SYNTHESIS OF THIAZOLINES AND THIAZOLIDINES

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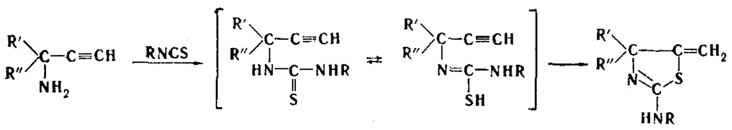
Primary α-ethynylamines form thiazolines with isothiocyanates, while secondary α-ethynylamines give thiazolidines. Data on the IR, PMR, and UV spectra of the compounds obtained are presented.

Primary α-ethynylamines react with isocyanates to form the corresponding ethynylureas [1,2]. However, we were unable to obtain the ethynylthioureas indicated by Easton and co-workers [1] on reaction with isothiocyanates. The thioureas formed are immediately converted to thiazolines as a result of intramolecular cyclization. The cyclization process apparently includes thiol-thione tautomerism as a compulsory step.



I-XIII

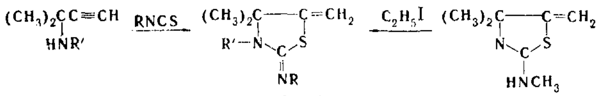
R', R''=Alk; R=Alk, Ph

The absorption bands characteristic for the stretching vibrations of C≡C and ≡C−H groups (2100, 3300 cm^{-1}) and frequencies associated with the absorption of the =N−C=S group in thioureas [3] are absent in the IR spectra of freshly prepared I-XIII. All of the reaction products have absorption bands at 860-870 and 3100 cm^{-1}, which correspond to the deformation and stretching vibrations of the terminal methylene group. The stretching vibrations of the N−H group are responsible for the absorption at 3200 cm^{-1}; we assign the two bands in the 1600 cm^{-1} region (1610 and 1650 cm^{-1}) to the absorption of the C=C and C=N groups. It should be noted that an intense band at 1550 cm^{-1}, which is affiliated with the absorption of the thiazole ring [4], is observed for all of the thiazolines.

The PMR spectra (Fig. 1) completely confirm the structure of the substances obtained. The signals at 4.9-5.0 ppm in the region of olefin protons correspond to the presence of geminal protons. The magnetic nonequivalence of the olefin protons increases as alkyl radical R' decreases [Δδ 0 Hz (XII), 1.5 Hz (XI), 3.0 Hz (X)], which is possibly associated with the diamagnetic effect on the shielding of the alkyl groups attached to the C_4. The structure of the signals in the aliphatic proton region corresponds to the structure of the alkyl radicals.

In the UV region, the thiazolines obtained have an intense absorption maximum at 195-210 nm (Table 3). A slight bathochromic shift of the maximum and a certain increase in intensity are observed during the formation of the hydrochlorides.

Secondary α-ethynylamines form thiazolidines with isothiocyanates. The reaction of isothiocyanates with secondary amines proceeds more slowly than with primary amines; in contrast to the crystalline thiazolines, the thiazolidines formed are yellow, readily distilled liquids that form hydrochlorides.



XIV-XVIII

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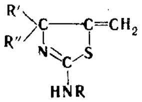
Institute of Chemical Sciences, Academy of Sciences of the Kazakh SSR, Alma Ata. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 471-474, April, 1972. Original article submitted February 1, 1971.

TABLE 1



Compound	R	R'*	mp, °C†	Empirical formula	Found, %				Calc., %				Yield, %
					C	H	N	S	C	H	N	S	
I	CH_3	CH_3	86 (170)	$C_7H_{12}N_2S$	54,3	8,2	17,5	20,5	54,8	7,7	17,9	20,5	81,0
II	CH_3	C_2H_5	90 (158)	$C_8H_{14}N_2S$	56,4	8,2	16,3	18,8	56,4	8,2	16,4	18,8	80,0
III	CH_3	C_3H_7	92	$C_9H_{16}N_2S$	—	—	14,8	18,2	—	—	15,2	17,4	87,0
IV	C_2H_5	CH_3	108 (130)	$C_8H_{14}N_2S$	57,0	8,5	16,3	18,8	56,5	8,2	16,4	18,8	92,0
V	C_2H_5	C_2H_5	60 (120)	$C_9H_{16}N_2S$	59,0	9,1	14,9	17,5	58,7	8,7	15,2	17,3	90,0
VI	C_2H_5	C_3H_7	68 (130)	$C_{10}H_{18}N_2S$	—	—	13,8	—	—	—	14,1	—	90,0
VII	$CH_2{=}CHCH_2$	CH_3	82	$C_9H_{14}N_2S$	59,8	8,0	15,5	17,5	59,3	7,7	15,3	17,5	82,0
VIII	$CH_2{=}CHCH_2$	C_2H_5	118—120 (5)	$C_{10}H_{16}N_2S$	61,3	8,6	—	15,7	61,2	8,1	—	16,3	80,0
IX	$CH_2{=}CHCH_2$	C_3H_7	118—120 (5)	$C_{11}H_{18}N_2S$	—	—	12,9	15,5	—	—	13,3	15,2	83,0
X	C_6H_5	CH_3	171	$C_{12}H_{13}N_2S$	66,4	6,5	—	—	66,0	6,4	—	—	76,0
XI	C_6H_5	C_2H_5	121	$C_{13}H_{15}N_2S$	67,2	6,7	—	—	67,2	6,8	—	—	93,0
XII	C_6H_5	C_3H_7	146	$C_{14}H_{18}N_2S$	68,3	7,4	—	—	68,2	7,3	—	—	99,0
XIII	C_6H_5		181	$C_{15}H_{18}N_2S$	69,9	8,1	—	—	69,7	8,4	—	—	90,0

