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ELECTROPHILIC TRANS QUATERNIZATION OF SUBSTITUTED 2-[2-CYCLOHEXEN-1-YLTHIO(SELENO)]PYRIDINES TO 4a, 10-a-cis-4,4a-trans-1,2,3,4,4a,10a-HEXAHYDROBENZOTHIAZOLO(SELENAZOLO)-[3,2-a]PYRIDINIUM SALTS

A. M. Shestopalov, V. N. Nesterov, Yu. A. Sharanin,
V. P. Litvinov, V. Yu. Mortikov, V. E. Shklover,
and Yu. T. Struchkov

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It was established that the electrophilic quaternization of substituted 2-[2-cyclohexen-1-ylthio(seleno)]pyridines is a stereoselective process and proceeds as trans quaternization with the formation of 4a,10a-cis-4,4a-trans-1,2,3,4,4a,10a-hexahydrobenzothiazolo(selenazolo)[3,2-a]pyridinium salts.

The study of the mechanism and stereochemistry of electrophilic heterocyclization — quaternization — was associated with its extensive use as a general method in the synthesis of various heterocycles [1-6]. Thus, this reaction was used in the synthesis of annelated pyridinium salts. Imidazo-, oxazolo-, thiazolo-, and selenazolo[3,2-a]pyridinium salts, respectively, were obtained in the bromination or iodination of 2-N-, O-, S-, and Se-allylpyridines [7, 8]. However, the use of 2-N-, O-, S-, and Se-allylpyridines in electrophilic quaternization did not make it possible to form a judgment regarding the stereochemistry of this reaction and its mechanism. In order to develop stereochemical concepts of the investigated reaction we synthesized a number of substituted 2-[2-cyclohexen-1-ylthio(seleno)]pyridines, studied their reaction with various electrophilic reagents, and investigated the structures of the annelated pyridinium salts obtained.

Substituted 2(1H)-pyridinethiones and -selenones Ia-c [9, 10] and 3-bromo-1-cyclohexene (II) were convenient and accessible reagents for the synthesis of IIIa-c; the alkylation of pyridines Ia-c with 3-bromo-1-cyclohexene (II) in DMF in the presence of an equimolar amount of KOH proceeds regioselectively exclusively at the sulfur or selenium atom with the formation of 2-[2-cyclohexen-1-ylthio(seleno)]pyridines IIIa-c.

T. G. Shevchenko Voroshilovgrad State Pedagogical Institute, Voroshilovgrad 348011. A. N. Nesmeyanov Institute of Heteroorganic Compounds, Academy of Sciences of the USSR, Moscow 117334. N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow 117334. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, pp. 1506-1514, November, 1988. Original article submitted April 20, 1987.

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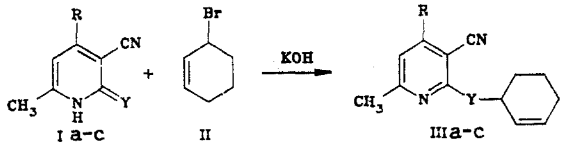
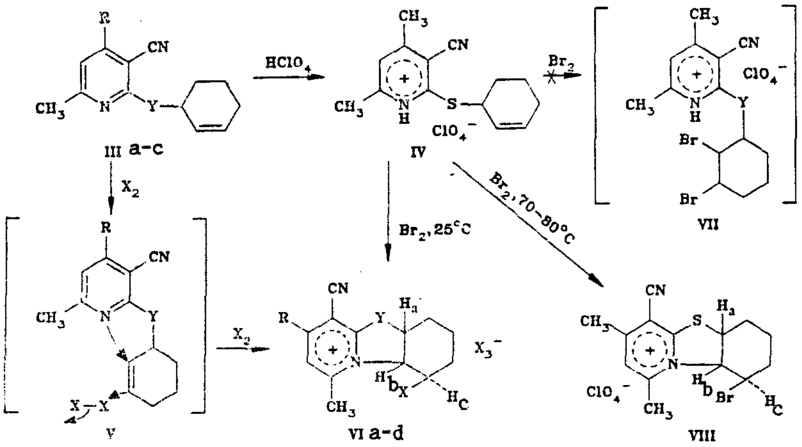


I, III a R=CH_3, Y=S; b R=CH_3, Y=Se; c R=H, Y=S

The results of elementary analysis and the IR and PMR spectroscopic data do not contradict the structures of the IIIa-c obtained (Table 1).

