CONDENSED PYRIDINES.

6.* SYNTHESIS AND STRUCUTRE OF ADAMANTYL-, CYCLOPROPYL- AND ALKYL-SUBSTITUTED 3-HALOMETHYL-2,3-DIHYDRO-8-CYANOTHIAZOLO[3,2-a]PYRIDINIUM SALTS AND THEIR OXAZOLO AND SELENAZOLO DERIVATIVES

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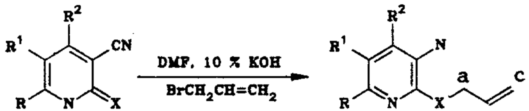
The reaction of substituted 2-cyanopyridin-2(1H)-ones and their thione and selenone derivatives with allyl bromide gives the corresponding 2-allyloxy-, 2-allylmercapto-, and 2-allylseleno-3-pyridines, which upon treatment with halogens, form intramolecular quaternization products, namely, 3-halomethyl-2,3-dihydro-8-cyanooxazole[3,2-a]pyridinium salts and their thiazolo and selenazolo analogs. X-ray diffraction structural analysis was used to determine the structure of 3-bromomethyl-2,3-dihydro-5,7-dimethyl-8-cyanothiazolo[3,2-a]pyridinium perchlorate.

In a search for new biologically active condensed pyridines, we have already synthesized previously unknown 3-halo-2,3-dihydro-5,6,7-alkyl-8-cyanothiazolo[3,2-a]pyridinium salts and their oxazolo and selenazolo analogs. In this regard, we note that thiazolo[3,2-a]-pyridinium derivatives are analgesics [2] and display anti-inflammatory [3] and hypoglycemic activity [4].

Various methods have been described for the preparation of thiazolo[3,2-a]pyridinium and oxazolo[3,2-a]pyridinium salts [5-10]. Their selenium analogs have not been reported.

We have studied the reaction of substituted 3-cyanopyridine-2(1H)-thiones Ia-e [11-15], pyridone If [16] and selenones Ig and Ih [16, 17] with allyl bromide and showed that Ia-h are selectively alkylated by allyl bromide in the presence of aqueous alkali in DMF with the formation of alkylation products IIa-h in 50-86% yield. The alkylation of pyridone If proceeds under more vigorous conditions entailing heating at 100°C for 2 h and with lower yield than its sulfur and selenium analogs. The starting pyridone remains in the reaction mixture. 6-(1-Adamantyl)-3-cyano-2-allyloxopyridine (IIf) was separated from unreacted pyridone If by extraction with hot hexane and subsequent recrystallization from hexane. The yield of IIf was 52%.



I a-h

II a-h

I, II $X=S$; a $R=CH_3$, $R^1=R^2=H$; b $RR^1=(-CH_2-)_4$, $R^2=H$; c $R=R^2=CH_3$, $R^1=H$; d $R^1=$ cyclopropyl $R^1=R^2=H$; e $R=Ad$, $R^1=R^2=H$, $X=O$; f $R=Ad$, $R^1=R^2=H$:, $X=Se$; g $R=Ad$, $R^1=R^e=H$; h $R=R^2=CH_3$, $R^1=H$, Ad = adamantyl

The structures of O-allyl, S-allyl and Se-allyl derivatives IIa-h were checked by spectroscopy and elemental analysis.

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*For Communication 5, see [1].

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TABLE 1. Spectral Indices for IIa-h

