Preparation of New Nitrogen-bridged Heterocycles. 11.[1] A New Synthetic Method of Pyrazolo[1,5-*a*]pyridines from the Alkaline Treatment of 1-[(Acylmethylthio)-methyleneamino]pyridinium Salts

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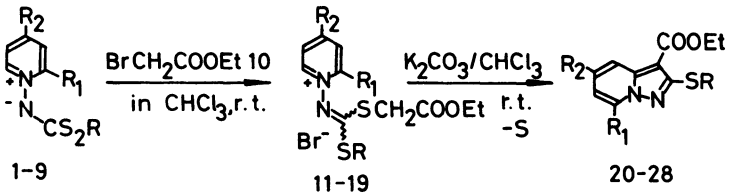
Alkaline treatment of 1-[(acylmethylthio)methyleneamino]pyridinium halides gave unexpectedly 3-acyl- or 3-(acylthio)pyrazolo[1,5-*a*]pyridine derivatives in 35—87% yields. Some 4,4a-dihydropyrido[1,2-*d*][1,3,4]thiadiazine intermediates involved in these reactions could be detected by their nmr follows and three related 4a,8-dimethyl derivatives were isolated. Substituent effect and possible mechanisms are also discussed.

In our previous communication[2] we have reported abnormal syntheses of 2-alkylthio-3-acyl- and 2-alkylthio3-(acylthio)pyrazolo[1,5-*a*]pyridine derivatives by the reactions of 1-[(acylmethlthio)methyleneamino]pyridinium salts with base, and assumed that these reactions must proceed *via* the desulfurization and the rearrangement of transient pyrido[1,2-*d*][1,3,4]-thiadiazine intermediates. Recently, Schmidt[3] has descrirbed that the 1,3,4-thiadiazinyl anions generated from the deprotonation of 6*H*-thiadiazines are thermally labile and are converted smoothly to desulfurized pyrazoles and the rearranged 4-mercaptopyrazoles. Our intermediates stated above are isoelectronic with such anions and are very intriguing molecules which have an antiaromatic (or a nonaromatic) 12-pi electron system. In this paper we wish to report a new synthetic method for 2-alkylthio-3-acyl- and 3-(acylthio)pyrazolo[1,5-*a*]pyridine derivatives and our attemps to detect the intermediates involved in the synthetic reactions of these compounds.

Result and Discussion

Reactions of Pyridinium Salts with Base. Treatment of 1-[(ethoxycarbonylmethylthio)methyleneamino]pyridinium bromides **11—19**. Obtainable by the alkylations of the corresponding pyridinium *N*-ylides **1—9** with ethyl bromoacetate **10** in quantitatively yields, with excess potassium carbonate in chloroform at room temperature afforded ethyl pyrazolo-[1,5-*a*]pyridine-3-carboxylate **20—28** in 35—82% yields along with the release of sulfur. (Scheme 1) The same pyrazolopyridines **20—22** could be aslo obtained from similar reactions of pyridinium iodides **30—32** which were prepared from the *N*-ylides **7—9** and methyl iodide **29**. The reaction of unsymmetrically substituted 3-methylpyridinium salt **34** with base gave a *ca.* 2:1 mixure of the corresponding 4-methyl- **35** and 6-methylpyrazolopyridine derivative **36** in 83% yield. (Scheme 2) On the other hand, the alkaline treatment of 1-[(phenacylthio)methyleneamino]pyridinium bromides **42—62** prepared from *N*-ylides **1—6** and phenacyl bromides **37—41** did not yield the initially expected 3-aroylpyrazolo[1,5-*a*]pyridines such as **63** at all, but, instead of them, afforded 3-(aroylthio)pyrazolo[1,5-*a*]pyridine derivatives in good yields, respectively. (Scheme 3) Similarly, unsymmetrical 3-methylpyridinium bromides **85** and **86** provided the corresponding isomeric mixtures **87** and **88** (its ratio was *ca.* 9:7), and **89** and **90** (its ratio was *ca.*



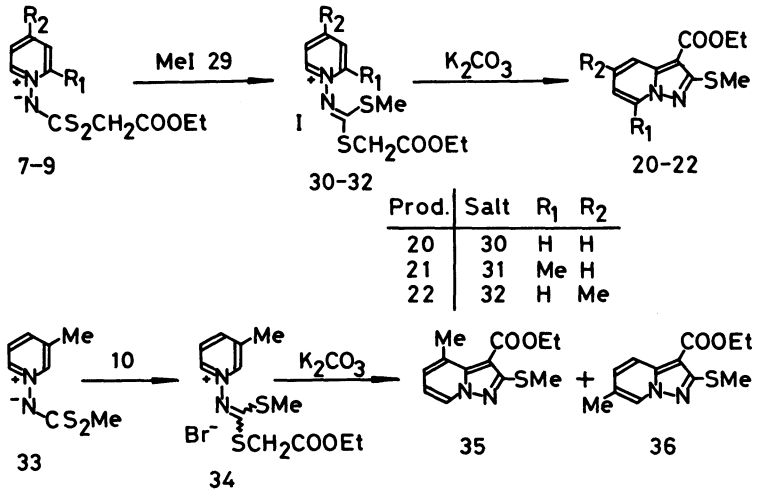
	R_1	R_2	R
1	H	H	Me
2	Me	H	Me
3	H	Me	Me
4	H	H	Et
5	Me	H	Et
6	H	Me	Et
7	H	H	CH_2COOEt
8	Me	H	CH_2COOEt
9	H	Me	CH_2COOEt

Prod.	Salt	R_1	R_2	R
20	11	H	H	Me
21	12	Me	H	Me
22	13	H	Me	Me
23	14	H	H	Et
24	15	Me	H	Et
25	16	H	Me	Et
26	17	H	H	CH_2COOEt
27	18	Me	H	CH_2COOEt
28	19	H	Me	CH_2COOEt

Scheme 1.

