X=Y$ alkenes afford, generally, cyclopropanes[1–3] ($Ad_N-E_{1,3}$ mechanism), but sometimes these reactions may yield five-membered heterocycles due to the participation of the activating X=Y group (—X=Y = $-NO_2$, —N=O, or —N=NAr) ($Ad_N-E_{1,5}$ mechanism):[2,4,5]



The reactions of sulfur ylides with α,β-unsaturated amides can give 2-pyrrolidones due to the participation of the amide nitrogen atom.[6] Presently, reactions of sulfur ylides with α,β-unsaturated thioamides (—X=Y = $-C(NH_2)=S$) are poorly known.[7] However, the reactions of the latter compounds with pyridinium ylides stabilized by the carbonyl group have been studied. Generally, these reactions afford the corresponding pyridinethiones as a result of attack of the N atom of the thioamide fragment on the carbonyl group.[8] However, if molecules of the reagents contain bulky substituents, products of the $Ad_N-E_{1,5}$ reaction, namely, 2-aminodihydrothiophenes, can be obtained.[9–11]

We have found that the reactions of arylmethylenecyanothioacetamides of the general formula $ArCH=C(CN)CSNH_2$ (**1**) with sulfonium ylides $Me_2S^+C^-HCOR$ stabilized by the carbonyl group, which are generated *in situ* from the corresponding sulfonium salts **2**, yielded 2-aminodihydrothiophenes **3** and cyclopropanethiocarboxamides **4**. A mixture of the corresponding aldehyde and cyanothioacetamide $NCCH_2CSNH$ can be used instead of arylmethylenecyanothioacetamides.



Ar = 2-MeC_6H_4 (**1a**, **3a**, **4a**); 2-$NO_2C_6H_4$ (**1b**, **3b**, **4b**); 4-$MeOC_6H_4$ (**1c**, **3c**, **4c**); 3-pyridyl (**1d**, **3d**,**e**,**g**, **4d**,**e**); 2-thienyl (**1e**, **3f**)

R = Ph (**2a**, **3a**,**b**,**d**, **4a**,**b**,**d**); 2-thienyl (**2b**, **3c**,**e**, **4c**,**e**); *cyclo*-C_3H_5 (**2c**, **3f**,**g**)

In most cases, the major products were dihydrothiophenes **3**. In the case of R = *cyclo*-C_3H_5, cyclopropanes **4** were not isolated. The ^1H NMR spectra of cyclopropanes are characterized by an upfield shift of

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Table 1. ^{1}H NMR spectra of dihydrothiophenes **3a,c—g**[a]

Compound	δ (*J*/Hz)			
	H(4)	H(5)	NH_2	Other signals[b]
3a	5.11 (d, *J* = 2.7)	5.30 (d, *J* = 2.7)	6.40 (br.s)	2.30 (s, 3 H, CH_3); 7.2—7.3 (m, 3 H), 7.47 (d, 1 H), 7.56 (t, 2 H), 7.69 (t, 1 H), 8.02 (d, 2 H) (all H_{Ar})
3c	4.85 (d, *J* = 4.2)	5.08 (d, *J* = 4.2)	6.43 (br.s)	3.80 (s, 3 H, OCH_3); 6.93 (d, 2 H, H_{Ar}); 7.22 (t, 1 H, H_T); 7.34 (d, 2 H, H_{Ar}); 7.87 (d, 1 H, H_T); 7.99 (d, 1 H, H_T)
3d	5.00 (d, *J* = 3.2)	5.30 (d, *J* = 3.2)	6.45 (br.s)	7.39 (dd, 1 H, H_{Py}); 7.53 (t, 2 H, H_{Ar}); 7.65 (t, 1 H, H_{Ar}); 7.83 (br.d, 1 H, H_{Py}); 7.99 (d, 2 H, H_{Ar}); 8.51 (dd, 1 H, H_{Py}); 8.67 (d, 1 H, H_{Py})
3e	4.93 (d, *J* = 4.0)	5.20 (d, *J* = 4.0)	6.62 (br.s)	7.22 (t, 1 H, H_T); 7.39 (dd, 1 H, H_{Py}); 7.84 (br.d, 1 H, H_{Py}); 7.91 (d, 1 H, H_T); 8.00 (d, 1 H, H_T); 8.52 (dd, 1 H, H_{Py}); 8.68 (d, 1 H, H_{Py})
3f	5.03 (d, *J* = 2.8)	4.50 (d, *J* = 2.8)	6.47 (br.s)	0.9—1.1 (m, 4 H), 2.18 (q, 1 H) (all H_{Cp}); 6.97 (t, 1 H), 7.05 (d, 1 H), 7.35 (d, 1 H) (all H_T)
3g	4.77 (d, *J* = 3.0)	4.53 (d, *J* = 3.0)	6.80 (br.s)	0.9—1.1 (m, 4 H), 2.15 (q, 1 H) (all H_{Cp}); 7.37 (dd, 1 H, H_{Py}); 7.77 (br.d, 1 H, H_{Py}); 8.50 (dd, 1 H, H_{Py}); 8.60 (d, 1 H, H_{Py})

[a] The spectrum of compound **3b** was reported previously.[7]

[b] Notations are as follows: H_{Ar} are the protons of the benzene ring, H_T are the protons of the thiophene ring, H_{Py} are the protons of the pyridine ring, and H_{Cp} are the protons of the cyclopropane ring. The spin-spin coupling constants for these protons are not given.

