Isothiocyanates and their synthetic producers. XIV. Synthesis and spectral properties of 1,5-disubstituted dithiobiurets and of their cyclization products with aldehydes and ketones

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Received 27 October 1975

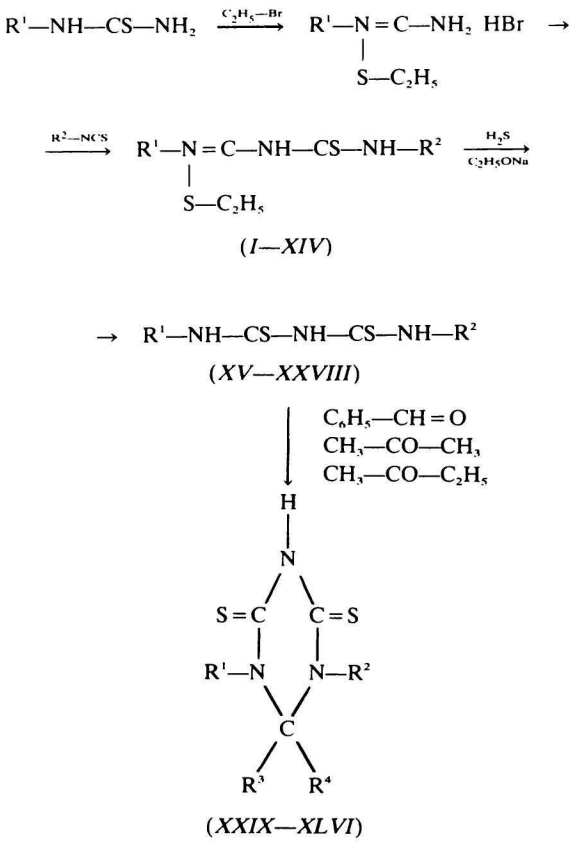
The synthesis of dithiobiurets substituted in positions 1 and 5 by aromatic and/or alicyclic substituents was studied. Cyclization of these compounds with aldehydes and ketones in glacial acetic acid led to the formation of substituted 1,3,5-triazine-2,4--dithiones. The structures of the synthesized compounds were confirmed by i.r. and u.v. spectrometry.

Был изучен синтез 1,5-двухзамещенных дитиобиуретов с ароматическими, а также с алициклическими заместителями. Кроме этого осуществилась циклизация указанных соединений с альдегидами и кетонами в среде ледяной уксусной кислоты, в результате которой образовались замещенные 1,3,5-триазин--2,4-дитионы. Структура синтезированных соединений была подтверждена при помощи ИК и УФ спектров.

The importance of studies dealing with the biological activity of compounds having the $>N-\underset{|}{C}=S$ group in their molecule has been stressed already in our previous papers [1—3]. To this type of compounds belong also the substituted dithiobiurets and the substituted 1,3,5-triazine-2,4-dithiones formed by cyclization of dithiobiurets with aldehydes and ketones, respectively. The biological activity of these compounds was investigated by *Fairfull* [4].

The synthesis and properties of 1,5-disubstituted dithiobiurets were studied by several authors [5—9]. The best method for their preparation has been proved to be that of *Fullhart* [10] who synthesized a series of 1-aryl-5-alkyldithiobiurets by reactions of *S*-alkylisothiourea with corresponding isothiocyanates followed by thiohydrolysis of formed isodithiobiurets with sodium alcoholate and H_2S.

The condensation of dithiobiurets with aldehydes and ketones was described by *Fromm et al.* [11—13]. *Gatewood* [14] and *Peak* [15] have demonstrated prevalent formation of 6-membered triazine ring over the 4-membered diazocyclobutane formation in the course of alkaline and acid hydrolysis.



Scheme 1

As the starting compounds for the synthesis of 1,5-disubstituted dithiobiurets (Scheme 1) we used isothiocyanates prepared by thiophosgene reaction [16—19]. From these by reaction with alcoholic ammonia we prepared *N*-substituted derivatives of thiourea [20] that upon condensation with ethyl bromide afforded hydrobromide of *S*-ethyl-*N*-substituted derivatives of isothiourea [21]. The condensation of free bases of *S*-ethyl-*N*-substituted isothiourea with corresponding isothiocyanates yielded *S*-ethyl-1,5-disubstituted isodithiobiurets [7] that were converted to 1,5-disubstituted dithiobiurets by means of thiohydrolysis with sodium alcoholate and H_2S [22, 23]. The substituted 1,3,5-triazine-2,4-dithiones were prepared by cyclization of 1,5-disubstituted dithiobiurets with aldehydes and ketones in glacial acetic acid [24].

