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Preparation of New Nitrogen-Bridged Heterocycles. XIV.¹⁾ Further Investigation of the Desulfurization and the Rearrangement of Pyrido[1,2-*d*]-1,3,4-thiadiazine Intermediates

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The formation of pyrazolo[1,5-*a*]pyridine derivatives *via* the desulfurization and the rearrangement of pyrido[1,2-*d*]-1,3,4-thiadiazine intermediates having various substituents at the 2- and 4-positions was investigated, and the wide applicability of this approach to the syntheses of pyrazolo[1,5-*a*]pyridines was established. The substituent effect in these reactions was also clarified. The possibility of the extension of this reaction to other heterocyclic systems such as pyrido[1,2-*b*]-pyridazine and pyrido[2,1-*f*]-1,2,4-triazine was examined, but only pyridinium 1-aminide and 1,2,4-triazolo[1,5-*a*]pyridine were obtained instead of the expected heterocyclic compounds.

Keywords—desulfurization; rearrangement; pyrazolo[1,5-*a*]pyridine; pyrido[1,2-*d*]-1,3,4-thiadiazine; pyridinium 1-(thiocarbonyl)aminide; 1,2,4-triazolo[1,5-*a*]pyridine; pyridinium 1-aminide; 1-[(methylthio)methyleneamino]pyridinium bromide

Recently, we developed a new convenient method for the preparation of 2-alkylthio-3-cyano-, 3-acyl- and 3-(aroylthio)pyrazolo[1,5-*a*]pyridine derivatives, involving the desulfurization and the rearrangement of transient pyrido[1,2-*d*]-1,3,4-thiadiazines generated *in situ* by the alkaline treatment of 1-[substituted (methylthio)methyleneamino]pyridinium halides.²⁾ Mechanistically, this reaction can be considered to be the same as that described in the conversion of a 1,3,4-thiadiazinyl anion to the desulfurized pyrazole and the rearranged 5-mercaptopyrazole,³⁾ since the neutral pyrido[1,2-*d*]-1,3,4-thiadiazine (A) is a high-energy 12 π bicyclic species and has a contributing structure (B) isoelectronic with the 1,3,4-thiadiazinyl anion (C), as shown in Fig. 1.

In particular, we were interested in the generality of this reaction and the substituent effect, since there is no precedent for the migration of a group other than a hydrogen onto the sulfur atom in this type of reaction, and the factors affecting this reaction are still uncertain. In this paper we wish to report the generations of pyrido[1,2-*d*]-1,3,4-thiadiazine intermediates possessing various substituents at the 2- and 4-positions, and an examination of the behavior of the desulfurization and the rearrangement. Some attempts to extend the reaction to other heterocyclic systems such as pyrido[1,2-*b*]pyridazine and pyrido[2,1-*f*]-1,2,4-triazine are also described.

Fig. 1

Results and Discussion

Preparation of Pyridinium 1-Aminides

We selected alkyl, aryl, amino, alkoxyl groups as the 2-substituent of pyrido[1,2-*d*]-1,3,4-thiadiazine and cyano, ester, and aroyl groups as the 4-substituent, in order to examine the generality of this reaction and the substituent effect. From the nature of the reaction,²⁾ the 2-substituent is generally derived from pyridinium 1-aminide as a starting material. We prepared the corresponding pyridinium 1-(thiocarbonyl)aminides (**8—19**) in good yields from the reactions of *N*-unsubstituted pyridinium 1-aminides, generated *in situ* by the alkaline treatment of 1-aminopyridinium iodides (**1—3**), with methyl dithiocarboxylates (**4, 5**, and **7**), and thiocarbamoyl chloride (**6**) (Chart 1). The structures of these pyridinium 1-(thiocarbonyl)aminides (**8—19**) were determined on the basis of elementary analyses, spectral comparisons with other pyridinium 1-aminides,⁴⁾ and the comparison of **17** with an authentic sample.⁵⁾

Preparation and Reaction of 1-[(Substituted Methylthio)methyleneamino]pyridinium Bromides

Since the 4-substituent of the pyridothiadiazine is derived from the alkylating agent used, we employed bromoacetonitrile (**20**), ethyl bromoacetate (**21**), phenacyl bromide (**22**), and *p*-chlorophenacyl bromide (**23**) as alkylating agents for the purpose of introducing cyano, ester, and aroyl groups. Treatment of pyridinium 1-[(ethyl)thiocarbonyl]aminides (**8—10**) with alkylating agents (**20—23**) in chloroform at room temperature gave the corresponding 1-[(substituted methylthio)methyleneamino]pyridinium bromides (**24—35**) in quantitative yields. The reactions of the pyridinium salts (**24—35**) with excess anhydrous potassium carbonate in chloroform at room temperature for 1 d afforded the desulfurized 3-cyano- (**36—38**) and 3-ethoxycarbonyl-2-ethylpyrazolo[1,5-*a*]pyridines (**39—41**) and the rearranged 3-aroylethio-2-ethylpyrazolo[1,5-*a*]pyridines (**42—47**), respectively. Similarly, the alkylations of pyridinium 1-[(phenyl)thiocarbonyl]aminides (**11—13**) and 1-[(dimethylamino)thiocarbonyl]aminides (**14—16**) with **20—23** followed by the alkaline treatment of the resulting pyridinium bromides (**48—59** and **72—83**) at room temperature provided 2-phenyl- (**60—71**) and 2-(dimethylamino)pyrazolo[1,5-*a*]pyridine derivatives (**84—95**) in good yields (Chart 2). On the other hand, the reactions of pyridinium salts (**96—107**), obtained from pyridinium 1-[(ethoxy)thiocarbonyl]aminides (**17—19**) and **20—23**, with base at room temperature gave only complex mixtures and no pyrazolopyridine product could be isolated. When the alkaline treatment of pyridinium salts (**96—107**) was performed in an ice bath under stirring for 3 d, however, the expected 2-ethoxypyrazolo[1,5-*a*]pyridines (**108—113** and **120—125**) were

Chart 1

Chart 2

obtained in low yields, together with pyridinium 1-[(substituted methylthio)carbonyl]aminides (**114**—**119** and **126**—**131**). The same pyridinium 1-aminides (**114**—**119** and **126**—**131**) were also formed in good yields by keeping the corresponding salts (**96**—**107**) in chloroform at room temperature or by heating them at 50—60°C in a water bath, respectively (Chart 3).