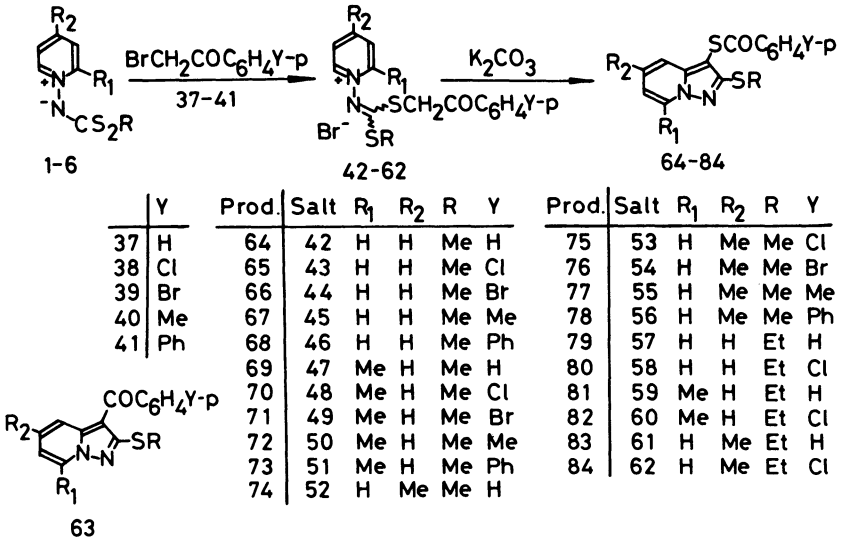
4:3) in 69 and 86% yields. (Scheme 4)

In order to investigate further the substituent effect in these reactions, we examined the reactions of pyridinium salts having an acetyl and a cyano group. The reactions of salts **93** and **95** synthesized from *N*-ylides **1** and **3** and bromoacetone **91** with base afforded only 3-(acetylthio)pyrazolopyridines **99** and **101**, but similar reactions of iodides **96** and **98** prepared from the same *N*-ylides and chloroacetone **92** in the presence of sodium iodide gave 3-acetyl derivatives **102** and **104** as major products together with the formation of a small amount of 3-acetylthio compound **101**. However, no 7-methylpyrazolopyridine derivatives such as **100** and **103** could be obtained from the reactions of 2-methylpyridinium bromide **94** and iodide **97**. (Scheme 5) On the other



Prod.	Salt	R_1	R_2
20	30	H	H
21	31	Me	H
22	32	H	Me

Scheme 2.

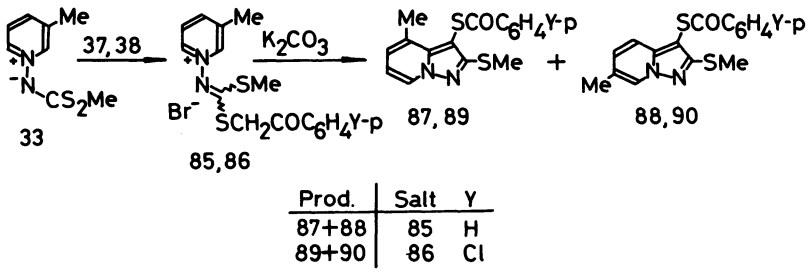


	Y
37	H
38	Cl
39	Br
40	Me
41	Ph

Prod.	Salt	R_1	R_2	R	Y
64	42	H	H	Me	H
65	43	H	H	Me	Cl
66	44	H	H	Me	Br
67	45	H	H	Me	Me
68	46	H	H	Me	Ph
69	47	Me	H	Me	H
70	48	Me	H	Me	Cl
71	49	Me	H	Me	Br
72	50	Me	H	Me	Me
73	51	Me	H	Me	Ph
74	52	H	Me	Me	H

Prod.	Salt	R_1	R_2	R	Y
75	53	H	Me	Me	Cl
76	54	H	Me	Me	Br
77	55	H	Me	Me	Me
78	56	H	Me	Me	Ph
79	57	H	H	Et	H
80	58	H	H	Et	Cl
81	59	Me	H	Et	H
82	60	Me	H	Et	Cl
83	61	H	Me	Et	H
84	62	H	Me	Et	Cl

Scheme 3.

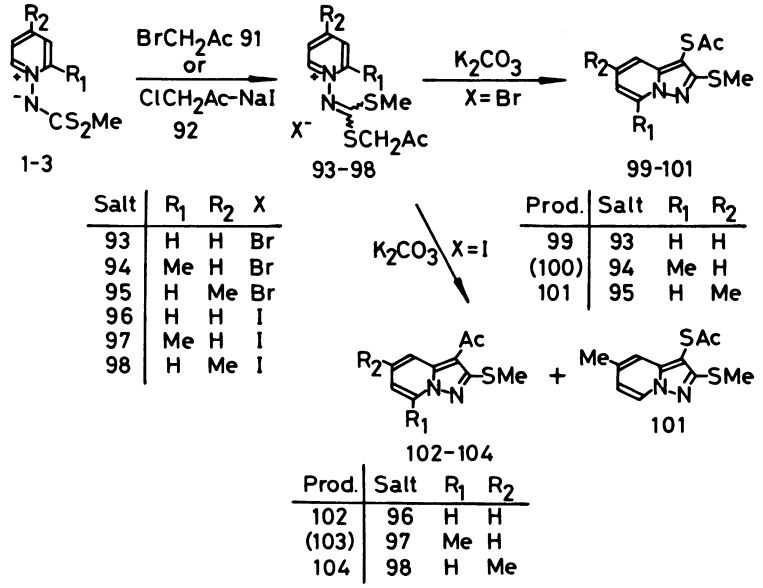


Prod.	Salt	Y
87+88	85	H
89+90	86	Cl

Scheme 4.

hand, the reactions of 1-[(cyanomethylthio)methyleneamino]pyridinium salts **107—112** with base gave only 3-cyano derivatives **113—115** in 32—55% yield but not 3-(thiocyanato)pyrazolopyridines at all. (Scheme 6)

The structures of 3-ethoxycarbonyl- **20—28**, **35**, and **36**, 3-acetyl- **102** and **104**, and 3-cyanopyrazolo[1,5-*a*]-pyridines **113—115** were decided by their physical and spectral inspections and partly by the comparisons of **20—22** with authentic samples prepared independently.[4] In particular, the chemical shifts and the signal patterns attributable to the skeletal protons in their NMR spectra (See Table 1) were quite similar to those of known pyrazolo[1,5-*a*]-pyridine-3-carboxylate[5] and 3-vinylpyrazolo[1,5-*a*]-pyridines.[6] Their microanalyses and mass spectra were in good accord with the molecular compositions involving only one sulfur atom, and the detection of the sulfur from the reaction mixtures also supported our proposed structures. On the other hand, their analyses and some mass spectra of products **64—84** and **87—90** obtained from 1-[(phenacylthio)methyleneamino]pyridinium bromides **42—62**, **85** and **86**, showed results different apparently from those of 3-aroylpyrazolo[1,5-*a*]pyridine derivatives such as **63** expected initially, that is, they suggested the molecular compositions having two sulfur atoms. In order to obtain further information about these structures, we attempted the syntheses of some 3-benzoylpyrazolopyridines and the comparisons of the resulting products with 3-aroylthio derivatives. As might be expected, 3-benzoyl-2-(methylthio)pyrazolo-[1,5-*a*]pyridines **120—122** were synthesized in very good yields by the reactions of 1-aminopyridinium iodides **116—118** with 2-benzoyl-1,1-bis(methylthio)-ethylene **119** in the presence of excess potassium carbonate in chloroform. (Scheme 7) There was little difference between both NMR spectra (See Table 1) of these 3-benzoylthio-3-(methylthio)pyrazolopyridines **64**, **69**, and **74** and 3-benzoyl compounds **120—122**, but, in their IR spectra, the large differences between their carbonyl absorptions were observed: Each band of **64**, **69**, and **74** appeared at much

