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Preparation of New Nitrogen-Bridged Heterocycles. 15.[1] Synthesis and Reaction of 1,9a-Dihydropyrido[2,1-*c*][1,4]thiazines

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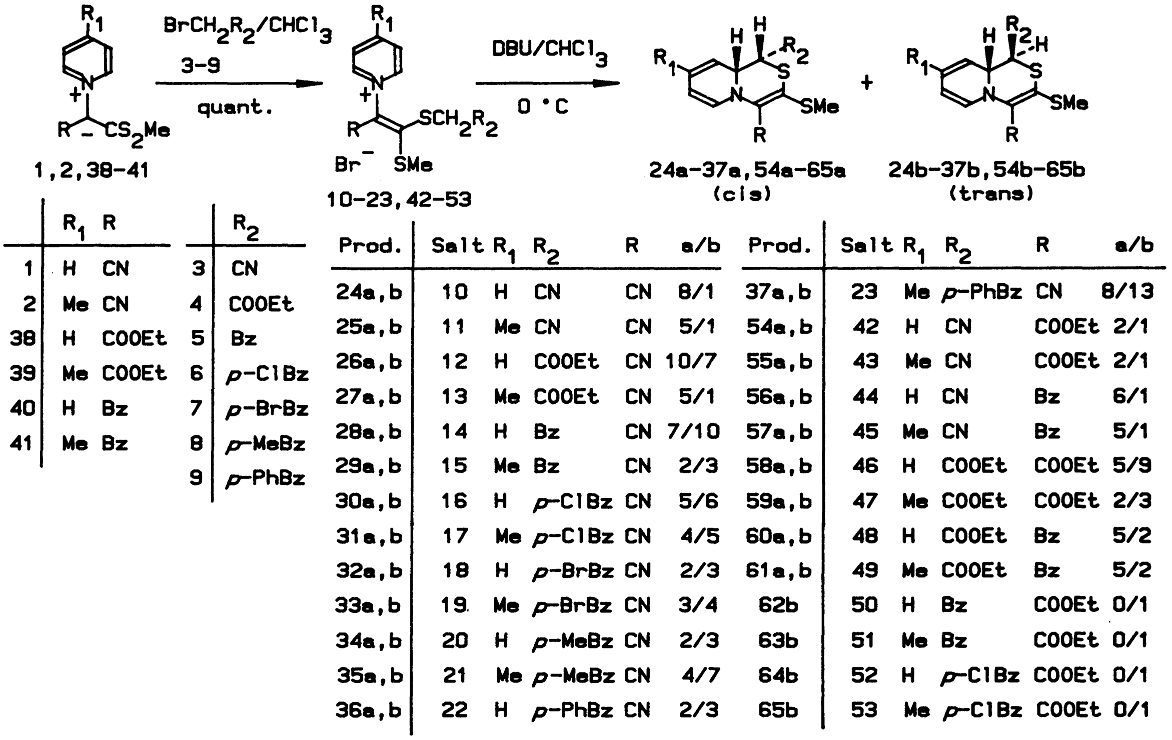
Alkaline treatment of 1-[2-(substituted methylthio)vinyl]pyridinium bromides, readily obtainable from the *S*-alkylation of pyridinium 1-(thiocarbonyl)methylides with various alkyl bromides such as bromoacetonitrile, ethyl bromoacetate, and some phenacyl bromides, gave smoothly 1,9a-dihydropyrido[2,1-*c*][1,4]thiazine derivatives as almost isomeric mixtures. These dihydropyridothiazines are very unstable and decomposed rapidly at ordinary temperature, but by treating them with a dehydrogenating agent such as lead tetraacetate (LTA) or 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) at 0 °C the desulfurized and the rearranged aromatic indolizine derivatives were formed in moderate to good yields.

A compound having a planar cyclic $4n\pi$ system is very intriguing molecule because various interesting reactions to avoid the high energic state caused by its resonance destabilization can be expected. Our recent reports[1,2] showed that neutral pyrido[1,2-*d*][1,3,4]thiadiazines bearing a planar 12π system are 1,3,4-thiadiazinyl anion congeners[3] and undergo smoothly the desulfurization or the rearrangement to give the aromatized pyrazolo[1,5-*a*]pyridine derivatives in good yields. On the other hand, the extension of this reaction to its 1-deaza analogue gave only 1,9a-dihydropyrido[2,1-*c*][1,4]thiazine derivatives and did not afford the initially expected indolizine derivatives except a few examples.[4] All our attempts to obtain the corresponding aromatic indolizines from these primary bicyclo adducts in the presence or absence of various dehydrogenating agents at ordinary temperature were unsuccessful, but we found that the treatment of them with LTA and DDQ at the limited temperature (0 °C) afforded the expected indolizines in moderate to good yields. In this paper we wish to report convenient syntheses of 1,9a-dihydropyrido[2,1-*c*][1,4]thiazines and their dehydrogenative transformations to the desulfurized and the rearranged indolizine derivatives.

Results and Discussion

Preparations of 1,9a-Dihydropyrido[2,1-*c*][1,4]thiazines. The treatment of 1-[1-cyano-2-methylthio-2-(substituted methylthio)vinyl]pyridinium bromides **10 —23**, obtainable quantitatively from the *S*-alkylations of the corresponding pyridinium (thiocarbonyl)-methylides **1** and **2** with bromoacetonitrile (**3**), ethyl bromoacetate (**4**), phenacyl bromide (**5**), *p*-chlorophenacyl bromide (**6**), *p*-bromophenacyl bromide (**7**), *p*-methylphenacyl bromide (**8**), and *p*-phenylphenacyl bromide (**9**), with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in chloroform at 0°C for 10 min afforded unstable yellow products **24—37** in 43—84% yields, respectively. Similar reactions of 1-[1-[1-(ethoxycarbonyl) and 1-benzoyl]-2-methylthio-2-(substituted methylthio)vinyl]pyridinium bromides **42—53** with DBU gave the corresponding compounds **54—65** in 39—89% yields and those of pyridinium bromides **68—78** possessing a methyl group at the 2-position yielded compounds **79—89** in 49—97% yields (Schemes 1 and 2). All products except **62—65**, **82**, **84**, and **86** were isomeric mixtures, and their isolatons other than **24a** were unsuccessful because of their thermal instability. These isomeric ratios (see Schemes 1 and 2) determined by their proton NMR (^{1}H NMR) spectra suggest the following inclinations for the substituent effect in these cyclization reactions: 1) In the adducts **24a,b—37a,b**, **54a,b—65a,b**, and **79a,b—89a,b** having 9a-hydrogen, the formations of the trans isomers (type b) increase with the increase of the steric hindrance of the substituent (R_2) derived from the alkylating agents **3—9**. 2) In the adducts **79c,d—89c,d** bearing a 9a-methyl group, the cis isomer (type c) is always predominant or exclusive. 3) The 2-methyl group of salts **68—78** does not cause large steric hinderance toward the cyclization at the 2-position. 4) When the group (R) is an ethoxycarbonyl and the substituent (R_2) is a bulky aroyl group, their cyclization reactions afford sole products **62b—65b**, **84b**, and **86b**, respectively.