The structures of these pyrazolo[1,5-*a*]pyridines were determined from their molecular compositions and their infrared (IR) and proton nuclear magnetic resonance (¹H-NMR) spectra. For example, the IR spectra each exhibit characteristic absorption bands at 2196—2210 cm⁻¹ (α,β-unsaturated cyano group), at 1670—1708 cm⁻¹ (α,β-unsaturated ester carbonyl group), and at 1654—1688 cm⁻¹ (aryl carbonyl group). In particular, the positions of the absorption bands due to the cyano or the carbonyl group in the 3-substituents on the pyrazolopyridine skeleton are almost the same as those of 2-(alkylthio)pyrazolopyridines reported earlier by us.²⁾ As can be seen in Table I, the chemical shifts and the signal patterns are very similar to those of 2-(alkylthio)pyrazolo[1,5-*a*]pyridines²⁾ and other pyrazolo[1,5-*a*]pyridines.^{4a,6)} Furthermore, ethyl 2-phenylpyrazolo[1,5-*a*]pyridine-3-carboxylates (**63** and **65**) were identical with authentic samples prepared independently.⁷⁾

The extent of the desulfurization and the rearrangement observed above were all the

Chart 3

same as in the case of the 2-(alkylthio)pyrazolo[1,5-*a*]pyridines described earlier by us,²⁾ and this indicates that the course of this reaction depends on only the 4-substituent in the pyridothiadiazine intermediates but not at all on the 2-substituent.

On the other hand, the structural assignment of pyridinium 1-[substituted (methylthio)carbonyl]aminides (114—119 and 126—131) was accomplished on the basis of elementary analyses and ¹H-NMR spectral inspection. In particular, the chemical shifts and the signal patterns due to the protons on the pyridine ring in the ¹H-NMR spectra (Table II) of these compounds (114—119 and 126—131) are quite different from those in the pyrazolo[1,5-*a*]pyridine derivatives (36—47, 60—71, 84—89, 108—113, and 120—125) but the same as those (Table II) of pyridinium 1-(thiocarbonyl)aminides (8—19) and other pyridinium 1-aminides.⁴⁾ The absence of ethoxy proton signals and the presence of the proton signals derived from the *S*-alkyl moiety also represent strong evidence for the proposed ylidic structure.

Attempts to Extend the Reaction to Other Heterocyclic Systems

Since the generality and wide applicability of this reaction were well established, its extension to other heterocyclic systems containing no sulfur atom was examined. Pyrido[1,2-*b*]pyridazine and pyrido[2,1-*f*]-1,2,4-triazine were selected as model compounds, and the corresponding pyridinium salts (135—138) were prepared by alkylations of pyridinium 1-vinylaminides (132 and 133)⁸⁾ and 1-imidoaminide (134)⁹⁾ with bromoacetonitrile (20) and ethyl bromoacetate (21). The alkaline treatment of these pyridinium salts (135—138), however, did not give the expected compounds (139) and/or the pyrazolopyridines formed *via* 139 at all: for example, the reaction of the salt 135 with base gave only the *N*-unsubstituted pyridinium 1-aminide (140), whose structure was confirmed by formation of its *N*-benzoyl derivative (142, 13%, mp 177—179 °C), while the similar treatment of salt 136 afforded only an intractable tarry product. On the other hand, the treatment of the salts 137 and 138 with 1,8-diazabicyclo[5.4.0]-7-undecene (DBU) yielded the same product, 7-methyl-2-phenyl-1,2,4-