Compound	UV spectrum in EtOH, λ_{max}, nm (log ε)	IR spectrum (KBr), ν, cm^{-1}, CN	PMR spectrum, *δ, ppm, J, Hz					
			4-H (d)	5-H (d)	4-H 5-H	R	Other protons	$^3J_{XCH^aH^b}$, $^3J_{H^bH^c}$cis-, $^3J_{H^bH^c}$trans-
IIa	219 (4,23), 270 (4,09), 313 (3,55)	2230	8,09	7,13	10,5	2,52 (3H, s, CH_3)	3,98 (2H, d, $—SCH_2—$); 5,06 (1H, d, *cis*-$CH_2=CH—$); 5,29 (1H, d *trans*-$CH_2=CH—$); 5,85 (1H, m, $—CH=CH_2$)	7,0 9,5 18,0
IIb	222 (4,23), 271 (4,12), 321 (3,60)	2223				1,80 (4H, m, $—CH_2—$); 2,79 (4H, m, $—CH_2—$) cyclohexone	3,86 (2H, d, $—SCH_2—$); 5,16 (1H, d., *cis*-$CH_2=CH—$); 5,28 (1H, d, *trans*-$CH_2=CH—$); 5,81 (1H, m, $—CH=CH_2$); 7,84 (1H, s, (arom.)	7,5 10,0 18,0
IIc	224 (4,21), 270 (4,08), 312 (3,63)	2220				2,40 (3H, s, CH_3)**	3,93 (2H, d, $—SCH_2—$); 5,14 (1H, d, *cis*-$CH_2=CH—$); 5,33 (1H, d, *trans*-$CH_2=CH—$); 5,91 (1H, m., $—CH=CH_2$); 7,08 (1H, s, (arom.)	7,0 10,0 18,0
IId	227 (4,16), 236 (4,17), 270 (4,10), 320 (3,78)	2225	8,00	7,23	8,0	1,13 (4H, m); 2,03 (1H, m) cyclopropane	3,85 (2H, d, $—SCH_2—$); 5,11 (1H, d, *cis*-$CH_2=CH—$); 5,28 (1H, d., *trans*-$CH_2=CH—$); 5,98 (1H, m, $—CH=CH_2$)	6,5 9,5 17,0
IIe	222 (4,32), 268 (4,13), 314 (3,69)	2220	7,74	7,04	8,0	1,80 (6H, s δ-H—Ad); 1,98 (6H, s β-H—Ad); 2,12 (3H, s, γ-H—Ad) adamantane	3,96 (2H, d, $—SCH_2—$); 5,15 (1H, d, *cis*-$CH_2=CH—$); 5,33 (1H, d., *trans*-$CH_2=CH—$); 6,00 (1H, m, $—CH=CH_2$)	6,5 9,5 17,0
IIf	205 (4,24), 236 (4,03), 294 (4,04)	2230	8,16	7,08	8,0	1,78 (6H, s, δ-H—Ad); 1,90 (6H, s, β-H—Ad); 2,05 (3H, s, γ-H—Ad)	4,95 (2H, d, $—OCH_2—$); 5,27 (1H, d, *cis*-$CH_2=CH—$); 5,42 (1H, d, *trans*-$CH_2=CH—$); 6,09 (1H, m, $—CH=CH_2$)	6,5 9,5 17,0
IIg	226 (4,25), 281 (4,01), 320 (3,57)	2220	8,0	7,08	8,0	1,80 (6H, s, δ-H—Ad); 1,98 (6H, s, β-H—Ad); 2,13 (3H, s, γ-H—Ad)	4,02 (2H, d, $—SeCH_2—$); 5,08 (1H, d, *cis*-$CH_2=CH—$); 5,30 (1H, d, *trans*-$CH_2=CH—$); 6,10 (1H, m, $—CH=CH_2$)	6,5 9,5 17,0
IIh	224 (4,11), 282 (3,95), 320 (3,55)	2220				2,40 (3H, s, CH_3)***	3,96 (2H, $—SeCH_2$); 5,04 (1H, d, *cis*-$CH_2=CH—$); 5,20 (1H, d., *trans*-$CH_2=CH—$); 5,97 (1H, m, $—CH=CH_2$); 7,13 (1H, s., arom.)	7,0 10,5 18,0

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*The spectra of IIa-d, f, and h were taken in DMSO-d_6, while the spectra of IIe and IIg were taken in $CDCl_3$.

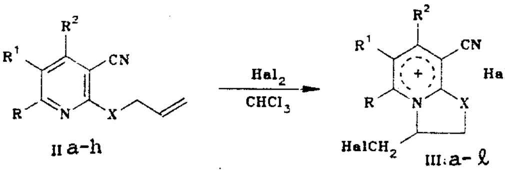
**R^2 = 2.48 ppm (3H, s, CH_3).

***R^2 = 2.52 ppm (3H, s, CH_3).

Thus, the IR spectra of IIa-h show a strong nitrile group band at 2220-2230 cm^{-1}. The IR spectrum of IIf lacks a CO group band while the PMR signal for the O–CH$_2$ group protons appears at 4.96 ppm, which is in accord with our previous data [17].

The PMR spectra have signals for the protons of the allyl group bound to the exocyclic heteroatom in addition to the signals of all the molecular fragments in their corresponding regions. Thus, the doublet for the protons of the CH$_2$X group appears at 3.85-4.96 ppm ($^3J_{XCH^aH^b}$ = 6.5-7.0 Hz), two doublets for the vinyl protons ($H_{c,cis,trans}$) appear at 5.06-5.30 ppm ($^3J_{H^bH^c_{cis}}$ = 9.5-10 Hz) and 5.20-5.46 ppm ($^3J_{H^bH^c_{trans}}$ = 17-18 Hz) and a multiplet for the proton at the double bond (H_b) appears at 5.81-6.10 ppm.

Products IIa-f and IIh react readily with halogens (1 eq of bromine or 2 eq iodine) in dry chloroform to form salts IIIa-j and IIIℓ in yields from 23 to 86%.



II a-h III a-ℓ

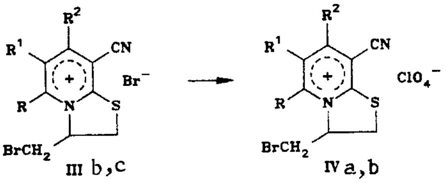
III Hal=Br, Hal$^-$=Br$^-$, X=S; **a** R=CH$_3$, R^1=R^2=H; **b** RR^1=(CH$_2$-)$_4$, R^2=H; **c** R=R^2=CH$_3$, R^1=H; **d** R=cyclopropyl, R^1=R^2=H; **e** R=Ad, R^1=R^2=H; X=O; **f** R=Ad, R^1=R^2=H; Hal=I, Hal$^-$=I$_3^-$, X=S; **g** R=R^2=CH$_3$, R^1=H; **h** R=cyclopropyl R^1=R^2=H; **i** R=Ad, R^1=R^2=H; X=O; **j** R=Ad, R^1=R^2=H; X=Se; **k** R=Ad, R^1=R^2=H; **ℓ** R=R^2=CH$_3$, R^1=H

The nature of the substituent at C$_{(6)}$ in the pyridine ring affects the yield of salt III under these conditions. The yield of the quaternization products with the adamantyl substituent is somewhat lower. This behavior is apparently related to the shielding effect of the adamantyl group. The ease of quaternization also depends on the nature of exocyclic heteroatom: the reaction of allylselenopyridines IIg and IIh with bromine does not proceed under the indicated conditions and only the starting allylselenopyridines are isolated from the reaction mixture. Treatment of IIg with two equivalents of iodine led to the formation of a 1:1 mixture of products with mp 77-83°C (dec.) as indicated by PMR spectroscopy. One of these products is 3-iodomethyl-2,3-dihydro-5-(1-adamantyl)-8-cyanoselenazolo[3,2-a]pyridinium iodide (IIIk), while the other could not be identified. On the other hand, the quaternization of 4,6-dimethyl-3-cyano-2-allylselenopyridine (IIh) proceeds readily to give IIIℓ in 86% yield.

