Tetrahedron Vol. 48, No. 33, pp. 6863-6874, 1992
Printed in Great Britain

0040-4020/92 $5.00+.00
Pergamon Press Ltd

A NOVEL CYCLOCONDENSATION OF XANTHATES CONTAINING ACTIVE METHYLENE GROUPS WITH ISOTHIOCYANATES.
SPECTRAL DATA AND X-RAY STRUCTURES OF THE PRODUCTS

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(*Received in UK* 29 *June* 1992)

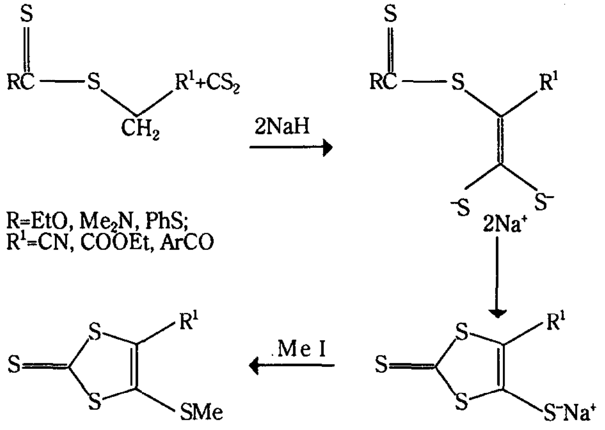
Abstract

A cyclocondensation reaction of S–(alkoxycarbonylmethyl)– and S–(cyanomethyl)dithiocarbonate O–esters with isothiocyanates in the presence of sodium tert–butoxide is described. Spectral data and X–ray structures of the main products are given.

Introduction

In the process of our investigations on the synthesis of unknown 4–aminosubstituted 1,3–dithiole–2–thiones we have examined the reaction of S–(alkoxycarbonylmethyl)– and S–(cyanomethyl)dithiocarbonate O–esters with isothiocyanates in DMF in the presence of sodium tert–butoxide [1]. The analogous reaction with carbon disulfide investigated recently by M.Augustin et al. [2] allows the synthesis of 4–alkylthio–1,3–dithiole–2–thione–5–carboxylic acid esters

(Scheme 1).



Scheme 1.

In the series of subsequent works the reaction conditions were studied in detail [3–6], and straightforward approaches to 4–alkylthio–1,3–dithiole–2–thiones [7–9], thieno–condensed 1,3–dithiole–2–thiones [10], and 1,3–thiazole systems [11] were proposed. The main feature of all these methods is a ring closure on sulfur. In our case the peculiarity is connected formally with the possibility of two alternative pathways, A and B (scheme 2), leading to 1,3–dithiole (ring closure on sulfur) and thiazole derivatives (ring closure on nitrogen) respectively.

The known reaction of isocyanoacetate esters with isothiocyanates demonstrated the ring closure on sulfur to give the thiazole ring as more preferable [12].

In this paper we present our spectral data on the reaction products, and the X–ray structures of compounds Ia, g and II. The full synthetic details are also discussed. Mass spectral investigations of the main products were undertaken to confirm the cyclization direction and results were published recently [13].