TABLE I. ¹H-NMR Spectral Data for Pyrazolo[1,5-*a*]pyridines in CDCl₃

Compd. ^{a)}	C-4	C-5	C-6	C-7	R		R ₃	
36	7.75 br d	7.48 br t	7.00 dt	8.56 br d	1.42 t	2.99 q	—	
37	7.62 br d	7.47 q	6.80 br d	2.79 s	1.41 t	3.01 q	—	
38	7.49 br s	2.49 s	6.81 dd	8.41 d	1.42 t	2.99 q	—	
39	8.18 br d	7.41 br t	6.90 dt	8.51 br d	1.38 t	3.16 q	1.43 t	4.42 q
40	8.08 d	7.38 q	6.75 br d	2.77 s	1.38 t	3.18 q	1.43 t	4.42 q
41	7.93 br s	2.43 s	6.72 dd	8.37 d	1.32 t	3.10 q	1.40 t	4.39 q
42	<i>b)</i>	7.21 br t	6.81 dt	8.52 br d	1.33 t	2.89 q	7.3—8.3 m	
43	<i>b)</i>	7.09 q	6.60 br t	2.70 s	1.33 t	2.90 q	7.6—8.3 m	
44	7.18 br s	2.31 s	6.58 dd	8.36 d	1.33 t	2.85 q	7.3—8.3 m	
45	<i>b)</i>	7.23 br t	6.82 dt	8.51 br d	1.32 t	2.87 q	7.3—8.3 m	
46	7.40 d	7.18 q	6.70 br d	2.78 s	1.33 t	2.89 q	7.4—8.3 m	
47	7.20 br s	2.37 s	6.67 dd	8.39 d	1.32 t	2.83 q	7.4—8.3 m	
60	<i>b)</i>	<i>b)</i>	6.97 dt	8.54 br d	7.2—8.3 m		—	
61	<i>b)</i>	<i>b)</i>	6.83 br d	2.82 s	7.1—8.4 m		—	
62	<i>b)</i>	2.47 s	6.83 dd	8.47 d	7.3—8.3 m		—	
63	8.27 br d	<i>b)</i>	6.97 dt	8.55 br d	7.3—8.0 m		1.33 t	4.33 q
64	8.15 d	<i>b)</i>	6.78 br d	2.79 s	7.1—8.0 m		1.27 t	4.28 q
65	8.03 br d	2.47 s	6.79 dd	8.45 d	7.3—8.0 m		1.28 t	4.31 q
66	<i>b)</i>	<i>b)</i>	6.85 dt	8.56 br d	7.0—8.3 m		7.0—8.3 m	
67	<i>b)</i>	7.10 q	6.64 br d	2.75 s	7.2—8.3 m		7.2—8.3 m	
68	7.27 br s	2.42 s	6.71 dd	8.47 d	7.2—8.3 m		7.2—8.3 m	
69	<i>b)</i>	<i>b)</i>	6.85 dt	8.55 br d	7.0—8.3 m		7.0—8.3 m	
70	<i>b)</i>	<i>b)</i>	6.73 br d	2.81 s	7.0—8.3 m		7.0—8.3 m	
71	7.27 br s	2.37 s	6.73 dd	8.48 d	7.2—8.3 m		7.2—8.3 m	
84	7.0—7.5 m		6.76 dt	8.21 br d	3.18 s	—		
85	7.0—7.4 m		6.59 br d	2.62 s	3.19 s	—		
86	7.14 br s	2.36 s	6.55 dd	8.05 d	3.14 s	—		

TABLE I. (continued)

Compd. ^{a)}	C-4	C-5	C-6	C-7	R		R ₃	
87	8.03 br d	7.33 br t	6.80 dt	8.36 br d	3.09 s		1.42 t	4.39 q
88	7.91 br d	7.24 q	6.66 br d	2.67 s	3.08 s		1.40 t	4.38 q
89	7.77 br s	2.39 s	6.56 dd	8.22 d	3.06 s		1.40 t	4.36 q
90	<i>b)</i>	<i>b)</i>	6.67 dt	8.32 br d	3.13 s		7.1—8.3 m	
91	6.9—7.4 m		6.57 br d	2.70 s	3.16 s		7.4—8.3 m	
92	6.98 br s	2.32 s	6.47 dd	<i>b)</i>	3.12 s		7.4—8.3 m	
93	<i>b)</i>	<i>b)</i>	6.67 dt	8.33 br d	3.12 s		7.1—8.2 m	
94	6.8—7.3 m		6.54 br d	2.66 s	3.11 s		7.3—8.3 m	
95	6.98 br s	2.33 s	6.49 dd	8.18 d	3.11 s		7.3—8.3 m	
108	7.64 br d	7.47 br t	6.92 dt	8.38 br d	1.49 t	4.49 q	—	
109	7.1—7.7 m		6.76 br d	2.69 s	1.48 t	4.51 q	—	
110	7.29 br s	2.43 s	6.67 dd	8.16 d	1.47 t	4.42 q	—	
111	7.98 br d	7.34 br t	6.80 dt	8.28 d	1.50 t	4.49 q	1.40 t	4.37 q
112	7.88 br d	7.27 q	6.65 br d	2.65 s	1.49 t	4.52 q	1.37 t	4.37 q
113	7.80 br s	2.41 s	6.65 dd	8.19 d	1.51 t	4.49 q	1.40 t	4.38 q
120	<i>b)</i>	<i>b)</i>	6.71 dt	8.33 br d	1.45 t	4.47 q	7.0—8.3 m	
121	6.9—7.4 m		6.63 br d	2.71 s	1.46 t	4.55 q	7.3—8.3 m	
122	7.10 br s	2.36 s	6.60 dd	<i>b)</i>	1.44 t	4.47 q	7.0—8.3 m	
123	<i>b)</i>	<i>b)</i>	6.76 m	8.33 br d	1.44 t	4.47 q	7.0—8.3 m	
124	6.9—7.4 m		6.61 br d	2.69 s	1.46 t	4.53 q	7.3—8.3 m	
125	7.04 br s	2.33 s	6.55 dd	8.20 d	1.41 t	4.44 q	7.3—8.3 m	

a) The coupling constants are as follows: $J_{4,5}=9.0$, $J_{5,6}=J_{6,7}=7.0$, $J_{5,7}=2.0$, and $J_{E1}=7.0$ Hz. b) Overlapped with the phenyl proton signals.

triazolo[1,5-*a*]pyridine (**143**), in 11% and 72% yields, respectively, together with ethyl cyanoacetate (**144**) and diethyl malonate (**145**) (confirmed by gas chromatographic (GLC) monitoring of the reaction mixtures). The use of potassium carbonate as a base in the reaction of **137** also afforded the same product (**143**) in 11% yield.

