New mesoionic systems of azolopyridine series
2.* Synthesis, structures, and biological activity of 2-aminothiazolo[3,2-*a*]pyridinium salts and thiazolo[3,2-*a*]pyridinium 2-imidates

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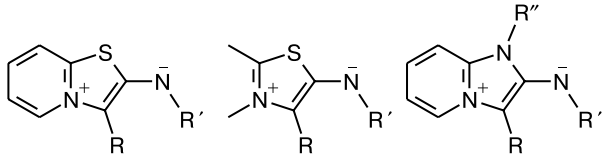
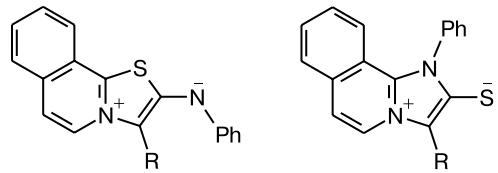
A new procedure was developed for the synthesis of 2-aminothiazolo[3,2-*a*]pyridinium salts **8** by the reaction of 2-halo-*N*-phenacylpyridinium salts with KSCN. The anion compositions of salts **8** were studied by ion chromatography. Acylation of salts **8** afforded representatives of the previously unknown bicyclic mesoionic thiazolo[3,2-*a*]pyridinium 2-imidate system **9**. The three-dimensional structures of 2-amino-3-(*p*-bromobenzoyl)thiazolo[3,2-*a*]pyridinium thiocyanate and *N*-trifluoroacetyl-3-(*p*-nitrobenzoyl)thiazolo[3,2-*a*]pyridinium 2-imidate were established by X-ray diffraction analysis.

Key words: mesoionic heterocycles, *N*-phenacylpyridinium salts, potassium rhodanide, thiazole, biological activity, ion chromatography.

Bicyclic mesoionic thiazolopyridinium 2-imidates **1** remain unknown although their monocyclic parent compounds **2** and isostructural imidates of the imidazopyridinium series **3** were described in the literature.[2,3]



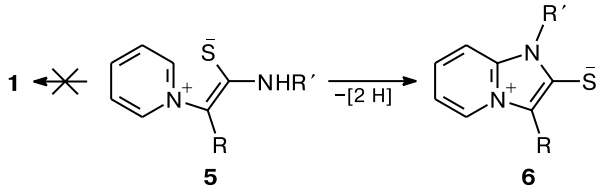
1 **2** **3**



4a **4b**

There are unconfirmed data on the preparation of the benzo analog of system **1** by 1,3-dipolar cycloaddition. In the early study,[4] the authors have assigned thiazole structure **4a** (R = *p*-NO_2Ph) to the adduct of isoquinolinium ylide with phenyl isothiocyanate without any spectroscopic evidence. However, it has later been demonstrated[5] that the reactions of *N*-phenacylisoquinolinium ylides with organic isothiocyanates result in the closure of the imidazole rather than thiazole ring to form structures **4b** (R = COAr). Consequently, cycloadduct **4a** more likely has imidazole-type structure **4b** (R = *p*-NO_2Ph). Similar pyridinium ylides readily form adducts with isothiocyanates having betaine structures (for example, **5**, R = CN). However, further oxidative cyclization leads (as in the latter case) to the closure of the imidazole (**6**) rather than thiazole (**1**) ring[6] (Scheme 1). The formation of the imidazole ring in the reactions of isothiocyanates with various pyridinium ylides[7—9] was unambiguously established by X-ray diffraction study of compound **6** (R′ = Ph, R = 2-benzimidazolyl). Therefore, fused thiazolium imidates **1** are still synthetically inaccessible.

Scheme 1



5 **6**

Synthesis of mesoionic system 1. We developed a new approach (Scheme 2) to the synthesis of mesoionic imidates **9** (first representatives of structural type **1**) by the previously unknown heterocyclization of 2-halo-*N*-phen-

* For Part 1, see Ref. 1.

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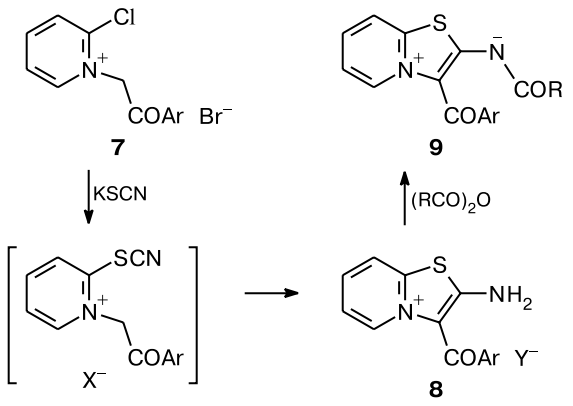
acylpyridinium salts **7** in the presence of KSCN followed by acylation of the resulting aminoheterocycles **8**.

