Preparation of New Nitrogen-Bridged Heterocycles. 18.[1] Facile Formations of 3-Arylpyrazolo[1,5-*a*]pyridines and 1-Arylindolizines

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The alkaline treatment of 1-[(substituted benzylthio)methyleneamino]pyridinium and 1-[2-(substituted benzylthio)vinyl]pyridinium bromides possessing an electron-withdrawing substituent such as a nitro or cyano group in the presence or absence of a dehydrogenating agent afforded the corresponding 3-arylpyrazolo[1,5-*a*]-pyridines and 1-arylindolizines in moderate to good yields, while the reactions of the parent pyridinium salts and those having an electron-releasing group did not produce any significant products. The mode of the reaction, a ring contraction-desulfurization, is the same as that observed in related monocyclic species.

In a series of papers,[1,2] we have described convenient syntheses of various indolizines and pyrazolo[1,5-*a*]pyridines from the reactions of 1-[2-(substituted methylthio)vinyl]pyridinium and 1-[(substituted methylthio)methyleneamino]pyridinium halides with base in the presence or absence of a dehydrogenating agent. In addition, we stated that transient bicyclic intermediates such as **A** having a 12π system (see Fig. 1) are involved in these reactions and that their rearrangement and desulfurization aptitudes to give the corresponding heteroarmatics depend predominantly on the class of the substituent (R′). On the other hand, it is well-documented that the monocyclic 1,3,4-thiadiazinyl anion and related compounds such as **B** afforded only the desulfurized pyrazoles or pyrroles unless the substituent (R′) is hydrogen.[3] Since their substituents (R′) in both species **A** and **B** are not the same and there are some differences between their reactivities, however, it is still doubtful to conclude their mechanistic similarity. Therefore, it is worthwhile to introduce the same type of groups (R′=aryl group) in our bicyclic system **A** and to compare their reactivity with that of the monocyclic system **B**. In this paper we wish to report the generation of 4-arylpyrido[1,2-*d*]-1,3,4-thiadiazine and 1-arylpyrido[2,1-*c*]-1,4-thiazine intermediates and their transformations to desulfurized 3-arylpyrazolo[1,5-*a*]pyridines and 1-arylindolizines.

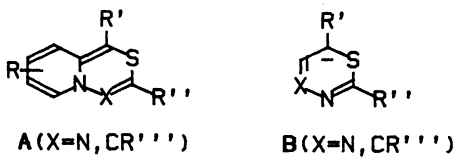
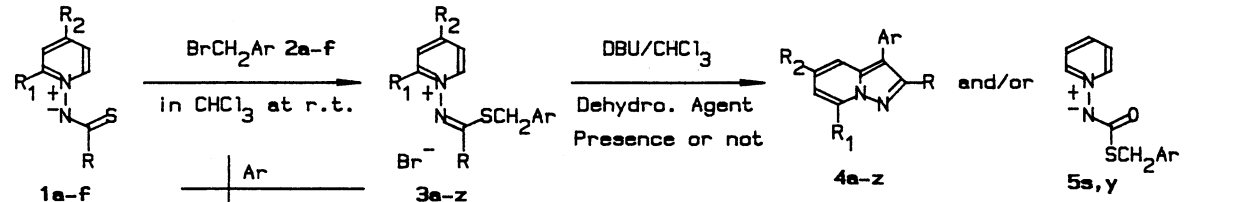


Fig. 1.

Results and Discussion

Preparations of 3-Arylpyrazolo[1,5-*a*]pyridines and 1-Arylindolizines. According to the procedure described in the syntheses of 3-cyano-, 3-ethoxycarbonyl-, and 3-aroylthiopyrazolo[1,5-*a*]pyridines,[2a,c,d] we examined first the reactions of 1-[(benzylthio)methyleneamino]pyridinium (**3a**) and 1-[(4-methylbenzylthio)-methyleneamino]pyridinium bromide (**3b**), readily obtainable from the *S*-alkylation of *N*-(1-pyridinio)-[(methylthio)thiocarbonyl]aminide (**1a**) with benzyl bromide (**2a**) and 4-methylbenzyl bromide (**2b**), in the presence of potassium carbonate in chloroform at room temperature. However, the expected heterocyclic products, 2-methylthio-3-phenyl- (**4a**) and 2-methylthio-3-(4-methylphenyl)pyrazolo[1,5-*a*]pyridine (**4b**), could not be detected. Similarly, the uses of other bases such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) or sodium hydride instead of potassium carbonate and of a dehydrogenating agent such as 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ), chloranil, or lead tetraacetate in these reactions afforded always intractable tarry materials and no significant product could be isolated from them.[4] Since the inaccessibility of these heterocycles **4a, b** was ascribed to the lack of the acidity of the benzyl proton, we focused our attention on the reactions of pyridinium salts possessing a benzyl group activated with an electron-withdrawing group. As expected, the treatment of 1-[(2-nitrobenzylthio)-methyleneamino]pyridinium bromides (**3c—h**) with DBU followed by the addition of chloranil or DDQ to the resulting reaction solutions at 0 °C gave the corresponding 3-(2-nitrophenyl)pyrazolo[1,5-*a*]pyridine derivatives (**4c—h**) in 46—89% yields, respectively. Similar reactions of 1-[(4-nitrobenzylthio)-(**3i—n**), 1-[(2-cyanobenzylthio)- (**3o—t**), and 1-[(4-cyanobenzylthio)-methyleneamino]pyridinium bromides (**3u—z**) in the presence or absence of a dehydrogenating agent afforded 3-arylpyrazolo[1,5-*a*]pyridines derivatives (**4i—z**) in considerable yields. In all cases, the possible alternatives, 3-(arylthio)pyrazolo[1,5-*a*]pyridines such as **6**, were not formed. In the reactions of the salts **3s, y**, *N*-(1-pyridinio)-[1-(2-cyanobenzylthio)-(**5s**) and 1-[1-(4-cyanobenzylthio)carbonyl]aminide (**5y**) were also formed in 14 and 24% yields together with pyrazolopyridines **4s** (34%) and **4y** (29%) (Scheme 1).