Compounds **142** and **143** were identical with authentic samples.^{4c, 9)}

Reaction Mechanisms

The mechanism for the formations of 2-ethyl- (**36—47**), 2-phenyl- (**60—71**), 2-

TABLE II. ¹H-NMR Spectral Data for Pyridinium 1-Aminides in CDCl₃

Compd. ^{a)}	C-2	C-3	C-4	C-5	C-6	Others
8	8.42 br d	————	7.6—8.3 m	————	8.45 br d	1.36 t 2.85 q
9	2.61 s	————	7.5—8.2 m	————	8.28 br d	1.40 t 2.88 q
10	8.29 br d	7.63 br d	2.59 s	7.63 br d	8.29 br d	1.34 t 2.82 q
11	————	————	————	7.3—9.3 m	————	————
12	2.66 s	————	————	7.3—8.4 m	————	————
13	7.2—8.5 m	————	2.51 s	————	7.2—8.5 m	————
14	8.38 br d	————	7.4—8.2 m	————	8.38 br d	3.30 s
15	2.58 s	————	7.3—8.1 m	————	8.28 br d	3.30 s
16	8.21 br d	7.40 br d	2.50 s	7.40 br d	8.21 br d	3.29 s
17	8.69 br d	————	7.8—8.6 m	————	8.69 br d	1.41 t 4.55 q
18	2.70 s	————	7.6—8.4 m	————	8.50 br d	1.43 t 4.51 q
19	8.51 br d	7.74 br d	2.67 s	7.74 br d	8.51 br d	1.43 t 4.56 q
114	8.85 br d	————	7.5—8.1 m	————	8.85 br d	3.68 s —
115	2.73 s	————	7.3—8.3 m	————	8.64 br d	3.72 s —
116	8.62 br d	7.51 br d	2.55 s	7.51 br d	8.62 br d	3.65 s —
117	8.86 br d	————	7.5—8.2 m	————	8.86 br d	3.73 s 1.30 t 4.22 q
118	2.71 s	————	7.4—8.2 m	————	8.66 br d	3.72 s 1.27 t 4.21 q
119	8.68 br d	7.51 br d	2.56 s	7.51 br d	8.68 br d	3.71 s 1.27 t 4.21 q
126	8.83 br d	————	7.3—8.3 m	————	8.83 br d	4.37 s 7.3—8.3 m
127	2.67 s	————	7.3—8.3 m	————	8.63 br d	4.39 s 7.3—8.3 m
128	8.65 br d	<i>b)</i>	2.55 s	<i>b)</i>	8.65 br d	4.38 s 7.3—8.3 m
129	8.84 br d	————	7.3—8.3 m	————	8.84 br d	4.31 s 7.3—8.3 m
130	2.68 s	————	7.3—8.3 m	————	8.61 br d	4.32 s 7.3—8.3 m
131	8.66 br d	<i>b)</i>	2.55 s	<i>b)</i>	8.66 br d	4.33 s 7.3—8.3 m

a) The coupling constants are as follows: $J_{2,3} = J_{5,6} = 7.0$, and $J_{E1} = 7.0$ Hz. b) Overlapped with the phenyl proton signals.

dimethylamino- (**84—95**), and 2-ethoxypyrazolo[1,5-*a*]pyridines (**108—113** and **120—125**) must be the same as that proposed for the formation of 2-(alkylthio)pyrazolo[1,5-*a*]pyridine derivatives.²⁾ On the other hand, the formation of pyridinium 1-aminides (**114—119** and

Chart 4

Chart 5

126—131) from the salts (96—107) seems to proceed *via* the nucleophilic dealkylation of the corresponding pyridinium salts (96—107) by the bromide ion and not *via* hydrolysis, since these reactions could be carried out in dry chloroform, and similar dealkylations of pyridinium salts⁵⁾ and sulfonium salts¹⁰⁾ have been reported recently. Interestingly, pyridinium 1-aminides (114—119 and 126—131) could not be alkylated at all by usual alkyl halides such as 20—23 and methyl iodide even under more drastic conditions (refluxing in chloroform for a week).

The possible mechanisms of formation of pyridinium 1-aminide (140) and 1,2,4-triazolo[1,5-a]pyridine (143) are summarized in Chart 5. Pyridinium 1-aminide (140) must be

formed by the hydrolysis of the carbon–nitrogen double bond in the 1-substituent of the salt **135**, though its counterpart, malonaldehydic ester, could not be detected in the reaction mixture. The low yield of **140** and the absence of **141** in the reaction of the salt **136**, however, mean that this route is not predominant. Finally, it seems that the main route in the reactions of salts **135** and **136** can not lead to any stabilized system such as aromatic pyrazolo[1,5-*a*]pyridine. On the other hand, 1,2,4-triazolo[1,5-*a*]pyridine (**143**) should be produced *via* the initial formation of the 1,6-zwitterion (**146**) followed by the migration of the ester group to the anionic center (path b) rather than the cyclization of **146** to 4,4a-dihydropyrido[2,1-*f*]-1,2,4-triazine (**139**) (path a), and the subsequent 1,5-dipolar cyclization of **147** and the aromatization of 1,8a-dihydro-1,2,4-triazolo[1,5-*a*]pyridine (**148**) to the final product (**143**) with the elimination of active methylene compounds (**144** and **145**).

Since anionic 1,2-sigmatropic suprafacial shift in this mechanism is a symmetry forbidden process,¹¹⁾ an aziridine intermediate may be involved *via* the nucleophilic attack of the anionic center on the ester carbonyl carbon in **146**. However, it is still uncertain why the ester rearrangement (path b) took place prior to the 1,6-cyclization (path a) to **139**.