Scheme 2



X = Br, Cl, Y = Cl, Br, SCN, ClO_4, or HSO_4.
9: Ar = *p*-$NO_2C_6H_4$, R = Me (**a**), CF_3 (**b**)

Note. Substituents for compounds **7a—h**, **8a—h** are given in Table 1.

The first step of the transformation of various 2-chloropyridinium salts **7b—h** (earlier, we have observed this transformation only for **7a** → **8a**)[10] proceeds in high yield (as a rule, in 60—90% yield, see Table 1).

The reactions occurred at high temperature for 5—10 min in a heterogeneous (acetonitrile) or homogeneous (aqueous ethanol) medium to give poorly soluble compounds, which were transformed into perchlorates **8**. The ^{1}H NMR spectra of perchlorates **8** (Table 2) show signals for the protons of the pyridine fragment and the aroyl residue but have no signals for the methylene group of the starting salts **7**. The spectra show a singlet of the NH_2 group at δ 7.9—8.2, which disappears upon the addition of D_2O.

Table 1. Characteristics of perchlorates **8**

Compound	Ar	Yield (%)	M.p./°C
8a[10]	4-$NO_2C_6H_4$	77	247—248
8b	4-FC_6H_4	57	158—160
8c	4-ClC_6H_4	89	180—182
8d	4-BrC_6H_4	83	210—211
8e	3-BrC_6H_4	79	140—141
8f	2,4-$Me_2C_6H_3$	35	128—130
8g	3,4-$Me_2C_6H_3$	85	175—176
8h	Ph	83	126—127

Apparently, the observed selectivity of the thiazole ring closure (rather than the imidazole ring closure observed in structures **4b** and **6**) is associated with the initial replacement of the halogen atom in salts **7** with the thiocyanate group followed by cyclization of 2-thiocyanatopyridinium salts. It should be emphasized that we discovered a new type of the thioazole ring closure. Although thiocyanates and isothiocyanates are classical reagents for the SCN + CC-type construction of the thiazole ring, the new cyclization belongs to another combination, *viz.*, "SC fragment of thiocyanate + CNC fragment of pyridinium salt" having no precedents (see Scheme 1). Only the thiadiazole ring closure by the reaction of *N*-aminopyridinium salts with KSCN, which has been described in the literature,[11] is similar in design.

Salts **8** are soluble in alkalis. However, we failed to isolate stable covalent compounds with imidate structures **1**. Attempts to introduce an additional electron-withdrawing fragment into the amino group by the reactions of salts **8** with benzoyl chloride or picryl chloride (in the presence of bases) led to the formation of mixtures, which are difficult to separate. It appeared that treatment of perchlorate **8a** with acetic or trifluoroacetic anhydrides afforded mesoionic imidates **9a,b** (Scheme 2). The signal

Table 2. ^{1}H NMR spectroscopic data for perchlorates **8** (DMSO-d_6, 360 MHz, δ, *J*/Hz)

Compound	Ar	H(5), d ($J_{5,6}$)	H(8), d ($J_{7,8}$)	H(7), m	NH_2, br.s	H(6), m	H (Ar/Me)
8a[10]	4-$NO_2C_6H_4$	9.24 (6.7)	8.63 (8.0)	8.15	8.56	7.78	8.38, 8.02
8b	4-FC_6H_4	9.21 (7.0)	8.59 (8.6)	8.10	8.05	7.76	7.89, 7.31
8c	4-ClC_6H_4	9.23 (6.8)	8.57 (8.5)	8.00—8.20	8.10	7.70—7.90	7.80, 7.58
8d	4-BrC_6H_4	9.23 (6.2)	8.58 (8.2)	8.11	8.11	7.70—7.80	7.70—7.80
8e	3-BrC_6H_4	9.22 (6.8)	8.58 (8.1)	8.11	8.11	7.70—7.85	7.94 (m, 1 H, H(2′), $J_{2',4'} = J_{2',6'} = 1.7$); 7.70—7.85 (m, 2 H, H(4′), H(6′)); 7.50 (m, 1 H, H(5′), $J_{4',5'} = J_{5',6'} = 7.8$)
8f	2,4-$Me_2C_6H_3$	9.29 (6.8)	8.60 (9.2)	8.11	8.04	7.75	7.36 (d, 1 H, H(6′), $J_{5',6'} = 7.8$); 7.24 (br.s, 1 H, H(3′)); 7.16 (br.d, 1 H, H(5′), $J_{5',6'} = 7.8$); 2.06, 2.41 (both s, 3 H each, Me)
8g	3,4-$Me_2C_6H_3$	9.16 (6.7)	8.57 (8.2)	8.09	7.91	7.73	7.57 (s, 1 H, H(2′)); 7.52 (d, 1 H, H(6′), $J_{5',6'} = 7.7$); 7.31 (d, 1 H, H(5′), $J_{5',6'} = 7.7$); 2.37, 2.34 (both s, 3 H each, Me)
8h	Ph	9.16 (6.5)	8.63 (8.3)	8.10	8.10	7.50—7.80	7.50—7.80 (m, 5 H, Ph)