The reactions of 2-[2-cyclohexen-1-ylthio(seleno)]pyridines III with electrophilic reagents (bromine, iodine, perchloric acid) proceed in different directions depending on the nature of the electrophile. The reaction of IIIb with perchloric acid in acetic acid at 25°C proceeds with the formation of pyridinium perchlorate IV rather than a benzothiazolo[3,2-a]pyridinium salt. This reaction pathway is associated with the rather high basicity of pyridine. Benzothiazolo(selenazolo)[3,2-a]pyridinium trihalides VIa-d are formed in high yields in the reaction of IIIa-c with a twofold excess of bromine or iodine in chloroform; triiodides VIb-d are always formed regardless of the amount of iodine introduced into the reaction. The starting IIIa-c remain unchanged when there is insufficient iodine. Quarternized azine VIa was also obtained in the bromination of perchlorate IV in acetic acid at 25°C. The direction of this reaction depends on the temperature of the reaction mixture and excludes the possibility of the occurrence of such quaternizations via a nucleophilic mechanism through intermediate VII. The bromination of IV in acetic acid at 70-80°C leads to benzothiazolo[3,2-a]pyridinium perchlorate VIII.



VI a R=CH_3, Y=S, X=Br; b R=CH_3, Y=S, X=I; c R=CH_3, Y=Se, X=I; d R=H, Y=S, X=I

A decrease in the intensity of the absorption band of the CN group and its shift to the high-frequency region to 2234-2239 cm^{-1} occur in the IR spectra on passing from IIIa-c to VIa-d and VIII; this is associated with delocalization of the positive charge in the pyridine fragment of the molecules of these compounds. Delocalization of the positive charge in the pyridine fragment of VIa-d and VIII leads to an increase in the polarization of the pyridine protons and the protons of the alkyl substitutents bonded to the pyridine ring; a shift of the signals of these protons in the PMR spectra of VIa-d and VIII to weak field is observed. Thus, for IIIa and VIa the differences in the chemical shifts of the protons of the R, CH_3, and pyridine CH groups are, respectively, 0.29, 0.61, and 0.78 ppm. The protons of the 6-CH_3 group of VIa-d and VIII are more polarized than the protons of the 8-CH_3 group. Signals of protons of the benzothia(selena)zole fragment are also present in the PMR spectra of VIa-d and VIII. Multiplets of protons of YCH and HalCH groups appear at 4.98-5.20 and 4.77-4.92 ppm, respectively. The signal of the proton of the NCH group of VIa-d and VIII shows up in the form of a double doublet at 6.02-6.17 ppm with $^3J_{cis}$ = 4.7-5.2 Hz and $^3J_{trans}$ = 9.9-10.6 Hz. This multiplicity of the signal of the proton of the NCH group in the series of these compounds is a consequence of the high stereoselectivity of the quaternization of azines IIIa-c to VIa-d and VIII. The assignment of the spin–spin coupling constants (SSCC) to the group of $YCH_aCH_bCH_cHal$ protons was made on the basis of double-resonance experiments in the spectra of VIa-d and VIII. Irradiation at the frequency of the proton of the CHHal group contracts

TABLE 1. Characteristics of Substituted 3-Cyano-2-[2-cyclohexen-1-yl-thio(seleno)]pyridines IIIa-c

Compound	mp, °C	IR spectrum, cm^{-1}, C≡N	PMR spectrum (d_6-DMSO), δ, ppm (multiplicity), J, Hz						Found, %				Empirical formula	Calc., %				Found, %
			R (s)	CH_3 (s)	5-H (s)	CH=CH (m)	Y—CH (m)	$(-CH_2-)_3$ (m)	C	H	N	S or Se		C	H	N	S or Se	
IIIa	47...49	2220	2,38	2,46	7,08	5,75; 5,89	4,66	1,68; 1,82; 2,03	68,5	6,5	11,7	12,8	$C_{14}H_{16}N_2S$	68,8	6,6	11,5	13,1	84
IIIb	72...74	2217	2,39	2,48	7,14	5,86	4,75	1,72; 1,98; 2,08	57,4	5,2	9,8	27,4	$C_{14}H_{16}N_2Se$	57,7	5,5	9,6	27,1	81
IIIc	93	2219	8,03; J_{45} = =7,4	2,46	7,02	5,73; 5,86	4,69	1,69; 1,83; 2,04	67,9	6,4	12,2	13,8	$C_{13}H_{14}N_2S$	67,8	6,1	12,2	13,9	91
IV	168... ...173 (dec.)	2236	2,43	2,49	7,16	5,74; 5,88	4,73	1,69; 1,96; 2,05	48,6	4,8	8,4	8,9	$C_{14}H_{17}ClN_2O_4S$	48,8	5,0	8,1	9,3	51

TABLE 2. Characteristics of Substituted 4a,10a-cis-4,4a-trans-1,2,3,4,4a,10a-hexahydrothiazolo(selenazolo)[3,2-a]-pyridinium Salts VIa-d and VIII