Synthesis

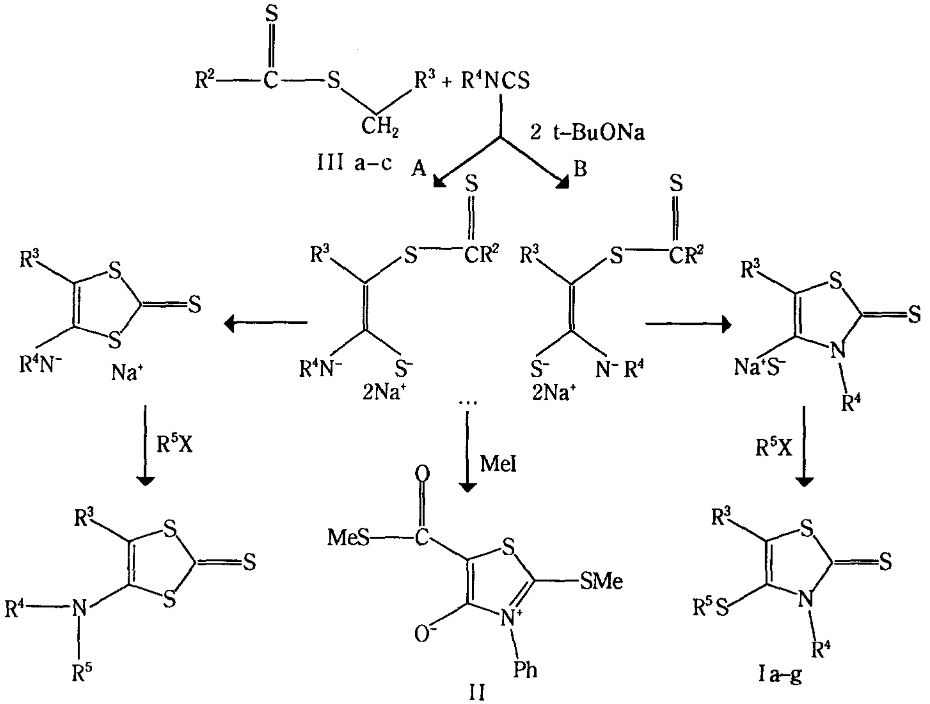
In the reaction of O–methyl S–(methoxycarbonylmethyl)dithiocarbonate (or xanthate) [15] and phenylisothiocyanate two products were obtained. On the basis of the spectral data analysis of both compounds (R^2=Me, R^3=COOMe, R^4=Ph, R^5=Me) it was not possible to assign them to the alternative products (routes A and B, scheme 2). The main products of the title reaction appeared to be 1,3–thiazoline–2–thione Ia [1]. This is confirmed by the X–ray data given below in this paper. An unexpected by–product 2–methylthio–3–phenyl–5–methylthiocarbonyl–1,3–thiazole–4–olate (II) was isolated, for which the X–ray investigations were also undertaken [14]. ^{1}H–NMR data of these compounds are given in Table 1.

The compound Ia was isolated after alkylation of the reaction mixture by methyliodide, diluting by water and filtering. Further purification by dissolving in benzene, filtering through silica gel, evaporation of the filtrate and recrystallization from methanol led to a 45 per cent yield of Ia. The product II remains on the silica gel during the filtration. It was isolated by elution with acetone evaporation of the solvent, and recrystallization from methanol in less than 1% yield. The yield of compound II can be increased to up to 6% by the change of the reaction conditions and mode of addition of reagents [14]. Searches for analogous products in the cases of Ib–g were unsuccessful. The possible reaction pattern is shown in Scheme 2. Yields, elemental analysis data and melting points of Ia–g are given in Table 2.

^{1}H-NMR, IR and UV spectra for Ia–g, II are given in Table 3.

X - Ray Structures

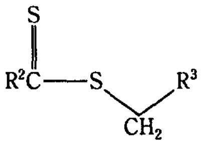
Geometry and final atom coordinates of molecule Ia are given in Figure I and Table 4 respectively. The five- and six-membered rings are planar. The dihedral angle between the rings is 85.3°, what hinders conjugation between them and leads to an increase in the bond distance C6–N(1.443(4)A). The atoms S2, C6, S3, C13 are almost coplanar in the five-membered ring plane.



I R^3, R^4, R^5=COOMe, Ph, Me(a), COOMe, Me, Me(b), COOMe, Ph, PhCO(c), COOEt, Ph, Me(d), COOEt, Me, Me(e), CN, Ph, Me(f), CN, Me, Me(g)

Scheme 2.

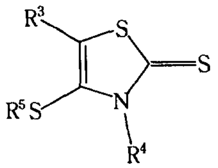
Table 1.



III a–c

N	R^2	R^3	^{1}H-NMR ($CDCl_3$), δ (ppm)
IIIa	MeO	COOMe	3.68 (s, 3H, COOMe) 3.88 (s, 2H, CH2) 4.10 (s, 3H, CSOMe)
IIIb	EtO	COOEt	1.22 (t, 3H, Me) 1.34 (t, 3H, Me) 3.84 (s, 2H, CH_2) 4.15 (q, 2H, CH_2Me) 4.59 (q, 2H, CH_2Me)
IIIc	EtO	CN	1.40 (t, 3H, Me) 3.84 (s, 2H, CH_2) 4.66 (q, 2H, CH_2Me)

Table 2.