Table 2. ^{1}H NMR spectra of cyclopropanes **4a—e**

Compound	δ (*J*/Hz)			
	H(3)	H(2)	$CSNH_2$	Other signals[a]
4a	4.00 (d, *J* = 10.3)	4.41 (d, *J* = 10.3)	9.03, 9.62 (both br.s)	2.31 (s, 3 H, CH_3); 7.05—7.10 (m, 2 H), 7.20—7.30 (m, 2 H), 7.65 (t, 2 H), 7.75 (t, 1 H), 8.20 (d, 2 H) (all H_{Ar})
4b	4.27 (d, *J* = 10.0)	4.53 (d, *J* = 10.0)	9.10, 9.72 (both br.s)	7.60—7.80 (m, 6 H), 8.02 (d, 2 H), 8.15 (d, 1 H) (all H_{Ar})
4c[b]	3.68 (d, *J* = 10.5)	4.28 (d, *J* = 10.5)	9.02, 9.58 (both br.s)	2.09 (s, 6 H, acetone); 3.77 (s, 3 H, OCH_3); 6.85 (d, 2 H, H_{Ar}); 7.23 (d, 2 H, H_{Ar}); 7.29 (t, 1 H), 8.00 (d, 1 H), 8.10 (d, 1 H) (all H_T)
4d	4.00 (d, *J* = 10.3)	4.47 (d, *J* = 10.3)	9.12, 9.70 (both br.s)	7.33 (dd, 1 H, H_{Py}); 7.61 (t, 2 H, H_{Ar}); 7.70—7.75 (m, 2 H, H_{Ar}, H_{Py}); 8.13 (d, 2 H, H_{Ar}); 8.50 (d, 1 H, H_{Py}); 8.59 (d, 1 H, H_{Py})
4e	3.95 (d, *J* = 10.1)	4.36 (d, *J* = 10.1)	9.14, 9.69 (both br.s)	7.20—7.30 (m, 2 H, H_{Py}, H_T); 7.74 (br.d, 1 H, H_{Py}); 8.03 (d, 1 H, H_T); 8.14 (d, 1 H, H_T); 8.50 (dd, 1 H, H_{Py}); 8.58 (d, 1 H, H_{Py})

[a] For the notations, see Table 1.

[b] The solvate with one acetone molecule.

the signals of the protons of the ring (H(2) and H(3)) relative to the signals of the corresponding protons of dihydrothiophenes (H(5) and H(4)) and by the presence of two signals of the protons of the thioamide group, whereas the amino group in the spectra of dihydrothiophenes gives one signal (Tables 1 and 2). An analogous upfield shift of the signals of the corresponding carbon atoms is observed in the ^{13}C NMR spectra of cyclopropanes **4**. In addition, these spectra are characterized by a low-field signal of the C atom of the thioamide group (Table 3). In the IR spectra of compounds **4**, the narrow intense absorption bands of the conjugated nitrile group at 2190—2200 cm^{-1} and of the C=C bond of the β-enaminonitrile fragment at 1590—1600 cm^{-1}, which are typical of dihydrothiophenes **3**, are absent, but the low intensity absorption band of the nonconjugated nitrile group at 2240—2250 cm^{-1} and the intense band of the C=S bond at 1225—1250 cm^{-1} are observed (Table 4).

The stereochemistry of the reaction is of most interest. In the molecules of the resulting dihydrothiophenes **3**, the substituents at the C(4) and C(5) atoms are in *trans* positions, which follows from the values of the spin-spin coupling constant ($J_{H(4),H(5)}$ = 2.7—4.2 Hz) and which is confirmed by the data of X-ray structural analysis of compound **3b**.[7] In the molecules of cyclopropanes **4**, the above-mentioned substituents are in *cis* positions, which is evidenced by the values of the spin-spin coupling constant ($J_{H(2),H(3)}$ = 10.0—10.5 Hz) typical of *cis*-protons in cyclopropanes.[12] This conclusion was confirmed by X-ray structural analysis of product **4b**. Figure 1 shows the overall view of molecule **4b**. The bond lengths and bond angles are given in Tables 5 and 6, respectively. The data on the structures of cyclopropanes that contain the thioamide fragment are unavailable in the Cambridge Structural Database (April 1997).

As can be seen from the Newman projection along the C(3)—C(2) bond (Fig. 2), the bulky substituents

