INVESTIGATION OF THE STRUCTURES OF QUATERNARY SALTS OF ISOMERIC 2-ALKYL- AND 2-ARYLAMINOTHIAZOLINES

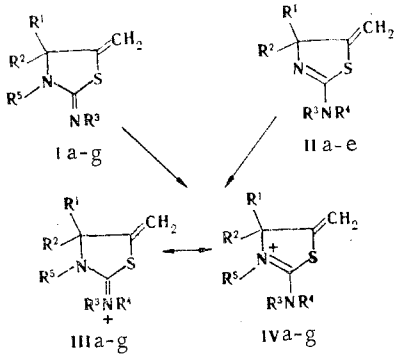
L. A. Tsoi, V. B. Rozhnov, and N. N. Rubanyuk

UDC 547.789.1.07:543.422.25

Isomeric 2-amino- and 2-imino-4,4-dialkyl-5-methylenethiazolines give identical methiodides with primary contribution of the imino structure for the anilino derivatives and the amino structure for the alkylamino derivatives. Thermolysis of the salts gives mixtures of thiazolines with amino and imino structures in a ratio of 2:1.

It has been shown [1, 2] that in the quaternization of isomeric amino and iminothiazolines and oxazolines the quaternization centers do not always coincide with the subsequent localization of positive charge. In this connection, in the investigation of isomeric bases, in addition to the problems of determination of the quaternization center, it is necessary to examine the problems of the structures of quaternary salts [3]. In the present paper we examine the problems of the structures of the methiodides of alkyl and aryl derivatives of 2-amino-4,4-dialkyl-5-methylene-1,3-thiazoline and 2-imino-4,4-dialkyl-5-methylene-1,3-thiazolidine.

In the quaternization of bases I and II with methyl iodide we obtained quaternary salts III and IV.



R	a	a′	b	c	c′	d	e	e′	f	g
	I–IV	I, III, IV	I–IV	I–IV	III, IV	I–IV	I–IV	III, IV	I, III, IV	I, III, IV
R^1	CH_3	CH_3	CH_3	CH_3	CH_3	CH_3	CH_3	CH_3	CH_3	CH_3
R^2	CH_3	CH_3	C_2H_5	CH_3	CH_3	C_2H_5	C_2H_5	C_2H_5	C_2H_5	CH_3
R^3	C_6H_5	C_6H_5	C_6H_5	CH_3	CH_3	CH_3	C_2H_5	C_2H_5	p-$CH_3C_6H_4$	C_2H_5
R^4	CH_3	CD_3	CH_3	CH_3	CD_3	CH_3	CH_3	CD_3	CH_3	CH_3
R^5	CH_3	CH_3	CH_3	CH_3	CH_3	CH_3	CH_3	CH_3	CH_3	CH_3

The development of positive charge on the nitrogen atoms during quaternization gives rise to deshielding of the alkyl groups bonded to them and, consequently, weak-field shifts in the NMR spectra [4, 5], from which we attempted to estimate the distribution of positive charge on the nitrogen atoms in quaternary thiazoline salts. In the case of aryl derivatives the maximum weak-field shift in the ^{13}C NMR spectra is observed for the substituents attached to the exocyclic nitrogen atom ($\Delta\delta$ 7.8 and 7.4 ppm, respectively, as compared with $\Delta\delta$ 6.0 and

Institute of Chemical Sciences, Academy of Sciences of the Kazakh SSR, Alma Ata 480100.
Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 8, pp. 1044-1047, August, 1983. Original article submitted July 19, 1982.

