13. R. Neidlein, W. Kramer, and R. Leidholdt, *Helv. Chim. Acta*, **66**, 2285 (1983).
14. St. Berger and A. Rieker, *Tetrahedron*, **28**, 3123 (1972).
15. G. Tóth and B. Podanyi, *J. Chem. Soc., Perkin Trans.* 2, No. 1, 91 (1984).
16. G. Hofle, *Tetrahedron*, **33**, 1963 (1977).
17. G. Levi and G. Nelson, *Handbook on Nuclear Magnetic Resonance of Carbon-13 for Organic Chemists* [in Russian], Mir, Moscow (1975).

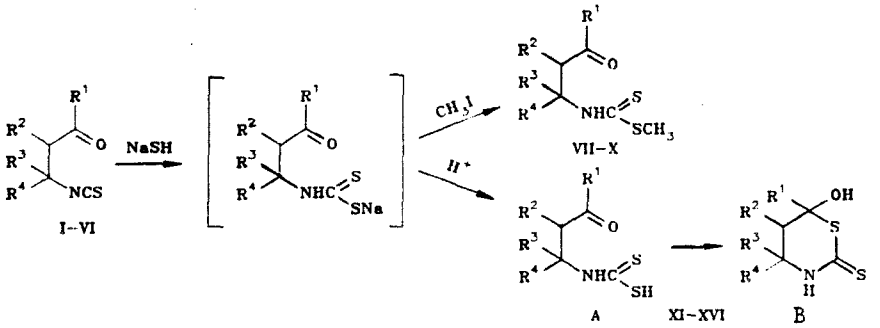
SYNTHESIS OF 6-HYDROXYTETRAHYDRO-1,3-THIAZINE-2-THIONES AND METHYL ESTERS OF 3-OXOALKYLDITHIOCARBAMIC ACIDS FROM 1,3-ISOTHIOCYANATO KETONES

A. S. Fisyuk and B. V. Unkovskii

UDC 547.869.07:543.422.25

Sodium salts of 3-oxoalkyldithiocarbamic acids were obtained by the reaction of 1,3-isothiocyanato ketones with sodum hydrosulfide. These salts were converted by reaction with methyl iodide into the corresponding dithiocarbamates, and with a mineral acid into the 6-hydroxytetrahydro-1,3-thiazine-2-thiones.

The presently known methods for the preparation of 6-hydroxytetrahydro-1,3-thazine-2-thiones and methyl esters of 3-oxoalkyl dithiocarbamic acids from 1,3-isothiocyanato ketones involve the use of the toxic and inflammable carbon disulfide [1, 2]. We found [3] that the reaction of 1,3-isothiocyanato ketones I-VI with sodium hydrosulfide or carbon disulfide in an alkaline medium leads to the formation of sodium salts of 3-oxoalkyldithiocarbamic acids, which convert by the action of methyl iodide into the corresponding esters VII-X, and by the action of mineral acids — into compounds XI-XVI, which in principle can exist in two tautomeric forms: the acyclic form of 3-oxoalkyldithiocarbamic acids XIA-XVIA and in the cyclic form of alkyl-substituted 6-hydroxytetrahydro-1,3-thiazine-2-thiones XIB-XVIB.



I, VII, XI $R^1=R^2=CH_3$, $R^3=R^4=H$; II, VIII, XII $R^1=R^3=R^4=CH_3$, $R^2=H$; III, IX, XIII $R^1=R^2=R^3=R^4=CH_3$; IV, XIV $R^1=C_2H_5$, $R^2=CH_3$, $R^3=R^4=H$; V, XV $R^1=C_2H_5$, $R^2=R^3=R^4=CH_3$; VI, X, XVI $R^1,R^2=(CH_2)_4$, $R^3,R^4=(CH_2)_5$

In contrast to the thioesters VII-X, in the IR spectra of compounds XI-XVI (Table 1), the band at 1680-1710 cm^{-1}, corresponding to the stretching vibrations of the C=O group, is absent, which suggests that in the crystalline state they exist in the cyclic form B.

The PMR spectra of compounds XII, XIII, and XVI, recorded immediately after their dissolution, confirm their presence in the cyclic form B (Table 2). Compound XIII is formed in the form of a mixture of cis- and trans-isomers in a ratio of 93:7, which indicates a dual set of signals corresponding to its structure.

The singlet signals ofthe $COCH_3$ group protons in the 2.08-2.20 ppm region, which are characteristic for acyclic analogs VIII and IX (Table 2), are absent in the case of compounds XII and XIII, while the 6-CH_3 group appears in the form of a singlet at 1.50 and 1.43 and 1.45 ppm, respectively. The proton signals at the $C_{(5)}$ atom of compounds XII and XIII are also present in the stronger-field region, compared with the signals of compounds VIII and IX.