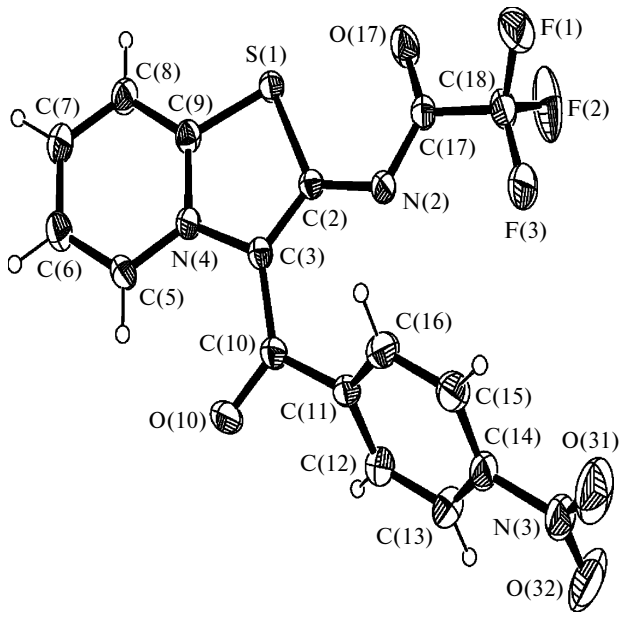


Fig. 1. Structure of new mesoionic system **9a** established by X-ray diffraction.

of the amino group, which was observed in the ^{1}H NMR spectrum of salt **8a**, *completely* disappeared in the spectra of compounds **9a,b** (due to acylation of the amino group accompanied by abstraction of the second proton). Another spectroscopic feature of compounds **9** is a small downfield shift of the signal for the proton H(5), which is hardly possible when going from the cation to the covalent (although mesoionic) molecule. The structure of imidate **9a** was unambiguously established by X-ray diffraction analysis (Fig. 1).

To analyze the structural features, let us compare the structure of molecule **9a** with that of its ionic analog, *viz.*, salt **8a** (for the X-ray diffraction data, see Ref. 10). The structure of the pyridine fragment and the C(9)—S(1) bond length depend slightly on whether they belong to the cation or the mesoionic system. In both molecules, the pyridine fragment is structurally similar to pyridine-2-thione (with a weakly pronounced quasi-diene structure). The S(1)—C(2) and N(4)—C(3) bonds in **9a** are longer than the corresponding bonds in molecule **8a** by approximately 0.02 Å. It should be noted that it is this pair of bonds that separates the pyridinethione fragment, on which the positive charge should be delocalized, and the remaining portion of the molecule, which should bear the negative charge. Both the endocyclic C(2)—C(3) bond and the exocyclic C(3)—C(10) bond remain virtually unchanged, whereas the *exo*-C(2)—N(2) bond (between the imidate fragment and the thiazole ring) is elongated to 1.35 Å. Hence, the structural changes can be approximately described as a tendency of molecule **9a** to be separated into two oppositely charged fragments with weakly pronounced bond delocalization in each fragment. It should be noted that a different tendency has been observed earlier for the related thiazolo[3,2-*a*]pyridinium-2-thiolate system (see the previous communication).[1]

To assess possible biological activities, some representatives of the previously unknown subclasses of heterocycles **8** and **9** were subjected to the corresponding assays. However, selected tests of mesoionic compound **9b** revealed no evidence of antitumor (*in vitro*, the *Hela* culture) and insecticidal (*in vivo*, Drosophilas) activities. For thiazolopyridinium salts of class **8**, agrochemical assays could be of particular interest (it is known that both the pyridine and thiazole structural fragments are involved in numerous modern pesticides and insecticides). However, salts **8** were isolated as perchlorates, which are unsuitable for biological assays. This stimulated us to investigate cyclization **7** → **8** in more detail from the viewpoint of the anion composition of salts **8**.

Anion compositions of the initially formed salts 8

The reaction **7** → **8** cannot be considered as a classical heterocyclization because it is accompanied by "inorganic" ion exchange of the "Salt 1 + Salt 2 = Salt 3 + Salt 4" type. The transformation involving the reagents in an equimolar ratio is described by the following stoichiometry:

$$[R—Cl]^+ + Br^- + K^+ + SCN^- = [RSCN]^+ + Cl^+ + Br^- + K^+,$$

where R is an organic fragment of the initial and final salts **7** and **8**, respectively.