0009-3122/83/1908-0835$07.50

TABLE 1. ^{13}C Chemical Shifts in the NMR Spectra of Thiazoline Bases and Their Methiodides (δ, ppm from tetramethylsilane)

Compound	R^1	R^2	R^3	R^4	R^5	$C_{(2)}$	$C_{(4)}$	$C_{(5)}$	$=CH_2$
Ia	26,6	26,6	123,2; 123,9 129,4; 152,2	—	29,7	157,0	67,9	149,1	104,5
Ib	26,6	8,2; 33,1	123,3; 123,9 129,3; 152,2	—	29,5	158,1	71,7	147,3	104,1
Ic	26,4	26,4	40,3	—	29,6	158,9	67,7	149,1	104,4
Id	26,9	8,2; 32,9	40,1	—	29,4	159,4	71,0	147,2	104,3
Ie	26,7	8,1; 32,9	16,7; 49,2	—	29,3	156,8	70,4	147,6	104,0
IIa	30,8	30,8	127,2; 127,7 129,9; 152,2	40,4	—	158,9	78,5	146,3	101,7
IIb	30,3	9,6; 37,1	127,0; 127,2	40,6	—	159,0	82,5	146,8	101,5
IIc	30,6	30,6	130,0; 155,7 39,8	39,8	—	158,8	78,3	149,2	101,7
IIe	30,2	8,6; 36,7	12,6; 48,0	40,0	—	158,0	81,2	149,3	101,5
IIIa, IVa	27,7	27,7	127,5; 130,5 131,1; 144,2	48,2	35,7	168,9	78,1	142,6	110,0
IIIa, IVa	27,7	27,7	127,5; 130,5 131,1; 144,2	—	35,7	168,9	78,1	142,6	110,0
IIIb, IVb	27,2	8,2; 33,3	127,4; 130,5 131,1; 151,9	48,0	35,1	169,3	81,9	143,9	109,9
IIIc, IVc	27,5	27,5	45,4	45,4	35,5	170,0	76,6	142,9	110,9
IIIc', IVc'	27,5	27,5	45,4	—	35,5	169,7	76,9	142,8	109,4
IIIg, IVg	27,5	27,5	13,3; 54,2	42,7	36,0	168,8	77,0	142,6	109,8
IIId, IVd	27,5	8,5; 33,5	46,3	46,3	36,0	171,1	80,9	140,1	109,9
IIIe', IVe'	27,5	8,5; 33,7	13,2; 54,2	—	35,8	169,4	80,9	140,7	109,8
IIIe, IVe	27,3	8,3; 33,6	13,2; 54,1	42,7	35,5	169,6	80,9	140,7	109,7

TABLE 2. PMR Spectra and Physical Characteristics of Thiazoline Bases and Their Methiodides

Compound	bp, °C [mm (Hg column)], mp, °C	Chemical shifts, ppm					
		R^1	R^2	R^3	R^4	R^5	$=CH_2$
Ia	70 [6]	1,35	1,35	7,00 m	—	2,87	1,85; 5,00
Ib	55 [6]	1,36	0,84 t; 1,67 q	7,07 m	—	2,90	5,02
Ic	oil [6]	1,35	0,80 t; 1,68 q	6,75 q; 2,24	—	2,90	4,94
Ic	79—82 (2) [9]	1,30	1,30	2,90	—	2,70	4,95; 5,05
Ig	88—90 (4) [7]	1,30	1,30	1,10 t; 3,00 q	—	2,70	4,92; 5,05
Id	120—122 (10)	1,30	0,75 t; 1,63 q	2,87	—	2,70	5,03
Ie	98—101 (3)	1,30	0,75 t; 1,60 q	1,10 t; 3,00 q	—	2,70	5,00
IIa	170—172 (1)	1,35	1,35	7,20	3,30	—	4,85
IIb	170—172 (1)	1,30	0,80 t; 1,60 q	7,20	3,30	—	4,80; 4,90
IIc	85—90 (5)	1,30	1,30	2,90	2,90	—	5,00
IId	89—95 (4)	1,30	0,75 t; 1,60 q	2,90	2,90	—	5,00
IIe	89—95 (4)	1,30	0,75 t; 1,60 q	1,10 t; 3,00 q	2,73	—	5,00
IIIa, IVa	163—165*	1,65	1,65	7,50 m	3,78	2,95	5,40 m
IIIa, IVa'	162—163	1,65	1,65	7,53 m	—	2,95	5,45 q
IIIb, IVb	155—158	1,65	0,90 t; 1,85 q	7,45 m	3,78	2,90	5,45
IIIf, IVf	183—184	1,60	0,86 t; 1,86 q	7,33 q; 2,28	3,70	2,85	5,40
IIIc, IVc	183—185	1,63	1,63	3,48 (3H)	3,48 (3H)	3,48 (3H)	5,45 q
IIIc', IVc'	152—153	1,65	1,65	3,50	—	3,47	5,36
IIIg, IVg	125—128	1,63	1,63	1,38 t; 3,65 q	3,50	3,50	5,40 q
IIId, IVd	203—204	1,60	0,85 t; 1,85 q	3,50 (3H)	3,50 (3H)	3,50 (3H)	5,50
IIIe', IVe'	152—153	1,65	0,85 t; 1,85 q	1,38 t; 3,65 q	—	3,45	5,50
IIIe, IVe	140—146	1,63	0,88 t; 1,83 q	1,36 t; 3,66 q	3,50	3,50	5,40