Experimental¹²⁾

Pyridinium 1-Aminides (8–19 and 132–134)—General Method A: An ethanolic solution (60 ml) of 1-aminopyridinium iodide (10 mmol) and methyl dithiopropionate (**4**, 12 mmol)¹³⁾ or *N,N*-dimethylthiocarbamoyl chloride (**6**, 12 mmol) was treated with ethanolic sodium ethoxide (10 mmol in 10 ml of ethanol or 20 mmol in 20 ml of ethanol) under stirring at room temperature for 1 d. The resulting solution was filtered to remove insoluble inorganic substances and the filtrate was concentrated under reduced pressure. The residue was separated by column chromatography on alumina using ether and chloroform as eluents, and the chloroform layer was concentrated under reduced pressure. The crude pyridinium 1-aminide thus obtained was purified by recrystallization from chloroform–

TABLE III. Some Data for Pyridinium 1-(Thiocarbonyl)aminides

Compd. No.	Reactants	Yield (%)	mp (°C)	$\nu_{\max}^{\text{KBr}}$ cm ⁻¹	Formula	Analysis (%)		
						Calcd (Found)		
						C	H	N
8	1 4	62	116–118	1421 1169	C ₈ H ₁₀ N ₂ S	<i>a)</i>		
9	2 4	64	115–116	1425 1170	C ₉ H ₁₂ N ₂ S	<i>a)</i>		
10	3 4	72	114–116	1406 1164	C ₉ H ₁₂ N ₂ S	<i>a)</i>		
11	1 5	75	152–153	1382 986	C ₁₂ H ₁₀ N ₂ S	67.26	4.70	13.07
						(67.30)	4.53	(13.07)
12	2 5	76	110–112	1400 982	C ₁₃ H ₁₂ N ₂ S	68.39	5.30	12.27
						(68.18)	5.55	(12.33)
13	3 5	96	135–137	1382 988	C ₁₃ H ₁₂ N ₂ S	68.39	5.30	12.27
						(68.31)	5.34	(12.31)
14	1 6	70	137–138	1325 1114	C ₈ H ₁₁ N ₃ S	53.01	6.12	23.18
						(53.32)	6.11	(22.88)
15	2 6	87	98–99	1337 1117	C ₉ H ₁₃ N ₃ S	55.35	6.71	21.52
						(55.25)	6.67	(21.66)
16	3 6	88	136–137	1330 1103	C ₉ H ₁₃ N ₃ S	55.35	6.71	21.52
						(55.51)	6.79	(21.28)
17	1 7	92	129–130 ^{b)}	1401 1199	Known compound ^{b)}			
18	2 7	93	105–106	1434 1200	C ₉ H ₁₂ N ₂ OS	54.79	6.13	14.20
						(54.96)	6.05	(14.36)
19	3 7	99	135–136	1411 1182	C ₉ H ₁₂ N ₂ OS	54.79	6.13	14.20
						(54.98)	6.30	(14.34)

a) Elemental analysis could not be performed because the compound sublimed readily. *b)* 130–131 °C, see ref. 5.

TABLE IV. Some Data for Pyrazolo[1,5-*a*]pyridines

Product ^{a)} No.	Salt (S.M. ^{b)})	Yield (%)	mp (°C)	$\nu_{\max}^{\text{KBr}}$ cm ⁻¹	Formula	Analysis (%) Calcd (Found)		
						C	H	N
36	24 (8, 20)	87	74—76	2206	C ₁₀ H ₉ N ₃	70.16 (70.17)	5.30 5.21	24.54 24.63)
37	25 (9, 20)	79	80—82	2201	C ₁₁ H ₁₁ N ₃	71.33 (71.46)	5.99 6.01	22.69 22.54)
38	26 (10, 20)	89	74—76	2208	C ₁₁ H ₁₁ N ₃	71.33 (71.03)	5.99 6.12	22.69 22.86)
39	27 (8, 21)	92	95—97	1670	C ₁₂ H ₁₄ N ₂ O ₂	66.04 (66.23)	6.47 6.56	12.84 12.55)
40	28 (9, 21)	81	54—56	1685	C ₁₃ H ₁₆ N ₂ O ₂	67.22 (67.14)	6.94 7.05	12.06 12.03)
41	29 (10, 21)	85	83—85	1690	C ₁₃ H ₁₆ N ₂ O ₂	67.22 (67.30)	6.94 6.95	12.06 11.97)
42	30 (8, 22)	71	109—111	1675	C ₁₆ H ₁₄ N ₂ OS	68.06 (67.90)	5.00 5.13	9.92 9.95)
43	31 (9, 22)	68	116—118	1660	C ₁₇ H ₁₆ N ₂ OS	^{c)}		
44	32 (10, 22)	79	106—108	1676	C ₁₇ H ₁₆ N ₂ OS	68.89 (68.96)	5.44 5.58	9.45 9.37)
45	33 (8, 23)	78	136—137	1688	C ₁₆ H ₁₃ ClN ₂ OS	60.66 (60.67)	4.14 4.03	8.84 8.94)
46	34 (9, 23)	75	97—98	1671	C ₁₇ H ₁₅ ClN ₂ OS	61.72 (61.69)	4.57 4.64	8.47 8.43)
47	35 (10, 23)	71	111—113	1672	C ₁₇ H ₁₅ ClN ₂ OS	61.72 (61.47)	4.57 4.67	8.47 8.62)
60	48 (11, 20)	90	143—145	2210	C ₁₄ H ₉ N ₃	76.70 (76.71)	4.14 4.14	19.17 19.26)
61	49 (12, 20)	91	96—97	2196	C ₁₅ H ₁₁ N ₃	77.23 (77.29)	4.75 4.66	18.01 18.04)
62	50 (13, 20)	96	143—145	2202	C ₁₅ H ₁₁ N ₃	77.23 (77.40)	4.75 4.60	18.01 17.76)
63	51 (11, 21)	97	82—84 ^{d)}	1700	Known compound ^{d)}			
64	52 (12, 21)	95	97—98	1675	C ₁₇ H ₁₆ N ₂ O ₂	72.84 (72.82)	5.75 5.71	9.99 10.05)
65	53 (13, 21)	78	90—91 ^{e)}	1708	Known compound ^{e)}			
66	54 (11, 22)	67	97—99	1670	C ₂₀ H ₁₄ N ₂ OS	72.70 (72.68)	4.27 4.27	8.48 8.66)
67	55 (12, 22)	65	79—81	1675	C ₂₁ H ₁₆ N ₂ OS	73.23 (73.07)	4.68 4.70	8.13 8.27)
68	56 (13, 22)	73	128—129	1673	C ₂₁ H ₁₆ N ₂ OS	73.23 (73.27)	4.68 4.67	8.13 8.10)
69	57 (11, 23)	80	141—143	1673	C ₂₀ H ₁₃ ClN ₂ OS	65.84 (65.79)	3.59 3.62	7.68 7.70)
70	58 (12, 23)	72	86—88	1671	C ₂₁ H ₁₅ ClN ₂ OS	66.57 (66.61)	3.99 4.20	7.39 7.24)
71	59 (13, 23)	67	172—174	1654	C ₂₁ H ₁₅ ClN ₂ OS	66.57 (66.87)	3.99 3.96	7.39 7.13)
84	72 (14, 20)	86	127—128	2200	C ₁₀ H ₁₀ N ₄	64.50 (64.55)	5.41 5.59	30.09 29.86)
85	73 (15, 20)	75	127	2199	C ₁₁ H ₁₂ N ₄	65.98 (65.90)	6.04 5.89	27.98 28.20)
86	74 (13, 21)	85	121—123	2200	C ₁₁ H ₁₂ N ₄	65.98 (65.79)	6.04 5.94	27.98 28.27)