Compound	mp, °C (dec.)	IR spectrum, cm^{-1}, C≡N	PMR spectrum (d_6-DMSO), δ, ppm (multiplicity), SSSC, J, Hz									Torsion angle (φ), deg		Found, %					Empirical formula	Calc., %					Yield, %
			R (c)	CH_3 (s)	CH—Hal (m)	CH—Y (m)	CH—N (dd)	7-H (s)	$(-CH_2-)_3$ (m)	$^3J_{cis}$	$^3J_{trans}$	φH_aH_b	φH_bH_c	C	H	Hal	N	S or Se		C	H	Hal	N	S or Se	
VIa	130...132	2234	2,67	3,07	4,81	5,06	6,17	7,86	1,74; 2,07; 2,33	5,2	9,9	52	148	29,5	2,6	56,9	4,7	5,4	$C_{14}H_{16}Br_4N_2S$	29,8	2,9	56,7	5,0	5,7	87
VIb	186...187	2237	2,68	3,16	4,77	4,98	6,09	7,82	1,68; 2,14; 2,39	5,1	10,6	53	152	22,1	1,9	67,9	3,4	3,9	$C_{14}H_{16}I_4N_2S$	22,4	2,2	67,5	3,7	4,3	91
VIc	173...174	2334	2,66	3,17	4,92	5,2	6,13	7,83	1,57; 1,76; 2,04; 2,28	4,7	10,6	56	152	20,8	1,8	63,1	3,2	9,6	$C_{14}H_{16}I_4N_2Se$	21,1	2,0	63,5	3,5	9,9	84
VId	160...161	2238	8,84 (d)	3,18	4,81	5,01	6,02	7,74 (d)	1,68; 1,76; 2,06; 2,37	5,1	10,5	53	151	21,1	1,8	68,4	3,5	4,7	$C_{13}H_{14}I_4N_2S$	21,2	1,9	68,8	3,8	4,3	95
VIII	231	2239	2,65	3,10	4,91	5,07	6,16	7,84	1,72; 2,12	5,2	9,9	52	148	40,9	3,6	19,1*	3,2	7,9	$C_{14}H_{16}ClBrNO_4$	41,0	3,9	19,5	3,4	7,8	72

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*The results of analysis for bromine are presented.

the components of the double doublet of the signal of the proton of the NCH group with a larger SSCC. The components of the double doublet of the proton of the NCH group with a smaller SSCC merge to give a doublet on irradiation at the frequency of the proton of the YCH group. It follows from this that the a-H and b-H protons have ^3J = 4.7-5.2 Hz, as compared with ^3J = 9.9-10.6 Hz for b-H and c-H. Using the dependence of the vicinal SSCC on the angle of the carbon–hydrogen bonds we calculated φH_aH_b and φH_bH_c dihedral angles from the Karplus–Conroy relationship [11] (Table 2). It follows from the calculated values that a-H and b-H protons have a cis configuration, while the benzothiazole (selenazole) ring is cis fused. The b-H and c-H protons have a trans conformation. The calculated values of the dihedral angles correspond to the assignment of the SSCC in the $YCH_aCH_bCH_cHal$ system of protons and are comparable to the results of x-ray diffraction analysis of VIb.

We subjected VIb to x-ray diffraction study in order to objectively establish the structure and also to unequivocally solve the problem of the cis-trans orientation of the protons in the $YCH_aCH_bCH_cHal$ fragments of the VIa-d and VIII molecules.

It was established that salt VIb is 4-iodo-6,8-dimethyl-9-cyano-1,2,3,4,4a,10a-hexahydrobenzothiazolo[3,2-a]pyridinium triiodide; its crystal is constructed from $[C_{14}H_{16}IN_2S]^+$ cations situated in a common position and two I_3^- anions that occupy separate positions in symmetrically independent inversion centers.

The bond and torsion angles in the VIb structure are presented in Tables 3 and 4, and the overall form of the cation with the lengths of the bonds in it is shown in Fig. 1.

The thiazolidine ring in molecules of different compounds can have different degrees of planarity and, in the case of a nonplanar structure, different conformations (envelope, twist, and mixed conformations). For a uniform description and comparison of the geometry of this ring in different compounds it is expedient to use the modified Cremer–Pople method [12], which gives good results as applied to rings with considerably different bond lengths. We calculated the modified parameters [12] of Cremer–Pople [13] in VIb and in 3-bromomethyl-2,3-dihydro-5,7-dimethyl-8-cyanothiazolo[3,2-a]pyridinium perchlorate (IX) [8]. It was established that the heteroring in both compounds has a twist conformation (φ_2 = 73.4° and q_2 = 0.574 Å for VIb; φ_2 = 175.7° and q_2 = 0.468 Å for IX). This heteroring has a similar conformation in the 2,3-dihydro-3-hydroxy-5H-thiazolo[3,2-a]pyrimidin-5-one (X) structure [14]. At the same time, the heteroring has an envelope conformation in cis-2,3-(3-cyclohexanon-1,2-ylene)-5-methyl-8-ethoxydihydrothiazolo[3,2-a]pyridinium bromide (XI) [15], trans-2-carboxy-5-methyldihydrothiazolo[3,2-a]pyridinyl-3-carboxylate (XII) [16], and 2-(2,6-dimethylphenyl)imino-3-(2-methylbenzoyl)thiazolidine (XIII) [17].