*Compounds III and IV were recrystallized from alcohol.

5.6 ppm for the methyl groups of the ring nitrogen atom, Table 1). The same sequence in the change in the shifts, but more pronounced, is also observed in the PMR spectra: The maximum weak-field shift (Δδ 0.48 ppm) is noted for the protons of the methyl group attached to the exocyclic nitrogen atom, while the shift of the 3-CH_3 group is either absent (IIIb-IVb) or is very very insignificant (Δδ 0.08 ppm, IIIa and IVa, Table 2). We explain these data by primary localization of the positive charge on the exocyclic nitrogen atom and, consequently, a large contribution of structure III for salts IIIa,b-IVa,b.

In the case of methiodides of alkyl derivatives of thiazoline the maximum weak-field shifts are observed for substituents attached to the ring nitrogen atom (Δδ 6.0-6.6 ppm),

but they differ only slightly from the shifts of the alkyl groups of the amino nitrogen atom ($\Delta\delta$ 5.9-6.4 ppm, Table 1). The same principle is observed in the PMR spectra of thiazolinium iodides IIIc-g to IVc-g: The methyl groups of the ring nitrogen atom have the maximum weak-field shift ($\Delta\delta$ 0.75-0.80 ppm), and a somewhat smaller shift is observed for the alkyl substituents of the exocyclic nitrogen atom (0.58-0.60 ppm, Table 2). In the case of IIIc,d to IVc,d a simultaneous weak-field shift leads to combining of the signals of the R^3, R^4 and R^5 methyl groups and their appearance in the PMR spectra as one singlet signal at 3.50 ppm (9H). On the basis of this, according to [8], one may conclude that the methyl groups are equivalent, i.e., one may assume quaternization at the exocyclic nitrogen atom to give a 2-trimethylammonium salt of thiazoline. However, the identical character of the quaternary salts obtained from 2-methylamino-3-methylthiazolidine (Ic) and 2-dimethylaminothiazoline (IIc) excludes this quaternization pathway. The ^{13}C NMR spectrum confirms the equivalence of only two methyl groups (45.4 ppm, 2C), and the R^5 methyl group resonates at stronger field (35.5 ppm). The simultaneous deshielding of the alkyl groups of the ring nitrogen atom and the amino nitrogen atom constitutes evidence for the high degree of delocalization of the positive charge along the —N=C—N< amidine system with a small shift to the ring nitrogen atom and, consequently, slight preponderance of the contribution of structures IV.

The thermal decomposition of thiazolinium iodides IIIc-g and IVc-g gives mixtures of bases with amino (II) and imino (I) structures in a ratio of 2:1. The thermolysis products were analyzed from the ratio of the signals in the ^{13}C NMR spectra of the decomposition products. The resonance signals of the alkyl groups of amino compounds II in the ^{13}C NMR spectra are shifted to weaker field with respect to the signals of imino compounds I. The percentage compositions were calculated most graphically from the ratios of the signals of the methylene group (=CH_2), the shifts of which remain unchanged for the imino (104.0-104.7 ppm) and amino (101.5-101.7 ppm) groups in all of the investigated thiazolines. The signals of the carbon atoms of the thiazoline ring in the amino compounds either coincide with the signals of the imino compounds [$C_{(2)}$ and $C_{(5)}$] or are shifted to strong field [$C_{(4)}$].