TABLE IV. (continued)

Product ^{a)} No.	Salt (S.M. ^{b)})	Yield (%)	mp (°C)	$\nu_{\max}^{\text{KBr}} \text{ cm}^{-1}$	Formula	Analysis (%)		
						Calcd (Found)		
						C	H	N
87	75 (14, 21)	93	79—80	1686	C ₁₂ H ₁₅ N ₃ O ₂	61.79 (61.56)	6.48 (6.53)	18.01 (18.19)
88	76 (15, 21)	88	78—79	1681	C ₁₃ H ₁₇ N ₃ O ₂	63.14 (62.89)	6.93 (6.91)	16.99 (17.27)
89	77 (16, 21)	82	81—83	1673	C ₁₃ H ₁₇ N ₃ O ₂	63.14 (63.17)	6.93 (7.02)	16.99 (16.87)
90	78 (14, 22)	65	125—127	1675	C ₁₆ H ₁₅ N ₃ OS	64.62 (64.60)	5.08 (5.10)	14.13 (14.12)
91	79 (15, 22)	78	102—103	1672	C ₁₇ H ₁₇ N ₃ OS	65.57 (65.77)	5.50 (5.49)	13.49 (13.30)
92	80 (16, 22)	83	129—131	1670	C ₁₇ H ₁₇ N ₃ OS	65.57 (65.54)	5.50 (5.45)	13.49 (13.57)
93	81 (14, 23)	76	138—140	1675	C ₁₆ H ₁₄ ClN ₃ OS	57.91 (57.69)	4.25 (4.27)	12.66 (12.87)
94	82 (15, 23)	73	140—142	1670	C ₁₇ H ₁₆ ClN ₃ OS	59.04 (58.74)	4.66 (4.74)	12.15 (12.37)
95	83 (16, 23)	84	148—149	1672	C ₁₇ H ₁₆ ClN ₃ OS	59.04 (58.74)	4.66 (4.84)	12.15 (12.37)
108 (114)	96 (17, 20)	26 (6)	126—127	2205	C ₁₀ H ₉ N ₃ O	64.16 (63.98)	4.85 (4.93)	22.45 (22.56)
109 (115)	97 (18, 20)	22 (34)	109—111	2203	C ₁₁ H ₁₁ N ₃ O	65.66 (65.43)	5.51 (5.56)	20.88 (21.06)
110 (116)	98 (19, 20)	22 (36)	101—103	2207	C ₁₁ H ₁₁ N ₃ O	65.66 (65.64)	5.51 (5.68)	20.88 (20.73)
111 (117)	99 (17, 21)	37 (33)	85—86	1705	C ₁₂ H ₁₄ N ₂ O ₃	61.53 (65.35)	6.02 (6.03)	11.96 (11.67)
112 (118)	100 (18, 21)	27 (18)	87—89	1703	C ₁₃ H ₁₆ N ₂ O ₃	62.89 (63.17)	6.50 (6.48)	11.28 (11.02)
113 (119)	101 (19, 21)	33 (29)	63—64	1697	C ₁₃ H ₁₆ N ₂ O ₃	62.89 (62.60)	6.50 (6.39)	11.28 (11.05)
120 (126)	102 (17, 22)	36 (13)	82—84	1671	C ₁₆ H ₁₄ N ₂ O ₂ S	64.41 (64.46)	4.73 (4.72)	9.39 (9.21)
121 (127)	103 (18, 22)	34 (24)	95—97	1672	C ₁₇ H ₁₆ N ₂ O ₂ S	65.36 (65.39)	5.16 (5.26)	8.97 (9.03)
122 (128)	104 (19, 22)	33 (20)	89—90	1671	C ₁₇ H ₁₆ N ₂ O ₂ S	65.36 (65.52)	5.16 (5.15)	8.97 (8.82)
123 (129)	105 (17, 23)	48 (35)	136—138	1669	C ₁₆ H ₁₃ ClN ₂ O ₂ S	57.74 (57.98)	3.94 (3.78)	8.42 (8.34)
124 (130)	106 (18, 23)	22 (40)	137—139	1674	C ₁₇ H ₁₅ ClN ₂ O ₂ S	58.87 (58.77)	4.36 (4.28)	8.08 (8.22)
125 (131)	107 (19, 23)	39 (30)	116—118	1670	C ₁₇ H ₁₅ ClN ₂ O ₂ S	58.87 (58.86)	4.36 (4.31)	8.08 (8.14)