The structures of compounds **24—37**, **54—65**, and **79—89**, were determined by their analytical and spectral inspections and by the mechanistic consideration of their transformations to indolizine derivatives. Adducts **24**, **25**, **28—37**, **54—56**, **59**, **61—65**, **79**, **80**, **83—86**, and **88** gave the satisfactory elemental analyses, though almost adducts of them were isomeric mixtures, and more evidently their ^{1}H NMR spectra (Table 1) supported our proposed 1,9a-dihydropyrido[2,1-*c*][1,4]-thiazine structure. For example, the spectrum of compound **24** indicated the proton signals due to the major isomer at δ 2.50 (3H, s, MeS), 4.02 (1H, d, *J*= 2.0 Hz, 1-H), 4.60 (1H, m, 9a-H), 4.99 (1H, br t, *J*=7.0 and 6.0 Hz, 7-H), 5.41 (1H, br q, *J*=10.0 and 4.0 Hz, 9-H), 6.21 (1H, br q, *J*=10.0 and 6.0 Hz, 8-H), and 6.72 (1H, br d, *J*=7.0 Hz, 6-H), together with weak proton

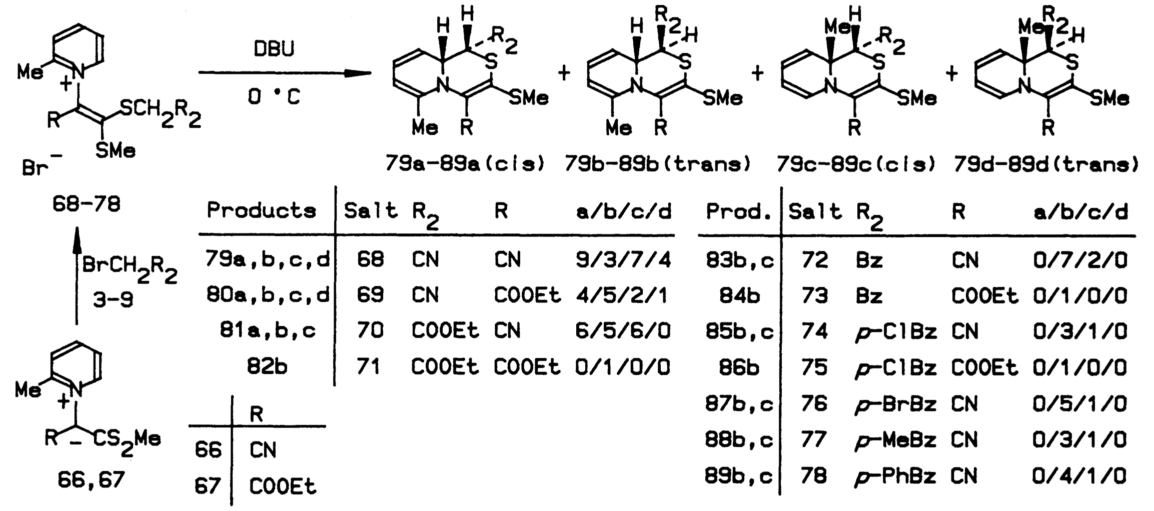


	R_1	R
1	H	CN
2	Me	CN
38	H	COOEt
39	Me	COOEt
40	H	Bz
41	Me	Bz

	R_2
3	CN
4	COOEt
5	Bz
6	*p*-ClBz
7	*p*-BrBz
8	*p*-MeBz
9	*p*-PhBz

Prod.	Salt	R_1	R_2	R	a/b	Prod.	Salt	R_1	R_2	R	a/b
24a,b	10	H	CN	CN	8/1	37a,b	23	Me	*p*-PhBz	CN	8/13
25a,b	11	Me	CN	CN	5/1	54a,b	42	H	CN	COOEt	2/1
26a,b	12	H	COOEt	CN	10/7	55a,b	43	Me	CN	COOEt	2/1
27a,b	13	Me	COOEt	CN	5/1	56a,b	44	H	CN	Bz	6/1
28a,b	14	H	Bz	CN	7/10	57a,b	45	Me	CN	Bz	5/1
29a,b	15	Me	Bz	CN	2/3	58a,b	46	H	COOEt	COOEt	5/9
30a,b	16	H	*p*-ClBz	CN	5/6	59a,b	47	Me	COOEt	COOEt	2/3
31a,b	17	Me	*p*-ClBz	CN	4/5	60a,b	48	H	COOEt	Bz	5/2
32a,b	18	H	*p*-BrBz	CN	2/3	61a,b	49	Me	COOEt	Bz	5/2
33a,b	19	Me	*p*-BrBz	CN	3/4	62b	50	H	Bz	COOEt	0/1
34a,b	20	H	*p*-MeBz	CN	2/3	63b	51	Me	Bz	COOEt	0/1
35a,b	21	Me	*p*-MeBz	CN	4/7	64b	52	H	*p*-ClBz	COOEt	0/1
36a,b	22	H	*p*-PhBz	CN	2/3	65b	53	Me	*p*-ClBz	COOEt	0/1

Scheme 1.



	R
66	CN
67	COOEt

Products	Salt	R_2	R	a/b/c/d	Prod.	Salt	R_2	R	a/b/c/d
79a,b,c,d	68	CN	CN	9/3/7/4	83b,c	72	Bz	CN	0/7/2/0
80a,b,c,d	69	CN	COOEt	4/5/2/1	84b	73	Bz	COOEt	0/1/0/0
81a,b,c	70	COOEt	CN	6/5/6/0	85b,c	74	*p*-ClBz	CN	0/3/1/0
82b	71	COOEt	COOEt	0/1/0/0	86b	75	*p*-ClBz	COOEt	0/1/0/0
					87b,c	76	*p*-BrBz	CN	0/5/1/0
					88b,c	77	*p*-MeBz	CN	0/3/1/0
					89b,c	78	*p*-PhBz	CN	0/4/1/0

Scheme 2.

signals of the minor one appeared at δ 4.03 (1H, d, J=8.0 Hz, 1-H), 4.41 (1H, br q, J=8.0 and 4.0 Hz, 9a-H), and 6.45 (1H, br d, J=7.0 Hz, 6-H). The chemical shifts (δ 4.02—6.72) and the signal patterns of these skeletal protons indicated distinctly the presence of a nonaromatic 1,2-dihydropyridine moiety in **24**, and the presence of the two kinds of the 1-H signals coupled with 2.0 or 8.0 Hz showed that **24** was a cis and trans mixture at the 1- and 9a-positions. From the consideration of Karplus relationship between the coupling constant and the dihedral angle using Dreiding models, we concluded that the major isomer (its dihedral angle is about 60°) is *cis* (**24a**) and the other (its dihedral angle is about 180°) is *trans* (**24b**). The ^{1}H NMR spectrum of **79** obtained from the alkaline treatment of 2-methylpyridinium salt **68** exhibited four methyl proton singlets at δ 1.43, 1.54, 2.08, and 2.25, and a pair of the 6-proton signals at δ 6.54 (br d, J=7.0 Hz) and 6.82 (br d, J=7.0 Hz), together with two methylthio singlets (δ 2.50 and 2.57) and many undistinguishable multiplets in the range of δ 4.0—6.5. From these spectral data we also concluded that