Products IIIa-ℓ are highly colored compounds with UV bands at 274-298 nm (log ε 3.97-4.68) and 320-369 nm (log ε 3.33-4.38).

In going from IIa-h to salts IIIa-ℓ, the IR spectra show a decrease in the nitrile group band intensity and its shift toward higher frequencies (2237-2250 cm^{-1}). This behavior is apparently related to charge delocalization in the pyridine ring in IIIa-ℓ.

The PMR spectra of IIIa-ℓ show a downfield displacement of the signals for the protons on the pyridine ring and the alkyl substituent bound to this ring ($\Delta\delta$ = 0.25-0.91 and $\Delta\delta$ = 0.14-0.57 ppm, respectively), which confirms the delocalization of positive charge in the pyridine ring. The PMR spectrum also shows signals for the protons of the oxazole, thiazole or selenazole fragment: the methine proton multiplet appears at 5.96-6.70 ppm while the multiplets for the XCH$_2$ and HalCH$_2$ groups of IIIa-d overlap and are found at 4.01-4.09 and 4.20-4.22 ppm. The proton multiplets ofthe XCH$_2$ and HalCH$_2$ groups of IIIe-ℓ appear at 3.93-5.37 and 3.03-3.98 ppm, respectively. A downfield displacement of the chemical shifts of the BrCH$_2$ group signals is observed in comparison with the signals of the iodine derivatives (compare IIId and IIIh, IIIe and IIIi, IIIf, and IIIj). The nature of the heteroatom affects the chemical shift of the methylene protons of the five-membered ring. Thus, the shifts of the methylene protons of the oxazolo[3,2-a]pyridinium ions (IIIf and IIIj) (5.12-5.37 ppm) are downfield relative to the signals for these protons in the corresponding sulfur (IIIe and IIIi) and selenium (IIIk) analogs (3.93-4.35 ppm).