Evidently, both the bromide and chloride ions (the bromide ion is the counterion of salt **7**, while the chloride ion appears due to the displacement of the initially covalent chlorine atom from the chloropyridinium salt) can equally serve as the anion for the resulting cation of **8**. It is difficult to predict the qualitative ion composition of salts **8**. Attempts to solve this analytical problem by conventional elemental analysis failed. The anion compositions of salts **8** were unambiguously determined by anion chromatography (chromatograms were calibrated against KCl, KBr, and KSCN). The results of selected experiments are given in Table 3.

It can be seen that the reactions of the reagents in an equimolar ratio gave **8d** and **8g** contaning the Br^- anion as the major counterion, both salts containing up to 20% of chloride. The thiocyanate ion can also be present in the product (salts **8g** and **8b**). It should be noted that rhodanide of the product was predominantly obtained for compound **8b** even in the reaction of the reagents in an equimolar ratio, *i.e.*, KSCN is consumed as both the covalent and ionic components due to which the yield in the reaction decreases to 57%. Therefore, solubility of the final product and stability of the crystal lattices have a decisive effect on the compositions of the organic salts.

Table 3. Anion compositions of the initially formed salts **8** determined by ion chromatography

Cation	**7** : KSCN*	Counterion in salts **8**		
		Cl^-	Br^-	SCN^-
8d	1 : 1	0.89	***4.30***	0
	1 : 2	0.13	0.05	***1.44***
8g	1 : 1	0.44	***2.03***	0.89
8b	1 : 1	0.13	0.09	***4.12***
	1 : 2	0.08	0.48	***2.00***

* The reagent molar ratio.

In the presence of a twofold excess of KSCN, the percentage of thiocyanate ions in the salts sharply increases. In the presence of a threefold excess of KSCN, the resulting salts **8** appeared to be thiocyanates. This fact was unambiguously confirmed by single-crystal X-ray diffraction analysis (Fig. 2) of **8d** isolated from the reaction mixture (*cf.* X-ray diffraction data for thiocyanate **8a**[10] prepared analogously). The structural tendencies observed for cation **8d** are analogous to those discussed earlier[10] for cation **8a**.

Therefore, one can prepare compounds **8** as either mixed salts or thiocyanates by varying the reaction conditions. Unfortunately, rhodanides of organic compounds are often unsuitable for biological assays. The conversion of mixed salts into hygroscopic hydrosulfates by the reactions with concentrated H_2SO_4 proved to be an efficient procedure for the preparation of water-soluble salts based on salts **8** (counterions can be removed due to volatility of the acids displaced). Finally, the use of the starting salt **7** as *perchlorate* provides an unusual approach to the synthesis of the target final product as *chloride*. In this case, bromide ions are virtually absent in the system. The reaction of perchlorate of the chloropyridinium salt with KSCN afforded poorly water-soluble $KClO_4$ and soluble organic chloride **8**.

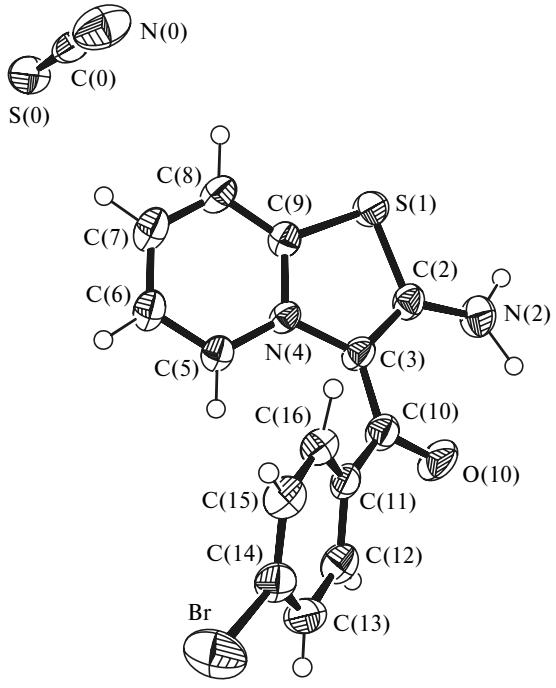


Fig. 2. Structure of rhodanide **8d** established by X-ray diffraction.

Biological assays. Hydrosulfates of compounds **8** (and thiocyanate **8a**) do not exhibit insecticidal and fungicidal activities in standard *in vitro* assays. Rhodanide **8a** shows no evidence of antitumor (*in vitro*, the *Hela* culture) and insecticidal (*in vivo*, Drosophilas) activities. Mixed halide **8d** (Br/Cl = 4.30/0.89, see Table 3) appeared to be active and suppress growth of golden staphylococcus at a concentration of 500 μg mL^{-1}.

Ionic compounds **8**, which were prepared by the reaction of the reagents in an equimolar ratio (see Table 3), possess pesticidal properties. Compounds **8b** and **8g** show moderate herbicidal activity (necrosis), and compounds **8b**, **8d**, and **8g** weakly suppress seed germination.