The synthesized compounds were studied with respect to the relations between structure and biological activity (results not presented here). The found spectral properties of the synthesized compounds should serve to expand our range of knowledge on the structure and physicochemical properties of these compounds.

Table 1. Characteristics of *S*-ethyl-1,5-disubstituted isodithiobiurets

No.	R^1	R^2	Formula	*M*	Calculated/found % N	Calculated/found % S	Yield %	M.p., °C
I	CH_3—O—C_6H_4	CH_3—O—C_6H_4	$C_{18}H_{21}N_3O_2S_2$	375.18	11.19 11.02	17.05 16.89	68.2	138—139
II	CH_3—O—C_6H_4	Br—C_6H_4	$C_{17}H_{18}N_3OS_2Br$	424.17	9.66 9.42	15.08 14.83	85.2	139—141.5
III	CH_3—O—C_6H_4	C_6H_5	$C_{17}H_{19}N_3OS_2$	345.17	12.16 12.30	18.54 18.29	53.4	106—107
IV	C_6H_5	C_6H_5	$C_{16}H_{17}N_3S_2$	315.16	13.39 13.11	20.30 20.18	73.6	91—92
V	C_6H_5	CH_3—C_6H_4	$C_{17}H_{19}N_3S_2$	329.17	12.76 12.58	19.44 19.31	46.2	93—94
VI	C_6H_5—CH_2	Br—C_6H_4	$C_{17}H_{18}N_3S_2Br$	408.17	10.28 10.05	15.67 15.42	40	88—90
VII	C_6H_5—CH_2	C_6H_5	$C_{17}H_{19}N_3S_2$	329.17	12.75 12.48	19.44 19.18	67.8	74—75.5
VIII	C_6H_5—CH_2	CH_3—C_6H_4	$C_{18}H_{21}N_3S_2$	343.18	12.23 11.98	18.64 18.50	58.7	92—94
IX	C_6H_5—CH_2	NO_2—C_6H_4	$C_{17}H_{18}N_4O_2S_2$	374.17	14.96 14.68	17.10 16.82	58.6	121—123
X	C_6H_5—CH_2	$C_{10}H_7$	$C_{21}H_{21}N_3S_2$	379.21	11.07 10.84	16.87 16.54	51.2	97—100
XI	C_6H_{11}	C_6H_5	$C_{16}H_{23}N_3S_2$	321.16	13.07 12.80	19.92 19.70	54.4	78—80
XII	CH_3—C_6H_4	CH_3—C_6H_4	$C_{18}H_{21}N_3S_2$	343.18	12.23 11.98	18.64 18.50	98.5	102—106
XIII	CH_3—C_6H_4	Br—C_6H_4	$C_{17}H_{18}N_3S_2Br$	408.17	10.28 9.98	15.67 15.46	97.7	126—127
XIV	Br—C_6H_4	Br—C_6H_4	$C_{16}H_{15}N_3S_2Br_2$	473.16	8.87 8.56	13.52 13.80	85.3	123—126

Table 2. Characteristics of 1,5-disubstituted dithiobiurets

No.	R^1	R^2	Formula	*M*	Calculated/found % N	Calculated/found % S	Yield %	M.p., °C
XV	CH_3—O—C_6H_4	CH_3—O—C_6H_4	$C_{16}H_{17}N_3O_2S_2$	347.16	12.09 11.91	18.43 18.34	66.2	131—132
XVI	CH_3—O—C_6H_4	Br—C_6H_4	$C_{15}H_{14}N_3OS_2Br$	396.15	10.62 10.27	16.15 16.32	60.5	155—156
XVII	CH_3—O—C_6H_4	C_6H_5	$C_{15}H_{15}N_3OS_2$	317.15	13.24 13.05	20.17 19.89	69.7	138—139
XVIII	C_6H_5	C_6H_5	$C_{14}H_{13}N_3S_2$	287.14	14.62 14.70	22.27 22.58	54.9	144—145
XIX	C_6H_5	CH_3—C_6H_4	$C_{15}H_{15}N_3S_2$	301.15	13.94 13.72	21.25 20.97	62.1	148—150
XX	C_6H_5—CH_2	Br—C_6H_4	$C_{15}H_{14}N_3S_2Br$	380.33	11.04 11.38	16.82 16.49	51	157—160
XXI	C_6H_5—CH_2	C_6H_5	$C_{15}H_{15}N_3S_2$	301.15	13.94 13.67	21.25 21.04	38.6	142—144.5
XXII	C_6H_5—CH_2	CH_3—C_6H_4	$C_{16}H_{17}N_3S_2$	315.16	13.32 13.42	20.30 20.47	79.4	172—173
XXIII	C_6H_5—CH_2	NO_2—C_6H_4	$C_{15}H_{14}N_4O_2S_2$	346.15	16.17 16.20	18.47 18.39	86.5	186—188
XXIV	C_6H_5—CH_2	$C_{10}H_7$	$C_{19}H_{17}N_3S_2$	351.19	11.95 11.78	18.22 18.36	50.7	168—169
XXV	C_6H_{11}	C_6H_5	$C_{14}H_{19}N_3S_2$	293.14	14.33 14.69	21.81 21.51	33.5	150—152
XXVI	CH_3—C_6H_4	CH_3—C_6H_4	$C_{16}H_{17}N_3S_2$	315.16	13.32 13.45	20.30 20.53	77.4	140—142
XXVII	CH_3—C_6H_4	Br—C_6H_4	$C_{15}H_{14}N_3S_2Br$	380.15	11.04 10.70	16.82 16.64	83.2	176.5—178
XXVIII	Br—C_6H_4	Br—C_6H_4	$C_{14}H_{11}N_3S_2Br_2$	445.14	9.43 9.72	15.44 15.57	76.2	184—186