Table 1. ^{1}H NMR Data of Pyrido[2,1-*c*][1,4]thiazines

Compd a)	C-1	C-6	C-7	C-8	C-9	C-9a	SMe	R_2		R	
24a	4.02 d	6.72 br d	4.99 br t	6.21 br q	5.41 br q	4.60 m	2.50 s	—		—	
24b	4.03 d	6.45 br d	b)	b)	b)	4.41 br q	b)	—		—	
25a	4.00 d	6.70 d	4.90 dd	1.85 s	5.29 br s	4.56 m	2.52 s	—		—	
25b	3.96 d	6.42 d	b)	b)	5.49 br s	b)	b)	—		—	
26a	3.90 d	6.62 br d	4.85 br t	6.02 br q	5.38 br q	4.61 m	2.50 s	1.24 t	4.18 q	—	
26b	4.00 d	6.48 br d	4.98 br t	b)	b)	b)	2.51 s	1.32 t	4.29 q	—	
27a	3.84 d	6.59 d	4.73 dd	1.74 s	5.08 br s	4.50 m	2.48 s	1.21 t	4.15 q	—	
27b	b)	6.42 d	b)	b)	b)	b)	b)	1.33 t	4.15 q	—	
28a	4.98 d	6.72 br d	c)	5.80 br q	4.4—5.2 m		2.50 s	7.4—8.2 m		—	
28b	5.08 d	6.54 br d	c)	5.90 br q	5.38 br q	c)	2.50 s	7.4—8.2 m		—	
29a	b)	6.64 d	d)	1.42 s	4.3—5.2 m		2.50 s	7.4—8.2 m		—	
29b	4.99 d	6.50 d	d)	1.65 s	4.3—5.2 m		2.50 s	7.4—8.1 m		—	
30a	4.91 d	6.68 br d	c)	5.78 br q	b)	c)	2.50 s	7.3—8.2 m		—	
30b	5.00 d	6.53 br d	c)	5.91 br q	5.33 br q	c)	2.50 s	7.3—8.2 m		—	
31a	b)	6.62 d	e)	1.47 s	4.3—5.3 m		2.55 s	7.3—8.1 m		—	
31b	4.96 d	6.49 d	e)	1.64 s	4.3—5.3 m		2.55 s	7.3—8.1 m		—	
32a	c)	6.70 br d	c)	5.79 br q	b)	c)	2.49 s	7.5—8.2 m		—	
32b	c)	6.55 br d	c)	5.94 br q	5.35 br q	c)	2.49 s	7.5—8.2 m		—	
33a	b)	6.65 d	e)	1.45 s	4.3—5.3 m		2.50 s	7.5—8.1 m		—	
33b	4.97 d	6.52 d	e)	1.63 s	4.3—5.3 m		2.50 s	7.5—8.1 m		—	
34a	4.98 d	6.73 br d	b)	5.78 br q	b)	4.88 m	2.48 s	7.2—8.1 m	2.44 s	—	
34b	5.07 d	6.56 br d	4.77 br t	5.93 br q	5.37 br q	4.59 br q	2.48 s	7.2—8.1 m	2.44 s	—	
35a	b)	6.66 d	d)	1.41 s	4.3—5.2 m		2.48 s	7.2—8.1 m	2.44 s	—	
35b	4.99 d	6.51 d	d)	1.60 s	4.3—5.2 m		2.48 s	7.2—8.1 m	2.44 s	—	
36a	5.02 d	6.75 br d	b)	5.80 br q	b)	b)	2.49 s	7.4—8.3 m		—	
36b	5.12 d	6.57 br d	4.88 br t	5.96 br q	5.40 br q	4.61 br q	2.49 s	7.4—8.3 m		—	
37a	b)	6.69 d	e)	1.41 s	4.3—5.3 m		2.49 s	7.3—8.3 m		—	
37b	5.07 d	6.55 d	e)	1.61 s	4.3—5.3 m		2.49 s	7.3—8.3 m		—	
54a	3.90 d	6.10 br d	4.88 br t	6.10 br q	5.46 br q	f)	2.40 s	—		1.38 t	4.40 q
54b	f)	b)	5.05 br t	b)	b)	b)	2.45 s	—		1.33 t	f)
55a	3.85 d	6.10 d	4.77 dd	1.82 s	5.13 br s	f)	2.40 s	—		1.38 t	4.37 q
55b	f)	5.97 d	4.92 dd	1.84 s	5.44 br s	f)	2.45 s	—		1.34 t	f)

Table 1. (Continued)