Table 3. ^{13}C NMR spectra (δ) of compounds **3d—g** and **4c—e**

Compound	C(2)	C(3)	C(4)	C(5)	CN	Other signals[a]
3d	161.3	70.1	48.1	55.2	117.9	123.7, 134.2, 135.0, 148.5, 148.7 (all C_{Py}); 128.6, 128.7, 133.5, 137.0 (all C_{Ar}); 192.6 (CO)
3e	162.5	71.0	49.7	56.9	118.7	124.6, 135.9, 137.8, 149.5 (all C_{Py}); 129.7, 135.0, 136.8, 142.1 (all C_T); 187.4 (CO)
3f	161.8	74.2	48.0	63.2	117.8	12.1, 19.3 (all C_{Cp}); 125.5, 127.7, 146.8 (all C_T); 206.2 (CO)
3g	162.0	69.9	48.5	60.9	118.0	11.8, 18.8 (all C_{Cp}); 123.9, 134.9, 137.2, 148.5, 148.7 (all C_{Py}); 203.9 (CO)
Compound	$CSNH_2$	C(1)	C(3)[b]	C(2)[b]	CN	Other signals[a]
4c	196.6	34.7	38.9	40.0	115.5	55.2 (OCH_3); 113.8, 123.3, 130.5, 158.9 (all C_{Ar}); 129.2, 134.3, 136.1, 144.1 (all C_T); 183.9 (CO); 30.7, 204.7 (acetone)
4d	196.0	34.8	37.7	38.1	115.4	123.4, 128.1, 137.1, 148.7, 150.3 (all C_{Py}); 128.4, 129.2, 134.3, 136.89 (all C_{Ar}); 191.5 (CO)
4e	195.8	34.8	37.2	37.9	115.3	123.4, 128.0, 137.1, 148.7, 150.4 (all C_{Py}); 129.3, 134.8, 136.6, 144.1 (all C_T); 183.8 (CO)

[a] For the notations, see Table 1.
[b] The opposite assignments of the signals of the C(2) and C(3) atoms are possible.

Table 4. Physicochemical characteristics and IR spectra of compounds **3** and **4**

Compound	Yield (%)	R_f (eluent)[a]	M.p./°C	Found / Calculated (%) C	H	N	S	Molecular formula	IR, ν/cm^{-1}
3a	42	0.35 (*A*)	180—182	71.32 71.22	5.22 5.03	8.48 8.74	10.10 10.01	$C_{19}H_{16}N_2OS$	3220, 3330, 3440 (NH_2); 2200 (CN); 1685 (C=O); 1650 (δ(NH_2)); 1600 (C=C)
3b	40	0.17 (*A*)	*Cf.* Ref.[7]	—	—	—	—	$C_{18}H_{13}N_3O_3S$	*cf.* Ref. 7
3c	57	0.15 (*A*)	191—192	59.83 59.63	4.00 4.12	8.14 8.18	19.01 18.72	$C_{17}H_{14}N_2O_2S_2$	3230, 3330, 3420 (NH_2); 2195 (CN); 1680 (C=O); 1650 (δ(NH_2)); 1595 (C=C)
3d	53	0.15 (*B*)	223—225 (with decomp.)[b]	66.64 66.43	3.98 4.26	13.75 13.67	10.50 10.43	$C_{17}H_{13}N_3OS$	3340, 3120 (NH_2); 2195 (CN); 1695 (C=O); 1670 (δ(NH_2)); 1590 (C=C)
3e	19	0.15 (*B*)	196—199	57.70 57.49	3.52 3.54	13.03 13.41	20.19 20.46	$C_{15}H_{11}N_3OS_2$	3150—3250, 3340 (NH_2); 2190 (CN); 1650—1670 (C=O, δ(NH_2)); 1595 (C=C)
3f	65	0.35 (*A*)	157—159	56.22 56.50	4.44 4.38	10.00 10.14	23.63 23.20	$C_{13}H_{12}N_2OS_2$	3230, 3330, 3420 (NH_2); 2200 (CN); 1700 (C=O); 1650 (δ(NH_2); 1590 (C=C)
3g	70	0.2 (*B*)	216—218 (with decomp.)	61.88 61.97	4.57 4.83	15.75 15.49	12.19 11.82	$C_{14}H_{13}N_3OS$	3100—3150, 3320 (NH_2); 2190 (CN); 1710 (C=O); 1670 (δ(NH_2)); 1590 (C=C)
4a	13	0.4 (*A*)	169—171 (with decomp.)	71.39 71.22	4.89 5.03	9.06 8.74	10.22 10.01	$C_{19}H_{16}N_2OS$	3000—3150, 3370 (NH_2); 2245 (CN); 1630—1690 (C=O); 1235 (C=S)
4b	16	0.3 (*A*)	194—196 (with decomp.)	61.40 61.53	3.78 3.73	12.12 11.96	8.81 9.12	$C_{18}H_{13}N_3O_3S$	3220, 3320, 3430 (NH_2); 2245 (CN); 1670 (C=O); 1530, 1350 (NO_2); 1230 (C=S)
4c	11	0.33 (*A*)	137—139	60.43 59.98	5.10 5.03	6.76 6.99	16.03 16.01	$C_{20}H_{20}N_2O_3S_2$	3220, 3330, 3380 (NH_2); 2240 (CN); 1600—1680 (C=O); 1250 (C=S)
4d	15	0.32 (*B*)	decomp. >170	66.49 66.43	4.36 4.26	13.94 13.67	10.20 10.43	$C_{17}H_{13}N_3OS$	3000—3200, 3370 (NH_2); 2250 (CN); 1630—1700 (C=O); 1225 (C=S)
4e	24	0.28 (*B*)	177—180 (with decomp.)	57.64 57.49	3.30 3.54	13.59 13.41	20.33 20.46	$C_{15}H_{11}N_3OS_2$	3000—3200, 3350 (NH_2); 2245 (CN); 1620—1680 (C=O); 1250 (C=S)

[a] Silufol UV-254 plates; *A*, a 2 : 1 petroleum ether—AcOEt mixture; *B*, a 1 : 1 petroleum ether—AcOEt mixture.
[b] Published data:[10] m.p. 225—226 °C (with decomp.).