On the other hand, similar treatment of 1-[2-(benzylthio)-(**8a**) and 1-[2-(4-methylbenzylthio)vinyl]-pyridinium bromide (**8b**) prepared from 1-(1-pyridinio)-



1a-f

	R_1	R_2	R
1a	H	H	SMe
1b	Me	H	SMe
1c	H	Me	SMe
1d	H	H	Ph
1e	H	H	OEt
1f	H	H	NMe_2

	Ar
2a	Ph
2b	C_6H_4Me-*p*
2c	$C_6H_4NO_2$-*o*
2d	$C_6H_4NO_2$-*p*
2e	C_6H_4CN-*o*
2f	C_6H_4CN-*p*

6

	Ar
5s	C_6H_4CN-*o*
5y	C_6H_4CN-*p*

3a-z

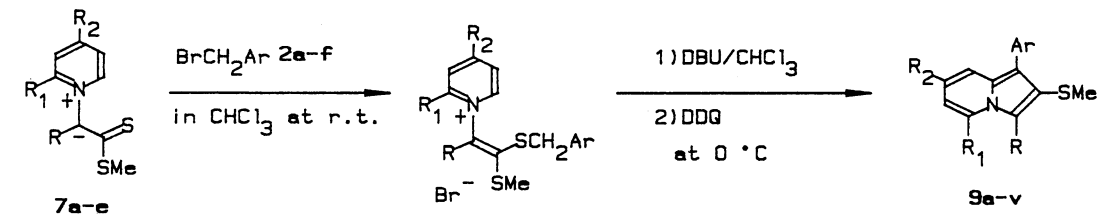
Prod.	Salt	R_1	R_2	R	Ar
(4a)	3a	H	H	SMe	Ph
(4b)	3b	H	H	SMe	C_6H_4Me-*p*
4c	3c	H	H	SMe	$C_6H_4NO_2$-*o*
4d	3d	Me	H	SMe	$C_6H_4NO_2$-*o*
4e	3e	H	Me	SMe	$C_6H_4NO_2$-*o*
4f	3f	H	H	Ph	$C_6H_4NO_2$-*o*
4g	3g	H	H	OEt	$C_6H_4NO_2$-*o*
4h	3h	H	H	NMe_2	$C_6H_4NO_2$-*o*
4i	3i	H	H	SMe	$C_6H_4NO_2$-*p*
4j	3j	Me	H	SMe	$C_6H_4NO_2$-*p*
4k	3k	H	Me	SMe	$C_6H_4NO_2$-*p*
4l	3l	H	H	Ph	$C_6H_4NO_2$-*p*
4m	3m	H	H	OEt	$C_6H_4NO_2$-*p*

4a-z

Prod.	Salt	R_1	R_2	R	Ar
4n	3n	H	H	NMe_2	$C_6H_4NO_2$-*p*
4o	3o	H	H	SMe	C_6H_4CN-*o*
4p	3p	Me	H	SMe	C_6H_4CN-*o*
4q	3q	H	Me	SMe	C_6H_4CN-*o*
4r	3r	H	H	Ph	C_6H_4CN-*o*
4s(+5s)	3s	H	H	OEt	C_6H_4CN-*o*
4t	3t	H	H	NMe_2	C_6H_4CN-*o*
4u	3u	H	H	SMe	C_6H_4CN-*p*
4v	3v	Me	H	SMe	C_6H_4CN-*p*
4w	3w	H	Me	SMe	C_6H_4CN-*p*
4x	3x	H	H	Ph	C_6H_4CN-*p*
4y(+5y)	3y	H	H	OEt	C_6H_4CN-*p*
4z	3z	H	H	NMe_2	C_6H_4CN-*p*

5s,y

Scheme 1.