Compd[a)]	C-1	C-6	C-7	C-8	C-9	C-9a	SMe	R_2	R
56a	3.97 d	6.02 br d	4.73 bt t	6.05 br q	5.40 br q	4.88 m	2.07 s	—	7.3—8.3 m
56b	4.16 d	b)	b)	b)	b)	b)	2.25 s	—	7.3—8.3 m
57a	3.98 d	6.05 d	4.64 dd	1.78 s	5.16 br s	4.84 m	2.08 s	—	7.3—8.3 m
57b	4.14 d	5.91 d	b)	b) s	b)	b)	2.28 s	—	7.3—8.3 m
58a	3.78 d	b) br t	4.70 br t	b)	b)	b)	2.36 s	g)	g)
58b	f)	6.01 br d	4.90 br t	5.98 br q	5.35 br q	f)	2.41 s	g)	g)
59a	3.74 d	6.00 d	4.61 dd	1.73 s	5.11 br s	f)	2.39 s	g)	g)
59b	f)	6.00 d	4.80 dd	1.73 s	5.11 br s	f)	2.44 s	g)	g)
60a	3.85 d	5.90 br d	4.57 br t	5.90 br q	5.35 br q	4.81 m	2.08 s	7.3—8.3 m	1.29 4.23 t q
60b	b)	b)	b)	b)	b)	b)	2.27 s	7.3—8.3 m	1.32 4.27 t q
61a	3.84 d	5.88 d	4.48 dd	1.69 s	5.13 br s	4.72 m	2.07 s	7.3—8.3 m	1.28 4.23 t q
61b	b)	b)	b)	b)	b)	b)	2.27 s	7.3—8.3 m	1.34 4.29 t q
62b	5.23 d	6.12 br d	4.92 br t	5.95 br q	5.40 br q	f)	2.42 s	7.3—8.3 m	1.38 4.36 t q
63b	5.12 d	6.05 br d	4.81 br d	1.59 s	5.05 br s	f) m	2.40 s	7.3—8.3 m	1.34 4.33 t q
64b	5.15 d	6.11 br d	4.91 br t	5.93 br q	5.34 br q	4.40 m	2.40 s	7.3—8.2 m	1.36 4.33 t q
65b	5.05 d	5.99 br d	4.85 br d	1.60 s	4.99 br s	4.30 m	2.41 s	7.3—8.1 m	1.36 4.34 t q
79a	4.00 d	2.25 s	4.8—6.5 m				h)	—	—
79b	b)	2.08 s	b)	b)	b)	b)	h)	—	—
79c	3.63 s	6.82 br d	b)	b)	b)	1.43 s	h)	—	—
79d	b)	6.54 br d	b)	b)	b)	1.54 s	h)	–	—
80a	3.97 d	1.90 s	4.92 br d	6.25 q	5.39 br q	f)	2.50 s	—	1.36 4.32 t q
80b	f)	1.77 s	i)	i)	i)	f)	2.53 s	—	g)
80c	3.59 s	i)	i)	i)	i)	1.43 s	2.39 s	—	g)
80d	f)	b)	b)	b)	b)	1.54 s	2.44 s	—	g)
81a	3.90 d	2.12 s	i)	i)	i)	f)	2.57 s	g)	—
81b	f)	2.07 s	b)	b)	b)	f)	2.57 s	g)	—
81c	3.46 s	6.75 br d	b)	b)	b)	1.40 s	2.45 s	g)	—
82b	f)	1.73 s	4.88 br d	6.00 q	5.28 br q	3.86 q	2.46 s	g)	g)
83b	5.21 d	2.13 s	4.99 br d	5.92 q	5.35 br q	4.18 q	2.54 s	7.3—8.2 m	—
83c	4.52 s	6.86 br d	b)	b)	b)	1.53 s	2.38 s	7.3—8.2 m	—
84b	5.38 d	1.81 s	4.92 br d	5.97 q	5.31 br q	f)	2.40 s	7.3—8.2 m	1.33 4.31 t q

Table 1. (Continued)

Compd[a)]	C-1	C-6	C-7	C-8	C-9	C-9a	SMe	R_2		R	
85b	5.12 d	2.11 s	5.00 br d	5.93 q	5.33 br q	4.13 q	2.54 s	7.3—8.1 m		—	
85c	4.46 s	6.87 br d	b)	b)	b)	1.53 s	2.38 s	7.3—8.1 m		—	
86b	5.28 d	1.80 s	4.92 br d	5.95 q	5.23 br q	f)	2.47 s	7.3—8.1 m		1.33 t	4.30 q
87b	5.15 d	2.12 s	4.99 br d	5.95 q	5.33 br q	4.16 q	2.52 s	7.4—8.1 m		—	
87c	4.46 s	6.87 br d	b)	b)	b)	1.53 s	2.37 s	7.4—8.1 m		—	
88b	5.17 d	2.11 s	4.97 br d	5.90 q	5.33 br q	4.16 q	2.50 s	7.1—8.1 m	2.43 s	—	
88c	4.47 s	6.85 br d	b)	b)	b)	1.51 s	2.36 s	7.1—8.1 m	2.43 s	—	
89b	5.24 d	2.13 s	4.99 br d	5.94 q	5.38 br q	4.20 q	2.51 s	7.3—8.3 m		—	
89c	4.55 s	6.90 br d	b)	b)	b)	1.53 s	2.37 s	7.3—8.3 m		—	

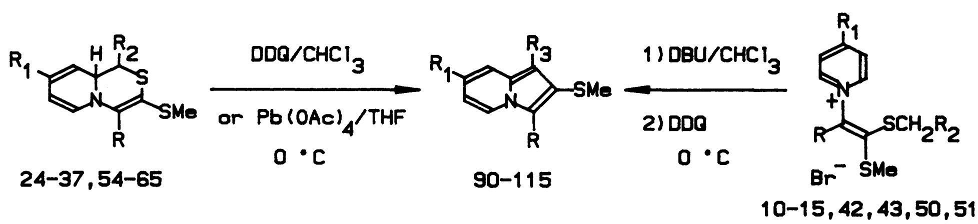
a) The coupling constants are as follows: $J_{1,9a}=2.0$(cis) or 8.0(trans), $J_{6,7}=7.0$, $J_{7,8}=6.0$, $J_{8,9}=10.0$, $J_{9,9a}=4.0$, $J_{7,9}=2.0$, $J_{Et}=7.0$ Hz. b) Overlapped with the signals of the major isomer. c) Overlapped with the signals at δ 4.4—5.2. d) Overlapped with the signals at δ 4.3—5.2. e) Overlapped with the signals at δ 4.3—5.3. f) Overlapped with the signals at δ 3.9—4.7. g) Overlapped with each others at δ 1.0—1.6 and 4.0—4.7. h) 2.57 or 2.50 (s). i) Overlapped with each others at δ 3.7—6.5.

compound **79** consisted of both cis and trans mixtures of 6-methyl and 9a-methyl derivatives and both cyclization to 2- and 6-positions on the pyridine ring took place. In the same way the distinction between the cis isomer and the trans one in the 9a-methyl derivatives **79c,d—89c,d** were carried out by the comparisons of the chemical shifts (δ 6.75—6.90 for the cis isomers **79c**, **81c**, **83c**, **85c**, and **87c—89c**, and δ 6.54 for the trans isomer **79d**) of each 6-proton with those (δ 6.59—6.73 for the cis isomers **24a—37a** and δ 6.42—6.57 for the trans isomers **24b—37b**) of the 9a-H derivatives. These chemical shifts and the signal patterns were very similar to those of 4,4a-dihydropyrido[1,2-*d*][1,3,4]-thiadiazine derivatives synthesized earlier by us.[2b)] Furthermore, the transformations of these compounds **24—37**, **54—65**, and **79—89** to the corresponding indolizine derivatives using a dehydrogenating agent supported strongly our proposed structures (See below).