III b,c IV a,b

IV **a** R=R^2=CH$_3$, R^1=H; **b** RR^1=(—CH$_2$—)$_4$, R^2=H

TABLE 2. Spectral Indices of IIIa-ℓ, IVa and IVb

Compound	UV spectrum in DMF, λ_{max}, nm (log ε)	IR spectrum (KBr) ν, cm^{-1} CN	PMR Spectrum in DMSO-d_6, δ, ppm, J, Hz				
			4-H (d)	5-H (d)	4-H—5-H	R	Other protons
IIIa	284 (3,60), 350 (3,93)	2245	8,81	7,86	9,0	2,93 (3H, s, CH_3)	4,09 (4H, m, —SCH_2—, —CH_2Br); 6,30 (1H, m, $BrCH_2CH$—)
IIIb	285 (4,13), 350 (3,81)	2240				1,75 (4H, s, —CH_2—); 2,88 (2H, s, —CH_2—); 3,27 (2H, s., —CH_2—) cyclohexane	4,02 (3H, m, —SCH—, —CH_2Br); 4,20 (1H, m, —SCH—); 6,14 (1H, m, $BrCH_2CH$—); 8,75 (1H, s, arom.)
IIIc	283 (3,97), 349 (3,75)	2240				2,60 (3H, s CH_3) [R^2=2,90 ppm. (3H,s , CH_3)]	4,01 (3H, m, —SCH—, —CH_2Br); 4,23 (1H, m , —SCH—); 6,14 (1H, m , $BrCH_2CH$—); 7,80 (1H, s, arom.)
IIId	276 (4,53), 347 (3,90)	2245	8,73	7,48	8,0	1,30—1,50 (2H, m); 1,65 (2H, m); 2,60 (1H, m)cyclopropane	4,05 (3H,m , —SCH—, CH_2Br); 4,22 (1H, m, —SCH—); 6,40 (1H, m, $BrCH_2CH$—)
IIIe	276 (4,47), 350 (4,13)	2255	8,90	7,97	8,0	1,80 (6H,s , β-H—Ad); 1,98—2,28 (6H,m, δ-H—Ad); 2,15 (3H, , γ-H—Ad)	3,44 (2H, m, —CH_2Br); 4,00—4,25 (2H, m , —SCH_2—); 6,40 (1H,m , $BrCH_2CH$—)
IIIf	274 (4,56), 320 (4,18)	2250	9,00	7,90	8,0	1,76 (6H, s, β-H—Ad); 2,05—2,20 (6H,m , δ-H—Ad); 2,15 (3H,s, γ-H—Ad)	3,82—3,96 (2H, m, —CH_2Br); 5,12—5,37 (2H, m, —OCH_2—); 6,42 (1H,m , $BrCH_2CH$—)
IIIg	296 (4,57), 365 (4,30)	2237				2,63 (3H,s , CH_3) [R^2=2,87 ppm (3H, s, CH_3)]	3,70—3,98 (2H, m, —CH_2I); 4,17 (2H, —SCH_2); 5,97 (1H, m, ICH_2CH—); 7,78 (1H, s, arom.)
IIIh	294 (4,61), 358 (4,38)	2240	8,72	7,50	8,0	1,25—1,50 (2H,m); 1,60 (2H,m); 2,55 (1H,m)cyclopropane	3,70 (2H, m, —CH_2I); 4,00—4,20 (2H, m., —SCH_2—); 6,26 (1H, m, ICH_2CH—)
IIIi	294 (4,69), 365 (4,26)	2250	8,88	7,94	8,0	1,78 (6H,s , β-H—Ad); 1,95—2,25 (6H, m , δ-H—Ad); 2,18 (3H, s, γ-H—Ad)	3,03—3,82 (2H, m, —CH_2I); 4,01—4,20 (2H, m, —SCH_2—); 6,35 (1H, m , ICH_2CH—)
IIIj	298 (4,69), 369 (4,36)	2250	9,00	7,88	8,0	1,76 (6H, s, β-H—Ad); 2,07—2,20 (6H, m δ-H—Ad); 2,13 (3H, s, γ-H—Ad)	3,40—3,70 (2H, m, —CH_2I); 5,12—5,26 (2H, m, —OCH_2—); 6,27 (1H, m , ICH_2CH—)
IIIk*	297 (–), 368 (–)	2240	8,00	7,86	10,0	1,70 (6H, s, β-H—Ad); 1,96 (6H, s , δ-H—Ad); 2,10 (3H, s γ-H—Ad)	3,50—3,90 (2H, m, —CH_2I); 4,35 (2H, m, —$SeCH_2$—); 6,70 (1H, m, ICH_2CH—)
IIIℓ	295 (4,63), 362 (3,33)	2235				2,57 (3H,s , CH_3) [R^2=2,85 ppm. (3H,s , CH_3)]	3,65 (2H, m, —CH_2I); 3,93—4,26 (2H, m., —$SeCH_2$—); 5,96 (1H, m, ICH_2CH—); 7,73 (1H,s, arom)
IVa	284 (3,97), 340 (3,77)	2240				2,54 (3H, s , CH_3) [R^2=2,90 ppm (3H,s , CH_3)]	4,00 (3H, m, —SCH—, —CH_2Br); 4,18 (1H, m, —SCH—); 6,08 (1H, m , $BrCH_2CH$—); 7,78 (1H, s, arom.)
IVb	286 (3,99), 355 (3,68)	2240				1,84 (4H,s , —CH_2—); 2,78 (2H,s , —CH_2—); 3,23 (2H,s , —CH_2—) cyclohexane	4,09 (4H, m, —SCH_2—, —CH_2Br); 6,06 (1H, m, $BrCH_2CH$—); 8,58 (1H, s ,arom.)

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*Not a single compound.

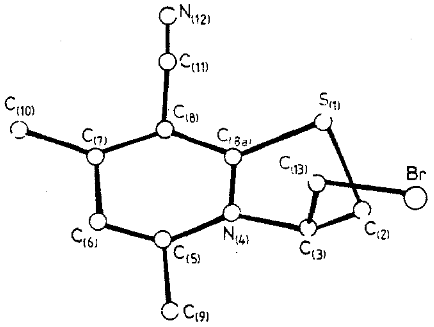

Fig. 1. Structure of the cation of IVa. The hydrogen atoms are not shown.

Bromides IIIb and IIIc may be converted to the corresponding perchlorates IVa and IVb by treatment with perchloric acid upon heating in acetic acid in the presence of acetic anhydride.

Comparison of the PMR spectra of pyridinium salts IIIa-ℓ and IVa, b with different anions indicates that the nature of the anion does not have a significant effect on the chemical shifts of the alkyl substituents and the pyridine ring protons. This indicates their existence in ionic form.

In order to establish the structure of the compounds synthesized, we investigated the crystal and molecular structure of 3-bromomethyl-2,3-dihydro-5,7-dimethyl-8-cyanothiazolo[3,2-a]pyridinium perchlorate (IVa) by x-ray diffraction structural analysis.

The bond lengths and angles in the structure of IVa are given in Tables 5 and 6. A general view of the cation is shown in Fig. 1.

The thiazolidine heterocycle has envelope conformation with $C_{(2)}$ extruding by −0.536(7) Å from the plane of the other four atoms (the departure of these atoms from the mean plane does not exceed 0.044(5) Å). The distribution of torsion angles in the heterocycle is given in Table 7. An analogous conformation of the thiazolidine ring is found in trans-2-carboxy-5-methylhydrothiazolo[3,2-a]pyridinium-3-carboxylate (V) [18] and 2-(2,6-dimethylphenyl)-imino-3-(2-methylbenzoyl)thiazolidine (VI) [19] (the carbon atom extrudes from the plane of the four ring atoms by 0.57 and 0.55 Å, respectively), while this ring in 2,3-dihydro-3-hydroxy-5H-thiazolo[3,2-a]pyrimidin-5-one (VII) [20] has half-chair conformation. A similarity is correspondingly observed in the distribution of the torsion angles in the thiazolidine fragments in IVa-VI. Short nonbonding contacts involving the axial bromomethyl group are retained in the observed conformation of the thiazolidine heterocycle in the cation of IVa: $S_{(1)}\cdots S_{(13)}$, 3.374(6) Å; $C_{(5)}\cdots C_{(13)}$, 3.187 (8) Å, $C_{(8a)}\cdots C_{(13)}$, 3.184(8) Å (the sum of the van der Waals radii for S and C and for C and C are 3.5 and 3.4 Å, respectively [21]).