I a–g

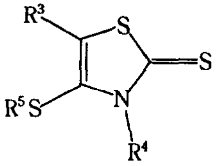
№	R^3	R^4	R^5	m.p. (°C)	Solvent for re-cryst.	Elemental analysis calcd./found C	H	N	S	Yield (%)
Ia	COOMe	Ph	Me	171	MeOH	48.46	3.73	4.71	32.34	45
						48.12	3.69	4.64	32.71	
Ib	COOMe	Me	Me	117	MeOH	35.73	3.85	5.95	40.87	25
						35.70	3.78	5.89	40.39	
Ic	COOMe	Ph	PhCO	152	MeOH				24.82	28
									24.79	
Id	COOEt	Ph	Me	132	EtOH	50.14	4.21	4.50	30.88	63
						49.78	3.76	4.50	30.19	

Table 2 cont'd ...

Ie	COOEt	Me	Me	110	EtOH				64.39 63.98	35
If	CN	Ph	Me	211	*	49.97 50.08	3.05 3.08	10.59 10.74	36.38 35.20	71
Ig	CN	Me	Me	101	MeOH	35.62 35.31	2.99 2.62	13.85 13.76	47.54 47.29	30

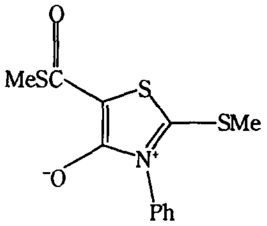
* The compound If was obtained pure enough without additional recrystallization.

Table 3.



I a-g

and



II

Nº	IR(cm^{-1})	UV, λ max (lgε) (nm)		^{1}H-NMR (CDCl$_3$), δ (ppm)
Ia	1732, 1595, 1533, 1490, 1310, 1235, 1080,	EtOH CHCl$_3$	309(3.98) 350(4.12) 312(3.97) 353(4.09)	2.25 (s, 3H, SMe) 3.81 (s, 3H, OMe) 7.25–7.48 (m, 5H, NPh)
Ib	1715, 1530, 1308, 1255, 1198, 1148, 1098, 1048		—	2.53 (s, 3H, SMe) 3.84 and 3.87 (s, 6H, NMe and OMe)
Ic	1728, 1683, 1593, 1533, 1307, 1258, 1233, 1203, 1175, 1160, 1080, 1063, 1055		—	3.85 (s, 3H, OMe) 7.05–7.80 (m, 10H, Ph)
Id	1717, 1525, 1310, 1295, 1235, 1127, 1100, 1062, 1028		—	1.33 (t, 3H, Me) 2.25 (s,3H, SMe) 4.32 (q, 2H, CH$_2$) 7.25–7.48 (m, 5H, NPh)
Ie	—		—	1.30 (t, 3H, Me) 2.48 (s, 3H, SMe) 3.76 (s, 3H, NMe) 4.29 (q, 2H, CH$_2$)

Table 3 cont'd ...

If	2210, 1590, 1523,	EtOH	268(3.92)	2.52 (s, 3H, SMe)
	1483, 1348, 1306,		312(3.91)	7.30–7.54 (m, 5H, NPh)
	1237, 1053		348(4.15)	
Ig	2188, 1513, 1311,	EtOH	267(3.78)	2.68 (s, 3H, SMe)
	1286, 1181, 1100		298(3.89)	3.73 (s, 3H, NMe)
	1050		348(4.13)	
II	1665, 1570, 1490,	EtOH	258(4.04)	2.27 (s, 3H, SMe)
	1355, 1220		388(4.10)	2.56 (s, 3H, SMe)
		$CHCl_3$	263(4.05)	7.25–7.50 (m, 5H, NPh)
			400(4.15)	

The atoms C13, 01, 02, C14 are situated in a plane which is slightly turned relative to the five membered ring (the dihedral angle value is 6.7°). The torsion angle N–C4–S3–C12 is 108.2°. The distances between molecules in the crystal do not exceed the sum of the van–der–Waals atom radii.

The geometry of molecule II, atom numbers, and the atom coordinates of II are shown in Figure 2 and Table 5 respectively. All five thiazole ring atoms are coplanar. The values show that the substituents in the positions 2, 4, 5 are included in the conjugate system of the molecule. The dihedral angle between the benzene ring and the heterocycle is 68.3°.

Table 4.
Final atom coordinates in molecule Ia.