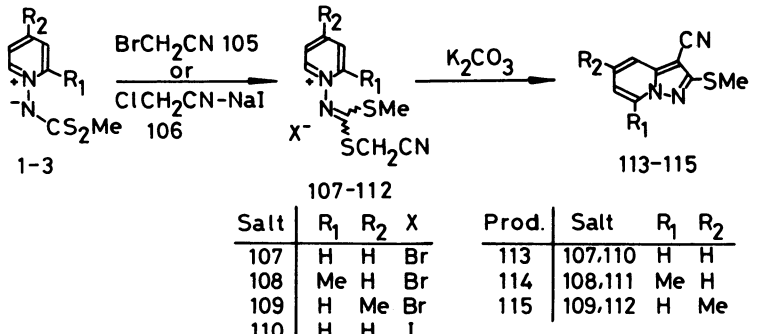


Salt	R_1	R_2	X
93	H	H	Br
94	Me	H	Br
95	H	Me	Br
96	H	H	I
97	Me	H	I
98	H	Me	I

Prod.	Salt	R_1	R_2
99	93	H	H
(100)	94	Me	H
101	95	H	Me

Prod.	Salt	R_1	R_2
102	96	H	H
(103)	97	Me	H
104	98	H	Me

Scheme 5.



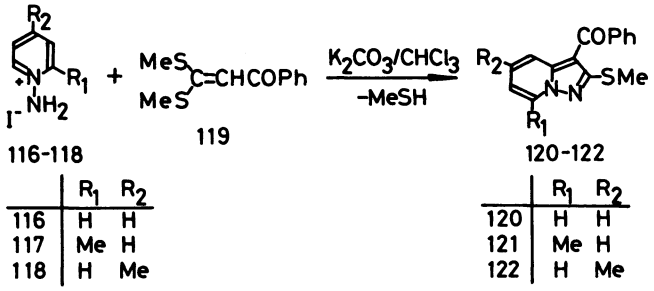
Salt	R_1	R_2	X
107	H	H	Br
108	Me	H	Br
109	H	Me	Br
110	H	H	I
111	Me	H	I
112	H	Me	I

Prod.	Salt	R_1	R_2
113	107,110	H	H
114	108,111	Me	H
115	109,112	H	Me

Scheme 6.

higher region (1665—1675 cm^{-1}) than those (1600—1610 cm^{-1}) of **120—122**, indicative of the absence of the conjugation between the benzoyl and the aromatic pyrazolopyridine ring. Further structural support for compounds **64—84**, **87—90**, **99**, and **101** was provided by their acid hydrolyses. Disulfides **123—125** could be obtained easily by heating 3-(benzoylthio)pyrazolopyridines **64**, **69**, and **74** with concentrated hydrochloric acid. (scheme 8) Compound **123** was also obtained by only heating 3-(acetylthio)pyrazolopyridine **99** with ethanol. The structures of **123—125** were assigned to be bis[2-(methylthio)pyrazolo-[1,5-*a*]pyridine-3-yl] disulfides, because their NMR spectra showed both presences of a methylthio group and a pyrazolopyridine skeleton and their Mass spectra exhibited the molecular weights bearing four sulfur atoms in each molecule.

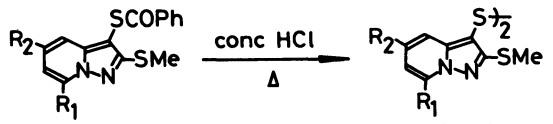
The X-ray analysis of 3-(*p*-chlorobenzoylthio)-7-methyl-2-(methylthio)pyrazolo[1,5-*a*]pyridine **70** was carried out (See Fig. 1), and the structures of other rearranged products **64—69**, **71—84**, **87—90**, **99**, and **101** were finally concluded by the physical and spectral analogies with **70**.



	R_1	R_2
116	H	H
117	Me	H
118	H	Me

	R_1	R_2
120	H	H
121	Me	H
122	H	Me

Scheme 7.



Prod.	R_1	R_2
123	H	H
124	Me	H
125	H	Me

Scheme 8.

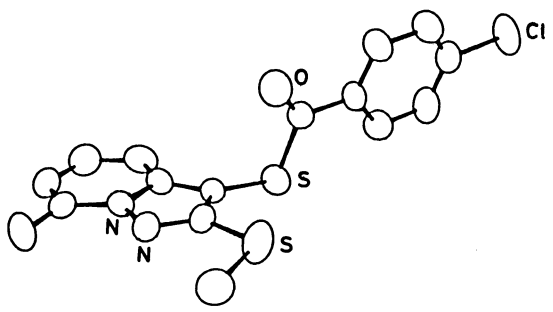
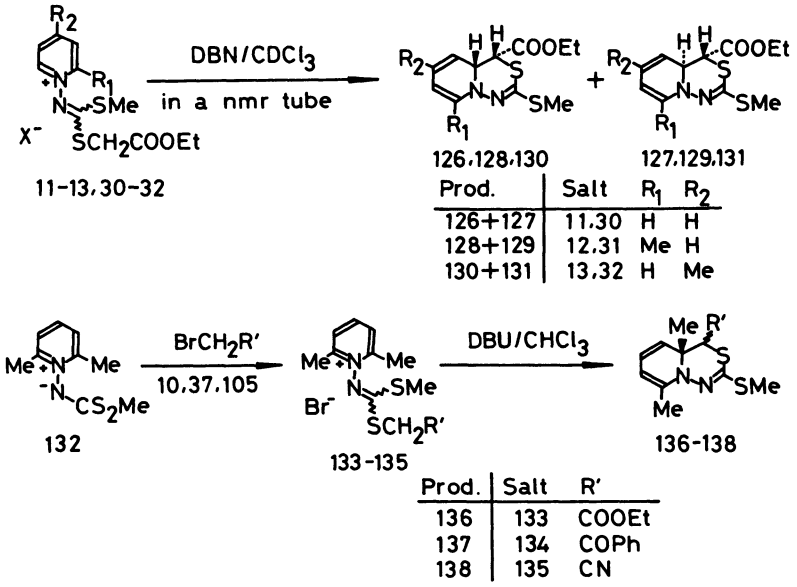