7a-e

	R_1	R_2	R
7a	H	H	COOEt
7b	Me	H	COOEt
7c	H	Me	COOEt
7d	H	H	CN
7e	H	H	COPh

8a-v

Prod.	Salt	R_1	R_2	R	Ar
(9a)	8a	H	H	COOEt	Ph
(9b)	8b	H	H	COOEt	C_6H_4Me-*p*
9c	8c	H	H	COOEt	$C_6H_4NO_2$-*o*
9d	8d	Me	H	COOEt	$C_6H_4NO_2$-*o*
9e	8e	H	Me	COOEt	$C_6H_4NO_2$-*o*
9f	8f	H	H	CN	$C_6H_4NO_2$-*o*
9g	8g	H	H	COPh	$C_6H_4NO_2$-*o*
9h	8h	H	H	COOEt	$C_6H_4NO_2$-*p*
9i	8i	Me	H	COOEt	$C_6H_4NO_2$-*p*
9j	8j	H	Me	COOEt	$C_6H_4NO_2$-*p*
9k	8k	H	H	CN	$C_6H_4NO_2$-*p*

9a-v

Prod.	Salt	R_1	R_2	R	Ar
9l	8l	H	H	COPh	$C_6H_4NO_2$-*p*
9m	8m	H	H	COOEt	C_6H_4CN-*o*
9n	8n	Me	H	COOEt	C_6H_4CN-*o*
9o	8o	H	Me	COOEt	C_6H_4CN-*o*
9p	8p	H	H	CN	C_6H_4CN-*o*
9q	8q	H	H	COPh	C_6H_4CN-*o*
9r	8r	H	H	COOEt	C_6H_4CN-*p*
9s	8s	Me	H	COOEt	C_6H_4CN-*p*
9t	8t	H	Me	COOEt	C_6H_4CN-*p*
9u	8u	H	H	CN	C_6H_4CN-*p*
9v	8v	H	H	COPh	C_6H_4CN-*p*

Scheme 2.

[(methylthio)thiocarbonyl]methylide (**7a**) and benzyl bromides (**2a, b**) did not afford any products, but those of pyridinium salts **8c—v** obtained from methylides **7a—e** and bromides **2c—f** gave the corresponding 1-aryl-2-(methylthio)indolizine dervatives (**9c—v**) in moderate yields, respectively (Scheme 2).

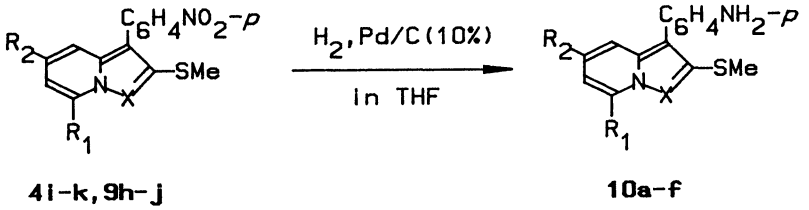
The structures of 3-arylpyrazolo[1,5-*a*]pyridines (**4c—z**), and 1-arylindolizines (**9c—v**) were determined mainly by their elemental analyses and their IR and ^{1}H NMR spectral inspections. For example, the elemental analyses of pyrazolopyridines **4c—z** and indolizines **9c, e—m, o—v** were in good accord with the proposed compositions but not with their arylthio analogs such as **6**. The chemical shifts and signal

patterns of the pyridine moiety in the ^{1}H NMR spectra (see Tables 1 and 2) of compounds **4c—z** and **9c—v** were similar to those of various pyrazolo[1,5-*a*]pyridine and indolizine derivatives previously reported.[1,2,5] The IR spectra of products **4c—n** and **9c—l** showed two characteristic nitro absorption bands at near 1510 and 1340 cm^{-1} and compounds **4o—z** and **9m—v** exhibited a cyano absorption band at near 2220 cm^{-1}. The structures of *N*-(1-pyridinio)[1-(substituted benzylthio)carbonyl]aminides (**5s, y**) were established by their spectral inspection and their independent syntheses. In particular, the elemental analyses and the ^{1}H NMR spectra of **5s, y** clearly showed the absence of the ethoxy moiety in these molecules, and the thermolyses of pyridinium salts **3s, y** in chloroform at the reflux temperature gave the same *N*-ylides **5s, y** in 88 and 90% yields. From these results and our previous observation of the smooth dealkylation of 1-(2-alkoxyvinyl)pyridinium halides[2b] we concluded compounds **5s, y** are *N*-(1-pyridinio) aminides.

Reductions of the Nitro Group. Since the versatility of a nitro group to various functional groups is well-known, the transformations of some 4-nitrophenyl derivatives to 4-aminophenyl compounds were investigated. The hydrogenation of 2-methylthio-3-(4-nitrophenyl)pyrazolo[1,5-*a*]pyridines (**4i—k**) and ethyl 2-methylthio-1-(4-nitrophenyl)indolizine-3-carboxylates (**9h—j**) over palladium on charcoal (10%) in THF proceeded smoothly to give the corresponding 4-aminophenyl derivatives **10a—f** in good yields, respectively. These transformations complement our present method in which an aryl group having an electron-donating group can not be introduced to the corresponding heteroaromatics.