The six-membered pyridine ring in IVa, as in V, is planar (the deviations of the atoms form the mean plane do not exceed 0.010(5) and 0.009 Å, respectively), while marked nonplanarity of the pyridine ring is noted in 3-bromomethyl-5-(2-furyl)-3,8-dimethyl-1,2,3-dihydro-1H-indolizine bromide (VIII) [22] (the maximum deviations of the atoms from their mean ring plane are 0.033(6) Å). The dihedral angle between the plane of the pyridine ring and the planar fragment of the thiazolidine ring is 4.03°, i.e., these fragments in IVa are apparently coplanar.

The short $S_{(1)}\cdots C_{(11)}$ nonbonding contact in IVa (3.066(7) Å) (the sum of the van der Waals radii is 3.5 Å [21]) leads to the extrusion of $S_{(1)}$ from the plane of the pyridine heterocycle by −0.065(2) Å, while $C_{(11)}$ is coplanar to the heterocycle (the corresponding deviation is only 0.004(7) Å). While the bromomethyl group, in principle, may have different orientations relative to the thiazolidine ring, the twist about the $C_{(3)}{-}C_{(13)}$ bond in the conformation found in the crystal forms a shoft nonbonding $Br\cdots C_{(2)}$ contact (3.372(7) Å) (the sum of the van der Waals radii for these atoms is 3.55 Å [21]). This is probably a result of packing in the crystal of IVa.

The $S_{(1)}{-}C_{(8a)}$ bond length in the cation of IVa (1.737(6) Å) is somewhat less than the standard $S{-}C_{(sp^2)}$ single bond (1.77 Å) and is in accord with the mean length of this bond in the case of partial π-character (1.74 Å [19]). Analogous $C{-}S_{(sp^2)}$ bond lengths are seen

TABLE 3. Pyridinium Salts IIIa-j, IIIℓ, IVa and IVb

Compound	mp,* °C	Found, %					Chemical yield	Calculated, %					Yield, %
		C	H	Hal	N	S (Se)		C	H	Hal	N	S (Se)	
IIIa	214—215	34,2	2,7	45,5	8,1	9,2	$C_{10}H_{10}Br_2N_2S$	34,3	2,9	45,6	8,0	9,2	85
IIIb	258**	39,9	3,5	41,0	7,0	8,3	$C_{13}H_{14}Br_2N_2S$	40,0	3,6	41,0	7,1	8.0	64
IIIc	235—238	35,8	3,2	44,1	7,8	9,0	$C_{11}H_{12}Br_2N_2S$	36,3	3,3	43,9	7,7	8,8	78
IIId	105—108	39,0	3,5	42,8	7,3	8,7	$C_{12}H_{12}Br_2N_2S$	38,3	3,2	42,5	7,4	8,5	60
IIIe	187—190	48,1	4,5	34,1	6,0	7,1	$C_{19}H_{22}Br_2N_2S$	48,5	4,7	34,0	6,0	6,9	23
IIIf	173—175	50,0	4,8	35,4	6,3		$C_{19}H_{22}Br_2N_2O$	50,2	4,9	35,2	6,2		51
IIIg	220—222	18,5	1,7	71,4	4,1	4,4	$C_{11}H_{12}I_4N_2S$	18,6	1,7	71,3	4,0	4.5	86
IIIh	138—140	20,0	1,8	70,2	3,6	4,4	$C_{12}H_{12}I_4N_2S$	19,9	1,7	70,1	3,9	4,4	73
IIIi	149—150	27,0	2,5	62,9	3,4	4,1	$C_{19}H_{22}I_4N_2S$	27,9	2,7	62,1	3,4	3,9	49
IIIj	68—70	28,5	2,7	63,5	3,3		$C_{19}H_{22}I_4N_2O$	28,5	2,8	63,3	3,5		52
IIIℓ	204—206**	16,9	1,6	67,1	3,6	10,9	$C_{11}H_{12}I_4N_2Se$	17,4	1,6	66,9	3,7	10,4	86
IVa	214—216**	35,0	3,4	Br 20,8 Cl 9,2	7,3	8,3	$C_{11}H_{12}BrClN_2O_4S$	34,4	3,2	Br 20,8 Cl 9,2	7,3	8,4	74
IVb	247—248	38,0	3,2	Br 19,3 Cl 8,6	6,8	7,9	$C_{13}H_{14}BrClN_2O_4S$	38,1	3,1	Br 19.5 Cl 8,6	6,8	7,8	68

*IIIℓ melts without decomposition, while the other compounds melt with decomposition.
**From nitromethane.