Experimental

The ^1H NMR spectra were recorded on a Bruker AC 400 instrument. The chemical shifts are given in the δ scale. Ion chromatography was carried out on a Dionex DX-120 chromatograph equipped with an AS4-A chromatographic column (1.7 *mM* Na_2CO_3/1.8 *mM* $NaHCO_3$ as the eluent); the flow rate was 1 mL min^{-1}. The starting pyridinium salts **7** were synthesized according to known procedures[12–14] and were used without additional purification.

Synthesis of perchlorates 8 (general procedure). Salt **7** (5 mmol) was dissolved in a mixture of ethanol (15 mL) and water (5 mL) (if necessary, the solution was heated to 50 °C). Then a solution of KSCN (1.46 g, 15 mmol) in ethanol (6 mL) and water (4 mL) was added. The reaction mixture was kept at ~20 °C for 4—5 h. The precipitate was separated, washed with 80% aqueous ethanol, and dried. Concentrated H_2SO_4 (0.5 mL) was added dropwise with vigorous stirring (Caution! Gas evolution!) to the precipitate. The mixture was kept at room temperature for 1—2 h, and then 71% perchloric acid (0.1 mL, 1 mmol) was added. The reaction mixture was kept for 1 h and then diluted with water to 1—2 mL, after which perchlorate **8** precipitated. The precipitate was filtered off, washed on a filter with a small amount of ice water, pressed out, and dried. Perchlorates **8** can be recrystallized from ethanol. The characteristics of perchlorates **8** are given in Table 1. The ^1H NMR spectroscopic data are listed in Table 2.

Synthesis of hydrosulfates 8 (general procedure). Solutions of salts in sulfuric acid were prepared as described above. Then the solutions were kept at room temperature for 1—2 h, anhydrous diethyl ether (100 mL) was added, and the mixture was thoroughly stirred for 30 min, after which the ether was decanted and the solid residue was again treated with diethyl ether (to remove traces of sulfuric acid) until a fine suspension of the solid substance was obtained. The precipitate was filtered off and dried *in vacuo* over P_2O_5. The ^1H NMR spectra of the

Table 4. Types of biological assays

Agriculture	Disease	Disease agent	Type of assay
Apple tree (Malus domestica)	Apple scab	Venturia inaequalis	Addition to a cultivation vessel
Common bean (Phaseolus vulgaris)	Gray mould	Botrytis cinerea	Treatment of a blooming plant
Wheat (Triticum)	Powdery mildew	Erysiphe graminis	Addition to a cultivation vessel
Tomato (Lycopersicon esculentum)	Late blight	Phytophthora infestans	Addition to a cultivation vessel
Grape (Vitis)	Downy mildew	Plasmopala viticola	Addition to a cultivation vessel

hydrosulfates differ from those of perchlorates **8** only by the presence of an additional broad signal of the HSO_4^- anion. The hydrosulfates are very hygroscopic.

Synthesis of 2-amino-3-(*p*-fluorobenzoyl)thiazolo[3,2-*a*]pyridinium chloride (8b). 2-Chloro-1-(*p*-fluorophenacyl)pyridinium bromide (**7b**) (0.27 g, 0.82 mmol) was dissolved in ethanol (10—15 mL). Then $NaClO_4$ (0.23 g, 1.64 mmol) was added. The solution was refluxed for 10 min and cooled. Crystals of organic perchlorate were filtered off and recrystallized from ethanol. Perchlorate **7b** was obtained in a yield of 0.24 g. Then perchlorate **7b** (0.07 g, 0.2 mmol) was dissolved in ethanol (4 mL) and mixed with a solution of KSCN (0.02 g, 0.2 mmol) in ethanol (1.5 mL). The reaction mixture was heated to 70 °C and then allowed to cool to ~20 °C. The precipitate of $KClO_4$ was filtered off. Evaporation of the filtrate under reduced pressure afforded chloride **8b** with 94% purity (the counterion was monitored by anion chromatography). The ^{1}H NMR spectrum of the sample was identical to that of perchlorate **8b**.

Table 5. Crystallographic data and details of X-ray diffraction study for **8d** and **9a**