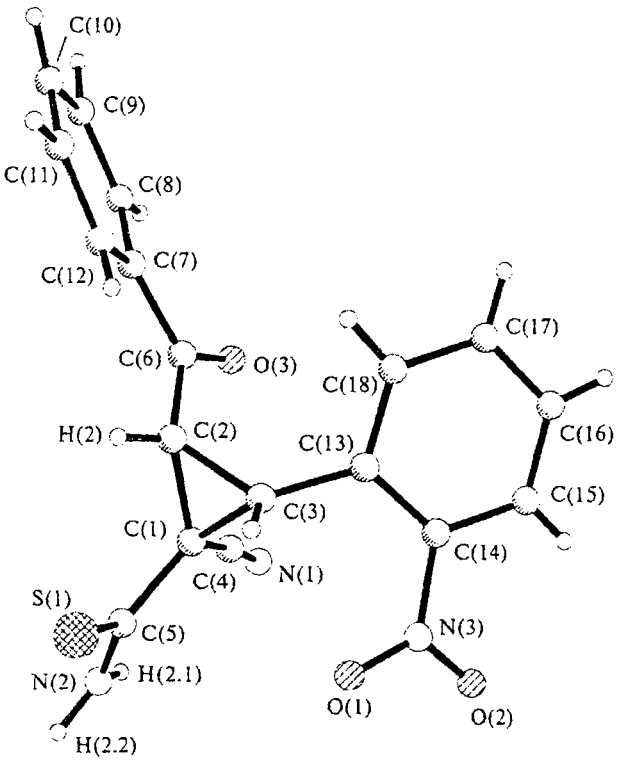

Fig. 1. Overall view of molecule **4b**.

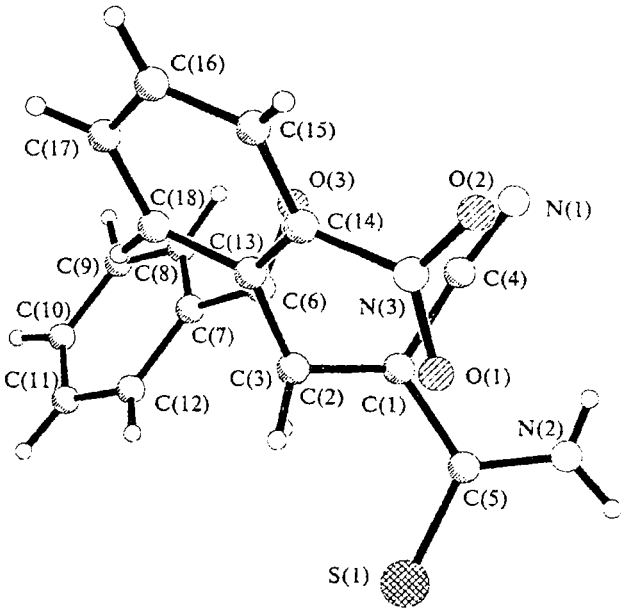

Fig. 2. Newman projection of molecule **4b** along the C(3)—C(2) bond.

are in a completely eclipsed *cis* conformation (the C(6)—C(2)—C(3)—C(13) and H(2)—C(2)—C(3)—H(3) torsion angles are 3.5° and −3.4°, respectively). The thioamide fragment is located below the plane of the ring. The observed mutual orientation of the substituents with respect to the three-membered ring leads to a number of forced shortened nonbonded intramolecular contacts: O(1)...C(1), 2.918(7) Å; O(1)...C(3), 2.697(7) Å; O(1)...H(3), 2.64(4) Å; O(1)...C(4), 3.192(7) Å; O(1)...C(5), 3.177(7) Å; O(3)...C(4), 2.736(7) Å; O(3)...C(13), 3.171(7) Å; O(3)...C(18), 3.117(7) Å; C(4)...C(14), 3.338(7) Å; C(4)...H(2.1), 2.34(5) Å; C(6)...C(18), 3.114(7) Å; S(1)...H(2), 2.81(4) Å; and S(1)...H(3), 2.65(4) Å (the sums of the van der Waals radii of the atoms are as follows:[13] O and C, 3.35 Å; O and H, 2.68 Å; C and C, 3.54 Å; C and H, 2.87 Å; and S and H, 2.91 Å). Of the above-mentioned contacts, the interactions with the participation of the C(4) atom are worthy of notice. These contacts result, apparently, in the substantial distortion of the

Table 5. Bond lengths (*d*) in molecule **4b**

Bond	*d*/Å	Bond	*d*/Å
S(1)—C(5)	1.664(6)	C(6)—C(7)	1.486(7)
O(1)—N(3)	1.221(6)	C(7)—C(8)	1.391(7)
O(2)—N(3)	1.225(6)	C(7)—C(12)	1.408(7)
O(3)—C(6)	1.225(6)	C(8)—C(9)	1.367(8)
N(1)—C(4)	1.145(7)	C(9)—C(10)	1.391(8)
N(2)—C(5)	1.316(7)	C(10)—C(11)	1.378(9)
N(3)—C(14)	1.457(7)	C(11)—C(12)	1.388(8)
C(1)—C(4)	1.461(7)	C(13)—C(18)	1.395(8)
C(1)—C(5)	1.511(7)	C(13)—C(14)	1.404(7)
C(1)—C(3)	1.511(7)	C(14)—C(15)	1.394(8)
C(1)—C(2)	1.538(7)	C(15)—C(16)	1.369(9)
C(2)—C(6)	1.477(8)	C(16)—C(17)	1.393(8)
C(2)—C(3)	1.526(7)	C(17)—C(18)	1.393(8)
C(3)—C(13)	1.492(7)		