Transformations to Indolizine Derivatives. Because of the thermal instability, the transformations from these dihydropyridothiazines to the corresponding indolizines did not take place except in compounds **26**, **27**, and **58**, and their treatment with an oxidizing or a dehydrogenating agent at a temperature over 0 °C resulted always in polymeric tars. Among many reagents examined for purpose of this transformation, we found that LTA and DDQ gave satisfactory results only when they were used at 0 °C. The reactions of dihydropyridothiazines **24—27** and **54—61** bearing a cyano or an ethoxycarbonyl group at the 1-position with LTA in tetrahydrofuran (THF) or with DDQ in chloroform in an ice bath afforded the desulfurized indolizines **90—101**, and those of compounds **28—37** and **62—65** having an aroyl group at that position with the same reagents gave the rearranged indolizines **102—115** in considerable yields. On the other hand, the reactions of dihydropyridothiazines **79—89**, synthesized from 2-methylpyridinium bromides **68—78**, with LTA or DDQ gave always only 5-methylindolizine derivatives **116—126** which were convertible from 9a-H adducts (types a and b), and did not afford any significant product which might be derived from 9a-methyl compounds (types c and d). The reaction of 1,4-dicyano adduct **79** with LTA, however, gave only 6-acetoxy-1,3-dicyano-5-methyl-2-methylthioindolizine **127** in very low yield (3%) instead of the expected 1,3-dicyano-5-methyl-2-methylthioindolizine **116**, while that of **79** with DDQ yielded normal product **116**. These results are summarized in Schemes 3 and 4. These dehydrogenating agents, LTA and DDQ, were effective to the same extent unless the substituents R and/or R_2 were an ethoxycarbonyl group, but, when the group(s) was so, the latter reagent was superior in the yield and the easy separation to the former.

The same indolizine derivatives could be also synthesized by adding directly DDQ to 1,9a-dihydropyridothiazines generated in situ from the alkaline treatment of the corresponding pyridinium salts (See Scheme 3). It was found that this method has high synthetic value because it can be carried out without the isolation of unstable dihydropyridothiazines.

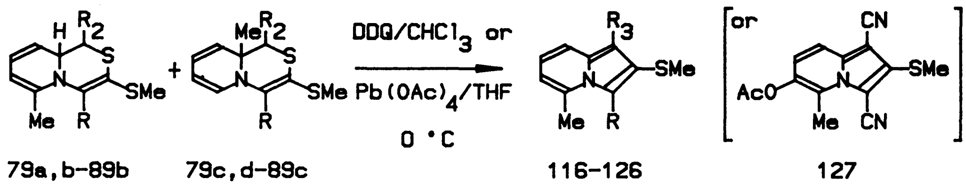
In above reactions, the desulfurized indolizines **90—**



Prod.	React.	R_1	R_3	R
90	24	H	CN	CN
91	25	Me	CN	CN
92	26	H	COOEt	CN
93	27	Me	COOEt	CN
94	54	H	CN	COOEt
95	55	Me	CN	COOEt
96	56	H	CN	Bz
97	57	Me	CN	Bz
98	58	H	COOEt	COOEt
99	59	Me	COOEt	COOEt
100	60	H	COOEt	Bz
101	61	Me	COOEt	Bz
102	28	H	BzS	CN

Prod.	React.	R_1	R_3	R
103	29	Me	BzS	CN
104	30	H	*p*-ClBzS	CN
105	31	Me	*p*-ClBzS	CN
106	32	H	*p*-BrBzS	CN
107	33	Me	*p*-BrBzS	CN
108	34	H	*p*-MeBzS	CN
109	35	Me	*p*-MeBzS	CN
110	36	H	*p*-PhBzS	CN
111	37	Me	*p*-PhBzS	CN
112	62	H	BzS	COOEt
113	63	Me	BzS	COOEt
114	64	H	*p*-ClBzS	COOEt
115	65	Me	*p*-ClBzS	COOEt

Scheme 3.



Prod.	React.	R_3	R
116	79	CN	CN
117	80	CN	COOEt
118	81	COOEt	CN
119	82	COOEt	COOEt
120	83	BzS	CN
121	84	BzS	COOEt

Prod.	React.	R_3	R
122	85	*p*-ClBzS	CN
123	86	*p*-ClBzS	COOEt
124	87	*p*-BrBzS	CN
125	88	*p*-MeBzS	CN
126	89	*p*-PhBzS	CN

Scheme 4.

101 and **116**—**119** were always formed when R_2 was a cyano or an ethoxycarbonyl group, and the rearranged indolizines **102**—**115** and **120**—**126** were obtained whenever R_2 was an aroyl group. These substituent effects are all the same as those observed in the formations from 4,4a-dihydropyrido[1,2-*d*][1,3,4]thiadiazines to the desulfurized and rearranged pyrazolo[1,5-*a*]pyridines.[1,2]

The structures of these indolizines **90**—**127** were determined mainly by their spectral and elementary analyses and in part by the comparison with authentic samples **94** (mp 142—143°C, Lit,[5] mp 139°C) and **96** (mp 143—144 °C, Lit,[5] mp 138—139 °C). In particular, the chemical shifts and signal patterns due to the skeletal protons in their ^{1}H NMR spectra (Table 2) were grossly similar to those of known indolizine derivatives prepared by us[6] and by other investigators.[5,7] The mass spectra of compounds **90**, **92**, **102**, **104**, **106**, **108**, and **110** gave molecular ion peaks at *m*/*z* 213, 260, 324, 360, 404, 338, and 401, respectively. On the other hand, the structure of unusual 6-acetoxyindolizine **127** was decided on the basis of the presences of a AB type signal coupled with 9.0 Hz (vicinal coupling) at δ 7.18 and 7.63 and of an acetoxy methyl signal at δ 2.41

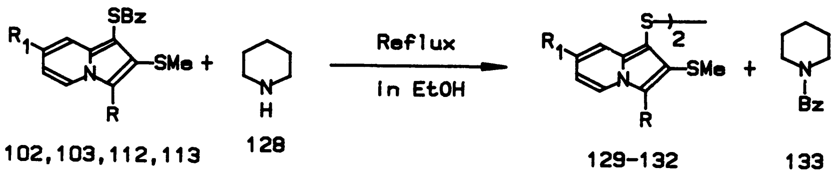
Table 2. ^{1}H NMR Data of Indolizines in $CDCl_3$