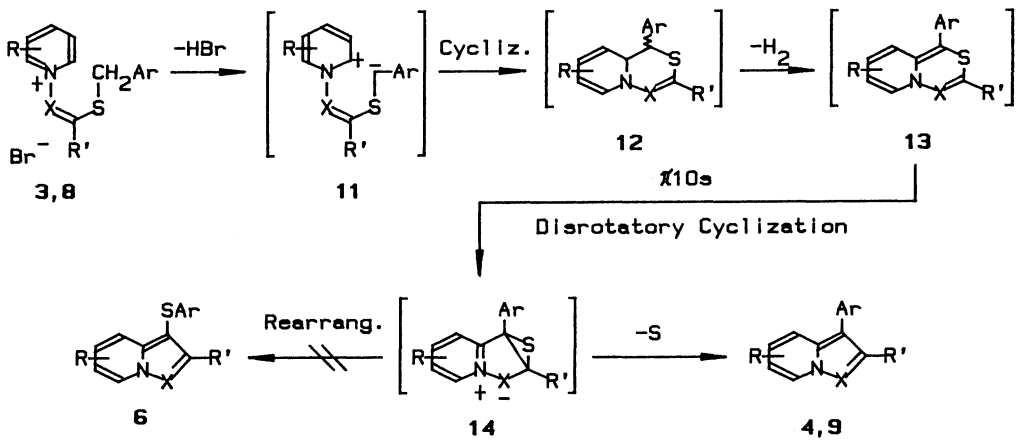
The structures of these compounds **10a—f** were determined mainly by the presence of the primary amino absorption bands appeared in the range of 3321—3620 cm^{-1} and by the absence of the nitro bands in their IR spectra.

Reaction Mechanism. A possible mechanism for these reactions is shown in Scheme 4. The corresponding 3-arylpyrazolo[1,5-*a*]pyridines (**4c—z**) and 1-aryl-



Prod.	React.	R_1	R_2	X
10a	**4i**	H	H	N
10b	**4j**	Me	H	N
10c	**4k**	H	Me	N
10d	**9h**	H	H	CCOOEt
10e	**9i**	Me	H	CCOOEt
10f	**9j**	H	Me	CCOOEt

Scheme 3.



Scheme 4.

indolizines (**9c—v**) were formed only from pyridinium salts **3c—z** and **8c—v** having a benzyl substituent activated by an electron-withdrawing group but not from those **3a, b** and **8a, b** possessing a parent or methyl-substituted benzyl group; accordingly it can be presumed that the benzyl proton must be acidic for the generation of the zwitterionic intermediate **11**. Furthermore, it is noted that these reactions proceeded via the ring contraction-desulfurization of transient 1-arylpyrido[2,1-*c*]-1,4-thiazine and its 4-aza-analog such as **13** but not via their ring contraction-rearrangement leading to arylthio derivatives such as **6**. This behavior is the same as that in related monocyclic species, since Schmidt and Huth reported already the smooth transformations of monocyclic 2,6-diphenyl-1,3-thiazinyl and 6-phenyl-1,3,4-thiadiazinyl anions to the desulfurized 2,3-diphenylpyrrole and 4-phenylpyrazole.[3]

Our method for the preparation of 3-arylpyrazolopyridines and 1-arylindolizines, even if a parent phenyl and electron-rich aryl groups could not be introduced into them, has still a high value because of the cheapness and ready availability of the starting materials, and the wide versatility of the heterocycles formed.

Table 1. ^{1}H NMR Spectral Data of Pyrazolopyridines in $CDCl_3$

Compd[a]	C-4	C-5	C-6	C-7	R		Ar
4c	[b]	[b]	6.76 dt	8.49 br d	2.58 s		7.4—8.3 m
4d	[b]	[b]	6.65 m	2.76 s	2.59 s		7.4—8.3 m
4e	7.00 br s	2.33 s	6.60 dd	8.37 d	2.58 s		7.4—8.3 m
4f	[c]	[c]	6.83 dt	8.58 br d	7.1—8.2 m		7.1—8.2 m
4g	[c]	7.18 br t	6.71 dt	8.35 br d	1.41 t	4.41 q	7.3—8.2 m
4h	[d]	[d]	6.65 m	8.33 br d	2.82 s		7.3—8.2 m
4i	7.66 br d	7.29 br t	6.81 dt	8.51 br d	2.69 s		7.6—8.5 m
4j	7.59 br d	7.21 q	6.69 br d	2.78 s	2.71 s		7.6—8.5 m
4k	7.41 br s	2.40 s	6.65 dd	8.41 d	2.68 s		7.6—8.5 m
4l	[c]	[c]	6.85 dt	8.55 br d	7.0—8.4 m		7.0—8.4 m
4m	7.68 br d	7.23 br t	6.71 dt	8.29 br d	1.48 t	4.48 q	7.6—8.4 m
4n	7.58 br d	7.22 br t	6.73 dt	8.41 br d	2.90 s		7.7—8.6 m
4o	[c]	[c]	6.77 dt	8.48 br d	2.64 s		7.0—8.0 m
4p	[c]	[c]	6.66 br d	2.75 s	2.66 s		7.0—8.0 m
4q	7.17 br s	2.38 s	6.66 dd	8.42 d	2.63 s		7.3—8.0 m
4r	[c]	[c]	6.85 dt	8.59 br d	7.0—8.0 m		7.0—8.0 m
4s	[c]	[c]	6.70 dt	8.33 br d	1.47 t	4.50 q	7.0—8.0 m
4t	[c]	[c]	6.63 m	8.32 br d	2.81 s		6.9—8.0 m
4u	7.64 br d	7.26 br t	6.81 dt	8.52 br d	2.69 s		7.5—8.0 m
4v	7.58 br d	7.20 q	6.68 br d	2.78 s	2.70 s		7.5—8.0 m
4w	7.38 br s	2.41 s	6.64 dd	8.39 d	2.67 s		7.5—8.0 m
4x	[c]	[c]	6.85 dt	8.58 br d	7.0—7.9 m		7.0—7.9 m
4y	7.52 br d	7.22 br t	6.72 dt	8.34 br d	1.49 t	4.49 q	7.5—8.0 m
4z	7.48 br d	7.11 br t	6.65 dt	8.34 br d	2.87 s		7.76 s