Table 6. Bond angles (ω) in molecule **4b**

Angle	ω/deg	Angle	ω/deg
O(1)—N(3)—O(2)	122.3(5)	O(3)—C(6)—C(7)	121.0(5)
O(1)—N(3)—C(14)	119.0(5)	C(2)—C(6)—C(7)	117.9(5)
O(2)—N(3)—C(14)	118.6(5)	C(8)—C(7)—C(12)	118.8(5)
C(4)—C(1)—C(5)	115.5(5)	C(8)—C(7)—C(6)	120.0(5)
C(4)—C(1)—C(3)	116.3(4)	C(12)—C(7)—C(6)	121.1(5)
C(5)—C(1)—C(3)	118.2(4)	C(9)—C(8)—C(7)	121.4(5)
C(4)—C(1)—C(2)	118.1(5)	C(8)—C(9)—C(10)	119.7(6)
C(5)—C(1)—C(2)	117.3(4)	C(11)—C(10)—C(9)	120.0(6)
C(3)—C(1)—C(2)	60.1(3)	C(10)—C(11)—C(12)	120.7(6)
C(6)—C(2)—C(3)	123.8(5)	C(11)—C(12)—C(7)	119.4(6)
C(6)—C(2)—C(1)	122.0(5)	C(18)—C(13)—C(14)	116.6(5)
C(3)—C(2)—C(1)	59.1(3)	C(18)—C(13)—C(3)	119.1(5)
C(13)—C(3)—C(1)	123.7(4)	C(14)—C(13)—C(3)	124.1(5)
C(13)—C(3)—C(2)	122.1(5)	C(15)—C(14)—C(13)	121.2(6)
C(1)—C(3)—C(2)	60.8(3)	C(15)—C(14)—N(3)	117.1(5)
N(1)—C(4)—C(1)	173.8(6)	C(13)—C(14)—N(3)	121.7(5)
N(2)—C(5)—C(1)	116.6(5)	C(16)—C(15)—C(14)	120.7(6)
N(2)—C(5)—S(1)	123.2(5)	C(15)—C(16)—C(17)	119.8(6)
C(1)—C(5)—S(1)	120.3(4)	C(18)—C(17)—C(16)	119.3(6)
O(3)—C(6)—C(2)	121.1(5)	C(17)—C(18)—C(13)	122.4(5)

C(1)—C(4)—N(1) bond angle [173.8(6)°] from the linear one.

The *o*-nitrophenyl ring is twisted by 131.0° relative to the cyclopropane ring. The nitro group is twisted about the C(14)—N(3) bond by 20.2°. This value is substantially smaller than the values observed in 4-(2-nitrophenyl)-1,4-dihydropyridines[14,15] (the NO_2 group is twisted by 31—44° with respect to the Ph ring) in which the contacts between one O atom of the nitro group and the H atom (C(4)H) are more pronounced (the O...H distances are 2.27—2.30 Å), whereas in molecule **4b**, the O(1)...H(3) distance [2.64(4) Å] is comparable with the sum of the van der Waals radii of the corresponding atoms. Apparently, in molecule **4b** the orientation of the *o*-nitrophenyl substituent relative to the three-membered ring is determined by the above-mentioned nonbonded interactions. The positions of other substituents relative to the ring are characterized by the following torsion angles: C(1)—C(2)—C(6)—O(3), −22.8°; C(7)—C(6)—C(2)—C(1), 160.0°; C(2)—C(6)—C(7)—C(8), −163.1°; C(2)—C(1)—C(5)—S(1), −40.2°; and C(2)—C(1)—C(5)—N(2), 138.9°. It should be noted that this mutual arrangement of the substituents leads to steric hindrance of the molecule as a whole, which is confirmed by the values of the bond lengths compared to the mean values.[16] In the crystal, molecules **4b** are linked in infinite chains along the *b* axis through the intermolecular N(2)—H(2.2)...O(3) (x, $1+y$, z) hydrogen bonds [N(2)...O(3) is 3.090(7) Å; N(2)—H(2.2) is 0.90(4) Å; H(2.2)...O(3) is 2.19(4) Å; and the N(2)—H(2.2)...O(3) angle is 172(3)°].

The *trans* orientation of the thioamide group relative to the two other substituents in the cyclopropane ring provides a reasonable explanation for the observed stereochemical peculiarities of the reaction. Apparently, this reaction yields dihydrothiophenes and cyclopropanes in which the bulkiest substituents are most remote from each other, *i.e.*, these substituents are in *trans* positions. In the case of dihydrothiophenes **3**, the Ar and RCO groups are, evidently, such substituents. In the case of cyclopropanes **4**, the situation is more complex because the mutual orientation of the three substituents, namely, Ar, RCO, and $CSNH_2$, should be considered (the CN group is not taken into account because it is, undoubtedly, the smallest one). Apparently, the thioamide group is the bulkiest substituent (because of the large size of the S atom), and the two other substituents should be in *trans* positions with respect to the thioamide group and, therefore, in *cis* positions with respect to each other.