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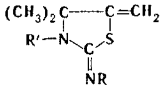
*For I-XII, R" = CH_3, while R' + R" = $(CH_2)_5$ for XIII.

† Compounds I-VII were recrystallized from petroleum ether, while X-XIII were recrystallized from heptane. The melting points of the hydrochlorides, the composition of which (B · HCl) was confirmed by determining the percentage of nitrogen, are indicated in parentheses. The boiling points are given for VIII and IX; n_D^{20} 1.5402 (VIII) and 1.5421 (IX).

TABLE 2



Comp.	R	R'	bp, °C (mm)	n_D^{20}	Empirical formula	Found, %		Calc., %		Yield, %	mp of hydrochloride, °C*
						N	S	N	S		
XIV	C_2H_5	CH_3	88—90 (4)	1,4770	$C_9H_{16}N_2S$	14,5	16,1	14,1	16,1	71,0	125
XV	C_2H_5	C_4H_9	108—110 (4)	1,5130	$C_{12}H_{22}N_2S$	12,8	14,3	12,3	14,1	87,0	130
XVI	C_6H_5	C_4H_9	148—150 (4)	1,5910	$C_{16}H_{22}N_2S$	9,6	—	10,2	—	96,0	165
XVII	CH_3	C_2H_5	88—90 (4)	1,5321	$C_9H_{16}N_2S$	14,9†	17,8	15,2	17,3	83,0	170
XVIII	C_6H_5	C_2H_5	128—130 (4)	1,6070	$C_{14}H_{18}N_2S$	—	—	—	—	71,0	165

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*The composition of the hydrochlorides (B · HCl) was confirmed by determining the percentage of nitrogen.

† Found: C 58.7; H 8.9%. Calculated: C 58.6; H 8.6%.

TABLE 3. Absorption Maxima in the Spectra of Aminothiazolines and Iminothiazolidines

Compound	λ_{max}, nm	lg ε
I	208	2,15
I · HCl	208	3,04
II	205	2,72
IV · HCl	212	2,74
VI	212	2,46
IX	209	2,43
XIV · HCl	215	2,40
XV · HCl	215	2,72
XVII · HCl	215	2,20
XVIII · HCl	203	2,56

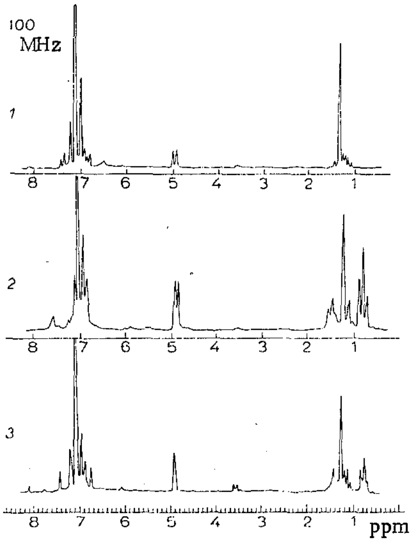

Fig. 1. PMR spectra of 2-phenylamino-2-thiazolines: 1) 2-phenylamino-4,4-dimethyl-5-methylene-2-thiazoline (X); 2) 2-phenylamino-4-ethyl-4-methyl-5-methylene-2-thiazoline (XI); 3) 2-phenylamino-4-methyl-4-propyl-5-methylene-2-thiazoline (XII).

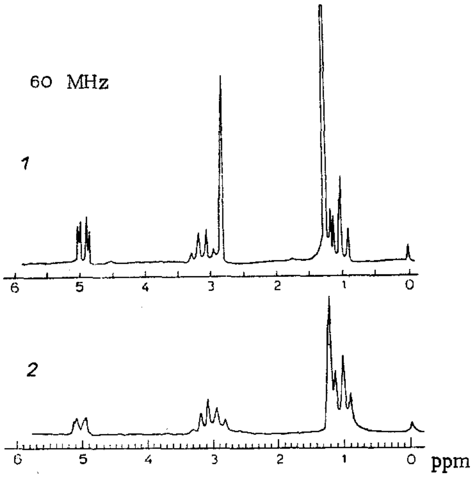

Fig. 2. PMR spectra of 2-alkylimino-thiazolidines: 1) 2-methylimino-3-ethyl-4,4-dimethyl-5-methylene-2-thiazolidine (XVII); 2) 2-ethylimino-3-ethyl-4,4-dimethyl-5-methylene-2-thiazolidine (XIV).