a) The coupling constants are as follows: $J_{4,5}$=9.0, $J_{5,6}$=$J_{6,7}$=7.0, $J_{4,6}$=2.0, J_{Et}=7.0. b) Overlapped with each other at δ 6.9—7.4. c) Overlapped with the phenyl proton signals. d) Overlapped with each other at δ 6.8—7.3.

Table 2. ^{1}H NMR Spectral Data of Indolizines in $CDCl_3$

Compd[a]	C-5	C-6	C-7	C-8	SMe	R		Ar
9c	9.57 br d	6.81 dt	7.03 br t	7.25 br d	2.23 s	1.46 t	4.47 q	7.4—8.3 m
9d	2.57 s	6.60 br d	6.92 q	7.17 br d	2.24 s	1.46 t	4.48 q	7.4—8.3 m
9e	9.48 d	6.72 dd	2.31 s	6.98 br s	2.25 s	1.47 t	4.49 q	7.4—8.3 m
9f	8.28 br d	6.88 dt	7.09 br t	7.28 br d	2.40 s	—		7.4—8.3 m
9g	9.55 br d	6.92 dt	7.18 br t	7.40 br d	1.74 s	7.0—8.3 m		7.4—8.3 m
9h	9.55 br d	6.91 dt	7.15 br t	7.55 br d	2.28 s	1.50 t	4.52 q	7.6—8.6 m
9i	2.57 s	6.60 br d	6.98 q	7.47 br d	2.20 s	1.47 t	4.50 q	7.6—8.5 m
9j	9.51 d	6.77 dd	2.31 s	7.34 br s	2.26 s	1.47 t	4.51 q	7.6—8.6 m
9k	[b]	6.98 dt	7.23 br t	7.67 br d	2.49 s	—		7.7—8.6 m
9l	9.52 br d	6.93 dt	7.23 br t	[b]	1.78 s	7.5—8.6 m		7.5—8.6 m
9m	9.59 br d	6.85 dt	7.08 br t	7.28 br d	2.32 s	1.49 t	4.51 q	7.3—8.0 m
9n	2.56 s	6.59 br d	6.93 q	7.15 br d	2.29 s	1.44 t	4.47 q	7.3—8.0 m
9o	9.49 d	6.73 dd	2.35 s	7.00 br s	2.35 s	1.48 t	4.50 q	7.2—8.0 m
9p	8.33 br d	6.90 dt	7.12 br t	7.35 br d	2.49 s	—		7.4—8.0 m
9q	9.60 br d	6.94 dt	[b]	[b]	1.77 s	7.1—8.1 m		7.1—8.1 m
9r	9.55 br d	6.87 dt	7.11 br t	7.51 br d	2.26 s	1.49 t	4.51 q	7.5—8.0 m
9s	2.58 s	6.62 br d	6.98 q	7.46 br d	2.21 s	1.48 t	4.51 q	7.5—8.0 m
9t	9.45 d	6.73 dd	2.34 s	7.27 br s	2.23 s	1.48 t	4.50 q	7.5—8.0 m
9u	8.31 br d	6.91 dt	7.16 br t	7.37 br d	2.46 s	—		7.4—8.0 m
9v	9.49 br d	6.90 dt	7.20 br t	[b]	1.77 s	7.4—8.0 m		7.4—8.0 m

a) The coupling constants are as follows: $J_{5,6}$=$J_{6,7}$=7.0, $J_{7,8}$=9.0, $J_{6,8}$=2.0, and J_{Et}=7.0 Hz. b) Overlapped with the phenyl proton signals.

Experimental

Melting points were measured with a Yanagimoto micro-melting point apparatus and are uncorrected. The microanalyses were carried out on a Perkin-Elmer elemental analyzer. The ^{1}H 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.

Materials. *N*-(1-Pyridinio) aminides (**1a—f**) and 1-(1-pyridinio) methylides (**7a—e**) employed in the above reactions were prepared according to the procedures described in the literatures.[2,6]

Preparations of 3-Arylpyrazolo[1,5-*a*]pyridines and 1-Arylindolizines. General Method A. A solution of pyridinum *N*-ylide (2 mmol) and benzyl bromide (2.2 mmol) in chloroform (20 ml) was kept at room temperature until the spot of the *N*-ylide completely disappeared (1—4 d, by TLC monitoring). The resulting solution was concentrated under reduced pressure and the residue was washed three times with ether to remove unaltered benzyl bromide. To the chloroform solution (30 ml) of the pyridinium salt, DBU (0.38g, 2.5 mmol) was added dropwise and the resulting mixture was stirred at room temperature for 1 d. The solution was concentrated at reduced pressure, and the residual oil was separated by column chromatography (alumina) using chloroform as eluent. The removal of the solvent and recrystallization from chloroform-hexane gave the corresponding pyrazolo[1,5-*a*]pyridines.

