HERBICIDAL HYDROXYLAMINE DERIVATIVES

XXXVII. 2,3-DISUBSTITUTED 2-IMINO-1,3-THIAZOLIDIN-4-ONES

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2-Arylimino-3-methoxy-1,3-thiazolidin-4-ones were obtained by the reaction of N-arylthiocarbamoyl-O-methylhydroxylamines with chloroacetyl chloride. The products are isomerized to 2-methoximino-3-aryl-1,3-thiazolidin-4-ones on heating with methanol in the presence of sodium methoxide. The UV, IR, and PMR spectra were used to determine the structures of the isomers.

The reactions of haloalkycarboxylic acid derivatives with N,N'-disubstituted thioureas with different substituents on the nitrogen atoms have been studied only in individual cases [2, 4]. The structure of the 2,3-disubstituted 1,3-thiazolidin-4-ones (pseudothiohydantoins) (I) obtained in the process could not, until recently, be considered to be rigorously proven.

	a $R = C_6 H_5$,	$R' = C_2 H_5$,	$X = CH_3$
P/N	b $R = C_2 H_5$,	$R' = C_6 H_5$,	$X = CH_3$
K I	c R=Ar,	R' = Alk,	X = H
RN S X	$d R = CH_3O$,	$R' = CH_3O_1$	X = H
1	e R=Ar,	$\mathbf{R}' = \mathbf{CH}_3\mathbf{O}$	X == H
	f R=CH ₃ O,	R' = Ar.	X = H

Andreasch [2], in a study of the reaction of N-phenyl-N'-ethylthiourea with ethyl α -bromopropionate, proposed two possible structures, Ia and Ib, for the compound he obtained.

Davis and Dains [3] ascribed the Ic structure, in which the aryl group is attached to the imino group, to the products of the reaction of ethyl chloroacetate with N-aryl-N'-alkylthioureas. To prove this structure they hydrolyzed the 5-benzal derivatives of Ic and isolated 3-alkyl-5-benzalthiazolidine-2,4-diones and the corresponding arylamines in the hydrolysis products. However, under severe hydrolysis conditions one cannot exclude the possibility of prior or subsequent isomerization of the benzal derivatives.

In a study of the reaction of chloroacetyl chloride with N-methyl-N'-methoxythiourea, which contains substituents with inductive effects of opposite sign, we obtained only one of the possible isomers of thiazolidinone Id in which the electronegative substituent is attached to the nitrogen in the imino group [5, 6]. The structure of the reaction product was unambiguously confirmed by the IR, UV, and PMR spectra. The structure that we established for Id confirms the structure proposed by Davis and Dains [3] for Ic, in which the electronegative aryl group is also attached to the imino group.

The reaction of chloroacetyl chloride with N,N'-disubstituted thioureas containing electronegative substituents on both carbon atoms should proceed in a considerably more complex manner. In this case, one would have expected the formation of two isomers that differ in the arrangement of the substituents in the 2 and 3 positions.

The possibility of the formation of two isomeric 2,3-disubstituted thiazolidinones was assumed by Meyer [7], but up to now no one has isolated such isomers [8].

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TABLE 1

RN -- N

Com-	4	D,	Ул. °С	Crystallization	Empirical		o puno	10	0	Calc. 7		Yield.
punod	4	4	- total	solvent	formula	ច	z	s	Ξ	z	s	d/o
*11	C ₆ H ₅	CH ₃ O	68	Methanol	CioH10N2O2S	1	12,6	14,3	I	12,6	14,4	92,5
111	2-CIC ₆ H ₄	CH ₃ O	104	Methanol	C ₁₀ H ₉ CIN ₂ O ₂ S	14,0	11,3	12,2	13,8	10,9	12,5	93,5
IV	3-CIC ₆ H₄	CH ₃ O	89		C ₁₀ H ₉ CIN ₂ O ₂ S	13,8	10,9	12,4	13,8	10,9	12,5	95,5
2	4-ClC ₆ H ₄	CH ₃ O	123		C ₁₀ H ₉ CIN ₂ O ₂ S	13,2	11,3	12,6	13,8	10,9	12,5	86,0
١٧	2-CH ₃ C ₆ H ₄	CH ₃ O	92	:	C ₁₁ H ₁₂ N ₂ O ₂ S	1	11,9	13,2	i	11,8	13,6	83,5
ΝI	3-CH ₃ C ₆ H ₄	CH ₃ O	99	Benzene	C ₁₁ H ₁₂ N ₂ O ₂ S	1	12,0	13,4		11,8	13,6	83,5
VIII	CH ₃ O	C ₆ H ₅	202	Methanol	C ₁₀ H ₁₀ N ₂ O ₂ S		12,5	14,4	I	12,6	14,5	93,0
XI	CH3O	2-CIC ₆ H ₄	144	Methanol	C ₁₀ H ₉ CIN ₂ O ₂ S	13,8	11,2	12,3	13,8	10,9	12,5	91,8
х	CH ₃ O	3-CIC ₆ H ₄	126127	4	C ₁₀ H ₉ CIN ₂ O ₂ S	13,7	10,8	12,2	13,8	10,9	12,5	92,0
IX	CH ₃ O	4-CIC ₆ H ₄	160		C ₁₀ H ₉ CIN ₂ O ₂ S	13,6	11,1	12,3	13,8	10,9	12,5	96,5
IIX	CH ₃ O	2-CH ₃ C ₆ H ₄	109		C ₁₁ H ₁₂ N ₂ O ₂ S	I	11,8	13,3	1	11,8	13,6	93,0
ХІН	CH ₃ O	3-CH ₃ C ₆ H ₄	148		C ₁₁ H ₁₂ N ₂ O ₂ S	1	11,8	13,3	I	11,8	13,6	90'0
XIV †	CH ₃ O	4-CH ₃ C ₆ H ₄	184		$C_{11}H_{12}N_2O_2S$	1	11,6	13,6	1	11,8	13,6	75,5
	1						-				-	