Apparently, thermodynamically most favorable configurations are selected due to epimerization of the final products **3** and **4**. Actually, it is well known that cyclopropanes that contain electron-withdrawing substituents undergo epimerization under the basic conditions.[17] As for dihydrothiophenes **3**, the H(5) proton should be even more labile (due to the adjacent S atom) compared to the corresponding H(2) proton in cyclopropanes, and hence, epimerization is also quite possible. Therefore, the proposed explanation is reasonable, although it is not unique. An alternative explanation for the observed stereochemistry involves the assumption that ylide is added stereoselectively at the C=C bond, and then Me_2S is eliminated, as has been suggested previously[10] for pyridinium ylides (kinetic control). The suggestion that in the course of the reaction, the initially formed cyclopropane is rearranged to dihydrothiophene was not confirmed. Thus, when a solution of compound **4a** in alcohol was heated at 50—60 °C for 40 min (the conditions were close to the reaction conditions), the formation of dihydrothiophene **3a** was not detected (according TLC) either in the absence of the base or in the presence of an equimolar amount of Et_3N.

Experimental

The ^1H NMR spectra were recorded on a Bruker-WM-250 instrument (250.13 MHz) in $(CD_3)_2CO$. The ^{13}C NMR spectra were measured on a Bruker-AM-300 instrument (75.47 MHz) in $(CD_3)_2SO$. The IR spectra were recorded on a Specord M-80 instrument. Compounds **3a—c,e,f** were recrystallized from alcohol, and compounds **4a—e** and **3d,g** were recrystallized from acetone. Dimethyl(phenacyl)sulfonium bromide **2a** was prepared according to a known procedure.[18]

Dimethyl(2-thienylcarbonylmethyl)sulfonium bromide (2b). Bromine (6.4 g, 40 mmol) was added dropwise to a solution of 2-acetylthiophene (5.0 g, 40 mmol) in MeOH (5 mL). The temperature of the reaction mixture was maintained at 20—25 °C (when approximately one-half of the amount of bromine was added, darkening of the mixture was observed). After completion of addition, methanol was distilled off. The residue (a dark-brown liquid) was dissolved (without isolation of 2-(bromoacetyl)thiophene) in acetone (10 mL), and then Me_2S (3.0 g, 48 mmol) was added. The mixture was kept at ~20 °C for 2 h. The precipitate of salt **2b** that formed was filtered off, washed with acetone, and dried. The yield was 6.5 g (61% calculated with respect to the starting 2-acetylthiophene), m.p. 199—200 °C (with decomp.).

Dimethyl(cyclopropylcarbonylmethyl)sulfonium bromide (2c). Me_2S (0.7 g, 11 mmol) was added to a solution of distilled bromoacetylcyclopropane[19] (1.63 g, 10 mmol) in acetone (3 mL). The reaction mixture was kept at 20 °C for 2 h (after 5 min, turbidity of the mixture was observed, and shortly thereafter a colorless oil was formed). The reaction mixture was kept in a refrigerator overnight. Then an oil crystallized out. The crystals were filtered off, washed with acetone, and dried. The yield was 1.85 g (82%), m.p. 115—120 °C (with decomp.).

Dihydrothiophenes 3 and cyclopropanes 4 (general procedure). Et_3N (0.2 g, 2 mmol) was added to a mixture of arylmethylenecyanothioacetamide **1** (or the corresponding aldehyde (2 mmol) and cyanothioacetamide (2 mmol)) and sulfonium salt **2** (2 mmol) in MeOH (3 mL). The suspension was heated until the reagents were dissolved (30—50 °C). Then the solution was cooled to ~20 °C. The products were isolated as described below. The poorer solubility of cyclopropanes **4a—c** in acetone compared to the corresponding dihydrothiophenes was used for isolation and purification. The compositions and purity of the products were checked by TLC. The yields, the melting points, the values of R_f, and the data of IR spectroscopy and elemental analysis for compounds **3** and **4** are given in Table 4.

***trans*-2-Amino-5-benzoyl-4-(2-tolyl)-4,5-dihydrothiophene-3-carbonitrile (3a) and *t*-2-benzoyl-*t*-3-(2-tolyl)-1-cyanocyclopropane-*r*-1-thiocarboxamide (4a).** The reaction of salt **2a** was carried out with *o*-toluic aldehyde (2 mmol) and cyanothioacetamide (2 mmol) instead of arylmethylenecyanothioacetamide **1a**. One drop of water was added to the cooled reaction mixture. When rubbing with a rod, a yellow precipitate of **3a** was formed. The precipitate was washed with water and dried. The yield was 0.27 g. The filtrate was diluted with water (10 mL). The yellowish precipitate (a mixture of **3a** and **4a**) that formed was filtered off, washed rapidly on a filter with acetone (1 mL), and dried. Pure product **4a** was obtained in a yield of 83 mg.

***trans*-2-Amino-5-benzoyl-4-(2-nitrophenyl)-4,5-dihydrothiophene-3-carbonitrile (3b) and *t*-2-benzoyl-*t*-3-(2-nitrophenyl)-1-cyanocyclopropane-*r*-1-thiocarboxamide (4b).** The reaction was carried out with the use of arylmethylenecyanothioacetamide **1b** and salt **2a**. The yellow precipitate of **3b** was formed from the warm solution. The precipitate was filtered off, washed with water, and dried. The yield was 0.28 g. The filtrate was diluted with water (10 mL). The brown precipitate (a mixture of **3b** and **4b**) that formed was filtered off, washed rapidly on a filter with acetone (1 mL), and dried. Pure product **4b** was obtained in a yield of 112 mg.