Method B. To the chloroform solution of pyridinium bromide (2 mmol) prepared in Method A, DBU (0.38g, 2.5 mmol) was added dropwise in an ice bath. After 10 min, chloranil (0.49 g, 2 mmol) was added and the resulting mixture was allowed to react for a further 12 h at that temperature (0 °C). The solution was filtered to remove insoluble substances and the filtrate was concentrated under reduced pressure. The same work-up as described above afforded pyrazolo[1,5-*a*]pyridines.

Method C. In the procedure described in Method B, DDQ (0.45g, 2 mmol) instead of chloranil was used as a dehydrogenating agent.

Only 3-(4-nitrophenyl)pyrazolo[1,5-*a*]pyridine derivatives **4i—n** were formed without a dehydrogenating agent (Method A), but none of the other pyrazolo[1,5-*a*]pyridines **4c—h, o—z** and indolizines **9c—v** could be obtained by this method because 4,4a-dihydropyrido[1,2-*d*]-1,3,4-thiadiazine[2c] and 1,9a-dihydropyrido[2,1-*c*]-1,4-thiazine derivatives[2a,e] such as **12** generated in situ from the corresponding pyridinium salts **3c—h, o—z** were not oxidized under the conditions employed here.

The reactions of pyridinium salts such as **3a, b** and **8a, b**, prepared from pyridinium *N*-ylides **1a** and **7a** and benzyl bromide (**2a**), 4-methylbenzyl bromide (**2b**), 4-chlorobenzyl bromide, and 4-bromobenzyl bromide, were carried out under several reaction conditions, but no significant products could be isolated.

Compounds **4c, e, g, k, m, n** and **9c, g** were obtained as orange prisms, **4d** and **9e, j** as orange needles, **4f, l** and **9f, h, i, k, l, v** as yellow needles, **4h** as violet needles, **4i, j** and **9q** as

Table 3. Some Physical and Analytical Data of 3-Arylpyrazolo[1,5-*a*]pyridines

Compd No.	Salt (SM[a])	Method (%)			Mp	$\nu^{KBr}_{NO_2 \text{ or } CN}$/cm^{-1}		Formula[b]
		A	B	C	θ_m/°C			
4a	**3a(1a,2a)**	0	0	0				
4b	**3b(1a,2b)**	0	0	0				
4c	**3c(1a,2c)**	0	75	83	125—127	1521	1352	$C_{14}H_{11}N_3O_2S$
4d	**3d(1b,2c)**		70	80	111—113	1514	1346	$C_{15}H_{13}N_3O_2S$
4e	**3e(1c,2c)**		88	89	109—111	1516	1347	$C_{15}H_{13}N_3O_2S$
4f	**3f(1d,2c)**		46	58	111—114	1512	1346	$C_{19}H_{13}N_3O_2$
4g	**3g(1e,2c)**		60	65	133—135	1504	1349	$C_{15}H_{13}N_3O_3$
4h	**3h(1f,2c)**		88		122—124	1513	1348	$C_{15}H_{14}N_4O_2$
4i	**3i(1a,2d)**	89			180—182	1508	1343	$C_{14}H_{11}N_3O_2S$
4j	**3j(1b,2d)**	79			169—172	1501	1344	$C_{15}H_{13}N_3O_2S$
4k	**3k(1c,2d)**	91			202—205	1503	1340	$C_{15}H_{13}N_3O_2S$
4l	**3l(1d,2d)**	74			188—190	1502	1336	$C_{19}H_{13}N_3O_2$
4m	**3m(1e,2d)**	54			168—170	1490	1309	$C_{15}H_{13}N_3O_3$
4n	**3n(1f,2d)**	89			121—123	1496	1341	$C_{15}H_{14}N_4O_2$[c]
4o	**3o(1a,2e)**		42		116—117	2219		$C_{15}H_{11}N_3S$
4p	**3p(1b,2e)**		38	54	117—119	2218		$C_{16}H_{13}N_3S$
4q	**3q(1c,2e)**		41	48	147—149	2218		$C_{16}H_{13}N_3S$
4r	**3r(1d,2e)**		34		144—146	2220		$C_{20}H_{13}N_3$
4s[d]	**3s(1e,2e)**			34	135—137	2216		$C_{16}H_{13}N_3O$
4t	**3t(1f,2e)**		37		122—123	2218		$C_{16}H_{14}N_4$
4u	**3u(1a,2f)**		51		207—209	2220		$C_{15}H_{11}N_3S$
4v	**3v(1b,2f)**		49		157—158	2218		$C_{16}H_{13}N_3S$
4w	**3w(1c,2f)**		55		217—219	2220		$C_{16}H_{13}N_3S$
4x	**3x(1d,2f)**		34		166—169	2218		$C_{20}H_{13}N_3$
4y[e]	**3y(1e,2f)**			29	157—159	2220		$C_{16}H_{13}N_3O$
4z	**3z(1f,2f)**		30		154—156	2220		$C_{16}H_{14}N_4$

a) Starting materials. b) Satisfactory analytical data (within 0.3% for C, H, and N) were obtained for all new compounds except **4n**. c) Found: C, 63.49; H, 5.03; N, 20.15%. Calcd for $C_{15}H_{14}N_4O_2$: C, 63.82; H, 5.00; N, 19.85%. d) Plus **5s**, 14%. e) Plus **5y**, 24%.