EXPERIMENTAL

The ^{13}C NMR spectra of solutions of the compounds in ethanol were recorded with a Brucker WP-80 spectrometer (20.15 MHz) at room temperature. The PMR spectra of 10% solutions in CCl_4 and $CDCl_3$ were recorded with a Tesla BS-467 spectrometer (60 MHz). Separation of the chloroform solutions of the quaternary salts into layers when ethanol (hexamethyldisiloxane) was added was eliminated by the addition of a few drops of CD_3OD.

2-Methylamino-3-methyl-4-methyl-4-ethyl-5-methylene-1,3-thiazolidine (Id). This compound was obtained by the method in [7] from 5.55 g (50 mmole) of 3-methylamino-3-methylpentyne and 3.05 g (50 mmole) of methyl isothiocyanate. Workup gave 7.74 g (90%) of a product with n_D^{25} 1.5365. Found: C 58.9; H 8.7; N 15.5; S 17.2%. $C_9H_{16}N_2S$. Calculated: C 58.7; H 8.7; N 15.2; S 17.4%.

2-Ethylamino-3-methyl-4-methyl-4-ethyl-5-methylene-1,3-thiazolidine (Ie). This compound was obtained by a similar method from 5.55 g (50 mmole) of 3-methylamino-3-methylpentyne and 3.75 g (50 mmole) of ethyl isothiocyanate. Workup gave 8.84 g (95%) of a product with n_D^{25} 1.5265. Found: C 60.8; H 9.0; N 14.2; S 16.3%. $C_{10}H_{18}N_2S$. Calculated: C 60.6; H 9.1; N 14.1; S 16.2%.

2-Methylanilino-4,4-dimethyl-5-methylene-1,3-thiazoline (IIa). A solution of 3.76 g of bicarbonate in 15 ml of water and 2.8 ml of dimethyl sulfate were added to an aqueous suspension of 2.18 g (10 mmole) of 2-phenylimino-4,4-dimethyl-5-methylenethiazolidine by the method in [10], after which the mixture was maintained at room temperature for 30 min and at 70°C for 1 h and then allowed to stand overnight. It was then made strongly alkaline with aqueous NaOH solution and heated at 60°C for 1 h. The organic layer was extracted with benzene, the solvent was removed by distillation, and the residue was fractionated in a stream of argon to give 1.15 g (50%) of a light-yellow oil with n_D^{25} 1.5850. Found: C 67.0; H 6.8; N 11.2; S 13.8%. $C_{13}H_{16}N_2S$. Calculated: C 67.2; H 6.9; N 12.1; S 13.8%.

2-Methylanilino-4-methyl-4-ethyl-5-methylenethiazoline (IIb). This compound was similarly obtained in 56% yield from 2-phenylimino-4-methyl-4-ethyl-5-methylenethiazolidine. The light-yellow oil had n_D^{25} 1.5780. Found: C 68.3; H 7.5; N 11.1; S 13.2%. $C_{14}H_{18}N_2S$. Calculated: C 68.3; H 7.3; N 11.4; S 13.0%.

The thermolysis of quaternary salts III and IV was carried out by heating the fused salts at 190-200°C with subsequent distillation of the decomposition products *in vacuo*.

2-Dimethylamino-4,4-dimethyl-5-methylenethiazoline (IIc). This compound was isolated by fractional distillation of the product of thermolysis of quaternary salts IIIc-IVc. The colorless liquid had n_D^{25} 1.5400. Found: C 56.7; H 8.4; N 16.2%. $C_8H_{14}N_2S$. Calculated: C 56.5; H 8.2; N 16.5%.