As in XI, the thiazolidine ring has cis fusion with the cyclohexane ring [torsion angle $H_{(4a)}C_{(4a)}C_{(10a)}H_{(10a)}$ is equal to 50.5°], and the trans orientation of the 4-H and 4a-H hydrogen atoms [torsion angle $H_{(4)}C_{(4)}C_{(4a)}$ = –149.6°] indicates that the electrophilic quaternization of 2-[2-cyclohexen-1-ylthio(seleno)]pyridines to benzothiazolo[3,2-a]pyridinium salts proceeds as a trans process. The substituted cyclohexane ring has a distorted chair conformation (see the torsion angles in Table 4). The distortion of the chair conformation is probably due to shortened nonbonding contacts with the participation of the equatorially oriented $I_{(5)}$ atom [torsion angles $I_{(5)}C_{(4)}C_{(4a)}C_{(10a)}$ and $I_{(5)}C_{(4)}C_{(3)}C_{(2)}$ are equal to –172.0° and –176.8°, respectively]: $I_{(5)}\cdots N_{(5)}$ 3.557(4) Å, $I_{(5)}\cdots C_{(6)}$ 3.692(4), and $I_{(5)}\cdots C_{(14)}$ 3.600(4) Å (in the case of sums of the van der Waals radii of the I and N and I and C atoms of 3.7 Å and 3.85 Å, respectively [18, 19]), as well as $S_{(10)}\cdots C_{(2)}$ and $S_{(10)}\cdots C_{(4)}$ contacts at distances of 3.332(4) Å and 3.215(4) Å (in the case of a sum of the van der Waals radii of 3.5 Å [19]).

The pyridine heteroring is not completely planar but has a sofa conformation: the $N_{(5)}$ atom deviates by –0.106(4) Å from the plane of the remaining five ring atoms [the deviations of which from the average plane do not exceed 0.026(6) Å]. The disruption of the planarity of the pyridine heteroring is evidently due to the above-indicated steric hindrance with the participation of the $I_{(5)}$ atom and was also observed in the 3-bromomethyl-5-(2-furyl)-3,8-dimethyl-1,2,3-dihydro-1H-indolizinium bromide (XIV) structure [20] [the maximum deviations of the atoms from the average plane of the ring are 0.033(6) Å], while this heteroring is completely planar in the IX, XI, and XII molecules (the deviations of the atoms do not exceed 0.01 Å).

As in IX, steric interaction of the $C_{(11)}{\equiv}N_{(12)}$ group with the $S_{(10)}$ atom and the 13-CH_3 group in VIb causes deviation of the $S_{(10)}$, $C_{(11)}$, and $C_{(13)}$ atoms from the planar fragment

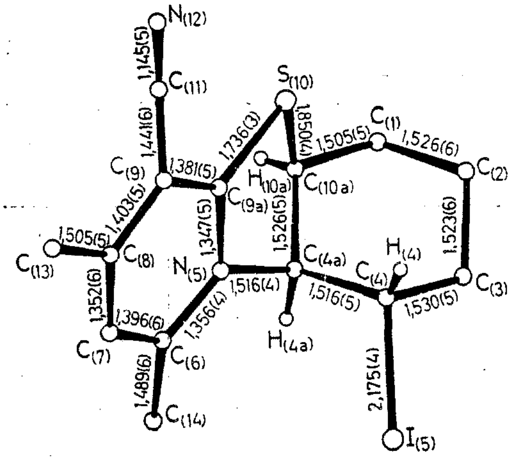


Fig. 1. Structure of the VIb cation. Only the hydrogen atoms that indicate cis fusion of the thiazolidine and cyclohexane rings and the trans orientation of the 4-H and 4a-H protons are depicted.

of the pyridine heteroring by 0.098(1), 0.216(6), and −0.027(7) Å, respectively. The nonbonding distances are $S_{(10)}\cdots C_{(11)}$ 3.065(4) Å and $C_{(11)}\cdots C_{(13)}$ 2.945(5) Å [3.066(7) Å and 2.96(1) Å in IX] vis-à-vis sums of the van der Waals radii of 3.5 Å and 3.4 Å, respectively [19].

The $S_{(10)}-C_{(9a)}$ bond length of 1.736(3) Å is somewhat decreased as compared with the standard value of the length of the $S-C^{(sp^2)}$ single bond of 1.77 Å [17]. Close values of the $S-C^{(sp^2)}$ bond length are observed in IX-XII [1.737(6), 1.736(3), 1.722(5), and 1.734(3) Å, respectively], while it is appreciably greater in XIII crystals and is equal to 1.772(5) Å.