Atoms	x	y	z
S1	0.2659(1)	0.06786(9)	0.47441(8)
C2	0.3764(5)	0.0963(4)	0.3354(3)
N3	0.5307(4)	0.2151(3)	0.3695(2)
C4	0.5604(6)	0.2816(4)	0.5011(3)
C5	0.4296(5)	0.2150(4)	0.5723(3)
S2	0.3060(1)	−0.00694(9)	0.19039(9)
C6	0.6530(5)	0.2611(3)	0.2728(3)
C7	0.5897(6)	0.3505(4)	0.1917(3)
C8	0.7006(6)	0.3877(4)	0.0947(4)
C9	0.8725(7)	0.3352(4)	0.0782(4)
C10	0.9360(7)	0.2468(4)	0.1613(4)
C11	0.8254(6)	0.2086(4)	0.2595(4)
S3	0.7516(1)	0.43657(9)	0.55391(8)
C12	0.9272(7)	0.3589(5)	0.6489(4)
C13	0.4202(6)	0.2506(4)	0.7125(4)
01	0.2651(4)	0.1593(3)	0.7441(2)
02	0.5310(4)	0.3451(3)	0.7898(2)
C14	0.2502(8)	0.1708(5)	0.8828(4)
H7	0.465(6)	0.381(4)	0.203(4)

Table 4 cont'd ...

H8	0.660(5)	0.444(4)	0.040(4)
H9	0.943(6)	0.353(4)	0.004(4)
H10	1.046(7)	0.202(5)	0.149(4)
H11	0.876(6)	0.144(5)	0.320(4)
H1(C12)	0.982(7)	0.283(5)	0.581(5)
H2(C12)	1.028(6)	0.441(5)	0.679(4)
H3(C12)	0.858(7)	0.322(5)	0.730(4)
H1(C14)	0.368(6)	0.137(4)	0.927(4)
H2(C14)	0.255(6)	0.267(5)	0.922(4)
H3(C14)	0.128(6)	0.106(4)	0.885(4)

The molecular structure and atom coordinates of Ig are given in Figure 3 and Table 6 respectively. The bond distances comparison of 1,3-thiazoline-2-thiones Ia, g, IVa-c, as well as the mesoionic compounds II, V given in Table 9, shows that bond distances SI-C2 of Ia, g do not change considerably, compared to the corresponding values of the earlier described compounds IVa-c. The small increase of the C2-N3 bond in Ia, g could be explained by the weak donor influence of the methylthiogroup.

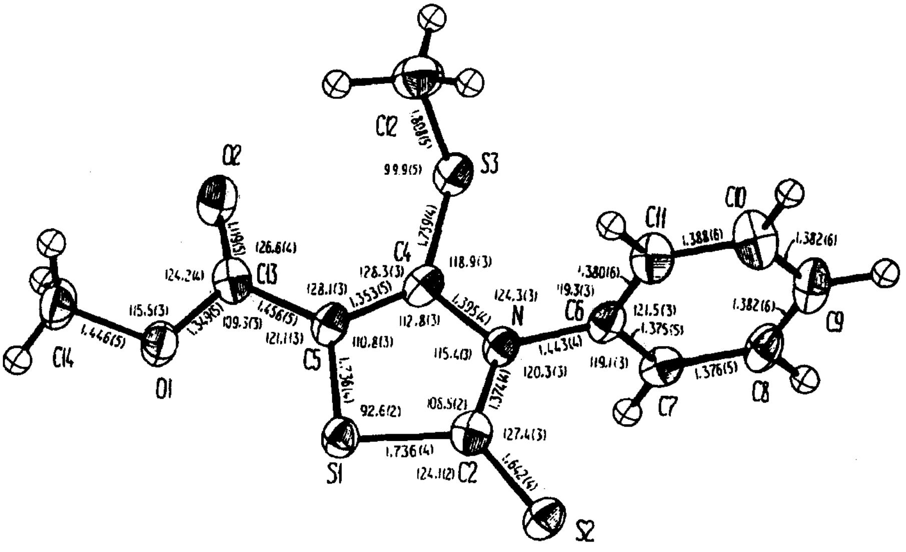
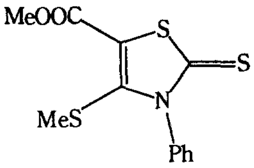
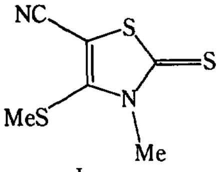