2-Dimethylamino-4-methyl-4-ethyl-5-methylenethiazoline (IId). This compound was obtained by fractional distillation of the product of thermolysis of quaternary salts IIId and IVd. The colorless liquid had n_D^{25} 1.5410. Found: C 58.5; H 8.8; N 15.5; S 16.9%. $C_9H_{16}N_2S$. Calculated: C 58.7; H 8.7; N 15.2; S 17.4%.

2-(Methyl)amino-4-methyl-4-ethyl-5-methylenethiazoline (IIe). This compound was isolated from the mixture of isomers obtained in the thermolysis of methiodides IIIe and IVe. The product had n_D^{25} 1.5410. Found: C 60.4; H 9.0; N 14.3; S 16.3%. $C_{10}H_{18}N_2S$. Calculated: C 60.6; H 9.1; N 14.1; S 16.2%.

LITERATURE CITED

1. L. A. Tsoi, S. T. Cholpankulova, G. K. Ryskieva, and A. D. Salimbaeva, Khim. Geterotsikl. Soedin., No. 7, 917 (1981).
2. L. A. Tsoi, A. D. Salimbaeva, and M. I. Goryaev, Dokl. Akad. Nauk SSSR, 259, 1123 (1981).
3. V. V. Zverev, T. N. Pylaeva, and L. V. Ermolaeva, in: The Chemistry of Hydrazones [in Russian], Nauka, Moscow (1977), p. 54.
4. J. W. Emsley, J. Feeney, and L. H. Sutcliffe, High-Resolution NMR Spectroscopy, Pergamon, Oxford (1965).
5. G. C. Levy and G. L. Nelson, Carbon-13 Nuclear Magnetic Resonance for Organic Chemists, New York (1972).
6. I. N. Azerbaev, L. A. Tsoi, S. T. Cholpankulova, and V. I. Artyukhin, Khim. Geterotsikl. Soedin., No. 6, 755 (1979).
7. I. N. Azerbaev, L. T. Kalkabaeva, M. Zh. Aitkhozhaeva, and L. A. Tsoi, Khim. Geterotsikl. Soedin., No. 4, 471 (1972).
8. G. B. Barlin and A. C. Young, J. Chem. Soc., B, No. 12, 2323 (1971).
9. N. R. Easton, D. P. Cassady, and P. D. Dillard, J. Org. Chem., 29, 1851 (1964).
10. Weygand-Hilgetag, Experimental Methods in Organic Chemistry [Russian translation], Khimiya, Moscow (1969), p. 463.

RING-CHAIN TAUTOMERISM OF β-KETO ESTER THIOBENZOYLHYDRAZONES

V. N. Nikolaev, S. I. Yakimovich, N. V. Koshmina, K. N. Zelenin, V. V. Alekseev, and V. A. Khrustalev

UDC 547.39'26'447.6'794.3:541.621.2:543.422

The products of condensation of thiobenzhydrazide with methyl acetoacetate and its α-alkyl-substituted homologs have the structure of the corresponding 2,3-dihydro-1,3,4-thiadiazoles; only the derivative of α-isopropylacetoacetic acid ester has the open hydrazone form. The products of the reaction of thiobenzhydrazide with the methyl esters of 2-oxocyclopentane- and 2-oxocyclohexanecarboxylic acid are mixtures of enehydrazine and thiadiazoline forms; the percentage of the latter decreases in polar solvents.

Thiobenzhydrazide — the most accessible of the thiohydrazides — is a promising reagent that can be used for the realization of various types of tautomeric equilibria in the products of its condensation with carbonyl compounds. Thus the products of condensation of thiobenzhydrazide with aldehydes and ketones serve as an example of hydrazone—1,3,4-thiadiazoline ring-chain tautomerism [1], whereas the product of the reaction with acetylacetone serves as an example of 1,3,4-thiadiazoline—5-hydroxypyrazoline ring—ring tautomerism [2]. In the case

A. A. Zhdanov Leningrad State University, Leningrad 199004. S. M. Kirov Academy of Military Medicine, Leningrad 195009.

Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 8, pp. 1048-1051, August, 1983. Original article submitted November 30, 1982.

0009-3122/83/1908-0838$07.50