Table 3

Characteristics of 1,5,6-trisubstituted 1,3,5-triazine-2,4-dithiones

No.	R^1	R^2	R^3	R^4	Formula	*M*	Calculated/found % N	Calculated/found % S	Yield %	M.p., °C
XXIX	C_6H_5	C_6H_5	H	C_6H_5	$C_{21}H_{17}N_3S_2$	375.21	11.19 11.36	17.05 17.21	8.67	202.5—205
XXX	C_6H_5—CH_2	C_6H_5	H	C_6H_5	$C_{22}H_{19}N_3S_5$	389.22	10.78 10.54	16.43 16.70	18.8	196.5—198
XXXI	C_6H_5—CH_2	NO_2—C_6H_4	H	C_6H_5	$C_{22}H_{18}N_4O_2S_2$	434.22	12.89 12.59	14.69 14.55	19.46	230—233
XXXII	C_6H_5—CH_2	CH_3—C_6H_4	H	C_6H_5	$C_{23}H_{21}N_3S_2$	403.23	10.41 10.76	15.80 15.49	20.9	208—211
XXXIII	CH_3—C_6H_4	CH_3—C_6H_4	H	C_6H_5	$C_{23}H_{21}N_3S_2$	403.23	10.41 10.70	15.80 15.52	25.3	198—200
XXXIV	CH_3—C_6H_4	Br—C_6H_4	H	C_6H_5	$C_{22}H_{18}N_3S_2Br$	468.22	8.97 9.11	13.60 13.98	18.96	210—213
XXXV	Br—C_6H_4	Br—C_6H_4	H	C_6H_5	$C_{21}H_{15}N_3S_2Br_2$	533.21	7.87 8.08	12.00 12.35	23.27	221—222
XXXVI	C_6H_5	C_6H_5	CH_3	CH_3	$C_{17}H_{17}N_3S_2$	327.17	12.83 13.02	19.56 19.47	12.07	242—245
XXXVII	C_6H_5—CH_2	C_6H_5	CH_3	CH_3	$C_{18}H_{19}N_3S_2$	341.18	12.31 12.42	18.63 18.49	27.2	245—247
XXXVIII	C_6H_5—CH_2	NO_2—C_6H_4	CH_3	CH_3	$C_{18}H_{18}N_4O_2S_2$	386.18	14.50 14.31	16.56 16.87	6.72	273—274.5
XXXIX	C_6H_5—CH_2	NO_2—C_6H_4	H	H	$C_{16}H_{14}N_4O_2S_2$	358.16	15.62 15.40	17.86 17.59	8.15	215—217
XL	C_6H_5—CH_2	CH_3—C_6H_4	CH_3	CH_3	$C_{19}H_{21}N_3S_2$	355.19	11.82 11.49	18.01 17.68	31.78	200—201.5
XLI	CH_3—C_6H_4	CH_3—C_6H_4	CH_3	CH_3	$C_{19}H_{21}N_3S_2$	355.19	11.82 11.52	18.01 18.29	32.57	233—235

Table 3 (Continued)