Table 4. Some Physical and Analytical Data of 1-Arylindolizines

Compd No.	Salt (SM[a])	Yield[b] %	Mp θ_m/°C	ν^{KBr}/cm^{-1}			Formula[c]
9a	**8a**(7a,2a)	0					
9b	**8b**(7a,2b)	0					
9c	**8c**(7a,2c)	56	98—100	1654	1513	1348	$C_{18}H_{16}N_2O_4S$
9d	**8d**(7b,2c)	18	[d]	1695	1520	1348[e]	[f]
9e	**8e**(7c,2c)	33	134—136	1660	1519	1343	$C_{19}H_{18}N_2O_4S$
9f	**8f**(7d,2c)	20	179—181	2198	1515	1346	$C_{16}H_{11}N_3O_2S$
9g	**8g**(7e,2c)	28	127—128	1592	1513	1348	$C_{22}H_{16}N_2O_3S$
9h	**8h**(7a,2d)	68	128—129	1662	1507	1344	$C_{18}H_{16}N_2O_4S$
9i	**8i**(7b,2d)	10	122—124	1709	1506	1334	$C_{19}H_{18}N_2O_4S$
9j	**8j**(7c,2d)	64	171—172	1672	1504	1329	$C_{19}H_{18}N_2O_4S$
9k	**8k**(7d,2d)	25	180—182	2201	1507	1340	$C_{16}H_{11}N_3O_2S$
9l	**8l**(7e,2d)	37	141—143	1590	1508	1336	$C_{22}H_{16}N_2O_3S$
9m	**8m**(7a,2e)	37	130—131	2221	1673		$C_{19}H_{16}N_2O_2S$
9n	**8n**(7b,2e)	21	[d]	2221	1699[e]		[f]
9o	**8o**(7c,2e)	28	144—145	2221	1660		$C_{20}H_{18}N_2O_2S$
9p	**8p**(7d,2e)	22	162—163	2220	2200		$C_{17}H_{11}N_3S$
9q	**8q**(7e,2e)	14	149—150	2223	1591		$C_{23}H_{16}N_2OS$
9r	**8r**(7a,2f)	53	110—111	2225	1665		$C_{19}H_{16}N_2O_2S$
9s	**8s**(7b,2f)	10	130—132	2224	1690		$C_{20}H_{18}N_2O_2S$
9t	**8t**(7c,2f)	21	157—159	2221	1664		$C_{20}H_{18}N_2O_2S$
9u	**8u**(7d,2f)	13	209—210	2221	2200		$C_{17}H_{11}N_3S$
9v	**8v**(7e,2f)	11	168—169	2225	1591		$C_{23}H_{16}N_2OS$

a) Starting materials. b) All of these yields were obtained by Method C. c) Satisfactory analytical data (within 0.3% for C, H, and N) were obtained for all new compounds except **9d**, **n**. d) Viscous oil. e) Neat. f) The preparation of a pure sample for analysis was unsuccessful.

yellow prisms, **4o—r**, **t**, **x** as colorless prisms, **4s**, **u—w** and **9m**, **p**, **s** as colorless needles, **4y**, **z** and **9o**, **r**, **t**, **u** as pale yellow needles, **9d** as orange viscous oil, and **9n** as yellow viscous oil.

These results together with some physical and analytical data are summarized in Tables 1—4.

Thermolyses of 1-[(2- or 4-Cyanobenzylthio)ethoxymethyleneanimo]pyridinium Bromides. General Method. Pyridinium bromide (**3s** or **3y**, 2 mmol) prepared as above was heated under reflux in chloroform (30 ml) on a water bath for 12 h. The usual work-up of the resulting solution and recrystallization from chloroform-ether gave *N*-(1-pyridinio)-[1-(2- or 4-cyanobenzylthio)carbonyl]aminides: **5s**, 88%, colorless needles, mp 119—121 °C, IR ν (KBr) 2218 (CN) and 1598 cm^{-1} (CO). ^{1}H NMR ($CDCl_3$) δ=4.33 (2H, s, SCH_2), 7.1—8.2 (7H, m, phenyl protons and 3-, 4-, and 5-protons), and 8.7—9.0 (2H, m, 2- and 6-protons). Anal. ($C_{14}H_{11}N_3OS$) C, H, N. **5y**, 90%, colorless needles, mp 135—136 °C, IR ν (KBr) 2221 (CN) and 1588 cm^{-1} (CO). ^{1}H NMR ($CDCl_3$) δ=4.14 (2H, s, SCH_2), 7.3—8.3 (7H, m, phenyl protons and 3-, 4-, and 5-protons), and 8.7—9.0 (2H, m, 2- and 6-protons). Anal. ($C_{14}H_{11}N_3OS$) C, H, N. These compounds **5s**, **y** were completely in accord with those obtained from the alkaline treatement of the salts **3s**, **y**.