Parameter	**8d**	**9a**
Molecular formula	$C_{15}H_{10}BrN_3OS_2$	$C_{16}H_8F_3N_3O_4S$
Molecular weight	392.29	395.31
Crystal system	Monoclinic	Triclinic
Space group	$P2_1/c$	$P\bar{1}$
a/Å	8.844(2)	4.4428(8)
b/Å	15.821(2)	13.2223(19)
c/Å	11.557(6)	13.5601(19)
α/deg	90	102.260(10)
β/deg	107.86(3)	89.620(10)
γ/deg	90	97.450(10)
V/Å^3	1539.3(9)	771.7(2)
Z	4	2
d_{calc}/g cm^{-3}	1.693	1.701
μ/mm^{-1}	2.945	2.499
Scan range, θ/deg	2.25—27.97	3.34—74.92
Range of indices	$-11 \le h \le 11$ $0 \le k \le 20$ $0 \le l \le 15$	$-5 \le h \le 5$ $-16 \le k \le 16$ $0 \le l \le 16$
Number of measured reflections	3885	3116
Number of reflections with $I > 2\sigma(I)$	3700	2996
Number of parameters in refinement	208	244
GOOF	1.023	1.054
R_1/wR_2 [$I > 2\sigma(I)$]	0.0830/0.2068	0.0858/0.2219
R_1/wR_2 for all reflections	0.1394/0.2469	0.1047/0.2368
Extinction	0.0073(9)	—
$\Delta\rho_{max}/\Delta\rho_{min}$, e • Å^{-3}	0.956/−1.002	0.352/−0.408

***N*-Trifluoroacetyl-3-(*p*-nitrobenzoyl)thiazolo[3,2-*a*]pyridinium 2-imidate (9a).** Trifluoroacetic anhydride (4 mL; distilled before use over P_2O_5) was added to perchlorate **8a** (0.5 g). The reaction mixture was cooled to 0 °C with stirring. Then the reaction mixture was kept at 0 °C for 1 h, and pyridine (0.5 mL, distilled over KOH) was added very carefully with vigorous stirring. The pale-yellow needle-like precipitate that formed was filtered off and dried on a filter. A crude product (0.8 g), which was contaminated with pyridinium trifluoroacetate, was recrystallized. The yield was 0.346 g (70%), m.p. 295—296 °C (from CH_3CN). Found (%): N, 10.55. $C_{16}H_8F_3N_3O_4S$. Calculated (%): N, 10.63. ^{1}H NMR (DMSO-d_6), δ: 10.05 (d, 1 H, H(5), $J_{5,6}$ = 6.8 Hz); 8.57 (d, 1 H, H(8), $J_{7,8}$ = 8.3 Hz); 8.26—8.23 (m, 2 H, Ar); 8.12 (m, 1 H, H(7)); 7.90—7.88 (m, 3 H, Ar + H(6)). The X-ray diffraction data are presented in Fig. 1 and in Tables 4—6.

***N*-Acetyl-3-(*p*-nitrobenzoyl)thiazolo[3,2-*a*]pyridinium 2-imidate (9b).** Acetic anhydride (5 mL, distilled before use over P_2O_5) was added to perchlorate **8a** (0.5 g). Then pyridine (0.2 g, distilled over KOH) was carefully added to the reaction mixture with vigorous stirring. The bright yellow amorphous precipitate

Table 6. Selected interatomic distances (d) in the structure of **8d**

Bond	d/Å	Bond	d/Å
Br(14)—C(14)	1.8993(9)	C(10)—O(10)	1.2083(6)
S(1)—C(9)	1.7270(6)	C(10)—C(11)	1.5558(5)
S(1)—C(2)	1.7548(6)	C(11)—C(16)	1.3935(7)
C(2)—N(2)	1.3417(7)	C(11)—C(12)	1.4031(6)
C(2)—C(3)	1.3639(5)	C(12)—C(13)	1.3811(8)
C(3)—N(4)	1.4276(7)	C(13)—C(14)	1.3918(9)
C(3)—C(10)	1.4454(6)	C(14)—C(15)	1.3687(8)
N(4)—C(5)	1.3277(8)	C(15)—C(16)	1.3740(9)
N(4)—C(9)	1.3424(8)	N(2)—H(2A)	0.83(3)
C(5)—C(6)	1.3587(10)	N(2)—H(2B)	0.90(3)
C(6)—C(7)	1.3804(8)	S—C	1.622(4)
C(7)—C(8)	1.3669(8)	N—C	1.141(5)
C(8)—C(9)	1.3913(9)		

Table 7. Selected bond angles (ω) in the structure of **8d**

Angle	ω/deg	Angle	ω/deg
C(9)—S(1)—C(2)	89.65(3)	O(10)—C(10)—C(3)	123.84(8)
N(2)—C(2)—C(3)	128.07(2)	O(10)—C(10)—C(11)	118.56(8)
N(2)—C(2)—S(1)	118.83(2)	C(3)—C(10)—C(11)	116.03(3)
C(3)—C(2)—S(1)	113.09(3)	C(16)—C(11)—C(12)	119.30(3)
C(2)—C(3)—N(4)	110.32(2)	C(16)—C(11)—C(10)	125.39(2)
C(2)—C(3)—C(10)	119.83(3)	C(12)—C(11)—C(10)	115.31(3)
N(4)—C(3)—C(10)	129.850(18)	C(13)—C(12)—C(11)	120.66(4)
C(5)—N(4)—C(9)	119.27(6)	C(12)—C(13)—C(14)	118.11(4)
C(5)—N(4)—C(3)	126.42(4)	C(15)—C(14)—C(13)	122.05(5)
C(9)—N(4)—C(3)	114.31(4)	C(15)—C(14)—Br(14)	118.40(5)
N(4)—C(5)—C(6)	122.23(4)	C(13)—C(14)—Br(14)	119.54(4)
C(5)—C(6)—C(7)	119.55(5)	C(14)—C(15)—C(16)	119.77(6)
C(8)—C(7)—C(6)	118.82(7)	C(15)—C(16)—C(11)	120.10(4)
C(7)—C(8)—C(9)	119.08(4)	C(2)—N(2)—H(2A)	118.8(19)
N(4)—C(9)—C(8)	121.06(5)	C(2)—N(2)—H(2B)	122.0(2)
N(4)—C(9)—S(1)	112.62(5)	H(2A)—N(2)—H(2B)	119.0(3)
C(8)—C(9)—S(1)	126.32(3)	N—C—S	178.5(3)