Omsk State University, Omsk. M. V. Lomonosov Moscow Institute of Fine Chemical Technology, Moscow. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 416-419, March, 1991. Original article submitted May 30, 1989.

0009-3122/91/2703-0339$12.50

TABLE 1. Physical Constants and Yields of Compounds VII-XVI

Compound	Empirical formula	mp, °C [bp, (mm, Hg)]	IR spectrum, cm^{-1}			Yield, %
			C=O (—OH)	CS	NH	
VII	$C_7H_{13}NOS_2$	[115...118 (0,05)]	1705	1510	3220	77,0
VIII	$C_8H_{15}NOS_2$	101	1710	1550	3180	83,9
IX	$C_9H_{17}NOS_2$	[128...130 (0,05)]	1710	1520	3225	55,9
X	$C_{14}H_{23}NOS_2$	106...107	1680	1500	3230	42,5
XI	$C_6H_{11}NOS_2$	71...72	(3320)	1560	3070	54,1
XII	$C_7H_{13}NOS_2$	113...114	(3260)	1535	3100	83,9
XIII	$C_8H_{15}NOS_2$	94...94,5	(3230)	1535	3090	67,9
XIV	$C_7H_{13}NOS_2$	66...67	(3300)	1530	3140	28,6
XV	$C_9H_{17}NOS_2$	79...80	(3270)	1535	3100	59,1
XVI	$C_{13}H_{21}NOS_2$	116...117	(3230)	1535	3090	47,2

*Solvent) an alcohol—acetone mixture.

TABLE 2. Chemical Shifts of Protons of Compounds VII-X, XII, XIII, and XVI

Compound	δ, ppm					
	2-H/5-H*	R^3, R^4	R^2	R^1	SCH_3	NH, OH
VII	3,05	3,87	1,12	2,12	2,48	8,30
VIII	3,26	1,53; 1,53	—	2,08	2,47	7,35
IX	3,87	1,58; 1,58	1,07	2,20	2,51	7,55
X	4,14	2,84...1,16		1,50	2,56	7,00
XII	1,84 (a);	1,28; 1,37	—	1,45	—	10,44; 6,56
XIII (7%)	2,06 (e)	1,19; 1,21	0,92	1,43	—	—
XIII (93%)	2,04	1,26; 1,28	1,00	—	—	10,20; 6,44
XVI	1,88	2,25	0,63		—	9,85; 6,35

*For compound J_{gem} = 14.5 Hz; for compounds XIII (7%) and XIII (93%), J = 7 Hz.

TABLE 3. Chemical Shifts of ^{13}C Nuclei of Compounds VII, VIII, X, XII, XIII, and XVI

Compound	δ, ppm							
	$C_{(1)}/C_{(6)}$	$C_{(2)}/C_{(5)}$	$C_{(3)}/C_{(4)}$	$C_{(4)}/C_{(2)}$	R^1	R^2	R^3, R^4	SCH_3
VII	210,3	44,6	47,2	198,1	27,4	13,4	—	17,0
VIII	206,6	49,8	57,2	196,7	30,4	—	26,7	17,7
X	211,0	54,0	33,1	195,5	42,9; 30,2; 29,6; 28,9; 27,6; 25,3; 24,9; 21,0; 20,8			17,9
XII	81,3	46,1	55,0	190,0	26,7	—	28,1; 28,8	—
XIII (7%)	86,4	45,4	59,0	190,2	22,0	—	28,1; 28,8	—
XIII (93%)	84,5	45,0	59,6	188,6	21,5	—	28,1; 28,8	—
XVI	86,0	36,0	60,5	130,5	33,7; 23,8; 23,8; 23,6; 23,6; 22,7; 22,1; 21,3; 21,1			—

In the ^{13}C NMR spectra of dithiocarbamates VII-X (Table 3), the signals of the carbonyl group (211.0-206.5 ppm), of the thiocarbamoyl fragment of the molecule (198.0-195.3 ppm) and the signals of the methyl group bound to the sulfur atom (17.9-17.0 ppm) [4] are the most characteristic. The chemical shifts of the ring $C_{(4)}$, $C_{(5)}$, and $C_{(2)}$ atoms of compounds XII, XIII, and XIV (Table 3) are similar to the chemical shifts of the corresponding atoms of the acyclic analogs VIII-X, while the signal of the sp^3 hydride nucleus at the $C_{(6)}$ atom is considerably shifted to the high-field region (81.3-81.0 ppm).

Thus, the data obtained show that 3-oxoalkyldithiocarbamic acids XI-XVIA, formed from isothiocyanato ketones as a result of the addition of sodium hydrosulfide, exist in an alkaline medium in the form of salts and can be converted into the corresponding esters by treatment with methyl iodide, while in an acid medium are cyclized into their isomeric 6-hydroxytetrahydro-1,3-thiazine-2-thiones XI-XVIB.