Compd a)	C-5	C-6	C-7	C-8	SMe	R_2	R
90	8.36 br d	7.10 dt	7.45 br t	7.77 br d	2.77 s	—	—
91	8.24 d	6.97 dd	2.49 s	7.51 br s	2.76 s	—	
92	8.29 br d	6.98 dt	7.37 br t	8.25 br d	2.81 s	1.44 4.42 t q	—
93	8.19 d	6.83 dd	2.44 s	8.03 br s	2.79 s	1.43 4.41 t q	—
94	9.59 br d	7.04 dt	7.41 br t	7.77 br d	2.89 s	—	1.47 4.50 t q
95	9.42 d	6.83 dd	2.47 s	7.48 br s	2.86 s	—	1.46 4.46 t q
96	9.48 br d	7.04 dt	b)	b)	2.52 s	—	7.3—8.0 m
97	9.32 d	6.84 dd	2.48 s	b)	2.50 s	—	7.3—8.9 m
98	9.47 br d	6.90 dt	7.29 br t	8.28 br d	2.53 s	1.47 c) t	1.47 c) t
99	9.40 d	6.79 dd	2.43 s	8.09 br s	2.54 s	1.48 d) t	1.48 d) t
100	9.25 br d	6.95 dt	b)	8.40 br d	2.28 s	1.47 4.49 t q	7.3—8.3 m
101	9.23 d	6.84 dd	2.49 s	8.20 br d	2.26 s	1.48 4.50 t q	7.3—8.0 m
102	8.36 br d	6.95 dt	b)	b)	2.63 s	7.2—8.3 m	—
103	b)	6.79 dd	2.37 s	7.26 br s	2.61 s	7.4—8.3 m	—
104	8.33 br d	6.95 dt	7.21 br t	b)	2.63 s	7.4—8.2 m	—
105	8.16 d	6.74 dd	2.36 s	7.20 br s	2.59 s	7.3—8.2 m	—
106	8.32 br d	6.94 dt	7.21 br t	7.51 br d	2.62 s	7.5—8.2 m	—
107	8.21 d	6.80 dd	2.39 s	7.26 br s	2.62 s	7.2—8.2 m	—
108	8.33 br d	6.92 dt	b)	b)	2.61 s	7.1—8.2 2.43 m s	—
109	8.18 d	6.77 dd	2.36 s	b)	2.59 s	7.2—8.2 2.43 m s	—
110	8.34 br d	6.95 dt	7.22 br t	b)	2.64 s	7.3—8.4 m	—
111	b)	6.79 dd	2.39 s	7.30 br s	2.63 s	7.4—8.4 m	—
112	9.55 br d	6.88 dt	7.15 br t	b)	2.50 s	7.3—8.3 m	1.48 4.49 t q
113	9.48 d	6.74 dd	2.36 s	7.30 br s	2.48 s	7.4—8.3 m	1.47 4.48 t q
114	9.54 br d	6.88 dt	7.14 br t	7.51 br d	2.48 s	7.4—8.1 m	1.47 4.49 t q
115	9.42 d	6.73 dd	2.36 s	7.24 br s	2.48 s	7.3—8.3 m	1.46 4.48 t q
116	3.03 s	6.82 br d	7.34 q	7.66 br d	2.76 s	—	—
117	2.57 s	6.78 br d	7.28 q	7.63 br d	2.70 s	—	1.44 4.48 t q
118	3.04 s	6.73 br d	7.30 q	8.32 br d	2.72 s	1.45 4.47 t q	—
119	2.57 s	6.67 br d	7.15 q	8.28 br d	2.50 s	1.44 e) t	1.44 e) t
120	3.04 s	6.70 br d	7.18 q	b)	2.57 s	7.3—8.3 m	—

Table 2. (Continued)

Compd$^{a)}$	C-5	C-6	C-7	C-8	SMe	R_2	R
121	2.60 s	6.71 br d	7.11 q	b)	2.46 s	7.3—8.4 m	1.47 4.51 t q
122	3.03 s	6.72 br d	7.16 q	b)	2.56 s	7.3—8.3 m	—
123	2.58 s	6.67 br d	7.07 q	b)	2.43 s	7.3—8.3 m	1.45 4.49 t q
124	3.03 s	6.69 br s	7.12 q	7.44 br d	2.55 s	7.6—8.2 m	—
125	3.02 s	6.68 br d	7.12 q	b)	2.57 s	7.2—8.2 2.46 m s	—
126	3.03 s	6.68 br d	7.13 q	b)	2.58 s	7.3—8.4 m	—
127	2.90 s	2.41 s	7.18 d	7.63 d	2.77 s	—	—

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. c) 4.48 or 4.44 (q). d) 4.48 or 4.49 (q). e) 4.47 or 4.49 (q).



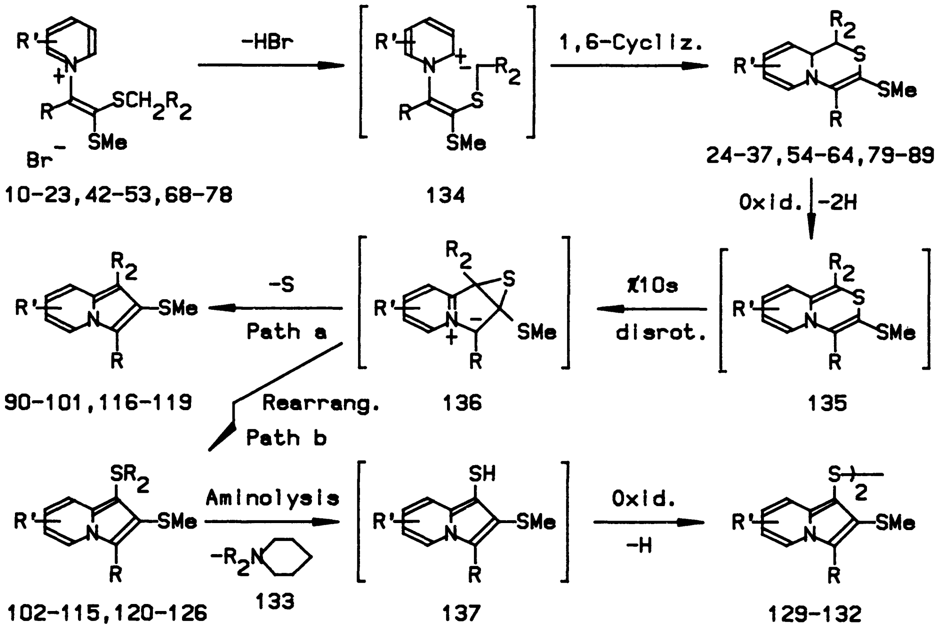
Prod.	React.	R_1	R
129	102	H	CN
130	103	Me	CN
131	112	H	COOEt
132	113	Me	COOEt

Scheme 5.

(s) and by the comparison of the chemical shifts of the pyridine protons in the ^{1}H NMR spectrum.

In order to obtain further evidences for the rearranged indolizine structure, the aminolysis of compounds **102**, **103**, **112**, and **113** with piperidine **128** were carried out in ethanol at the reflux temperature, and the corresponding disulfides **129**—**132** were obtained in good yields together with *N*-benzoylpiperidine **133** (Scheme 5). The structures of disulfides **129**—**132** were also determined by their IR and ^{1}H NMR spectral inspections in which the absence of the benzoyl group was clearly exhibited.