The sum $S_{(10)}-C_{(10a)}$ bond length of 1.850(4) Å is increased as compared with the standard value of the $S-C^{(sp^3)}$ bond length (1.817 Å [12]), as well as with the lengths of the corresponding bonds in IX, X, XII, and XIII [1.809(7), 1.809(3), 1.832(3), and 1.796(7) Å, respectively] and virtually coincides with the value of 1.844(5) Å in XI. The formation of the thiazolidine heteroring and its cis fusion with the cyclohexane ring, to which the electrophilic quaternization of substituted 2-[2-cyclohexen-1-ylthio(seleno)]pyridines leads, evidently gives rise to steric strain of the cyclic fragments of cation VIb, which is manifested (in addition to the above-indicated conformational peculiarities) also in the deformation of these fragments [the decrease in the $S_{(10)}C_{(10a)}C_{(4a)}$ bond angle to 103.2(2)° and the $C_{(10a)}C_{(4a)}N_{(5)}$ bond angle to 103.1(3)°] and in an increase in the $S_{(10)}-C_{(10a)}$ bond length. Similar changes are also observed in the XI cation with a similar structure.

The bond lengths in the pyridine heteroring are close to those found in unsubstituted pyridine [22] and coincide with the values observed in the IX, XI, XII, and XIV structures. One may note the increase in the $C_{(6)}N_{(5)}C_{(9a)}$ bond angle to 122.5(3)° as compared with 116.6(2)° in pyridine [22] [120.8(5)°, 123.5(4)°, 122.7(3)°, and 121.7(5)° in IX, XI, XII, and XIV, respectively].

The $I_{(5)}-C_{(4)}$ bond length of 2.175(4) Å is somewhat increased as compared with the standard value for the $I-C^{(sp^3)}$ bond [2.139(1) Å [23]] or, for example, with the length of 2.156(5) Å in phenacyl iodide (with Lere-Porte and coworkers [24] assume to be the usual length); this is evidently due to the above-examined short nonbonding contacts with the participation of the $I_{(5)}$ atom.

The $I_{(1)}-I_{(2)}$ [2.912(1) Å] and $I_{(3)}-I_{(4)}$ [2.919(1) Å] bond lengths in the linear centrosymmetric I_3^- anions in the VIb crystal virtually coincide with those observed in other structures [25].

In the VI b crystal the shortest contacts, viz., $I_{(1)}\cdots I_{(5')}$ (x + 1, y, z) 4.281(1) Å, $I_{(1)}\cdots C_{(11')}$ (1 − x, 1 − y, 1 − z) 3.831(4) Å, $I_{(3)}\cdots N_{(5')}$ (1 − x, 1 − y, −z) 3.717(4) Å,

TABLE 3. Bond Angles (ω, deg) in the VIb Structure

Angle	ω	Angle	ω
$C_{(10a)}C_{(1)}C_{(2)}$	112,5(3)	$C_{(6)}C_{(7)}C_{(8)}$	123,1(4)
$C_{(1)}C_{(2)}C_{(3)}$	110,0(4)	$C_{(7)}C_{(8)}C_{(9)}$	117,8(4)
$C_{(2)}C_{(3)}C_{(4)}$	109,9(4)	$C_{(7)}C_{(8)}C_{(13)}$	122,0(4)
$C_{(3)}C_{(4)}C_{(4a)}$	110,9(3)	$C_{(13)}C_{(8)}C_{(9)}$	120,2(4)
$C_{(3)}C_{(4)}I_{(5)}$	107,4(3)	$C_{(8)}C_{(9)}C_{(9a)}$	119,4(4)
$I_{(5)}C_{(4)}C_{(4a)}$	111,4(2)	$C_{(8)}C_{(9)}C_{(11)}$	122,8(3)
$C_{(4)}C_{(4a)}C_{(10a)}$	111,4(3)	$C_{(11)}C_{(9)}C_{(9a)}$	117,7(3)
$C_{(4)}C_{(4a)}N_{(5)}$	111,1(3)	$C_{(9)}C_{(9a)}N_{(5)}$	120,0(3)
$C_{(10a)}C_{(4a)}N_{(5)}$	103,1(3)	$C_{(9)}C_{(9a)}S_{(10)}$	125,7(3)
$C_{(4a)}N_{(5)}C_{(9a)}$	112,2(3)	$N_{(5)}C_{(9a)}S_{(10)}$	114,3(2)
$C_{(4a)}N_{(5)}C_{(6)}$	125,3(3)	$C_{(9a)}S_{(10)}C_{(10a)}$	89,3(3)
$C_{(6)}N_{(5)}C_{(9a)}$	122,5(3)	$S_{(10)}C_{(10a)}C_{(1)}$	111,7(3)
$N_{(5)}C_{(6)}C_{(7)}$	116,5(4)	$S_{(10)}C_{(10a)}C_{(4a)}$	103,2(2)
$N_{(5)}C_{(6)}C_{(14)}$	121,4(4)	$C_{(1)}C_{(10a)}C_{(4a)}$	116,0(3)
$C_{(14)}C_{(6)}C_{(7)}$	122,0(4)	$C_{(9)}C_{(11)}N_{(12)}$	177,5(3)