Figure 1. Geometry of molecule Ia

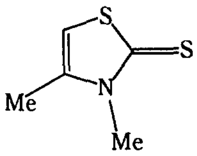
The bond distances SI-C5 of Ia, g are almost unchanged compared to the compounds IVa-c. On the other hand, the donor influence of methylthiogroup probably causes the N3-C4 bond increase. The tendency of the bond distances C4-C5 increments in the series IVa-IVb-IVc disappears in molecules Ia,g. In our opinion formula II demonstrates the compound structure approximately (Table 7).



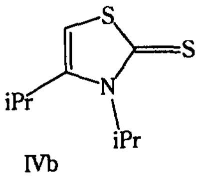
Ia



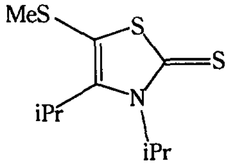
Ig



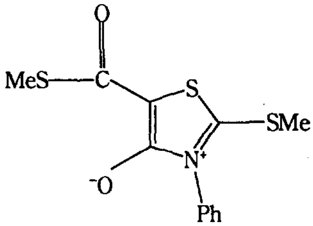
IVa



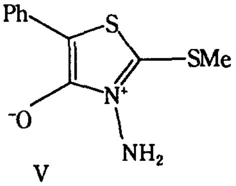
IVb



IVc



II



V

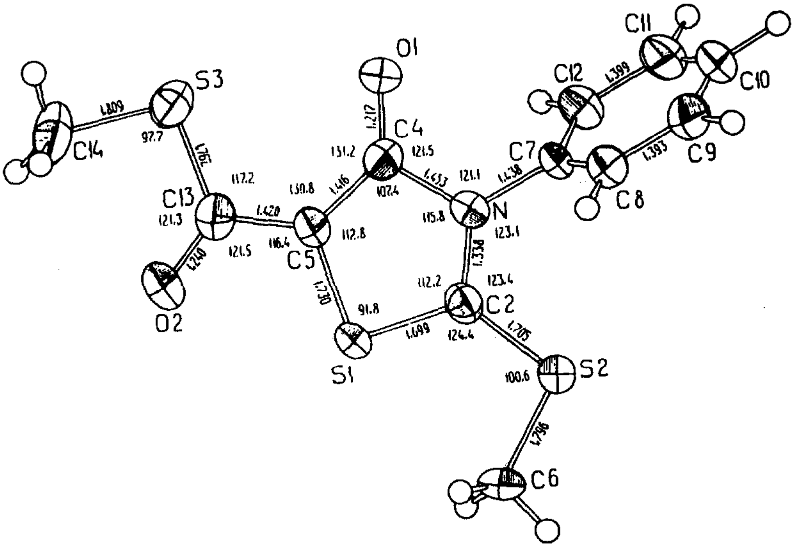


Figure 2. Geometry of molecule II

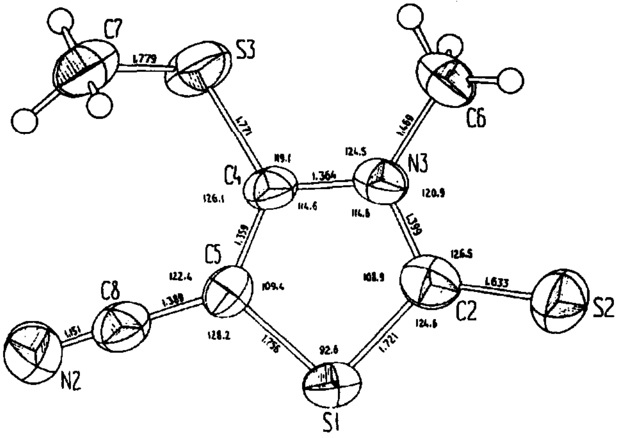


Figure 3. Geometry of molecule Ig

Table 5.
Atom coordinates in molecule II.