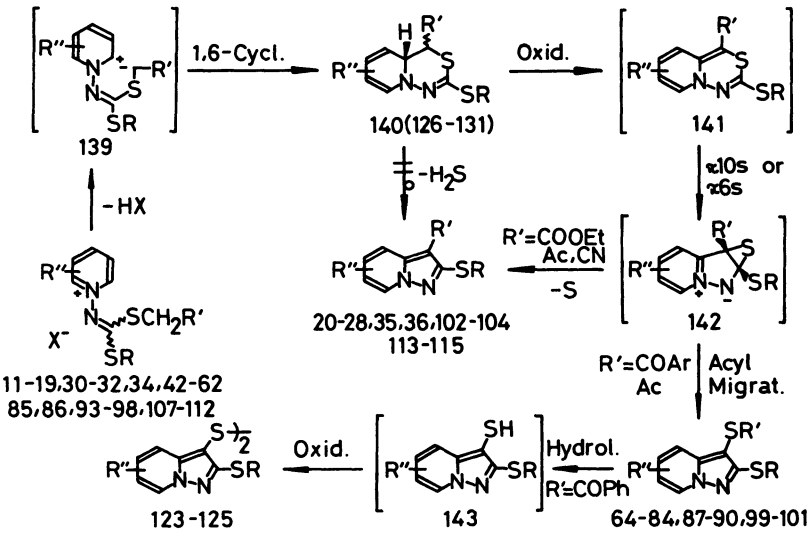
Fig. 1. ORTEP drawing of 3-(*p*-chlorobenzoylthio)-7-methyl-2-(methylthio)pyrazolo[1,5-*a*]pyridine Hydrogen atoms are not shown.

Detection and Isolation of Pyrido[1,2-d][1,3,4]thiadiazine Derivatives. On the TLC of the mixtures at the early reaction stage, we often observed certain significant spots different clearly from those of products described above. Our attempts to isolate these substances were unuccessful because of their thermal instability, but some of them could be detected by the NMR follows of the reactions of pyridinium salts with base. For example, treatment of pyridinium bromides **11—13** with DBN in deuteriochloroform in a NMR tube caused instantly the disappearance of the salts and the generations of new nonaromatic compounds **126—131**. The same products **126—131** were also observed in the reactions of pyridinium iodides **30—32** with DBN. In the NMR spectra of **126—131** (See Table 2), the signals due to all skeletal protons appeared in an olefinic region of δ 3.4—6.5 and not in an aromatic region as shown in those of pyrazolo[1,5-*a*]pyridine derivatives (Table 1). These values of **126—131** were considerably similar to those of 3,3a-dihydropyrazolo-[1,5-*a*]pyridines[7] and 1,9a-dihydropyrido[1,2-*b*][1,2,4]-triazines,[8] and this fact suggested strongly the presence of a 1,2-dihydropyridine moiety in these molecules. We next examined the syntheses of isolable pyridothiadiazines possessing a methyl group at the 4a-position, since the instability of these molecules might be caused by the susceptibility to the oxidation of the 4- and 4a-protons. The treatment of 2,6-dimethylpyridinium bromides **133—135** with DBU in chloroform gave considerably stable 4a,8-dimethyl-4,4a-dihydropyrido[1,2-*d*][1,3,4]thiadiazines **136—138** in 81, 43, and 78% yields, respectively. (Scheme 9) In contrast with the above reactions of **11—13** and **30—32**, compounds **136—138** were not *cis-trans* mixtures (See Table 2) but their configurations could not be decided because of the absence of the coupling constants between the 4- and the 4a-substituents.

Reaction Mechanisms. Possible mechanisms for these reactions are shown in Scheme 10. The reactions must be initiated by the dehydrohalogenation of pyridinium salts, and undergo the 1,6-cyclization of the resulting ionic intermediates **139** to give 4,4a-dihydropyridothiadiazines **140** as detected partly by their NMR spectrometry. The oxidation of **140** may afford antiaromatic (or nonaromatic) 12-pi pyridothiadiazines **141**, and their symmetry-allowed disrotatory cyclizations may give rise to tricyclic thiiranes **142**. The desulfurization of the reactive species **142** should provide 3-acyl- **20—28**, **35**, **36**, and **102—104** and 3-cyanopyrazolopyridines **113—115**, while the opening of the thiirane ring with the acyl migration



Scheme 9.



Scheme 10.

should lead to 3-(acylthio)pyrazolopyridines **64—84**, **87—90**, and **99—101**. An alternative route from dihydropyridothiadiazines **140** to 3-acyl- or 3-cyanopyrazolopyridines *via* the elimination of hydrogen sulfide is negligible, since no evolution of gaseous hydrogen sulfide could be observed. Of the reaction sequence the routes from pyridothiadiazines **141** to two types of pyrazolopyridines are the same with those described for the thiadiazinyl anion-pyrazoles transformation by Schmidt,[3] except the acyl migration in place of the proton transfer. The substituent effect which influences the desulfurization and the rearrangement in these reactions is still uncertain, but it may be related to the migrating or eliminating ability of these substituents. The formation of disulfides **123—125** can be interpreted reasonably by the acid hydrolyses of 3-(benzoylthio)pyrazolo[1,5-*a*]-pyridines **64**, **69**, and **74** followed by the air oxidation of the resulting thiols **143** to the disulfides.

Experimental

Melting points were measured with a Yanagimoto micromelting point apparatus and are uncorrected. Microanalyses were carried out on a perkin-Elmer 240 Elemental Analyzer. The NMR spectra were determined with a Varian EM360A Spectrometer in deuteriochloroform with tetramethylsilane as an internal standard. The chemical shifts are expressed in δ values. The IR spectra were taken with a Hitachi 260-10 Infrared Spectrophotometer. The Mass spectra were obtained with a JEOL JMS-01SG-2 Mass Spectrometer attached with a JEC-6 Spectrocomputer.

Preparations of Pyridinium N-Ylides. These pyridinium *N*-ylides **1—9**, **33**, and **132** were synthesized ac-