Reduction of the Nitro Group. General Method. A mixture of 4-nitrophenyl derivatives (0.5 mmol), palladium on carbon (10%, 0.5 g), and THF (50 ml) was stirred at room temperature under hydrogen (1 atmosphere) for 1 d. The resulting mixture was filtered to remove the catalyst, and the filtrate was concentrated under reduced pressure. The residue was separated by column chromatography on alumina using chloroform as eluent. The removal of the solvent and the recrystallizations from chloroform-hexane afforded the corresponding 4-aminophenyl compounds **10c—f**. On the other hand, 3-(4-aminophenyl)-2-(methylthio)pyrazolo-[1,5-*a*]pyridines **10a**, **b** were converted to the *N*-acetyl derivatives by the action of acetic anhydride/pyridine because they were unstable and the preparation of pure samples for analyses was unsuccessful.

Some physical and analytical data of these 4-aminophenyl derivatives are shown below: **10a**, 96%, unstable colorless crystals, IR ν (KBr) 3330 and 3420 cm^{-1} (NH_2), ^{1}H NMR ($CDCl_3$) δ=2.62 (3H, s, SMe), 3.62 (2H, br s, NH_2), 6.5—7.7 (7H, m, 4-, 5-, 6-H, and phenyl protons), and 8.48 (1H, br d, J=7.0 Hz, 7-H). Its *N*-acetyl derivative, pale yellow prisms, mp 140—143 °C. Anal. ($C_{16}H_{15}N_3OS+H_2O$) C, H, N. **10b**, 86%, unstable colorless crystals, IR ν (KBr) 3321 and 3419 cm^{-1} (NH_2), ^{1}H NMR ($CDCl_3$) δ=2.62 (3H, s, SMe), 2.73 (3H, s, 7-Me), 3.61 (2H, br s, NH_2), 6.88 (1H, br d, 6-H), and 6.7—7.6 (6H, m, 4-, 5-H, and phenyl protons). Its *N*-acetyl derivatives, pale yellow prisms, mp 77—79 °C. Anal. ($C_{17}H_{17}N_3OS+H_2O$) C, H, N. **10c**, 92%, colorless prisms, mp 115—118 °C, IR ν (KBr) 3325 and 3392 cm^{-1} (NH_2), ^{1}H NMR ($CDCl_3$) δ=2.33 (3H, s, 5-Me), 2.61 (3H, s, SMe), 3.24 (2H, br s, NH_2), 6.50 (1H, dd, J=7.0 and 2.0 Hz, 6-H), 6.7—7.6 (5H, m, 4-H and phenyl protons), and 8.32 (1H, d, J=7.0 Hz, 7-H). Anal. ($C_{15}H_{15}N_3S$) C, H, N. **10d**, 99%, pale yellow prisms, mp 104—107 °C, IR ν (KBr) 1670 (CO), 3341 and 3420 cm^{-1} (NH_2), ^{1}H NMR ($CDCl_3$) δ=1.46 (3H, t, J=7.0 Hz, $OCH_2C\underline{H}_3$), 2.21 (3H, s, SMe), 3.33 (2H, br s, NH_2), 4.48 (2H, q, J=7.0 Hz, $OCH_2C\underline{H}_3$), 6.6—7.6 (7-H, m, 6-, 7-, 8-H, and phenyl protons), 9.47 (1H, br d, J=7.0 Hz, 5-H). Anal. ($C_{18}H_{18}N_2O_2S$) C, H, N. **10e**, 57%, pale yellow prisms, mp 144—146 °C, IR ν (KBr) 1665 (CO), 3377 and 3462 cm^{-1} (NH_2), ^{1}H NMR ($CDCl_3$) δ=1.45 (3H, t, J=7.0 Hz, $OCH_2C\underline{H}_3$), 2.19 (3H, s, SMe), 2.53 (3H, s, 5-Me), 3.51 (2H, br s, NH_2), 4.47 (2H, q, J=7.0 Hz, $OC\underline{H}_2CH_3$), 6.51 (1H, br d, J=7.0 Hz, 6-H), and 6.6—7.6 (6H, 7-, 8-H, and phenyl pro-

tons). Anal. ($C_{19}H_{20}N_2O_2S$) C, H, N. **10f**, 99%, pale yellow prisms, mp 164—167 °C, IR ν (KBr) 1650 (CO), 3370 and 3456 cm^{-1} (NH_2), ^1H NMR ($CDCl_3$) δ=1.45 (3H, t, J=7.0 Hz, $OCH_2\underline{CH_3}$), 2.19 (3H, s, SMe), 2.28 (3H, s, 7-Me), 3.41 (2H, br s, NH_2), 4.46 (2H, q, J=7.0 Hz, $OC\underline{H_2}CH_3$), 6.59 (1H, dd, J=7.0 and 2.0 Hz, 6-H), 6.6—7.4 (5H, m, 8-H and phenyl protons), and 9.35 (1H, d, J=7.0 Hz, 5-H). Anal. ($C_{19}H_{20}N_2O_2S$) C, H, N.

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