TABLE 4. Torsion Angles (τ, deg) in the Thiazolidine Heteroring and Cyclohexane Ring of the VIb Cation

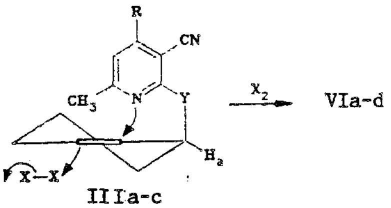
Angle	τ	Angle	τ
$S_{(10)}C_{(10a)}C_{(4a)}N_{(5)}$	42,5	$C_{(10a)}C_{(1)}C_{(2)}C_{(3)}$	52,8
$C_{(10a)}C_{(4a)}N_{(5)}C_{(9a)}$	−35,3	$C_{(1)}C_{(2)}C_{(3)}C_{(4)}$	−60,6
$C_{(4a)}N_{(5)}C_{(9a)}S_{(10)}$	10,2	$C_{(2)}C_{(3)}C_{(4)}C_{(4a)}$	61,2
$N_{(5)}C_{(9a)}S_{(10)}C_{(10a)}$	14,4	$C_{(3)}C_{(4)}C_{(4a)}C_{(10a)}$	−52,3
$C_{(9a)}S_{(10)}C_{(10a)}C_{(4a)}$	−33,4	$C_{(4)}C_{(4a)}C_{(10a)}C_{(1)}$	45,8
		$C_{(4a)}C_{(10a)}C_{(1)}C_{(2)}$	−46,2

$I_{(3)} \cdots C_{(6')}$ (1 − x, 1 − y, −z) 3.789(4) Å, $I_{(3)} \cdots C_{(9a')}$ (1 − x, 1 − y, −z) 3.815(4) Å, and $I_{(5)} \cdots C_{(7)}$ (−x, 1 − y, 1 − z) 3.768(4) Å, are realized between the anions and cations at distances that are comparable to the sums of the van der Waals radii of the I and I, I and C, and I and N atoms (4.3 Å [18], 3.85 Å, and 3.7 Å [19], respectively). The shortest contacts (I...I, I...C, and I...N) are observed between the cations and the linear I_3^- anions.

Thus, it was established unambiguously by x-ray diffraction investigation that the thiazolidine ring in the three-ring system of the cation is cis-fused with the cyclohexane ring [torsion angle $H_{(4a)}C_{(4a)}C_{(10a)}H_{(10a)}$ = 50.5°] and that torsion angle $H_{(4)}C_{(4)}C_{(4a)}H_{(4a)}$ is equal to −149.6°; this indicates a transoid orientation of the 4-H and 4a-H protons with respect to one another; this is comparable to the data from the PMR spectra of solutions of d_6-DMSO.

On the basis of the experimental data obtained it may be noted that the intramolecular quaternization of pyridines IIIa-c in VIa-d is an electrophilic process. The possibility of the noncyclic addition of halogen molecules to the multiple bond of the cyclohexene fragment and the occurrence of quaternization via a nucleophilic mechanism is excluded in the case of the formation of quaternized azines VIa and VIII from perchlorate IV.

The data from PMR spectroscopy and x-ray diffraction analysis of VIa-d and VIII indicate that electrophilic quaternization proceeds as a trans process and leads to the cis-annelated isomer.



IIIa-c

TABLE 5. Coordinates of the Atoms ($\cdot 10^5$ for the I atoms; $\cdot 10^4$ for the S, N, and C atoms; $\cdot 10^3$ for the H atoms) and Anisotropic Equivalent Heat Parameters of the Nonhydrogen Atoms (isotropic values for the H atoms)