a) Physical and analytical data for pyridinium 1-aminides (114—119 and 126—131) are listed in Table V. b) Starting materials. c) The elementary analysis of this compound could not be performed because it sublimed readily. d) 73—75 °C, see ref. 6. e) 88—90 °C, see ref. 6.

ether. Pyridinium 1-(thiocarbonyl)aminides (8—10 and 14—16) were prepared by this method.

General Method B: An ethanolic solution (60 ml) of 1-aminopyridinium iodide (10 mmol) and methyl dithiobenzoate¹³⁾ (5, 12 mmol) or methyl xanthogenate (7, 12 mmol)⁵⁾ was treated with anhydrous potassium carbonate (10 g) as a base at room temperature for 1 d under stirring. The isolation and the purification of pyridinium 1-aminide from the reaction mixture were accomplished according to the procedure mentioned in method A. By this method, pyridinium 1-(thiocarbonyl)aminides (11—13 and 17—19) were prepared.

These pyridinium 1-(thiocarbonyl)aminides were obtained as colorless prisms (**8**—**10**) or colorless needles (**11**—**19**), and compound **17** was identical with an authentic sample.⁵⁾ Some data for these compounds (**8**—**19**) are listed in Tables II and III.

On the other hand, pyridinium 1-vinylaminides (**132** and **133**) and 1-imidoylaminide (**134**) were prepared according to the literature.^{8,9)}

1-[(Substituted Methylthio)methyleneamino]pyridinium Bromides (24—35, 48—59, 72—83, and 96—107)—General Method: A chloroform solution (20 ml) of pyridinium 1-aminide (2 mmol) and an alkylating agent (2.5 mmol) such as bromoacetonitrile (**20**), ethyl bromoacetate (**21**), phenacyl bromide (**22**), or *p*-chlorophenacyl bromide (**23**) was kept at room temperature for 1—10 d until the pyridinium 1-aminide employed here was completely consumed (determined by thin layer chromatographic (TLC) monitoring). The resulting solution was concentrated under reduced pressure and the residue was washed three times with ether to remove the excess alkylating agent. Since all of the pyridinium salts were obtained quantitatively in an almost pure state, they were used directly for a subsequent reaction without further purification.

2-Ethyl- (36—47), 2-Phenyl- (60—71), 2-Dimethylamino- (84—95), and 2-Ethoxypyrazolo[1,5-*a*]pyridines (108—113 and 120—125)—General Method A: Pyridinium salt (2 mmol) was dissolved in chloroform (40 ml) and anhydrous potassium carbonate (5 g) was added. The reaction solution was stirred at room temperature for 1 d and then filtered to remove inorganic substances. The filtrate was concentrated under reduced pressure and the residue was separated by column chromatography (alumina) using hexane, ether, and chloroform as eluents. The combined ether and chloroform layer was concentrated under reduced pressure and the crude pyrazolopyridine was recrystallized from ethanol. By this route, 2-ethyl (**36**—**47**), 2-phenyl- (**60**—**71**), and 2-(dimethylamino)pyrazolo-[1,5-*a*]pyridines (**84**—**95**) were prepared.

General Method B: A chloroform solution (40 ml) of pyridinium salt (2 mmol) was treated with anhydrous potassium carbonate (5 g) in an ice bath under stirring for 3 d. Work-up of the resulting reaction mixture was carried out according to the procedure described in general method A. By this method, 2-ethoxypyrazolo[1,5-*a*]pyridines (**108**—**113** and **120**—**125**) were formed together with pyridinium 1-[(substituted methylthio)carbonyl]aminides (**114**—**119** and **126**—**131**).