TABLE 1. NMR DATA OF PYRAZOLO[1,5-*a*]PYRIDINE DERIVATIVES

Compd[a]	C-4	C-5	C-6	C-7	SR			R′	
20	8.05	7.37	6.84	8.45	2.65			1.43	4.41
	br d	br t	dt	d	s			t	q
21	7.93	7.29	6.68	2.73	2.67			1.43	4.39
	dd	q	br d	s	s			t	q
22	7.80	2.43	6.68	8.31	2.63			1.42	4.39
	br s	s	dd	d	s			t	q
23	8.11	7.42	6.90	8.50	1.46	3.29		1.48	4.44
	br d	br t	dt	d	t	q		t	q
24	8.01	7.35	6.77	2.77	1.47	3.33		1.51	4.45
	br d	q	br d	s	t	q		t	q
25	7.87	2.47	6.72	8.36	1.44	3.27		1.47	4.43
	br s	s	dd	d	t	q		t	q
26	8.13	7.42	6.91	8.46	4.05	1.30	4.28	1.44	4.43
	br d	br t	dt	br d	s	t	q	t	q
27	7.98	7.32	6.75	2.72	4.03	1.29	4.26	1.43	4.41
	dd	q	br d	s	s	t	q	t	q
28	7.80	2.43	6.68	8.25	3.99	1.28	4.23	1.42	4.38
	br s	s	dd	d	s	t	q	t	q
35	2.73	7.09	6.73	8.30	2.62			1.43	4.39
	s	br d	t	dd	s			t	q
36	7.93	7.09	2.37	8.25	2.63			1.43	4.39
	d	d	s	br s	s			t	q
64	b)	b)	6.76	8.47	2.67			7.0—8.3	
			dt	d	s			m	
65	b)	b)	6.78	8.46	2.68			7.0—8.2	
			dt	d	s			m	
66	7.39	7.20	6.79	8.48	2.68			7.5—8.1	
	br d	br t	dt	d	s			m	
67	b)	b)	6.75	8.45	2.67			7.0—8.1	2.43
			dt	d	s			m	s
68	b)	b)	6.77	8.46	2.68			7.0—8.3	
			dt	d	s			m	
69	b)	b)	6.63	2.77	2.69			7.0—8.3	
			br d	s	s			m	
70	b)	b)	6.67	2.78	2.69			7.0—8.3	
			br d	s	s			m	
71	b)	b)	6.63	2.77	2.68			7.0—8.1	
			br d	s	s			m	
72	b)	b)	6.63	2.77	2.69			7.0—8.1	2.44
			br d	s	s			m	s
73	b)	b)	6.63	2.77	2.70			7.0—8.4	
			br d	s	s			m	
74	7.12	2.36	6.60	8.33	2.65			7.3—8.3	
	br s	s	dd	d	s			m	
75	7.10	2.36	6.60	8.33	2.64			7.3—8.2	
	br s	s	dd	d	s			m	
76	7.11	2.38	6.62	8.34	2.67			7.4—8.1	
	br s	s	dd	d	s			m	
77	7.10	2.37	6.59	8.32	2.64			7.1—8.1	2.43
	br s	s	dd	d	s			m	s
78	7.13	2.36	6.60	8.33	2.64			7.3—8.3	
	br s	s	dd	d	s			m	
79	b)	b)	6.83	8.53	1.41	3.25		7.0—8.3	
			dt	d	t	q		m	
80	b)	b)	6.87	8.53	1.42	3.25		7.0—8.3	
			dt	d	t	q		m	

TABLE 1. Continued

Compd[a]	C-4	C-5	C-6	C-7	SR		R′
81	b)	b)	6.64 br d	2.76 s	1.42 t	3.25 q	7.0—8.3 m
82	b)	b)	6.67 br d	2.77 s	1.41 t	3.24 q	7.0—8.3 m
83	7.19 br s	2.38 s	6.67 dd	8.40 d	1.40 t	3.22 q	7.4—8.3 m
84	7.18 br s	2.41 s	6.68 dd	8.41 d	1.42 t	3.23 q	7.3—8.3 m
87	2.56 s	6.97 br d	6.69 t	8.38 dd	2.67 s		7.1—8.3 m
88	b)	6.97 d	2.34 s	8.32 br s	2.67 s		7.1—8.3 m
89	2.56 s	7.00 br d	6.70 t	8.41 br d	2.66 s		7.1—8.3 m
90	b)	7.01 d	2.34 s	8.34 br s	2.66 s		7.1—8.3 m
99	7.41 br d	7.28 br t	6.78 dt	8.47 d	2.67 s		2.43 s
101	7.12 br s	2.39 s	6.61 dd	8.32 d	2.64 s		2.42 s
102	8.18 br d	7.43 br t	6.90 dt	8.44 d	2.68 s		2.59 s
104	7.97 br s	2.47 s	6.73 dd	8.31 d	2.68 s		2.59 s
113	7.64 br d	7.45 br t	6.95 dt	8.49 d	2.72 s		—
114	7.60 br d	7.38 q	6.85 br d	2.79 s	2.77 s		—
115	7.39 br s	2.48 s	6.78 dd	8.37 d	2.71 s		—
120	b)	b)	6.83 dt	8.47 d	2.61 s		7.0—7.9 m
121	b)	b)	6.73 br	2.78 s	2.65 s		7.0—7.9 m
122	7.20 br s	2.31 s	6.68 dd	8.32 d	2.59 s		7.3—7.8 m
123	——6.5—7.0—— m			8.31 br d	2.58 s		—
124	6.6—7.0 m		6.48 br	2.68 s	2.61 s		—
125	6.53 br s	2.37 s	6.47 dd	8.21 d	2.59 s		—

a) The coupling constants are as follows: $J_{4,5}=9.0$, $J_{5,6}=J_{6,7}=J_{Et}=7.0$, $J_{4,6}=2.0$, and $J_{5,7}=1.0$ Hz. b) Overlapped with the phenyl proton signals.

cording to the procedure reported by us[6c] and by Yoshida *et al.*[9] Some data of new *N*-ylides are as follows: **3**, 87%, colorles needles, mp 126—127 °C. Found: C, 48.33; H, 5.10; N, 14.24%. Calcd for $C_8H_{10}N_2S_2$: C, 48.45; H, 5.08; N, 14.13%. **4**, 74%, colorless needles, mp 107—108 °C. Found: C, 48.61; H, 5.03; N, 14.03%. Calcd for $C_8H_{10}N_2S_2$: C, 48.45; H, 5.08; N, 14.13%. **6**, 75%, Colorless needles, mp 117—118 °C. Found: C, 50.93; H, 5.63; N, 13.24%. Calcd for $C_9H_{12}N_2S_2$: C 50.91; H 5.70; N, 13.19%. **7**, 47%, pale yellow needles, mp 94—95 ° C. Found: C, 46.62; H, 4.63; N, 10.85%. Calcd for $C_{10}H_{12}N_2O_2S_2$: C, 46.85; H,4.72; N, 10.93%. **8**, 82%, pale yellow needles, mp 105—107 °C. Found: C, 48.96; H, 5.09; N,10.40%. Calcd for $C_{11}H_{14}N_2O_2S_2$: C, 48.87; H, 5.22: N, 10.36%. **9**, 97%, pale yellow needles, mp 127—128 °C. Found: C, 48.58; H, 5.13: N, 10.17%. Calcd for $C_{11}H_{14}N_2O_2S_2$: C, 48.87; H 5.22; N, 10.36%. **33**, 84%, colorless needles, mp 117—118 °C. Found: C, 48.23; H, 5.08; N, 14.19%. Calcd for $C_8H_{10}N_2S_2$: C, 48.45; H, 5.08; N, 14.13%.

Preparations of Pyrazolo[1,5-a]pyridine Derivatives. *General Method A*: A chloroform solution (20 ml) of pyridinium *N*-ylide (2 mmol) was allowed to react overnight with a small excess of an alkylating agent (2.4 mmol) at room temperature. The resulting solution was then concentrated at reduced pressure and the residue was washed three times with ether to remove the remaining alkylating agent. The

almost pure pyridinium salt was dissolved again in chloroform (30 ml) and treated with potassium carbonate (5 g) at room temperature until the salt was completely consumed. (about 1 or 2 d) The reaction mixture was filtered to remove insoluble inorganic substances and the filtrate was concentrated at reduced pressure. The residue was separated by column chromatography on alumina using hexane, ether, and chloroform as eluents. Evaporation of the chloroform layer and recrystallzation of the resulting crude product from ethanol afforded pure pyrazolopyridine derivative.