Atom	x	y	z	B_{iso}^{eq}, Å
$I_{(1)}$	61043(7)	19161(5)	52251(4)	5,60(1)
$I_{(2)}$	1/2	1/2	1/2	4,37(1)
$I_{(3)}$	97456(6)	28896(4)	2516(3)	4,41(1)
$I_{(4)}$	0	0	0	3,41(1)
$I_{(5)}$	8378(7)	29286(5)	43137(3)	5,24(1)
$S_{(10)}$	4695(2)	4972(1)	1470(1)	3,11(3)
$N_{(5)}$	1415(5)	5443(4)	2282(3)	2,60(9)
$N_{(12)}$	4726(7)	8531(5)	1685(5)	5,2(1)
$C_{(1)}$	4921(7)	2297(5)	1029(4)	3,2(1)
$C_{(2)}$	5604(7)	1494(6)	1999(5)	3,7(1)
$C_{(3)}$	4055(9)	1499(6)	2829(5)	4,0(1)
$C_{(4)}$	2922(7)	3025(5)	3065(4)	3,1(1)
$C_{(4a)}$	2166(6)	3867(5)	2134(4)	2,6(1)
$C_{(6)}$	−310(7)	6188(6)	2596(4)	3,2(1)
$C_{(7)}$	−693(8)	7577(6)	2839(4)	3,4(1)
$C_{(8)}$	540(7)	8207(6)	2714(4)	3,3(1)
$C_{(9)}$	2263(7)	7441(5)	2273(4)	3,0(1)
$C_{(9a)}$	2268(6)	6052(5)	2061(4)	2,6(1)
$C_{(10a)}$	3610(6)	3761(5)	1214(4)	2,6(1)
$C_{(11)}$	3616(8)	8072(6)	1956(4)	3,5(1)
$C_{(13)}$	90(9)	9705(6)	2987(5)	4,4(2)
$C_{(14)}$	−1726(7)	5586(7)	2610(6)	4,3(1)
$H_{(1,1)}$	594(7)	237(5)	41(4)	3(1)
$H_{(1,2)}$	433(7)	201(5)	91(4)	3(1)
$H_{(2,1)}$	647(6)	196(5)	213(4)	2(1)
$H_{(2,2)}$	64(1)	34(1)	173(6)	9(2)
$H_{(3,1)}$	334(9)	82(6)	268(5)	5(2)
$H_{(3,2)}$	450(8)	109(6)	327(5)	4(1)
$H_{(4)}$	349(8)	339(6)	359(5)	5(2)
$H_{(4a)}$	126(6)	349(5)	208(4)	1,6(9)
$H_{(7)}$	−200(9)	815(6)	296(5)	5(1)
$H_{(10a)}$	332(8)	400(6)	78(5)	4(1)
$H_{(13,1)}$	26(8)	1036(6)	239(5)	4(1)
$H_{(13,2)}$	−100(8)	987(6)	339(4)	4(1)
$H_{(13,3)}$	68(8)	980(6)	361(5)	5(1)
$H_{(14,1)}$	−289(8)	630(6)	305(5)	4(1)
$H_{(14,2)}$	−15(1)	473(7)	273(6)	6(2)
$H_{(14,3)}$	−22(1)	56(1)	189(8)	12(3)

This high stereoselectivity — with respect to two systems of a-H and b-H and b-H and c-H protons — is probably ensured in the transition state and is determined by the synchronous effect of the donor (the electron pair of the pyridine nitrogen atom) and the acceptor (the halogen molecules) on the electrons of the multiple bond of the cyclohexene fragment of the molecules of IIIa-c.

The donor and acceptor act on the π electrons of the double bond in the transoid positions; the orientation of the a-H proton is strictly determined in the transition state, while the b-H and c-H protons are coplanar with the planar part of the cyclohexene fragment. The subsequent electrophilic cleavage of the multiple bond and the electrophilic quaternization occur synchronously; the b-H and c-H protons diverge in opposite directions and are oriented in a trans position opposite to the transoid orientation of the donor and acceptor. Thus, the intramolecular electrophilic quaternization of 2-[2-cyclohexen-1-ylthio)seleno)]-pyridines proceeds as synchronous trans quaternization with cis annelation to give hexahydrobenzothiazolo(selenazolo)[3,2-a]pyridinium salts.

In conclusion, we thank A. I. Yanovskii for his active assistance in setting up the experiments and deciphering the structures.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a UR-20 spectrometer. The PMR spectra of solutions in d_6-DMSO were recorded with a Bruker WM-250 spectrometer with tetramethylsilane (TMS) as the internal standard.

X-Ray Diffraction Analysis of VIb. The VIb crystals were triclinic with the following parameters: $a = 8.193(1)$, $b = 10.126(1)$, $c = 13.406(2)$ Å, $\alpha = 82.32(1)^\circ$, $\beta = 79.20(1)^\circ$, $\gamma = 68.94(1)^\circ$, $V = 1016.9$ Å^3, $d_{calc} = 2.46$ g/cm^3, $Z = 2[C_{14}H_{16}N_2SI]^+I_3^-$, space group $P\bar{1}$. The cell parameters and the intensities of 3121 independent reflections with $F^2 > 3\sigma$ were measured with an Enraf—Nonius CAD4 four-circle automatic diffractometer (20°C, λ Mo K_α, graphite monochromator, ratio of the scanning rates $\omega:\theta = 1.2:1$, $\theta_{max} = 25^\circ$). A correction for absorption was introduced by means of the DIFABS program [26]. The structure was deciphered by the direct method. Five symmetrically independent iodine atoms were localized in E synthesis. The remaining nonhydrogen atoms, as well as (in the final stages of the refinement) the hydrogen atoms, were localized from Fourier differential syntheses. The nonhydrogen atoms were refined by the complete-matrix method of least squares within the anisotropic approximation, while the hydrogen atoms were refined isotropically. The final divergence factors $R = 0.035$ and $R_W = 0.058$. All of the calculations were performed with an RDR-11/23 computer by means of SDP-PLUS programs [27]. The coordinates and isotropic equivalent heat parameters of the atoms are presented in Table 5.