Reaction Mechanisms. Possible mechanisms for the reactions of pyridinium sals **10**—**23**, **42**—**53**, and **68**—**78** to desulfurized indolizines **90**—**101** and **116**—**119**, and rearranged indolizines **102**—**115** and **120**—**126** and of the rearranged indolizines to disulfides **129**—**132** are summarized in Scheme 6. This mechanisms are formally the same as those proposed to the reactions of a 1,3,4-thiadiazinyl anion by Schmidt et al.[3] and of a pyrido[1,2-*d*][1,3,4]thiadiazine by us.[1,2] In contrast with our previos works[1,2] for its aza-analogue, 1,9a-dihydropyrido[2,1-*c*][1,4]thiazine intermediates could be separated actually and the effect of dehydrogenating agents in the conversion from them to aromatic indolizines derivatives was confirmed distinctly. On the other hand, the lowness of the stereoselectivity and the regioselectivity in the 1,6-cyclizations of the zwitterionic species **134** to 1,9a-dihydropyrido[2,1-*c*][1,4]thiazines **24**—**37**, **54**—**65**, and **79**—**89** may be largely owing to the one plane and one anionic pyramidal approach (see Fig. 1) which undergoes less steric hindrance than the two plane approach as seen in normal cycloaddition reactions. The increase of the formation ratios of the trans isomers to cis isomers with the increase of the bulkiness of the group R_2 in the 9a-H adducts **24**—**37**, **54**—**65**, and **79a,b**—**89a,b** can be explained reasonably by considering the sterically less hindered conformation (**B**) in the transition state, and the predominance of the cis isomers in 9a-methyl adducts **79c,d**—**89c,d** can be understand similarly by thinking the larger steric hindrance of the 2-methyl group than that of the flat pyridine ring. Furthermore, the fact that the



Scheme 6.

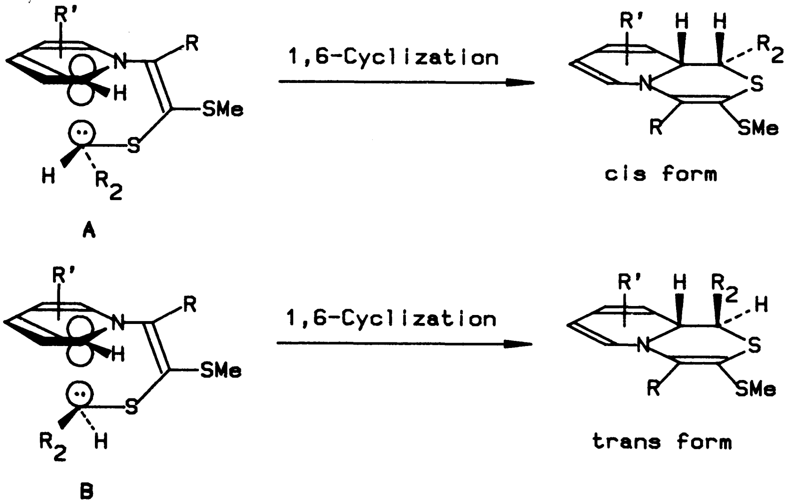


Fig. 1.

effect of the substituent R_2 in these reactions was all the same that as in the transformations of pyridothiadiazines to pyrazolo[1,5-*a*]pyridines suggests strongly a mechanistic similarity between these two reactions.

On the other hand, the mechanism for the formation of 6-acetoxyindolizine **127** is uncertain, but it may involve an attack of the acetoxyl radical generated from LTA onto the electron-rich sp^2 carbon in the pyridothiazine or indolizine intermediate.

Our reactions described here have a theoretical and practical values because only the desulfurizaion has been reported in the reaction of a 1,4-thiazinyl anion system[8] and the *S*-containing indolizine has been scarcely synthesized.[5,9]

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 ^{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, and the mass specta with a JEOL LMS-01SG-2 mass spectrometer attached with a JEC-6 spectrocomputer.

Preparations of Pyridinium 1-(Thiocarbonyl)methylides. These pyridinium 1-(thiocarbonyl)methylides **1**, **2**, **38—41**, **66**, and **67** were synthesized from the alkaline treatment of

Table 3. Some Data of 1,9a-Dihydropyrido[2,1-*c*][1,4]thiazines

Compd No.	Salt(S.Ma))	Yield %	Mp θ_m/°C	IR^{KBr} (cm^{-1})		Formula	Calcd%(Found%)		
							C	H	N
24a, b	**10**(1, 3)	47	131—133b)	2230	2210	$C_{11}H_9N_3S_2$	53.41 (53.21	3.67 3.63	16.99 17.23)
25a, b	**11**(2, 3)	56	c)	2230	2212	$C_{12}H_{11}N_3S_2$	55.15 (55.06	4.24 4.19	16.08 15.84)
26a, b	**12**(1, 4)	72	c)	2212	1728d)	Unstablee, f)			
27a, b	**13**(2, 4)	74	c)	2213	1722d)	Unstablee, g)			
28a, b	**14**(1, 5)	55	c)	2208	1677	$C_{17}H_{14}N_2OS_2$	62.55 (62.78	4.32 4.27	8.58 8.40)
29a, b	**15**(2, 5)	84	c)	2208	1664	$C_{18}H_{16}N_2OS_2$	63.50 (63.37	4.74 4.67	8.23 8.33)
30a, b	**16**(1, 6)	44	c)	2205	1687	$C_{17}H_{13}ClN_2OS_2$	56.58 (56.46	3.63 3.51	7.76 8.00)
31a, b	**17**(2, 6)	62	c)	2205	1678	$C_{18}H_{15}ClN_2OS_2$	57.67 (57.54	4.03 3.88	7.47 7.37)
32a, b	**18**(1, 7)	43	c)	2206	1670	$C_{17}H_{13}BrN_2OS_2$	50.37 (50.44	3.23 3.09	6.91 6.97)
33a, b	**19**(2, 7)	57	c)	2210	1679	$C_{18}H_{15}BrN_2OS_2$	51.55 (51.59	3.61 3.53	6.68 6.73)
34a, b	**20**(1, 8)	54	c)	2205	1670	$C_{18}H_{16}N_2OS_2$	63.50 (63.79	4.74 4.59	8.23 8.09)
35a, b	**21**(2, 8)	67	c)	2199	1663	$C_{19}H_{18}N_2OS_2$	64.38 (64.36	5.12 4.97	7.90 8.08)
36a, b	**22**(1, 9)	57	c)	2215	1670	$C_{23}H_{18}N_2OS_2$	68.63 (68.68	4.51 4.35	6.96 7.07)
37a, b	**23**(2, 9)	63	c)	2219	1668	$C_{24}H_{20}N_2OS_2$	69.20 (69.46	4.84 4.89	6.73 6.52)
54a, b	**42**(38, 3)	78	c)	2235	1710	$C_{13}H_{14}N_2O_2S_2$	53.04 (53.01	4.79 4.55	9.52 9.79)
55a, b	**43**(39, 3)	50	c)	2240	1717	$C_{14}H_{16}N_2O_2S_2$	54.52 (54.34	5.23 5.27	9.08 9.24)
56a, b	**44**(40, 3)	89	88—88c)	2232	1669	$C_{17}H_{14}N_2OS_2$	62.55 (62.55	4.32 4.30	8.58 8.60)
57a, b	**45**(41, 3)	82	c)	2230	1666d)	Unstablee)			
58a, b	**46**(38, 4)	50	c)	1720d)		Unstablee)			
59a, b	**47**(39, 4)	90	c)	1710		$C_{16}H_{21}NO_4S_2$	54.06 (53.95	5.95 5.87	3.94 3.84)
60a, b	**48**(40, 4)	82	c)	1731	1666d)	Unstablee)			
61a, b	**49**(41, 4)	72	c)	1716	1658	$C_{20}H_{21}NO_3S_2$	61.99 (61.83	5.46 5.42	3.61 3.82)
62b	**50**(38, 5)	80	94	1715	1675	$C_{19}H_{19}NO_3S_2$	61.10 (61.10	5.13 5.31	3.75 3.72)
63b	**51**(39, 5)	75	96—97	1670	1650	$C_{20}H_{21}NO_3S_2$	61.99 (61.98	5.46 5.37	3.61 3.71)
64b	**52**(38, 6)	63	92—94	1674		$C_{19}H_{18}ClNO_3S_2$	55.94 (55.86	4.45 4.59	3.43 3.36)
65b	**53**(39, 6)	39	106—108	1676	1640	$C_{20}H_{20}ClNO_3S_2$	56.93 (56.79	4.78 4.69	3.32 3.32)
79a, b, c, d	**68**(66, 3)	67	c)	2232	2203	$C_{12}H_{11}N_3S_2$	55.15 (55.05	4.24 4.21	16.08 16.20)
80a, b, c, d	**69**(67, 3)	91	c)	2235	1723	$C_{14}H_{16}N_2O_2S_2$	54.52 (54.50	5.23 5.14	9.08 9.19)
81a, b, c	**70**(66, 4)	77	c)	2205	1732d)	Unstablee)			
82b	**71**(67, 4)	89	Oil	1720	1687d)	Unstablee)			
83b, c	**72**(66, 5)	94	c)	2204		$C_{18}H_{16}N_2OS_2$	63.50 (63.64	4.74 4.84	8.23 7.99)
84b	**73**(67, 5)	58	91—92	1670		$C_{20}H_{21}NO_3S_2$	61.99 (61.96	5.46 5.22	3.61 3.88)
85b, c	**74**(66, 6)	97	c)	2207	1688	$C_{18}H_{15}ClN_2OS_2$	57.67 (57.58	4.03 3.99	7.47 7.60)
86b	**75**(67, 6)	49	99—100	1676		$C_{20}H_{20}ClNO_3S_2$	56.93 (56.64	4.78 4.70	3.32 3.52)