that formed was filtered off, washed three times with anhydrous acetonitrile, and dried on a filter. The yield was 0.29 g (68%). The compound (50 mg) was recrystallized, m.p. 305—306 °C (from CH_3CN). Found (%): N, 12.33. $C_{16}H_{11}N_3O_4S$. Calculated (%): N, 12.31. ^{1}H NMR (DMSO-d_6), δ: 10.21 (d, 1 H, H(5), $J_{5,6}$ = 6.9 Hz); 8.31—8.26 (m, 2 H, Ar); 8.05 (m, 1 H, H(7)); 7.90—7.80 (m, 2 H, Ar); 7.52 (d, 1 H, H(8), $J_{7,8}$ = 8.4 Hz); 7.42 (ddd, 1 H, H(6), $J_{5,6}$ = 6.9 Hz, $J_{6,7}$ = 7.4 Hz, $J_{6,8}$ = 0.9 Hz); 1.72 (s, 3 H, Ac).

Biological assays were carried out according to standard procedures on the following cultures: *imago D. virilis*, strain 101 (toxicity of compounds with respect to Drosophila); the *Hela* culture (antitumor activity); golden staphylococcus, strain 209_P (bacteriostatic action).

The pesticidal activity was assessed in laboratories of Nippon Soda Co. (Japan). The fungicidal properties were studied (*in vivo*) on plants and pathogens listed in Table 4.

In fungicidal assays (*in vitro*), the following cultures were examined: *Pseudomonas syringae*, *Pythium aphanidermatum*, *Rhisoctonia solani*, *Botritis cinerea* (both resistant and sensitive to benzimidazole), *Penicillium italicum*, *Cercospora beticola*, *Diaporthe citri*, *Alternaria alternate* (apple pathotype), *Gibberella fujikuroi*, and *Phytophthora infestans*.

Insecticidal assays were carried out on cotton aphid (*Aphis gossypii*), armyworms (*Pseudaletia unipuncta*), and spotted spider mite (*Tetrarhynchus*). Cypermethrin and dicofol were used as reference compounds.

The herbicidal activity was assessed on the following cultures: *Digitaria adscendence*, *Setaria faberi*, *Abutilon theophrasti*, *Amarantus retroflexus* (post-germination assays) and *Ethinochloa utilis*, *Cyperus iria*, *Lactuca sativa* (seed germination). Alachlor, atrazine, and glycophosphate were used as reference compounds.

X-ray diffraction analysis. The intensities of X-ray reflections for single crystals of **8d** and **9a** were measured at room temperature on a CAD-4 diffractometer[15] (λ(Mo-Kα) = 0.7107 Å for **8d** and (λ(Cu-Kα) = 1.5418 Å for **9a**, graphite monochromator, ω scanning technique). The crystallographic characteristics and details of X-ray study are given in Table 5. The unit cell parameters were determined and refined based on 25 reflections in the θ angle ranges of 14.5—15.5° and 30—35° for compounds **8d** and **9a**, respectively. No absorption corrections were applied because of the low linear absorption coefficients and small sizes of the crystals of **8d** and **9a**. The experimental data sets were preliminarily processed using the WinGX program package.[16] All subsequent calculations were carried out using the SHELX97 program package.[17] The structures were solved by direct methods and refined by the full-matrix least-squares method with anisotropic displacement parameters for all nonhydrogen atoms. The hydrogen atoms were placed in geometrically calculated positions and refined using a riding model. Selected interatomic distances and bond angles for compounds **8d** and **9a** are given in Tables 6—9. The crystallographic data for compounds **8d** and **9a** were deposited with the Cambridge Structural Database. The molecular structures of compounds **8d** and **9a**, which were drawn with the use of the