Atoms	x	y	z
S1	0.7054(1)	0.05898(9)	0.45591(5)
C2	0.6425(5)	−0.0075(4)	0.4119(2)
N	0.6952(4)	−0.1910(3)	0.4577(2)
C4	0.7914(5)	−0.1592(4)	0.5343(2)
C5	0.8045(5)	−0.0195(4)	0.5397(2)
S2	0.5262(2)	−0.10311(9)	0.32015(5)
C6	0.5035(8)	0.0672(4)	0.2920(3)
C7	0.6585(6)	−0.3259(3)	0.4342(2)
C8	0.4790(7)	−0.3707(4)	0.4204(2)
C9	0.4434(8)	−0.5029(5)	0.4008(3)
C10	0.5882(9)	−0.5852(5)	0.3965(3)
C11	0.7682(9)	−0.5398(5)	0.4111(3)
C12	0.8042(7)	−0.4073(4)	0.4303(3)
O1	0.8446(4)	−0.2451(2)	0.5810(1)
C13	0.8845(5)	0.0636(4)	0.6014(2)
S3	0.9725(2)	−0.0133(1)	0.68914(6)
C14	1.0217(9)	0.1334(7)	0.7463(4)
O2	0.8899(4)	0.1854(3)	0.5942(2)
H8	0.379(7)	−0.312(5)	0.427(3)
H9	0.308(8)	−0.537(5)	0.392(3)
H10	0.577(7)	−0.667(6)	0.383(3)
H11	0.881(8)	−0.603(5)	0.410(3)
H12	0.930(6)	−0.374(4)	0.441(2)
H1C6	0.426(7)	0.114(5)	0.325(3)
H2C6	0.633(7)	0.105(4)	0.298(3)
H3C6	0.438(7)	0.061(5)	0.239(3)

Table 5 cont'd ...

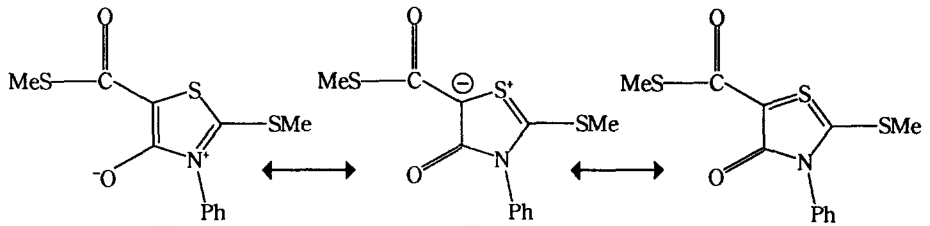
H1C14	1.124(9)	0.174(6)	0.731(3)
H2C14	1.062(9)	0.110(7)	0.795(4)
H3C14	0.896(9)	0.176(7)	0.744(4)

Table 6.
Final atom coordinates in molecule Ig.

Atoms	x	y	z
S1	0.7395(5)	0.4616(1)	0.3188(1)
C2	0.668(2)	0.3899(5)	0.2288(4)
N3	0.805(1)	0.2964(4)	0.2409(4)
C4	0.956(2)	0.2848(5)	0.3180(4)
C5	0.952(2)	0.3664(5)	0.3699(4)
S2	0.4657(6)	0.4265(2)	0.1447(1)
C6	0.782(3)	0.2195(7)	0.1737(7)
S3	1.1537(6)	0.1717(1)	0.3396(1)
C7	1.009(3)	0.1405(8)	0.4439(7)
C8	1.103(2)	0.3800(5)	0.4486(5)
N2	1.232(2)	0.3890(5)	0.5137(4)
H1(C6)	0.99(3)	0.202(9)	0.149(8)
H2(C6)	0.62(2)	0.228(6)	0.137(5)
H3(C6)	0.77(3)	0.156(9)	0.194(8)
H1(C7)	1.07(2)	0.095(5)	0.451(5)
H2(C7)	0.75(3)	0.164(7)	0.462(7)
H3(C7)	1.09(3)	0.176(7)	0.495(7)

Table 7.
Bond distances of the compounds Ia,g, II, Va–c, VI.