*Obtained without an acceptor.

† Obtained in the same way as III-VII.

TARLE 2 IR IIV and NMR Sheetral Data

*The integral intensity of the C = N band was measured together with the intensity of the completely symmetrical vibration band of the double bonds of the benzene ring in dioxane solution. $t \delta CH_3$ 3.35.

We have obtained a number of compounds with comparatively low melting points by carrying out the reaction of N-arylthiocarbamoyl-O-methylhydroxylamines with chloroacetyl chloride in methylene chloride in the presence of sodium acetate without a hydrogen chloride acceptor at -15 to -20° . These compounds were converted in virtually quantitative yield to higher melting substances with the same elementary composition by brief heating in methanol in the presence of sodium methoxide. Attempts to obtain low-melting products under other conditions using ethyl chloroacetate as the cyclizing agent were unsuccessful. In addition, we could not obtain a low-melting product in the case of N-(p-tolyl)-N'-methoxylthiourea. The structures of the compounds synthesized (Table 1) could be established from the UV, IR, PMR, and combination scattering (CS) spectra.

Comparison of the UV spectra (Table 2) of the high-melting VIII-XIV (structure If) with the spectrum of Id indicated that, despite replacement of methyl by aryl, the character of the spectra does not change. An increase in the intensity of the bands in the ~220-nm region and the appearance of an additional maximum in the ~270-nm region ($\varepsilon \sim 5000-10,000$) are observed in the spectra of low-melting products II-VII (structure Ie); this indicates the presence of a system of multiple bonds with participation of the aromatic ring. This makes it possible to assume that the two series of the compounds obtained with the same (analogous to Id) structure of the cyclic portion differ in the position of the aryl and methoxy groups: in the low-melting compounds the aryl group should be attached to the C = N bond, the π electrons of which are in conjugation with the π electrons of the aryl double bonds, while the methoxy group is attached to the ring nitrogen atom.

The IR spectra of II-XIV, like that of Id, contain two bands: $1708-1733 \text{ cm}^{-1}$ and $1608-1617 \text{ cm}^{-1}$ for high-melting products VIII-XIV, and $1733-1742 \text{ cm}^{-1}$ and $1642-1662 \text{ cm}^{-1}$ for low-melting products II-VII, which characterize the absorptions, respectively, of the C=O and C=N groups. The presence of these bands again attests to an analogy between the structures of the cyclic part of II-XIV and Id.

The intense band at $1584-1600 \text{ cm}^{-1}$ in the spectra of the low-melting products and the small shoulder on the low-frequency side of the band at $1608-1617 \text{ cm}^{-1}$ in the spectra of the high-melting compounds can be assigned to the completely symmetrical vibration of the system of conjugated double bonds of the benzene ring.

The integral intensity* of the indicated bands, calculated by means of the Wilson-Wells extrapolation method (Table 2), has a considerably higher value for the low-melting products, which confirms the assumption of conjugation, in these isomers, of an aromatic ring with a C = N bond. The higher intensities of the indicated bands in the CS spectrum of a solution of III in dimethyl sulfoxide [1579 cm⁻¹ (9), 1642 cm⁻¹ (10), 1741 cm⁻¹ (6)] as compared with high-melting IX [1583 cm⁻¹ (2), 1612 cm⁻¹ (3), 1725 cm⁻¹ (3)], is also evidence for this.

In the PMR spectra (Table 2) (in acetone) the chemical shift of the line from the methoxy group of Id and the high-melting products coincides with the limits of 0.1 ppm, which also attests to the same location of the methoxy group in these compounds. In the low-melting products, however, the methoxy group line is found at weaker field, while the methylene group line is found at stronger field, i.e., the methoxy group in these compounds is located somewhere else than in the high-melting isomers.

Derivatives of 1,3-thiazolidin-4-thione (XV and XVI) were synthesized by the action of P_2S_5 on III and VIII, respectively, in order to obtain additional data on the structures of the isomers. In XVI, which is the sulfur analog of III, the methoxy and methylene lines are shifted considerably to the weak-field side, which attests to the close spatial arrangement of the methoxy group with respect to the C=S and C=O groups in XVI and III, respectively. The shift of only one line of the CH₂ group in the spectrum of XV points to the location of the methoxy group in the 2 position in XV and VII.