***trans*-2-Amino-4-(4-methoxyphenyl)-5-(2-thienylcarbonyl)-4,5-dihydrothiophene-3-carbonitrile (3c) and *t*-3-(4-methoxyphenyl)-*t*-2-(2-thienylcarbonyl)-1-cyanocyclopropane-*r*-1-thiocarboxamide (4c).** The reaction was carried out with the use of arylmethylenecyanothioacetamide **1c** and salt **2b**. Compound **3c** was precipitated from the warm solution. The precipitate was filtered off, washed with water, and dried. The yield was 0.39 g. The filtrate was diluted with water (10 mL). The oil that formed was separated and dissolved in acetone (2 mL) with heating. After cooling, crystals of **4c** · Me_2CO were formed. The yield (after filtering off, washing with water, and drying) was 43 mg.

***trans*-2-Amino-5-benzoyl-4-(3-pyridyl)-4,5-dihydrothiophene-3-carbonitrile (3d) and *t*-2-benzoyl-*t*-3-(3-pyridyl)-1-cyanocyclopropane-*r*-1-thiocarboxamide (4d).** Arylmethylenecyanothioacetamide **1d** and salt **2a** were used in the reaction. Compound **3d** was precipitated from the warm solution. The precipitate was filtered off, washed with water, and dried. The yield was 0.33 g. After 30 min, compound **4d** that precipitated from the mother liquor was washed with water and dried. The yield was 93 mg.

***trans*-2-Amino-4-(3-pyridyl)-5-(2-thienylcarbonyl)-4,5-dihydrothiophene-3-carbonitrile (3e) and *t*-3-(3-pyridyl)-*t*-2-(2-thienylcarbonyl)-1-cyanocyclopropane-*r*-1-thiocarboxamide (4e).** The reaction of salt **2b** was carried out with nicotinic aldehyde (2 mmol) and cyanothioacetamide (2 mmol) instead of arylmethylenecyanothioacetamide **1d**. The precipitate (a mixture of **3e** and **4e**) was formed from the warm solution. The precipitate was filtered off, washed with water, and dried. The yield was 0.39 g (62%). A suspension of the precipitate in alcohol (5 mL) was boiled for 3 min. Undissolved compound **4e** was filtered off and dried. The yield was 0.15 g. Cooling of the filtrate gave yellow crystals of **3e**. The yield (after drying) was 0.12 g.

***trans*-2-Amino-4-(2-thienyl)-5-(cyclopropylcarbonyl)-4,5-dihydrothiophene-3-carbonitrile (3f).** The reaction was carried out with the use of arylmethylenecyanothioacetamide **1e** and salt **2c**. The compounds were dissolved at ~20 °C within 1 min. After 10 min, water (0.5 mL) was added to the reaction mixture. When rubbing with a rod, compound **3f** was precipitated. The precipitate was filtered off, washed with water, and dried. The yield was 0.36 g.

Table 7. Atomic coordinates ($\times10^4$; for H, $\times10^3$) and isotropic (equivalent for nonhydrogen atoms) thermal parameters for molecule **4b**

Atom	*x*	*y*	*z*	U_{eq}/Å^2
S(1)	7454(1)	244(2)	4655(1)	28(1)
O(1)	10182(3)	−1294(5)	6388(3)	38(1)
O(2)	11472(3)	−2297(6)	7562(3)	49(1)
O(3)	7402(3)	−5700(5)	6234(2)	26(1)
N(1)	8676(4)	−2926(6)	7681(3)	35(1)
N(2)	7729(4)	494(7)	6376(4)	26(1)
N(3)	10684(4)	−2474(6)	6840(4)	27(1)
C(1)	7995(4)	−2271(7)	5937(3)	19(1)
C(2)	7341(4)	−3555(8)	5211(4)	22(1)
C(3)	8499(4)	−3220(7)	5407(4)	17(1)
C(4)	8347(4)	−2711(7)	6905(4)	24(1)
C(5)	7734(4)	−457(7)	5709(4)	21(1)
C(6)	6962(4)	−5114(7)	5460(4)	20(1)
C(7)	6063(4)	−5991(6)	4730(4)	17(1)
C(8)	5496(4)	−7191(7)	4966(4)	20(1)
C(9)	4708(4)	−8092(7)	4310(4)	25(1)
C(10)	4459(5)	−7806(8)	3386(4)	27(2)
C(11)	5008(5)	−6624(8)	3134(4)	29(2)
C(12)	5798(4)	−5685(7)	3795(4)	24(1)
C(13)	9343(4)	−4499(7)	5826(3)	19(1)
C(14)	10366(4)	−4151(7)	6491(4)	22(1)
C(15)	11126(5)	−5400(8)	6840(4)	29(2)
C(16)	10912(5)	−6987(8)	6505(4)	29(2)
C(17)	9912(5)	−7375(8)	5833(4)	25(1)
C(18)	9149(5)	−6130(7)	5500(4)	22(1)
H(2.1)	787(4)	8(7)	687(4)	2(2)
H(2.2)	757(3)	159(6)	633(3)	3(2)
H(2)	686(4)	−307(8)	473(4)	4(2)
H(3)	859(4)	−251(6)	494(3)	2(1)
H(8)	568(4)	−744(6)	561(3)	2(1)
H(9)	432(4)	−909(7)	448(4)	3(2)
H(10)	406(5)	−853(9)	298(5)	6(2)
H(11)	482(5)	−647(8)	249(4)	4(2)
H(12)	620(4)	−492(7)	363(3)	2(1)
H(15)	1172(5)	−513(8)	719(4)	4(2)
H(16)	1133(5)	−790(8)	671(4)	5(2)
H(17)	979(4)	−849(7)	559(3)	2(1)
H(18)	850(3)	−645(5)	504(3)	2(2)