We proved the formation of five-membered rings in the case of secondary α-ethynylamines by means of the identical character of the products obtained and the product of the alkylation of thiazoline.

The IR spectra of thiazolidines XIV-XVIII contain the frequencies of a terminal methylene group, δ 860-870 cm^{-1} and ν 3100 cm^{-1}. The two bands in the 1600 cm^{-1} region (1610 and 1640 cm^{-1}) attest to the presence of C =C and C =N groups. The band at 1560 cm^{-1} characteristic for thiazolines is not present in the spectra of the thiazolidines. The geminal protons of the terminal methylene group in the PMR spectra of the thiazolidines appear as two doublets at 4.88 and 5.02 ppm with J_{gem} 2 Hz (Fig. 2) [5]. We assign the singlet with δ 1.25 ppm to the protons of the $(CH_3)_2C$ methyl groups. The protons of the methyl group attached to nitrogen appear as a singlet at 2.8 ppm, while the NCH_2CH_3 protons appear as a quartet at 3.1 ppm and a triplet at 1.0 ppm.

The UV spectra of the thiazolidines have an absorption maximum at 210 nm that is bathochromically shifted by 13 nm as compared with the corresponding thiazolines (Table 3).

It should be noted that the cyclization is hindered as R' becomes larger. Thus the cyclization proceeds quantitatively when R' = CH_3 (XIV) or C_2H_5 (XVII, XVIII), while cyclization is not observed when R' = C_6H_5 or $CH_2C_6H_5$. The possibility of cyclization is also reduced as R becomes larger. While the reaction proceeds to completion when R = Alk, a portion of the amine and the isothiocyanate is recovered unchanged from the reaction mixture when R = Ph. Similar peculiarities in the cyclization were previously noted, and the difficulties were explained by steric factors, which was confirmed by examination of Stuart models [1, 6].

EXPERIMENTAL

The IR spectra of KBr pellets and pure liquids were recorded with a UR-20 spectrometer. The PMR spectra were recorded with a JNM-100 spectrometer (with chloroform as the solvent and tetramethylsilane as the standard) and with a ZKP-60 spectrometer (as the pure liquid with hexamethyldisiloxane as the standard). The UV spectra of alcohol solutions were recorded with a Hitachi EPS-3T spectrometer.

2-Methylamino-4,4-dimethyl-5-methylene-2-thiazoline (I). A 1.46-g (0.02 mole) sample of methyl isothiocyanate was added in small portions with stirring to 1.66 g (0.02 mole) of 3-amino-3-methyl-1-butyne in such a way that the temperature did not rise above 50° (the reaction was exothermic), and the mixture was allowed to stand at 50° for 2 h. Compound I crystallized out when the mixture was cooled. It was purified by sublimation and subsequent crystallization from dry petroleum ether to give a product with mp 86° and R_f 0.41 (activity III Al_2O_3, petroleum ether–diethylether (1 :1)]. The hydrochloride of I was hygroscopic.

Compounds II-XIII (Table 1) were similarly obtained.

2-Methylamino-3-ethyl-4,4-dimethyl-5-methylenethiazolidine (XVII, Table 2). A) A 1.46-g (0.02 mole) sample of methyl isothiocyanate was added in portions with stirring to 2.22 g (0.02 mole) of 3-ethylamino-3-methyl-1-butyne (the reaction was exothermic), and the mixture was stirred at 50° for 2 h. Compound XVII was purified by vacuum distillation.

Compounds XIV-XVI, XVIII (Table 2) were similarly obtained.

B) (By the method in [7].) A methanol solution of 3.1 g (0.02 mole) of ethyl iodide was added with cooling and stirring to 1.6 g (0.01 mole) of 2-methylamino-4,4-dimethyl-5-methylene-2-thiazoline, and the mixture was heated at 60° for 2 h. A 5% solution of KOH was added to the solution, and the liberated oil was extracted with benzene. The extract was washed with water and dried over $MgSO_4$. Compound XVII was purified by vacuum distillation. The yield was 20%.

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LITERATURE CITED

1. N. R. Easton, D. R. Cassady, and R. D. Dillard, J. Org. Chem., 29, 1851 (1964).
2. I. N. Azerbaev, M. Zh. Aitkhozhaeva, and L. A. Tsoi, Acetylene Chemistry and Calcium Carbide Technology [in Russian], Alma Ata (1972), p. 216.
3. C. N. R. Rao and R. Venkataraghavan, Spectr. Acta, 18, 541 (1962).
4. S. G. Bogomolov, Yu. N. Sheinker, and I. Ya. Postovskii, Zh. Obshch. Khim., 24, 539 (1954).
5. N. S. Bhacca, L. F. Johnson, and G. N. Shoolery, NMR Spectra Catalog, Varian Associates (1962), pp. 17, 18, 23.
6. F. Ya. Perveev and R. A. Bogatkin, Zh. Organ. Khim., 2, 968 (1966).
7. K. K. Kuz'mina, N. G. Ostroumova, Yu. V. Markova, and M. N. Shchukina, Zh. Obshch. Khim., 32, 3215 (1962).