Compound Bond	IVa[16]	IVb[17]	IVc[18]	Ia	Ig	II	V[19]
S1–C2	1.694	1.727	1.739	1.736	1.721	1.699	1.768
C2–N3	1.349	1.361	1.366	1.374	1.399	1.388	1.266
S1–C5	1.745	1.723	1.740	1.736	1.756	1.730	1.812
N3–C4	1.410	1.404	1.423	1.359	1.364	1.453	1.473
C4–C5	1.319	1.346	1.377	1.353	1.359	1.416	1.310
C2–S2	1.708	1.678	1.688	1.642	1.633	1.705	1.719
C_{exo}–N3	1.462	1.489	1.542	1.443	1.469	1.438	—
C5–C_{exo}	—	—	1.508	1.456	1.389	1.420	1.508
C4–O_{exo}	—					1.217	1.326


II IIa IIb

The bond distances C2–N3, C4–C5 and C4–O$_{exo}$ of the compound V are also short, approaching the standard C=N, C=C and C–O, but C2–S1, C5–S1 and S4–N are long, approaching the ordinary C–S and C–N. These facts show positive charge localization on the nitrogen atom and negative on the exocyclic oxygen atom. On the other hand, the comparison of the corresponding values for the mesoionic compound V is evidence for the considerable contributions of the structures IIa and IIb. Probable assumption about the negative charge delocalization on atom group O1–C4–C5–C13–O2 in molecule II is refuted by the examination of the bond distances C=O. The bond distance C4–O1 is short approaching the standard value of a C=O distance and the distance C13–O2 is usual for thiolcarbonic acid esters.

EXPERIMENTAL

Synthesis.

IR spectra were recorded on a IR 75 for suspensions in paraffin oil, UV spectra on a Specord UV—VIS, ^{1}H-NMR on a Bruker WH-90/DS using TMS as an internal standard in CDCl$_3$.

1,3-Thiazoline-2-thiones(Ia–g). General procedure.

To the cooled on the ice bath mixture containing xathates IIIa–c (5.55 mmol) and isothiocyanate R^{4}NCS (5.55 mmol) in dry DMF (9 ml) sodium tert–butoxide (11.11 mmol) was added portionwise. Argon was passing continuously. After stirring for 2 hours and adding of R^{5}X (12.12 mmol) and further stirring for 2 hours the mixture was diluted by water (90 ml). The precipitate was filtered off, washed with water (4×8 ml), dried and dissolved in benzene (5 ml). The solution was filtered through silica gel and eluted with benzene (5×15 ml). After evaporation of the solvent the residue was recrystallized.

2–Methylthio–3–phenyl–5–methylthiocarbonyl–1,3–thiazol–4–olate(II).

To the stirred solution of phenylisothiocyanate in dry DMF (9 ml), cooled in on ice bath, sodium tert–butoxide (5.55 mmol) was added. After 10 min O–methyl S–(methoxycarbonylmethyl)dithiocarbonate (5.55 mmol) was added and the mixture was stirred for one hour at 20°C. Argon was passing continuously. Then the another portion of sodium tert–butoxide(5.55 mmol) was added and the mixture was stirred for 40 min. After the addition of methyliodide (12.12 mmol) stirring for one hour, and diluting with water (40 ml), the precipitated oil was isolated. Benzene (30 ml) was added, the precipitated crystals were filtered off, washed with hexane (3×3 ml), and recrystallized from methanol. Yield 0,1 g (6%), yellow needles, m.p. 244°C (d).

Crystal structure determination.

Crystals of Ia,g, II suitable for X–ray experiments were obtained by recrystallization from methanol. The most relevant data and experimental details are given in Table 8.

Table 8. Crystal data and experimental details.

	Ia	Ig	II
Space group	P 1	$P\,2_1/C$	$P\,2_1/C$
Cell parameters	a=6.884(1),	a=4.259(2),	a=7.405(1),
	b=9.476(2),	b=13.457(4),	b=10.110(2),
	c=10.396(2)A,	c=15.466(4)A,	c=18.130(2)A,
	=98.63,	=90.15(3)°,	=102.66(1)°
	=96.01(1),	V=886.4A^3,z=4,	V=1324.2A^3, z=4,
	=100.47(2)°	D_{cald}=1.632 g×cm^{-3}	D_{cald}=1.492 g×cm^{-3}
	V=653.2(2)A,		
	z=2,		
	D_{cald}=1.512 g×cm^{-3}.		
Radiation	CuK, graphite monochromator		
Number of unique reflections	1342	1370	1364
Final R	0.039	0.069	0.043
Syntex $P2_1$ diffractometer	$2\Theta_{max}$=100°	$2\Theta \leq 50°$	$2\Theta_{max}$=100°

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