No.	R^1	R^2	R^3	R^4	Formula	*M*	Calculated found N	Calculated found S	Yield	M.p. °C
XLII	CH_3—C_6H_4	Br—C_6H_4	CH_3	CH_3	$C_{18}H_{18}N_3S_2Br$	420.18	9.97 9.68	15.23 15.56	20.36	253—255
XLIII	Br—C_6H_4	Br—C_6H_4	CH_3	CH_3	$C_{17}H_{15}N_3S_2Br_2$	485.17	8.65 8.25	13.19 13.40	22.8	262—264
XLIV	CH_3—C_6H_4	CH_3—C_6H_4	CH_3	C_2H_5	$C_{20}H_{23}N_3S_2$	369.20	11.37 11.04	17.33 17.58	20.3	252—253
XLV	CH_3—C_6H_4	Br—C_6H_4	CH_3	C_2H_5	$C_{19}H_{20}N_3S_2Br$	434.19	9.67 9.35	14.74 14.93	20.67	287—290
XLVI	Br—C_6H_4	Br—C_6H_4	CH_3	C_2H_5	$C_{18}H_{17}N_3S_2Br_2$	499.18	8.40 8.12	12.84 13.16	21.7	310—312

Table 4. Infrared and ultraviolet absorption spectra of 1,5-disubstituted dithiobiurets

No.	R^1	R^2	$\tilde{\nu}$, cm^{-1}				λ_{max}, nm log ε	
			ν(C=C)	ν(—NH—C=S)				
XV	CH_3—O—C_6H_4	CH_3—O—C_6H_4	1600 1495	1540	1445	945	281 4.34	
XVI	CH_3—O—C_6H_4	Br—C_6H_4	1600 1494	1538	1435	942	286 4.31	
XVII	CH_3—O—C_6H_4	C_6H_5	1600 1495	1540	1440	945	284 4.32	
XVIII	C_6H_5	C_6H_5	1605 1515	1545	1445	950	280 4.31	
XIX	C_6H_5	CH_3—C_6H_4	1595 1493	1542	1440	946	293 4.34	
XX	C_6H_5—CH_2	Br—C_6H_4	1600 1495	1540	1440	—	284 4.30	
XXI	C_6H_5—CH_2	C_6H_5	1600 1490	1540	1420	—	285 4.28	
XXII	C_6H_5—CH_2	CH_3—C_6H_4	1600 1492	1538	1425	—	285 4.39	
XXIII	C_6H_5—CH_2	NO_2—C_6H_4	1600 1494	1535	1421	—	291 4.27	
XXIV	C_6H_5—CH_2	$C_{10}H_7$	1600 1490	1540	1430	—	285 4.27	300 4.05
XXV	C_6H_{11}	C_6H_5	1600 1495	1540	1432	945	266 4.35	
XXVI	CH_3—C_6H_4	CH_3—C_6H_4	1600 1510	1545	1445	950	290 4.34	
XXVII	CH_3—C_6H_4	Br—C_6H_4	1595 1495	1540	1445	950	290 4.41	
XXVIII	Br—C_6H_4	Br—C_6H_4	1600 1495	1540	1450	950	290 4.37	

Table 5

Infrared and ultraviolet absorption spectra of 1,5,6-trisubstituted 1,3,5-triazine-2,4-dithiones

No.	R^1	R^2	R^3	R^4	ν, cm^{-1}		λ_{max}, nm log ε
					$\nu(\geq N-\underset{\|}{C}=S)$	$\nu(C=C)$	
XXIX	C_6H_5	C_6H_5	H	C_6H_5	1550 1400 1310	1630	284 4.29
XXX	$C_6H_5—CH_2$	C_6H_5	H	C_6H_5	1530 1395 1305	1600	295 4.34
XXXI	$C_6H_5—CH_2$	$NO_2—C_6H_4$	H	C_6H_5	1535 1405 1315	1600	310 4.32
XXXII	$C_6H_5—CH_2$	$CH_3—C_6H_4$	H	C_6H_5	1540 1390 1300	1605	290 4.30
XXXIII	$CH_3—C_6H_4$	$CH_3—C_6H_4$	H	C_6H_5	1560 1410 1320	1630	294 4.28
XXXIV	$CH_3—C_6H_4$	$Br—C_6H_4$	H	C_6H_5	1550 1405 1315	1630	300 4.48
XXXV	$Br—C_6H_4$	$Br—C_6H_4$	H	C_6H_5	1560 1405 1315	1630	298 4.51
XXXVI	C_6H_5	C_6H_5	CH_3	CH_3	1535 1390 1300	1600	345 4.35
XXXVII	$C_6H_5—CH_2$	C_6H_5	CH_3	CH_3	1520 1385 1300	1610	336 4.28

Table (Continued)