***trans*-2-Amino-4-(3-pyridyl)-5-(cyclopropylcarbonyl)-4,5-dihydrothiophene-3-carbonitrile (3g).** The reaction was carried out with the use of arylmethylenecyanothioacetamide **1d** and salt **2c**. Compound **3g** was precipitated from the warm solution. The precipitate was filtered off, washed with water, and dried. The yield was 0.38 g.

X-ray structural analysis of compound 4b. Crystals of **4b** ($C_{18}H_{13}N_3O_3S$) are monoclinic, at −125 °C, a = 13.858(5) Å, b = 8.045(2) Å, c = 15.995(6) Å, β = 114.48(3)°, V = 1622.9(9) Å^3, d_{calc} = 1.438 g cm^{-3}, Z = 4, space group $P2_1/n$. The unit cell parameters and intensities of 2965 independent reflections were measured on an automated four-circle Siemens P3/PC diffractometer (Mo-Kα radiation, graphite monochromator, θ/2θ scanning technique, θ_{max} = 27°). The structure was solved by the direct method and refined by the full-matrix least-squares method with anisotropic thermal parameters for nonhydrogen atoms. The hydrogen atoms were located from the difference Fourier synthesis and refined isotropically. The final values of the R factors were as

follows: $R_1 = 0.074$ using 1477 independent reflections with $I > 2\sigma(I)$ and $wR_2 = 0.121$ using 2237 independent reflections. All calculations were carried out on an IBM PC/AT-486 computer using the SHELXTL PLUS and SHELXTL-93 programs. The atomic coordinates and isotropic thermal parameters (equivalent thermal parameters for nonhydrogen atoms) are given in Table 7.

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References

1. L. A. Yanovskaya, V. A. Dombrovskii, and A. Kh. Khusid, *Tsiklopropany s funktsional'nymi gruppami: sintez i primenenie* [*Cyclopropanes That Contain Functional Groups. Synthesis and Application*], Nauka, Moscow, 1980 (in Russian).
2. Yu. V. Belkin and N. A. Polezhaeva, *Usp. Khim.*, 1981, **50**, 909 [*Russ. Chem. Rev.*, 1981, **50** (Engl. Transl.)].
3. B. Trost, *J. Am. Chem. Soc.*, 1967, **89**, 138.
4. G. Kumaran and G. Kulkarni, *Synthesis*, 1995, 1545.
5. A. V. Samet, A. M. Shestopalov, and V. V. Semenov, *Khim. Geterotsikl. Soedin.*, 1996, 1136 [*Chem. Heterocycl. Compd.*, 1996, **32** (Engl. Transl.)].
6. H. König, H. Metzger, and K. Seelert, *Chem. Ber.*, 1965, **98**, 3712.
7. A. Samet, A. Shestopalov, V. Nesterov, and V. Semenov, *Synthesis*, 1997, 623.
8. A. Shestopalov, V. Litvinov, L. Rodinovskaya, and Yu. Sharanin, *Synthesis*, 1991, 402.
9. A. Shestopalov, O. Bogomolova, and V. Litvinov, *Synthesis*, 1991, 276.
10. L. A. Rodinovskaya, A. M. Shestopalov, and V. P. Litvinov, *Dokl. Akad. Nauk*, 1994, **339**, 214 [*Dokl. Chem.*, 1994 (Engl. Transl.)].
11. A. M. Shestopalov, O. P. Bogomolova, L. A. Rodinovskaya, V. P. Litvinov, and Yu. A. Sharanin, *Dokl. Akad. Nauk SSSR*, 1991, **317**, 112 [*Dokl. Chem.*, 1991 (Engl. Transl.)].
12. H. Gunther, NMR *Spectroscopy*, John Wiley and Sons, New York, 1980.
13. R. Rowland and R. Taylor, *J. Phys. Chem.*, 1996, **100**, 7384.
14. V. Nesterov, V. Shklover, Yu. Struchkov, Yu. Sharanin, A. Shestopalov, and L. Rodinovskaya, *Acta Crystallogr., C*, 1985, **41**, 1191.
15. V. N. Nesterov, L. A. Rodinovskaya, A. M. Shestopalov, and Yu. T. Struchkov, *Khim. Geterotsikl. Soedin.*, 1997, 643 [*Chem. Heterocycl. Compd.*, 1997, **33** (Engl. Transl.)].
16. F. Allen, O. Kennard, D. Watson, L. Brammer, A. Orpen, and R. Taylor, *J. Chem. Soc., Perkin Trans. 2*, 1987, S1.
17. *The Chemistry of Alkenes*, Ch. 7, Ed. S. Patai, Interscience Publishers, New York—London, 1964.
18. H. Böhme and W. Krause, *Chem. Ber.*, 1949, **82**, 426.
19. M. Calverley, *Tetrahedron*, 1987, **43**, 4609.

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