B: Pyridinium iodides **96—98** and **110—112** were prepared by the reactions of pyridinium *N*-ylides **1—3** (4 mmol) with a large excess of chloride **92** or **106** (5 g) in the presence of sodium iodide (5 g) in acetone (60 ml) at room temperature for 2 d. After the evaporation of acetone and the removal of excess chloride by repeated washings with ether, the resulting salts were dissolved in chloroform (60 ml) and allowed to react with potassium carbonate (10 g) at room temperature for 3 d. Similar work-ups of the reaction mixtures provided the corresponding pyrazolopyridine derivatives.

In the reactions of pyridinium salts **11—19**, **30—32**, and **34** with base the elimination of sulfur was observed, though its quantity could not be decided because of the heterogeneous reactions. On the other hand, no evolution of hydrogen sulfide from these reaction systems could be detected. Compound **99** was converted easily to disulfide **120** by the recrystallization from ethanol. The Mass spectra of **20—22**, **26—28**, **64—68**, and **113—115** gave satisfactory values 236, 250, 250, 308, 322, 322, 300, 336, 380, 314, 376, 189, 203, and 203, for each molecular ion, respectively. These results and some properties are listed in Tables 1 and 3.

Preparations of 3-Benzoylpyrazolo[1,5-a]pyridines 120—122. General Method: A mixture of 1-aminopyridinium iodide (2 mmol) and 2-benzoyl-1,1-bis(methylthio)ethylene **119** (2 mmol) was stirred with potassium carbonate (5 g) in chloroform (30 ml) at room temperature for 2 d. The reaction mixture was then filtered to remove inorganic substances and the filtrate was concentrated at reduced pressure. The residue was separated by column chromatography (alumina) using hexane, ether, and chloroform as eluents. After the evaporation of the solvent, recrystallization of the residue from ethanol afforded 3-benzoyl-2-(methylthio)-pyrazolo[1,5-*a*]pyridine derivative. Some data except their NMR spectra (see Table 1) of these products are as follows: **120**, 93%, colorless needles, mp 104—105 °C, ν (KBr) 1605 cm^{-1} (CO). Found: C, 67.22; H, 4.48; N, 10.43%. Calcd for $C_{15}H_{12}N_2OS$: C, 67.14; H, 4.51; N, 10.44%. **121**, 91%, colorless needles, mp 126—128 °C, ν (KBr) 1605 cm^{-1} (CO). Found: C, 68.01: H, 4.90; N, 10.09%. Calcd for $C_{16}H_{14}N_2OS$: C, 68.06; H, 5.00 N, 10.09%. **122**, 93%, colorless needles, mp 161—162 °C, ν (KBr) 1601 cm^{-1} (CO). Found: C, 67.98; H, 4.98; N, 9.85%. Calcd for $C_{16}H_{14}N_2OS$: C, 68.06; H, 5.00; N,9.92%.

Acid Hydrolyses of 3-(Benzoylthio)pyrazolo[1,5-a]pyridines 64, 69, and 74. General Method: A mixture of 3-benzoylthio derivative (1 mmol) and a concentrated hydrochloric acid (10 ml) was heated at 60—80 °C in a water bath for 30 min. After cooling to room temperature, the reaction mixture was neutralized carefully with an aqueous potassium carbonate and then extracted twice with 100 ml portion of chloroform. The combined extracts were filtered through phase-separating filter paper and the resulting solution was then concentrated at reduced pressure. The residue was separated by column chromatography on alumina using hexane and ether as eluents. The evaporation of the ether layer and recrystallization of the crude crystals from a mixture of ether—hexane gave the disulfide.

These disulfides **123—125** were also formed by refluxing

Table 2. NMR data of 4,4a-dihydropyrido[1,2-*d*][1,3,4]thiadiazines

Compd[a,b]	SMe	C-4	C-4a	C-5	C-6	C-7	C-8	R′	
126 or **127**	2.45	c)	c)	5.15	5.80	4.56	6.48	1.25	4.22
(Major)	s			br d	m	br t	d	t	q
127 or **126**	2.41	c)	c)	a)	5.80	4.64	6.48	1.33	4.25
(Minor)	s				m	br t	d	t	q
128 or **129**	2.50	c)	c)	5.16	5.90	4.51	2.01	1.25	4.23
(Major)	s			br d	m	br d	s	t	q
129 or **128**	2.48	c)	c)	c)	5.90	4.62	2.01	1.33	4.28
(Minor)	s				m	br d	s	t	q
130 or **131**	2.48	c)	c)	4.94	1.70	4.46	6.51	1.24	4.22
(Major)	s			br s	s	dd	d	t	q
131 or **130**	2.46	c)	c)	c)	1.70	4.56	6.47	1.32	4.28
(Minor)	s				s	dd	d	t	q
136	2.47	3.48	1.39	5.00	5.81	4.58	2.02	1.20	4.15
	s	s	s	d	q	br d	s	t	q
137	2.43	4.58	1.57	4.87	5.70	4.60	2.08	7.1—8.2	
	s	s	s	d	q	br d	s	m	
138	2.49	3.44	1.41	5.10	6.02	4.78	2.07	—	
	s	s	s	d	q	br d	s		

a) $J_{6,7}=J_{7,8}=7.0$, $J_{5,6}=9.0$, $J_{5,7}=1.5$, $J_{Et}=7.0$ Hz. b) The ratios of major and minor isomers could not be decided because of the absence of the signals separated clearly. c) These signals could not be assigned by their overlapping with those of DBN(and its salt) and the ethoxycarbonyl group.