TABLE V. Some Data for Pyridinium 1-Aminides

Compd.	Salt	Yield (%)	mp (°C)	$\nu_{\max}^{\text{KBr}}$ cm ⁻¹	Formula	Analysis (%)		
						Calcd	Found	
						C	H	N
114	96	79	130—132	2233 1603	C ₈ H ₇ N ₃ OS	49.73 (49.47)	3.65 3.57	21.75 21.63
115	97	99	87—89	2241 1609	C ₉ H ₉ N ₃ OS	52.16 (52.47)	4.38 4.46	20.28 20.02
116	98	100	156—157	2238 1605	C ₉ H ₉ N ₃ OS	52.16 (51.87)	4.38 4.32	20.28 20.33
117	99	80	61—62	1729 1603	C ₁₀ H ₁₂ N ₂ O ₃ S	49.99 (50.20)	5.03 4.84	11.66 11.64
118	100	95	58—59	1734 1601	C ₁₁ H ₁₄ N ₂ O ₃ S	51.95 (51.65)	5.55 5.47	11.02 11.30
119	101	89	122—123	1741 1609	C ₁₁ H ₁₄ N ₂ O ₃ S	51.95 (51.73)	5.55 5.47	11.02 11.32
126	102	83	142—143	1690 1600	C ₁₄ H ₁₂ N ₂ O ₂ S	61.75 (61.74)	4.44 4.50	10.29 10.24
127	103	93	146—148 ^{a)}	1682 1594 ^{b)}	C ₂₁ H ₁₇ N ₅ O ₉ S ^{a)}	48.93 (48.71)	3.32 3.25	13.59 13.43
128	104	77	139—140	1690 1598	C ₁₅ H ₁₄ N ₂ O ₂ S	62.92 (63.21)	4.93 4.88	9.78 9.48
129	105	87	125—126	1684 1580	C ₁₄ H ₁₁ ClN ₂ O ₂ S	54.81 (54.71)	3.61 3.60	9.13 9.19
130	106	63	113—114	1693 1598	C ₁₅ H ₁₃ ClN ₂ O ₂ S	56.16 (55.89)	4.08 4.03	8.73 8.53
131	107	82	138—140	1690 1601	C ₁₅ H ₁₃ ClN ₂ O ₂ S	56.16 (56.00)	4.08 4.02	8.73 8.84

a) Its picrate. b) Neat.

The application of method A to 1-(ethoxymethyleneamino)pyridinium bromides (**96**—**107**) gave only small amounts of pyridinium 1-aminides (**114**—**119** and **126**—**131**); the desulfurized 2-ethoxypyrazolopyridines (**108**—**113**) and the rearranged products, 2-arylthio-2-ethoxypyrazolopyridines (**120**—**125**), could not be obtained.

The products were obtained as colorless needles (**36**—**41**, **44**, **60**—**68**, **84**—**89**, and **108**—**113**) or pale yellow needles (**42**, **43**, **45**—**47**, **69**—**71**, **90**—**95**, and **120**—**125**) and some data for the products other than pyridinium 1-aminides (**114**—**119** and **126**—**131**, see Tables II and V) are summarized in Tables I and IV.

Pyridinium 1-[(Substituted (Methylthio)carbonyl)aminides (114**—**119** and **126**—**131**)**—General Method: A chloroform solution (30 ml) of pyridinium salt (2 mmol) was heated at 50—60 °C in a water bath until the spot of the salt had completely disappeared (about 5—10 d, by TLC monitoring). The reaction mixtures were purified by work-up as mentioned above to afford the corresponding pyridinium 1-aminides (**117**—**119** and **126**—**131**). On the other hand, the reactions of pyridinium salts (**96**—**98**) possessing a cyano group could be accomplished only by keeping them at room temperature for 2 d.

These compounds were obtained as colorless needles (**114**—**117**, **126**, **128**, **129**, and **131**) and colorless prisms (**118**, **119**, and **130**) from chloroform–ether. Some data are summarized in Tables II and V.

1-Propylideneamino- (135** and **136**) and 1-(Aminomethyleneamino)pyridinium Bromides (**137** and **138**)**—Pyridinium 1-vinylaminides (**132** and **133**) and 1-imidoilaminide (**134**) did not react at all with alkylating agents such as **20**—**23** under the conditions described for the preparations of 1-[(substituted methylthio)methyleneamino]-pyridinium bromides. However, the alkylations of **132**—**134** (2 mmol) with **20** or **21** (10 mmol) were accomplished in refluxing chloroform to afford the corresponding pyridinium salts (**135**—**138**) in quantitative yields. These salts were used in the next reactions without further purification.

Pyridinium 1-Aminide and Pyridinium 1-Benzoylaminide—A chloroform solution (30 ml) of 1-propylideneaminopyridinium bromide (**135**) (2 mmol) was treated with anhydrous potassium carbonate (5 g) under stirring at room temperature for 3 h. The reaction solution gradually turned blue, indicating the generation of pyridinium 1-aminide (**140**). When benzoyl chloride (0.28 g, 2 mmol) was added to the blue solution, the color changed to red. The solution was stirred for a further 2 h and then filtered. The filtrate was concentrated and the residual oil was separated by column chromatography on alumina using ether and chloroform. The chloroform layer was concentrated and recrystallization of the residue from ether–chloroform gave pyridinium 1-benzoylaminide (**142**, 52 mg, 13%, mp 177—179 °C (lit.^{4c}) 179—180.5 °C)). Compound **142** was identical with an authentic samples.^{4c})

On the other hand, the reaction of the salt **136** with base afforded only a polymeric tar and no significant product could be isolated.

1,2,4-Triazol[1,5-a]pyridine—General Method: A chloroform solution (30 ml) of 1-(aminomethyleneamino)-pyridinium bromide (2 mmol) was treated with DBU (0.30 g, 2 mmol) under stirring at room temperature for 1 d and the dark brown solution was concentrated under reduced pressure. The residue was separated by column chromatography on alumina using hexane and ether. The ether layer was concentrated and recrystallization of the residue from hexane gave 7-methyl-2-phenyl-1,2,4-triazolo[1,5-a]pyridine (**143**, mp 140—142 °C (lit.⁹) 140—142 °C)). Concentration of the hexane layer yielded an active methylene compound **144** or **145** which could be identified by GLC monitoring.

By this method, **143** was formed in 11% and 72% yields from the salts **137** and **138**, respectively. In the reaction of **137** with potassium carbonate as a base, triazolopyridine (**143**) was obtained in 11% yield.

References and Notes

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