No.	R^1	R^2	R	R^3	cm		nm
					ν(>N—C=S)	ν(C=O)	log ε
					‖		
XXXVIII	C_6H_5—CH_2	NO_2—C_6H_4	CH_3	CH_3	1520	1610	352
					1400		4.40
					1315		
XXXIX	C_6H_5—CH_2	NO_2—C_6H_4	H	H	1525	1620	357
					1405		4.31
					1315		
XL	C_6H_5—CH_2	CH_3—C_6H_4	CH_3	CH_3	1530	1625	340
					1390		4.39
					1305		
XLI	CH_3—C_6H_4	CH_3—C_6H_4	CH_3	CH_3	1520	1620	344
					1395		4.34
					1315		
XLII	CH_3—C_6H_4	Br—C_6H_4	CH_3	CH_3	1530	1610	345
					1390		4.36
					1300		
XLIII	Br—C_6H_4	Br—C_6H_4	CH_3	CH_3	1540	1595	345
					1390		4.11
					1310		
XLIV	CH_3—C_6H_4	CH_3—C_6H_4	CH_3	C_2H_5	1520	1600	350
					1395		4.04
					1315		
XLV	CH_3—C_6H_4	Br—C_6H_4	CH_3	C_2H_5	1520	1600	350
					1395		4.40
					1315		
XLVI	Br—C_6H_4	Br—C_6H_4	CH_3	C_2H_5	1540	1595	350
					1390		3.38
					1315		

Experimental

Tables 1—3 represent the lists of the synthesized *S*-ethyl-1,5-disubstituted isodithiobiurets (*I—XIV*; [7]), 1,5-disubstituted dithiobiurets (*XV—XXVIII* [22]), and 1,5,6-trisubstituted 1,3,5-triazine-2,4-dithiones (*XXIX—XLVI* [24]), respectively.

Infrared spectra were measured in the range 3400—700 cm using a UR-20 spectrophotometer (Zeiss, Jena) calibrated against a polystyrene foil. The samples were prepared for measurements in the form of KBr discs (0.5—0.8 mg of sample per 500 mg KBr).

Ultraviolet spectra were registered with a Perkin—Elmer spectrophotometer, Type 402, using anal. grade methanol as the solvent. The concentration of sample was 4×10^{-5}—4×10^{-4} M, cell thickness 1 cm, temperature 20 ± 2°C. The i.r. and u.v. data are summarized in Tables 4 and 5.

Discussion

The synthesized 1,5-disubstituted dithiobiurets are crystalline compounds, sparsely soluble in the common organic solvents. Their cyclization products are compounds having high melting points and limited solubility in organic solvents.

The spectral characteristics of 1,5-disubstituted dithiobiurets and their cyclization products have not been, so far, described in the literature.

There are three absorption bands in the investigated i.r. region which are characteristic of the $>N-\underset{|}{C}=S$ or $-NH-\underset{|}{C}=S$ group [25]. These bands arise as a result of mixed vibrations (copulation vibrations C—N, C=S, N—H). The spectra of investigated 1,5-disubstituted dithiobiurets exhibited for $-NH-\underset{|}{C}=S$ group the first absorption band (I) at 1535—1545 cm^{-1}, the second absorption band (II) at 1420—1450 cm^{-1}, and the third one (III) for the $-N=\underset{|}{C}-SH$ group at 942—950 cm^{-1}. In case when nitrogen atom was substituted with an aliphatic substituent (derivatives *XX—XXIV*) the third absorption band (III) corresponding to $-N=\underset{|}{C}-SH$ group was absent in the i.r. spectrum at 900—1000 cm^{-1}.

The spectra of 1,5,6-trisubstituted 1,3,5-triazine-2,4-dithiones exhibited the absorption band (I) for the $>N-\underset{|}{C}=S$ group at 1520—1560 cm^{-1}, the second band (II) at 1300—1410 cm^{-1}. The third absorption band (III) of the $>N-\underset{|}{C}=S$ group was not observed.

The absorption bands corresponding to the stretching vibrations of double bonds $\nu(C=C)$ were observed for all investigated compounds in the region 1480—1630 cm^{-1}. The u.v. absorption spectra of 1,5-disubstituted dithiobiurets exhibited intense absorption bands in the region 220—360 nm ($\log \varepsilon \doteq 4$). These bands can be attributed to the absorption of the two aromatic residues conjugated with the $-NH-\underset{|}{C}=S$ group in the molecule. In this case the $\pi \rightarrow \pi^*$ transitions accompanied with electron transfers due to p—π conjugation of the free electron couple of nitrogen with the double bond in the thione group are resulting in the so-called "N"-conjugation

$$Ar-\overset{\curvearrowright}{NH}-C\overset{\curvearrowright}{\leq}S$$

In case of the cyclized derivatives the change in the chromophore system does not take place and, consequently, the character of u.v. spectra remains unchanged.

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Translated by V. Farkaš