Table 3. Results and some properties of pyrazolo[1,5-*a*]pyridines

Compd No.	Reactants Ylide	Halide	(Salt)	Yield %	Mp θ_m/°C	$\nu_{C=O}^{KBr}$(CN)/cm^{-1}	Formula	Calcd (%) C	H	N	Found (%) C	H	N
20	**1**	**10**	(**11**)	75	102—103	1671	$C_{11}H_{12}N_2O_2S$	55.91	5.12	11.86	56.04	5.13	11.73
	1	**29**	(**30**)	83	102—103								
21	**2**	**10**	(**12**)	82	120—122	1666	$C_{12}H_{14}N_2O_2S$	57.58	5.64	11.19	57.71	5.67	11.03
	2	**29**	(**31**)	89	120—122								
22	**3**	**10**	(**13**)	79	139—140	1675	$C_{12}H_{14}N_2O_2S$	57.58	5.64	11.19	57.36	5.68	11.18
	3	**29**	(**32**)	87	139—140								
23	**4**	**10**	(**14**)	82	71—73	1690	$C_{12}H_{14}N_2O_2S$	57.58	5.64	11.19	57.41	5.64	11.14
24	**5**	**10**	(**15**)	76	64—66	1689	$C_{13}H_{16}N_2O_2S$	59.07	6.10	10.60	59.16	6.13	10.60
25	**6**	**10**	(**16**)	80	83—85	1682	$C_{13}H_{16}N_2O_2S$	59.07	6.10	10.60	58.90	6.09	10.53
26	**7**	**10**	(**17**)	72	90—91	1719 1691	$C_{14}H_{16}N_2O_4S$	54.53	5.23	9.08	54.59	5.29	8.97
27	**8**	**10**	(**18**)	48	125—126	1720 1680	$C_{15}H_{18}N_2O_4S$	55.89	5.63	8.69	55.92	5.56	8.72
28	**9**	**10**	(**19**)	35	110—111	1728 1672	$C_{15}H_{18}N_2O_4S$	55.89	5.63	8.69	55.99	5.57	8.64
35+**36**[a]	**33**	**10**	(**34**)	83	d)	1706	$C_{12}H_{14}N_2O_2S$	57.58	5.64	11.19	57.54	5.74	11.13
64	**1**	**37**	(**42**)	77	136—138	1668	$C_{15}H_{12}N_2OS_2$	59.97	4.03	9.33	60.10	4.10	9.44
65	**1**	**38**	(**43**)	87	158—160	1672	$C_{15}H_{11}N_2OS_2Cl$	53.81	3.31	8.37	53.66	3.34	8.65
66	**1**	**39**	(**44**)	80	177—179	1668	$C_{15}H_{11}N_2OS_2Br$	47.50	2.92	7.39	47.39	2.92	7.48
67	**1**	**40**	(**45**)	83	125—126	1670	$C_{16}H_{14}N_2OS_2$	61.12	4.49	8.91	60.89	4.50	9.22
68	**1**	**41**	(**46**)	73	138—141	1675	$C_{21}H_{16}N_2OS_2$	66.99	4.28	7.44	67.27	4.31	7.14
69	**2**	**37**	(**47**)	72	94—95	1667	$C_{16}H_{14}N_2OS_2$	61.12	4.49	8.91	61.00	4.41	8.82
70	**2**	**38**	(**48**)	64	136—138	1671	$C_{16}H_{13}N_2OS_2Cl$	55.08	3.76	8.03	54.91	3.72	7.95
71	**2**	**39**	(**49**)	69	154—156	1669	$C_{16}H_{13}N_2OS_2Br$	48.86	3.33	7.12	48.72	3.32	7.12
72	**2**	**40**	(**50**)	86	109—110	1663	$C_{17}H_{16}N_2OS_2$	62.17	4.91	8.53	61.94	4.93	8.45
73	**2**	**41**	(**51**)	66	148—149	1670	$C_{22}H_{18}N_2OS_2$	67.66	4.65	7.12	67.84	4.59	7.05
74	**3**	**37**	(**52**)	68	126—128	1672	$C_{16}H_{14}N_2OS_2$	61.12	4.49	8.91	61.17	4.53	9.19
75	**3**	**38**	(**53**)	66	162—164	1673	$C_{16}H_{13}N_2OS_2Cl$	55.08	3.76	8.03	54.93	3.73	7.98
76	**3**	**39**	(**54**)	79	167—170	1671	$C_{16}H_{13}N_2OS_2Br$	48.86	3.33	7.12	48.74	3.43	7.15
77	**3**	**40**	(**55**)	87	157—159	1669	$C_{17}H_{16}N_2OS_2$	62.17	4.91	8.53	61.90	5.00	8.81
78	**3**	**41**	(**56**)	58	196—197	1672	$C_{22}H_{18}N_2OS_2$	67.66	4.65	7.12	67.81	4.70	7.27
79	**4**	**37**	(**57**)	83	95—96	1673	$C_{16}H_{14}N_2OS_2$	61.12	4.49	8.91	61.30	4.56	8.85
80	**4**	**38**	(**58**)	81	117—120	1676	$C_{16}H_{13}N_2OS_2Cl$	55.08	3.76	8.03	55.24	3.87	7.76
81	**5**	**37**	(**59**)	66	115—116	1684	$C_{17}H_{16}N_2OS_2$	62.17	4.91	8.53	61.93	4.94	8.40
82	**5**	**38**	(**60**)	69	93—95	1671	$C_{17}H_{15}N_2OS_2Cl$	56.27	4.17	7.72	56.13	4.17	7.52
83	**6**	**37**	(**61**)	83	107—109	1676	$C_{17}H_{16}N_2OS_2$	62.17	4.91	8.53	62.16	4.99	8.45
84	**6**	**38**	(**62**)	83	119—121	1677	$C_{17}H_{15}N_2OS_2Cl$	56.27	4.17	7.72	56.14	4.12	7.51

87+**88**[c]	**33**	**37**	(**85**)	69	b)	1675	$C_{16}H_{14}N_2OS_2$	61.12	4.49	8.91	60.94	4.51	8.97
89+**90**[d]	**33**	**38**	(**86**)	86	b)	1670	$C_{16}H_{13}N_2OS_2Cl$	55.08	3.76	8.03	54.99	3.74	8.26
99[e]	**1**	**91**	(**93**)	62	92—94	1698	$C_{10}H_{10}N_2OS_2$	50.40	4.23	11.75	50.38	4.30	11.70
100	**2**	**91**	(**94**)	0									
101	**3**	**91**	(**95**)	76	104—105	1703	$C_{11}H_{12}N_2OS_2$	52.35	4.79	11.10	52.26	5.02	10.96
102	**1**	**92**	(**96**)	12	131—132	1639	$C_{10}H_{10}N_2OS$	58.23	4.89	13.58	58.53	4.57	13.60
103	**2**	**92**	(**97**)	0									
101+**104**[f]	**3**	**92**	(**98**)	*ca.* 25	124—126[g]	1640[g]	$C_{11}H_{12}N_2OS$[g]	59.97	5.49	12.72	60.13	5.56	12.49
113	**1**	**105**	(**107**)	32	136—137	(2218)	$C_9H_7N_3S$	57.12	3.73	22.21	57.05	3.63	22.38
	1	**106**	(**110**)	55	136—137								
114	**2**	**105**	(**108**)	38	128—129	(2215)	$C_{10}H_9N_3S$	59.09	4.46	20.67	58.93	4.36	20.93
	2	**106**	(**111**)	43	128—129								
115	**3**	**105**	(**109**)	47	134—135	(2200)	$C_{10}H_9N_3S$	59.09	4.46	20.67	58.98	4.38	20.87
	3	**106**	(**112**)	49	134—135								

a) The ratio of **35** to **36** was *ca.* 2 : 1. b) Mixture. c) The ratio of **87** to **88** was *ca.* 9 : 7. d) The ratio of **89** to **90** was *ca.* 4 : 3. e) This compound was recrystallized from chloroform–hexane at low temperature. f) The ratio of **101** to **104** was *ca.* 1 : 5. g) These physical data were those of pure 3-acetylpyrazolo[1,5-*a*]-pyridine **104**.