TABLE 4. Substituted 2-Allyloxo-, 2-Allylmercapto- and 2-Allylseleno-3-cyanopyridines IIa-h

Compound	mp,* °C	M⁺	Found, %				Chemical formula	Calculated, %				Yield, %
			C	H	N	S (Se)		C	H	N	S (Se)	
IIa	43	190	63.1	5,2	14,6	16,6	$C_{10}H_{10}N_2S$	63,1	5.3	14,7	16,8	74
IIb	51	230	67.6	6,0	12,0	13,7	$C_{13}H_{14}N_2S$	67,8	6,1	12,2	13,9	86
IIc	25	204	64,6	5,9	13,5	16.5	$C_{11}H_{12}N_2S$	64,7	5,9	13,7	16,7	82
IId	51—52	216	66.6	5,6	13,0	14,7	$C_{12}H_{12}N_2S$	66,6	5,5	12.9	14,8	50
IIe	105—107	310	73,9	7,3	9,1	10,3	$C_{19}H_{22}N_2S$	73,5	7,1	9,0	10,3	75
IIf	97—98	294	77,5	7,6	9,6		$C_{19}H_{22}N_2O$	77,5	7,5	9,5		52
IIg	108—109	358	63,8	6,3	7,8	(22,5)	$C_{19}H_{22}N_2Se$	63,8	6,2	7,8	(22,1)	67
IIh	28	252	52,5	4,8	11,0	(32,0)	$C_{11}H_{12}N_2Se$	52,6	4,8	11,1	(31,4)	73

*IIa, IIc, IId, and IIh were recrystallized from pentane, while IIb and IIe-g were recrystallized from hexane.

TABLE 5. Bond Lengths d (Å) in IVa

Bond	*d*	Bond	*d*	Bond	*d*
$Cl—O_{(1)}$	1,427(6)	$C_{(3)}—N_{(4)}$	1,485(7)	$C_{(7)}—C_{(10)}$	1,486(9)
$Cl—O_{(2)}$	1,425(5)	$C_{(3)}—C_{(13)}$	1,511(8)	$C_{(8)}—C_{(8a)}$	1,358(8)
$Cl—O_{(3)}$	1,393(6)	$N_{(4)}—C_{(5)}$	1,376(7)	$C_{(8)}—C_{(11)}$	1,437(9)
$Cl—O_{(4)}$	1,402(6)	$C_{(5)}—C_{(6)}$	1,353(8)	$C_{(8a)}—N_{(4)}$	1,362(7)
$S_{(1)}—C_{(2)}$	1,809(7)	$C_{(5)}—C_{(9)}$	1,479(9)	$C_{(11)}—N_{(12)}$	1,141(9)
$S_{(1)}—C_{(8a)}$	1,737(6)	$C_{(6)}—C_{(7)}$	1,391(9)	$C_{(13)}—Br$	1,935(6)
$C_{(2)}—C_{(3)}$	1,526(9)	$C_{(7)}—C_{(8)}$	1,395(8)		

in the structures of V (1.734(4) Å) and VII (1.736(3) Å), while the corresponding value in VI is 1.772(5) Å.

The $S_{(1)}$-$C_{(2)}$ bond length (1.809(7) Å) is in accord with the standard S—$C_{(sp^2)}$ bond length (1.817 Å [23]) and with the values found in VI (1.796(7) Å) and VII (1.809(3) Å) but is somewhat less than in V (1.832(3) Å).

The bond lengths in the pyridine heterocycle are close to those found in unsubstituted pyridine [24] and coincide with the values observed in V and VIII. We note the expansion of the $C_{(5)}N_{(4)}C_{(8a)}$ bond angle to 120.8(5)° in comparison for 116.6(2)° in pyridine [24] (the values are 122.7(3)° in V and 121.7(5)° in VIII).

TABLE 6. Bond Angles ω in IVa

Bond angle	ω°	Bond angle	ω°	Bond angle	ω°
$O_{(1)}ClO_{(2)}$	109,9(3)	$C_{(13)}C_{(3)}N_{(4)}$	106,8(4)	$C_{(10)}C_{(7)}C_{(8)}$	123,1(6)
$O_{(1)}ClO_{(3)}$	111,5(4)	$C_{(3)}N_{(4)}C_{(5)}$	124,8(4)	$C_{(7)}C_{(8)}C_{(8a)}$	120,0(5)
$O_{(1)}ClO_{(4)}$	105,7(3)	$C_{(3)}N_{(4)}C_{(8a)}$	114,3(4)	$C_{(7)}C_{(8)}C_{(11)}$	121.5(5)
$O_{(2)}ClO_{(3)}$	111.3(4)	$C_{(5)}N_{(4)}C_{(8a)}$	120,7(5)	$C_{(11)}C_{(8)}C_{(8a)}$	118,5(5)
$O_{(2)}ClO_{(4)}$	108,7(4)	$N_{(4)}C_{(5)}C_{(6)}$	117,6(5)	$C_{(8)}C_{(8a)}S_{(1)}$	125,9(4)
$O_{(3)}ClO_{(4)}$	109,5(4)	$N_{(4)}C_{(5)}C_{(9)}$	118,8(5)	$C_{(8)}C_{(8a)}N_{(4)}$	121,2(5)
$C_{(8a)}S_{(1)}C_{(2)}$	90,8(3)	$C_{(9)}C_{(5)}C_{(6)}$	123,5(5)	$N_{(4)}C_{(8a)}S_{(1)}$	112,9(4)
$S_{(1)}C_{(2)}C_{(3)}$	105,8(4)	$C_{(5)}C_{(6)}C_{(7)}$	123.6(6)	$C_{(8)}C_{(11)}N_{(12)}$	179,5(7)
$C_{(2)}C_{(3)}N_{(4)}$	104,6(4)	$C_{(6)}C_{(7)}C_{(8)}$	116,7(5)	$C_{(3)}C_{(13)}Br$	111,6(4)
$C_{(2)}C_{(3)}C_{(13)}$	115,4(5)	$C_{(6)}C_{(7)}C_{(10)}$	120,2(6)		

The $C_{(13)}$–Br bond length (1.935(6) Å) coincides with the standard C_{sp^3}–Br bond length (1.940(5) Å [25]) and with the value in VIII (1.943(7) Å). The other bond lengths and angles in the cation of IVa are ordinary.