Table 8. Selected interatomic distances (*d*) in the structure of **9a**

Bond	*d*/Å	Bond	*d*/Å
S(1)—C(9)	1.716(4)	C(11)—C(16)	1.381(6)
S(1)—C(2)	1.754(3)	C(11)—C(12)	1.386(6)
C(2)—N(2)	1.353(5)	C(12)—C(13)	1.387(6)
C(2)—C(3)	1.383(5)	C(13)—C(14)	1.370(7)
N(2)—C(17)	1.325(5)	C(14)—C(15)	1.376(7)
N(4)—C(9)	1.360(5)	C(14)—N(3)	1.477(5)
N(4)—C(5)	1.375(5)	C(15)—C(16)	1.377(6)
N(4)—C(3)	1.435(4)	C(17)—O(17)	1.236(5)
C(5)—C(6)	1.367(6)	C(17)—C(18)	1.535(5)
C(3)—C(10)	1.438(5)	C(18)—F(2)	1.308(5)
C(6)—C(7)	1.387(6)	C(18)—F(1)	1.309(5)
C(7)—C(8)	1.377(6)	C(18)—F(3)	1.318(6)
C(8)—C(9)	1.393(5)	N(3)—O(31)	1.207(7)
C(10)—O(10)	1.249(5)	N(3)—O(32)	1.217(7)
C(10)—C(11)	1.495(5)		

Table 9. Selected bond angles (ω) in the structure of **9a**

Angle	ω/deg	Angle	ω/deg	Angle	ω/deg
C(9)—S(1)—C(2)	90.48(17)	N(4)—C(9)—C(8)	121.2(3)	C(14)—C(15)—C(16)	118.2(4)
N(2)—C(2)—C(3)	124.3(3)	N(4)—C(9)—S(1)	113.1(3)	C(15)—C(16)—C(11)	120.6(4)
N(2)—C(2)—S(1)	122.9(3)	C(8)—C(9)—S(1)	125.7(3)	O(17)—C(17)—N(2)	128.5(4)
C(3)—C(2)—S(1)	112.3(3)	O(10)—C(10)—C(3)	121.9(4)	O(17)—C(17)—C(18)	116.1(4)
C(17)—N(2)—C(2)	117.1(3)	O(10)—C(10)—C(11)	114.4(3)	N(2)—C(17)—C(18)	115.4(3)
C(9)—N(4)—C(5)	120.0(3)	C(3)—C(10)—C(11)	123.7(3)	F(2)—C(18)—F(1)	106.8(4)
C(9)—N(4)—C(3)	113.2(3)	C(16)—C(11)—C(12)	119.8(4)	F(2)—C(18)—F(3)	107.5(4)
C(5)—N(4)—C(3)	126.6(3)	C(16)—C(11)—C(10)	122.1(4)	F(1)—C(18)—F(3)	107.2(4)
C(6)—C(5)—N(4)	119.5(4)	C(12)—C(11)—C(10)	118.1(4)	F(2)—C(18)—C(17)	110.6(4)
C(2)—C(3)—N(4)	110.9(3)	C(11)—C(12)—C(13)	120.3(4)	F(1)—C(18)—C(17)	111.2(3)
C(2)—C(3)—C(10)	127.4(3)	C(14)—C(13)—C(12)	118.0(4)	F(3)—C(18)—C(17)	113.4(4)
N(4)—C(3)—C(10)	120.1(3)	C(13)—C(14)—C(15)	123.0(4)	O(31)—N(3)—O(32)	122.8(5)
C(5)—C(6)—C(7)	121.2(4)	C(13)—C(14)—N(3)	118.4(4)	O(31)—N(3)—C(14)	119.0(5)
C(8)—C(7)—C(6)	119.3(4)	C(15)—C(14)—N(3)	118.6(4)	O(32)—N(3)—C(14)	118.3(5)
C(7)—C(8)—C(9)	118.8(4)				

ORTEP-3 program,[18] and the atomic numbering schemes are shown in Figs 1 and 2, respectively.

In the crystal of compound **8d**, one intramolecular N(2)—H(2A)...O(10) hydrogen bond (N(2)—H(2A), 0.83(3) Å; H(2A)...O(10), 2.16(3) Å; N(2)...O(10), 2.734(2) Å; N(2)—H(2A)...O(10), 127(2)°) and two intermolecular hydrogen bonds, N(2)—H(2A)...S^{i} (N(2)—H(2A), 0.83(3) Å; H(2A)...S^{i}, 2.89(3) Å; N(2)...S^{i}, 3.5189(11) Å; N(2)—H(2A)...S^{i}, 135(2)°; *i* is the symmetry operation [x, $1/2 - y$, $z - 1/2$]) and N(2)—H(2B)...S^{ii} (N(2)—H(2B), 0.90(3) Å; H(2B)...S^{ii}, 2.45(3) Å; N(2)...S^{ii}, 3.2856(17) Å; N(2)—H(2B)...S^{ii}, 155(3)°; *ii* is the symmetry operation [$-x$, $y + 1/2$, $1/2 - z$]), occur.

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