3-(benzoylthio)pyrazolopyridines **64**, **69**,and **74** in ethanol in the presence of an amine such as piperidine or DBU, but the reaction rate was generally slow and the separation of the disulfide from the unreacted starting material was difficult. Some data of **123**—**125** are as follows: **123**, 38%, pale yellow needles, mp 176—178 °C, ν (KBr) 757, 1362, and 1630 cm^{-1}. Found: C, 49.64; H,3.61; N, 14.31%; M^+, 390. Calcd for $C_{16}H_{14}N_4S_4$: C, 49.90; H, 3.61; N, 14.35%. **124**, 31%, pale yellow needles, mp 146—148 °C, ν (KBr) 771, 1342, and 1625 cm^{-1}. Found: C, 51.56; H, 4.21; N, 13.46%; M^+, 418. Calcd for $C_{18}H_{18}N_4S_4$: C, 51.64; H, 4.33; N, 13.38%. **125**, 45%, pale yellow needles, mp 177—178 °C, ν (KBr) 783, 1356, and 1639 cm^{-1}, Found: C, 51.82; H, 4.39; N, 13.14%; M^+, 418. Calcd for $C_{18}H_{18}N_4S_4$: C, 51.64; H, 4.33; N, 13.38%.

X-Ray Crystallography. The crystal of 3-(*p*-chlorobenzoylthio)-7-methyl-2-(methylthio)pyrazolo[1,5-*a*]pyridine **70** was grown from ethanol. A suitable crystal was mounted on a Rigaku AFC-6B diffractometer and the intensity data of $|F_o|>3\sigma|F_o|$ were colleted using Mo($K\alpha$) radiation of 0.71070 Å wave length within the range of $2\theta<55°$. Total reflections usd for the analysis were 1617. The structure was solved by the MULTAN method and the final R values was 9.1%.

The crystal data are as follows (see Fig. 2 for the bond lengths and the bond angles of this molecule): **70**, $C_{16}H_{13}N_2OS_2Cl$, F.W.=348.9, monoclinic, space group $P2_1/C$, a=16.816(6) Å, b=6.331(1) Å, c=17.026(5) Å, β=116.21(2)°, z=4, Dc=1.42 g/cm^3.

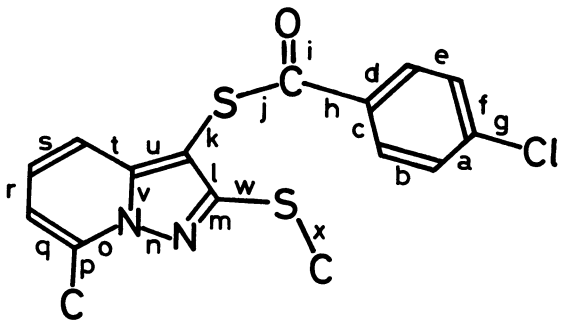


Fig. 2.

Bond lengths (Å): a=1.364(20), b=1.410(21), c=1.381(15), d=1.410(20), e=1.421(22), f=1.365(19), g=1.750(23), h=1.482(20), i=1.205(13), j=1.784(19), k=1.741(17), l=1.369(16), m=1.337(19), n=1.374(13), o=1.373(21), p=1.489(16), q=1.360(17), r=1.424(17), s=1.384(23), t=1.412(17), u=1.414(19), v=1.385(13). w=1.747(13), x=1.824(14).

Bond angles (°): ab=117.7(13), af=124.0(10), ag=117.8(12), bc=120.2(10), cd=121.3(10), ch=122.8(9), de=117.6(14), dh=115.9(13), ef=19.2(11), fg=118.2(9), hi=124.0(9), hj=114.0(11), ij=122.0(8), jk=102.9(10), kl=129.2(8), ku=124.0(10), lm=113.7(9), lu=106.1(10), lw=124.7(10), mn=103.3(9), mw=121.6(10), no=123.5(8), nv=113.0(11), op=118.0(11), oq=116.3(9), ov=123.4(11), pq=125.7(11), qr=123.2(12), rs=119.5(13) st=117.5(10), tu=136.0(9), tv=120.1(11), uv=103.9(12), wx=101.9(11).

Detections of 4,4a-Dihydropyrido[1,2-d][1,3,4]thiadiazines ***126—131.*** *General Method*: A deuteriochloroform solution (0.5 ml) of pyridinium halide (0.1 mmol) which was placed in a NMR tube was treated with two drops of DBN (about 40 mg, 0.26 mmol). The NMR spec-

trum of resulting solution which was turned instantly red was measured. However, our attempts to isolate these intermediates **126—131** from the reaction mixtures were unsuccessful because their column separations did not afford them at all but gave always only ethyl 2-(methylthio)pyrazolo[1,5-*a*]pyridine-3-carboxylates **20—22**. In addition, compounds **126—131** were completely decomposed by heating them at **50—60** °C for only a few minutes. The NMR spectral data of **126—131** are shown in Table 2.

Isolations of 4a,8-Dimethyl-4,4a-dihydropyrido[1,2-d][1,3,4]-thiadiazines 136—138. General Method: 2,6-Dimethylpyrildinium *N*-ylide **132** (424 mg, 2 mmol) was treated with bromide (3 mmol) in chloroform (20 ml) at room temperature for 1 d. The reaction mixture was then concentrated at reduced pressure and the residue was washed three times with ether to remove excess alkylating agent. The pyridinium salt was again dissolved in chloroform (15 ml) and the resulting solution was cooled to 0 °C in an ice bath. DBU (453 mg,3 mmol) was added dropwise into the solution under stirring at 0 °C and the reddish solution was immediately separated by column chromatography (two times) on alumina using chloroform as an eluent. The removal of chloroform at reduced pressure at below 40 °C afforded oils of **136—138**. However, the preparations of pure samples for the analyses were unsuccessful because of their thermal instability and the failure to their crystallization. These compounds **136—138** could be stored for about a week in the freezer but decomposed completely at room temperature for about 1 d. Some data except their NMR spectra (see Table 2) are as follow: **136**, 81%, orange oil, ν (Neat) 1738 (CO), 1630, 1368, 1150, 711 cm^{-1}. **137**, 43%, yellow oil, ν (Neat) 1681 (CO), 1491, 1370, 1210, 981 cm^{-1}. **138**, 78%, Orenge oil, ν (Neat) 2245 (CN),1648,1586,1370,1138,715 cm^{-1}.

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