The set of data makes it possible to assert that the high-melting (If) and low-melting (Ie) products are two isomeric forms in which the aryl and methoxy substituents are located in different positions.

The disubstituted 2-imino-1,3-thiazolidinones obtained are stable crystalline substances with all the properties of pseudothiohydantoins. They give 5-benzal derivatives in moderate yields on reaction with

^{*}The intensity was estimated on a ten-point scale with respect to the band at 1642 cm^{-1} in the spectrum of III, the intensity of which was taken as ten. All of the intensities were measured with respect to the 1386 cm^{-1} band of dimethyl sulfoxide.

benzaldehyde in the presence of small amounts of alkali; phosphorus pentasulfide in refluxing toluene converts them to the corresponding thiazolidinethiones without converting one isomer into the other. The stability of If to oxidizing and reducing agents is remarkable: the compounds were isolated unchanged from acetic acid solutions after the action of hydrogen peroxide or zinc metal on them.

EXPERIMENTAL

2-Arylimino-3-methoxy-1,3-thiazolidin-4-ones (II-VII). Sodium acetate (0.025 mole) was added to a solution of 0.01 mole of N-arylthiocarbamoyl-O-methylhydroxylamine in 50 ml of methylene chloride (or absolute ether), the mixture was cooled to -15 to -20° , and 0.01 mole of chloroacetyl chloride was carefully added to it. The mixture was stirred for 3 h, allowing it to gradually heat up to room temperature. The mixture was then washed with cold water (twice with 20-25-ml portions), dried, and the solvent was removed. The precipitate was recrystallized (Table 1).

The reaction can be carried out without an acceptor; in this case, the solution was washed at the end of the reaction with 0.5% aqueous sodium acetate.

2-Methoximino-3-aryl-1,3-thiazolidinones (VIII-XIV). A. A solution of 1.0 g of thiazolidinone Ie in 15-20 ml of about 0.2% sodium methoxide was refluxed for 15-20 min. The mixture was cooled, and water was added to precipitate the product, which was recrystallized from methanol, benzene, or hexane.

Compound XIV was obtained in the same way as II-VII. The reaction does not proceed without an acceptor.

B. The reaction of N,N'-disubstituted thiourea with chloroacetyl chloride under conditions similar to those used for the synthesis of II-VII, but in acetone without an acceptor, gave quantitative yields of the hydrochlorides of VIII-XIV, from which free VIII-XIV were isolated by the addition of alkali or another base.

C. The reaction of N,N'-disubstituted thioureas with ethyl chloroacetate in methylene chloride in the presence of triethylamine at room temperature gave 80% yields of VIII-XIV. When the solvent was replaced by acetone or the reaction was carried out without an acceptor, the reaction either did not occur or resin formation with sulfur evolution was observed.

<u>2-Methoximino-3-phenyl-1,3-thiazolidine-4-thione (XV).</u> Phosphorus pentasulfide [1.1 g (0.005 mole)] was added to a solution of 1.1 g (0.005 mole) of VIII in 75 ml of toluene and the mixture was refluxed with stirring for 3 h. Excess P_2S_5 was removed by filtration, the solvent was evaporated in vacuo, and the residue was recrystallized from benzene-heptane (1:10) to give 1.1 g (92%) of XV with mp 165°. Found %: N 11.9; S 27.2. $C_{10}H_{10}N_2OS_2$. Calculated %: N 11.7; S 26.9.

 $\frac{2-(\text{o-Chlorophenyl})\text{imino-3-methoxy-1,3-thiazolidine-4-thione (XVI).}}{\text{yield from 1.25 g (0.005 mole) of III and 1.1 g (0.005 mole) of P₂S₅ and had mp 152-153° (from hexane).}}{\text{Found }\%: N 10.1; Cl 12.5. C₁₀H₉N₂ClOS₂. Calculated \%: N 10.3; Cl 12.7.}}$

2-Methoximino-3-phenyl-5-benzal-1,3-thiazolidine-4-thione (XVII). A solution of two to three drops of 0.2% sodium methoxide and 0.8 g (0.08 mole) of benzaldehyde was added to a solution of 1.1 g (0.05 mole) of VIII in 30 ml of dimethylformamide, the mixture was heated at 153° for 6 h, cooled, and water was added to give 0.8 g (53.5%) of XVII with mp 180° (from methanol). Found %: N 8.9; S 10.6. $C_{17}H_{13}N_2O_2S$. Calculated %: N 9.0; S 10.4.

The IR spectra were obtained (KBr pellets) with a UR-10 spectrophotometer with slit program 4 and other standard conditions. The UV spectra in ethanol in a $6 \cdot 10$ -cm⁻³ thick cuvette were obtained with an SF-4 spectrometer. The CS spectra of 7% solutions in dimethyl sulfoxide were obtained with a DFS-12 spectrometer. The PMR spectra of 1% solutions in deuteroacetone were obtained with an RS-60 spectrometer.

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