EXPERIMENTAL

The ^{13}C and ^{1}H NMR spectra were recorded on Bruker WM 250 and Tesla 80 spectrometers for substituted dithiocarbamates VII-X in a $CDCl_3$ solution and for 6-hydroxythiazines XI-XVI — in DMSO-D_6. The IR spectra were run on the UR-10 spectrophotometer, the crystalline samples in a suspension in mineral oil, and the liquid samples in a thin layer. The elemental analysis data for C, H, and S for the newly synthesized compounds correspond to the calculated values.

4,4,6-Trimethyl-6-hydroxytetrahydro-1,3-thiazine-2-thione (XII). A. Carbon disulfide was passed in the course of 10 min, at 18-25°C, with stirring, through a solution of 5.58 g (35.5 mmoles) of isothiocyanato ketone II in 18 ml of methanol, and then a solution of 2.19 g (54.6 mmoles) of sodium hydrosulfide in 18 ml of methanol was added dropwise without interrupting the addition of carbon disulfide. Carbon disulfide was passed for another 30 min, after which the crystalline precipitate formed was filtered, washed with water and hexane, and dried in a vacuum desiccator. Yield 4.13 g (60.0%) of compound XII.

B. A solution of 3.16 g (20.1 mmoles) of isothiocyanato ketone II in 8 ml of methanol was added at 18-25°C, with stirring, to a solution of 1.61 g (28.7 mmoles) of sodium hydrosulfide in 14.5 ml of methanol. After 3 h 30 min, the reaction mixture was acidified with 10% HCl (pH 3-5), and poured into 50 ml of water. The crystalline precipitate that separated out was filtered off after 30 min and, following the above-described treatment, 3.22 g (83.9%) of compound XII was obtained.

Compounds XI and XIII-XVI were obtained in a way similar to method B, at reaction duration of 30 min-2 h.

Methyl N-(2-Methyl-3-oxobutyl-1)dithiocarbamate (VII). A 2.79 g portion (19.5 mmoles) of ketone I in 2.4 ml of methanol was added at 18-25°C, with stirring, in the course of 5 min to a solution of 1.42 g (24.4 mmoles) of sodium hydrosulfide in 9.5 ml of methanol, and after 15 min 1.6 ml (25.4 mmoles) methyl iodide was added. The reaction mixture was stirred for another 30 min, diluted with 50 ml of water, and extracted with chloroform (3 × 50 ml). The chloroform extract was washed with water, and a saturated solution of sodium chloride, dried over calcium chloride, evaporated, and the residue was distilled under vacuum. Yield 2.87 g of thioester VII.

Compound IX was obtained in a similar way.

Methyl N-(2-Methyl-4-oxopentyl-2)dithiocarbamate (VIII). A solution of 14.62 g (260 mmoles) of sodium hydrosulfide in 30 ml of methanol was added at 18-25°C, with stirring, to a solution of 24.23 g (154 mmoles) of ketone II in 56.5 ml of methanol, and after 2 h 12.1 ml (195 mmoles) of methyl iodide was added. The reaction mixture was stirred for 30 min diluted in 600 ml of water, the crystalline precipitate which formed was filtered, dried on the filter, and then in a vacuum desiccator. Yield 26.52 g of ester VIII.

2-[(Methylthio)thiocarbamoylcyclohexyl]cyclohexanone (X). A 17.8 g portion (75 mmoles) of isothiocyanato ketone VI was added at 18-25°C, with stirring, to a solution of 6.73 g (120 mmoles) of sodium hydrosulfide in 54 ml of methanol, and then 5.0 ml (90 mmoles) of methyl iodide was added in the course of 2 h, and the mixture was stirred for another 15 min. The reaction mixture was diluted with 150 ml of water and extracted with chloroform (3 × 50 ml). The combined chloroform extract was washed with water and a saturated solution of sodium chloride, and dried over magnesium sulfate. The solvent was evaporated, and the residue was dissolved in 100 ml of hexane; the solution was cooled. The crystalline precipitate that separated out was filtered off, washed with hexane, dried on a filter, and then in a vacuum desiccator. Yield 9.1 g of ester X.

LITERATURE CITED

1. I. E. Jansen and T. A. Mathes, *J. Am. Chem. Soc.*, **77**, 5431 (1955).
2. J. C. Ioachims and A. Abu-Taha, *Chem. Ber.*, **109**, 139 (1976).
3. A. S. Fisyuk and B. V. Unkovskii, USSR Inventor's Certificate, No. 1,252,326; *Byull. Izobret.*, No. 31, 104 (1986).
4. B. I. Ionin, B. A. Ershov, and A. I. Kol'tsov, *NMR Spectroscopy in Organic Chemistry* [in Russian], Khimiya, Leningrad (1983).