Substituted 3-Cyano-2-[2-cyclohexen-1-ylthio(seleno)]pyridines IIIa-c. A 5.6-ml sample of a 10% solution of KOH in water and 10 mmoles of 3-bromo-1-cyclohexene (II) were added successively with stirring to a suspension of 10 mmoles of the corresponding pyridine Ia-c in 20 ml of DMF, and the reaction mixture was stirred at 25°C. It was then diluted with 20 ml of water, and the mixture was allowed to stand for 2 h at 0°C. The precipitate was separated, washed with water, dried, and recrystallized from hexene (Table 1).

4,6-Dimethyl-3-cyano-2-(2-cyclohexen-1-yl)pyridinium Perchlorate (IV). A 4-mmole sample of IIIa was added to a solution prepared from 3 ml of 70% perchloric acid and 10 ml of AcOH, and the mixture was heated for 10 min at 40-45°C. It was then cooled to 25°C and diluted with 20 ml of ether. After 2 h, the precipitate was removed by filtration and washed with ether to give 0.7 g (51%) of IV (Table 1).

9-Cyano-4a,10a-cis-4,4a-trans-1,2,3,4,4a,10a-hexahydrobenzothiazolo(selenazolo)[3,2-a]pyridinium Trihalides VIa-d. A solution of 10 mmoles of bromine or iodine in 15-50 ml of chloroform was added dropwise with stirring at 25°C in the course of 10 min to a solution of 5 mmoles of the corresponding IIIa-c in 15 ml of chloroform, after which the mixture was stirred for 1 h at 25°C. The precipitate was removed by filtration and washed with chloroform and ether. Compounds VIb-d were recrystallized from nitromethane (Table 2).

6,8-Dimethyl-9-cyano-4-bromo-4a,10a-cis-4,4a-trans-1,2,3,4,4a,10a-hexahydrobenzothiazolo[3,2-a]pyridinium Tribromide (VIa). A 4-mmole sample of bromine was added to 25°C to a suspension of 2 mmoles of perchlorate IV in 5 ml of AcOH, after which the mixture was stirred for 10 min. The precipitate was removed by filtration and washed with AcOH and ether. The yield of VIa was 0.45 g (87%); the product had mp 130-132°C (dec.), and its IR spectrum was identical to that of the corresponding tribromide (Table 2).

6,8-Dimethyl-9-cyano-4-bromo-4a,10a-cis-4,4a-trans,1,2,3,4,4a,10a-hexahydrobenzothiazolo[3,2-a]pyridinium Perchlorate (VIII). A solution of 2 mmoles of bromine in 5 ml of AcOH was added dropwise with stirring in the course of 5 min to a heated (to 70-80°C) solution of 2 mmoles of perchlorate IV in 5 ml of AcOH, after which the mixture was cooled to 5°C and diluted with 10 ml of ether. The precipitate was removed by filtration and recrystallized from nitromethane.

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SYNTHESIS OF SUBSTITUTED 2-AMINOQUINOLINE-3-CARBOXYLIC ACID AMIDES

S. V. Ukhov and M. E. Konshin

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Substituted 3-(2-nitrophenyl)-2-cyanoacrylic acid amides were synthesized by the Knoevenagel reaction and were then reduced with iron in acetic acid to the corresponding 2-aminoquinoline-3-carboxylic acid amides.

Little study has been devoted to 2-aminoquinoline-3-carboxylic acid amides. The unsubstituted amide of this acid was obtained by the reaction of 2-aminobenzaldehyde with cyanoacetamide and was then used for the synthesis of biologically active pyrimido[4,5-b]quinolin-4-ones [1]. In order to synthesize substituted amides we used the reaction of 2-nitrobenzaldehyde with cyanoacetamides under the conditions of the Knoevenagel reaction to obtain 3-(2-nitrophenyl)-2-cyanoacrylic acid N-alkyl- and N-arylamides Ia-i (Table 1) in good yields; these products were used as the starting substances. The IR spectra of Ia-i contain bands at 1660-1690 (CO), 2230-2240 (CN), and 3340-3380 cm^{-1} (NH).

Substituted 2-aminoquinoline-3-carboxylic acid amides IIa-f (Table 1) are formed in the reduction of amides Ia-f with iron in acetic acid. The IR spectra of IIa-f contain absorption bands at 1630-1660 (CO), 3140-3290 (NH), and 3360-3380 and 3425-3480 cm^{-1} (NH_2). A multiplet centered at 7.5 ppm (9H, aromatic protons, and 2H, NH_2), a singlet at 8.33 ppm (1H, pyridine), and a singlet at 10.1 ppm (1H, NH) are observed in the PMR spectra of amide IIa.

Compounds IIa, b are identical to the substances described in [2], which were also synthesized by reduction of amides Ia, b and to which the 2-arylamino-3-cyanoquinoline structure was erroneously assigned.

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