The mean Cl–O bond length of the perchlorate anion (1.41(2) Å) is in good accord with the standard value for this bond (1.43(2) Å [25]), while the mean OClO bond angle (109(2)°) coincides with the tetrahedral value.

The following contacts are found in the crystal of IVa between the cation and the surrounding anions in positions (x, y, z), (x − 1, y, z), and (−1/2 − x, y − 1/2, 3/2 − z): $O_{(2)}\cdots N_{(4)}$ (x, y, z), 3.039(7) Å; $O_{(2)}\cdots C_{(8a)}$ (x, y, z), 3.079(8) Å; $O_{(3)}\cdots C_{(9)}$ (x, y, z) 3.223(9) Å; $O_{(4)}\cdots S_{(1)}$ (x, y, z) 2.941(6) Å; $O_{(4)}\cdots C_{(2)}$ (x − 1, y, z) 3.210(9) Å, and $O_{(1)}\cdots C_{(10)}$ (−1/2 − x, y − 1/2, 3/2 − z) 3.204(9) Å. These values are comparable to the van der Waals radii of the S–O, O–N, and O–C atom pairs (3.32, 3.07 and 3.22 Å, respectively (21)]. These contacts stabilize the checkerboard arrangement of the cations and anions in planes parallel to ab.

EXPERIMENTAL

The IR spectra were taken in KBr pellets on a UR-20 spectrometer. The UV spectra were taken on a Specord UV-vis spectrometer in ethanol and DMF. The PMR spectra were taken on a Bruker WM-250 spectrometer at 250 MHz in $CDCl_3$ and DMSO-d_6 with TMS as the internal standard. The mass spectra were taken on a Varian MAT-CH-6 mass spectrometer with direct sample inlet into the ion source at 70 eV. The reaction was monitored and the purity of the compounds synthesized was checked by thin-layer chromatography on Silufol UV-254 plates with 3:5 acetone–hexane as the eluent.

X-Ray Diffraction Structural Analysis of 3-Bromomethyl-2,3-dihydro-5,7-dimethyl-8-cyanothiazolo[3,2-a]pyridinium Perchlorate (IVa). The unit cell parameters for colorless monoclinic crystals of IVa at 20°C are as follows: a = 7.3823(5), b = 17.5944(8), c = 11.572(1) Å, β = 95.998(6)°, V = 1494.9(2) Å³, d = 1.705 g/cm³, Z = 4, $C_{11}H_{12}BrClN_2O_4S$, space group $P2_1/n$. The unit cell parameters and the intensities of 1718 independent reflections were taken on a Hilger–Watts automatic four-circle diffractometer using λMoK_α radiation, graphite monochromator and θ/2θ scanning to θ_{max} = 30°. The structure was solved by the direct method using the MULTAN program and refined by the full-matrix method of least squares in the anisotropic approximation for the nonhydrogen atoms using 1589 reflections with I > 2σ. The anomalous scattering of the bromine atom was taken into account but a correction for absorption was not introduced. The hydrogen atoms were revealed in the difference map and refined isotropically with fixed B_{iso} = 6.0Å. Final value of scattering factor R = 0.055 and R_w = 0.051. All the calculations were carried out on an Eclipse S/200 computer using the INEXTL program [26]. The coordinates and isotropic equivalent temperature parameters of the atoms are given in Table 8.

Alkyl-substituted 3-cyanopyridine-2(1H)-thiones (Ia-e) were obtained according to previous procedures [11-15], while 6-(1-adamantyl)-3-cyanopyridin-2(1H)-one (If) was obtained according to our previous method [16] and alkyl substituted 3-cyanopyridine-2(1H)-selenones (Ig and Ih) were obtained according to our procedures [16, 17].

The spectral indices, yields and elemental analysis data for IIa-h, IIIa-ℓ, IVa and IVb are given in Tables 1-4.

TABLE 7. Torsion Angles (τ) in the Thiazolidine Fragment in IVa

Angle	τ
$S_{(1)}C_{(2)}C_{(3)}N_{(4)}$	−34,6(4)
$C_{(2)}C_{(3)}N_{(4)}C_{(8a)}$	27,4(6)
$C_{(3)}N_{(4)}C_{(8a)}S_{(1)}$	−6,7(4)
$N_{(4)}C_{(8a)}S_{(1)}C_{(2)}$	−13,2(6)
$C_{(8a)}S_{(1)}C_{(2)}C_{(3)}$	27,9(6)

TABLE 8. Atomic Coordinates (×10^5 for Br, Cl and S, ×10^4 for O, N, C and ×10^3 for the H Atoms) and Isotopic Equivalent Temperature Parameters for Non-Hydrogen Atoms

Atom	*x*	*y*	*z*	B_{eq}^{iso}(Å)^2
Br	26275(11)	4389(4)	44062(8)	5,9(1)
$S_{(1)}$	29746(22)	24473(10)	69443(15)	4,1(1)
$O_{(2)}$	−1453(8)	2238(3)	8265(5)	7,0(2)
$O_{(4)}$	−4234(7)	1756(4)	8619(5)	8,7(2)
$N_{(12)}$	2373(10)	4527(3)	7299(5)	6,7(2)
$C_{(3)}$	737(7)	1451(3)	5798(5)	3,2(2)
$C_{(6)}$	−2569	3061(3)	5390(5)	3,7(2)
$C_{(8)}$	237(8)	3490(3)	6356(5)	3,2(2)
$C_{(9)}$	−3089(8)	1693(4)	4885(6)	4,5(2)
$C_{(11)}$	1433(9)	4066(4)	6880(6)	4,6(2)
Cl	−24388(21)	15605(8)	84527(13)	3,6(1)
$O_{(1)}$	−1702(7)	1207(3)	9508(5)	7,2(2)
$O_{(3)}$	−2446(11)	1066(3)	7512(5)	9,7(2)
$N_{(4)}$	−208(6)	2194(2)	5844(4)	2,7(1)
$C_{(2)}$	2218(9)	1470(4)	6821(6)	4,5(2)
$C_{(5)}$	−1962(8)	2336(3)	5370(5)	3,2(2)
$C_{(7)}$	−1526(8)	3662(4)	5872(5)	3,9(2)
$C_{(8a)}$	853(7)	2763(3)	6344(5)	2,9(1)
$C_{(10)}$	−2283(11)	4446(4)	5834(7)	6,7(3)
$C_{(13)}$	1412(8)	1397(3)	4612(6)	3,9(2)
$H_{(1C2)}$	314(8)	117(3)	661(5)	
$HC_{(3)}$	0(7)	101(3)	597(5)	
$H_{(1C9)}$	−272(8)	−138(3)	440(5)	
$H_{(3C9)}$	−421(8)	−190(3)	435(5)	
$H_{(2C10)}$	−203(8)	−462(3)	644(5)	
$H_{(1C13)}$	28(8)	142(3)	399(5)	
$H_{(2C2)}$	171(8)	143(3)	742(5)	
$HC_{(6)}$	−373(8)	−314(3)	515(5)	
$H_{(2C9)}$	−360(8)	−138(3)	539(5)	
$H_{(1C10)}$	−296(8)	−452(3)	531(5)	
$H_{(3C10)}$	−153(8)	−490(3)	533(5)	
$H_{(2C13)}$	245(8)	172(3)	447(5)	

6-(1-Adamantyl)-3-cyano-2-allylmercaptopyridine (IIe). A sample of 1.12 ml (2 mmoles) 10% aq. KOH was added with stirring to 0.54 g (2 mmoles) pyridinethione Ie in 10 ml DMF and then 0.26 ml (3 mmoles) allyl bromide was added. After 1 h, the reaction mixture was diluted with five volumes of water, maintained for 1 h at 0°C and the precipitate was filtered off, dried over P_2O_5 and recrystallized from hexane to give 0.46 g (74%) IIe, mp 105-107°C.

Products IIa-d, IIg and IIh were obtained analogously.

6-(1-Adamantyl)-3-cyano-2-allyloxopyridine (IIf). A sample of 2.64 ml (4.72 mmoles) 10% aq. KOH and 0.17 ml (2 mmoles) allyl bromide were added with stirring to a solution of 0.3 g (0.18 mmole) pyridone If in 30 ml DMF and heated at 100°C for 2 h. The reaction mixture was cooled and poured into 50 ml ice water. The precipitate was filtered off, dried and extracted with 20 ml hot hexane. Cooling of the extract gave 0.18 g (52%) IIf, mp 97-98°C. The residue (0.1 g) was the starting compound If, mp 317-318°C (identified by thin-layer chromatography).

3-Iodomethyl-2,3-dihydro-5-cyclopropyl-8-cyanothiazolo[3,2-a]pyridinium Iodide (IIIh). A sample of 0.51 g (2 mmoles) iodine dissolved in 25 ml $CHCl_3$ was added to a solution of

0.21 g (1 mmole) IId in 2 ml dry $CHCl_3$. The reaction mixture was maintained for 4 h at 20°C and then for 10 h at 0°C. The precipitate was filtered off and washed with 2 ml $CHCl_3$ and 10 ml ether. The yield was 0.53 g (73%), mp 138-140°C (dec.).

Products IIIg and IIIi-ℓ were obtained analogously.

3-Bromomethyl-2,3-dihydro-5-cyclopropyl-8-cyanothiazolo[3,2-a]pyridinium Bromide (IIId). A sample of 0.05 ml (0.94 mmole) bromine in 5 ml $CHCl_3$ was added to a solution of 0.20 g (0.93 mmole) IId in 2 ml dry $CHCl_3$. The precipitate formed was filtered and washed with 10 ml $CHCl_3$ to give 0.21 g (60%) (IIId), mp 105-108°C (dec.)

Products IIIa-c, IIIe and IIIf were obtained analogously.

General Procedure for the Preparation of Perchlorates IVa and IVb. A sample of 2.7 ml 57% perchloric acid and 2.5 ml acetic acid were added successively to 12 ml glacial acetic acid. Bromides IIb and IIc (2 mmoles) were added to the reaction mixture which was heated on a water bath at 80°C for 30 min. HBr was liberated and the starting reagent dissolved. The hot reaction mixture was filtered through a fluted filter, cooled to 25°C and diluted with 5 ml ether. The solution was maintained for 3 h at −4°C. The precipitate was filtered off, washed twice with 5 ml ether and recrystallized.

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