Table 3. (Continued)

Compd No.	Salt(S.M[a])	Yield %	Mp θ_m/°C	IR^{KBr} (cm^{-1})		Formula	Calcd%(Found%)		
							C	H	N
87b, c	**76**(**66**, **7**)	74	c)	2210	1668[d]	Unstable[e]			
88b, c	**77**(**66**, **8**)	76	c)	2199	1662	$C_{19}H_{18}N_2OS_2$	64.38	5.12	7.90
							(64.51	5.08	7.92)
89b, c	**78**(**66**, **9**)	77	c)	2210	1674[d]	Unstable[e]			

a) Starting materials. b) Cis isomer. c) Mixture. d) Neat. e) The preparation of pure sample for its analysis was unsuccessful because of its instability. f) This compound decomposed smoothly to indolizine **92** on standing in a freezer (76%). g) This compound decomposed smoothly to indolizine **93** on standing in a freezer (66%).

Table 4. Some Data of Indolizines

Compd No.	React	Method(%)			Mp θ_m/°C	IR^{KBr} (cm^{-1})		Formula	Calcd%(Found%)		
		A	B	C					C	H	N
90	**24**	41		27	140—141	2201		$C_{11}H_7N_3S+1/2H_2O$	59.94	3.63	18.96
									(59.46	3.72	18.80)
91	**25**	56		47	173—175	2201		$C_{12}H_9N_3S$	63.41	3.99	18.49
									(63.64	3.96	18.29)
92	**26**	42		43	152—154	2201	1678	$C_{13}H_{12}N_2O_2S$	59.98	4.65	10.76
									(60.14	4.75	10.50)
93	**27**	57		55	130—132	2201	1680	$C_{14}H_{14}N_2O_2S$	61.29	5.14	10.21
									(61.58	5.17	9.90)
94	**54**	33		65	142—143	2194	1669	Known Compound[a]			
95	**55**	63		51	168—169	2202	1671	$C_{14}H_{14}N_2O_2S$	61.29	5.14	10.21
									(61.40	5.18	10.06)
96	**56**	31	62		143—144	2212	1608	Known Compound[b]			
97	**57**	59	60		176—178	2203	1606	$C_{18}H_{14}N_2OS$	70.56	4.61	9.14
									(70.46	4.32	9.20)
98	**58**	23			58	1680	1660	$C_{15}H_{17}NO_4S$	58.62	5.58	4.56
									(58.46	5.42	4.48)
99	**59**	13			55	1680	1660	$C_{16}H_{19}NO_4S$	59.79	5.96	4.36
									(59.83	5.37	4.41)
100	**60**	62	53		126—128	1691		$C_{19}H_{17}NO_3S$	67.24	5.05	4.13
									(67.13	5.02	4.22)
101	**61**	56	45		84—85	1670		$C_{20}H_{19}NO_3S$	67.97	5.42	3.96
									(67.92	5.49	3.95)
102	**28**	50	81	57	134	2196	1672	$C_{17}H_{12}N_2OS_2$	62.94	3.73	8.63
									(62.68	3.68	8.52)
103	**29**	49	63	44	158—159	2196	1673	$C_{18}H_{14}N_2OS_2$	63.88	4.17	8.28
									(63.69	4.12	8.58)
104	**30**	58	94		139	2190	1670	$C_{17}H_{11}ClN_2OS_2$	56.90	3.09	7.81
									(56.80	3.07	7.64)
105	**31**	64	79		171—172	2192	1671	$C_{18}H_{13}ClN_2OS_2$	57.98	3.51	7.51
									(57.93	3.53	7.53)
106	**32**	54	83		141—142	2206	1679	$C_{17}H_{11}BrN_2OS_2$	50.63	2.75	6.95
									(50.46	2.58	6.69)
107	**33**	59	80		179	2189	1672	$C_{18}H_{13}BrN_2OS_2$	51.80	3.14	6.71
									(51.54	2.89	6.45)
108	**34**	59	61		140	2192	1668	$C_{18}H_{14}N_2OS_2$	63.88	4.17	8.28
									(63.73	4.12	8.48)
109	**35**	59	56		208—209	2204	1670	$C_{19}H_{16}N_2OS_2$	64.74	4.58	7.95
									(64.74	4.45	8.08)
110	**36**	57	93		174	2199	1676	$C_{23}H_{16}N_2OS_2$	68.97	4.03	6.99
									(68.98	3.95	7.13)
111	**37**	47	77		120—121	2185	1674	$C_{24}H_{18}N_2OS_2$	69.54	4.38	6.76
									(69.31	4.21	6.76)
112	**62**	22	68	53	89—90	1670		$C_{19}H_{17}NO_3S_2$	61.43	4.61	3.77
									(61.21	4.59	3.66)
113	**63**	37	53	51	105—106	1670		$C_{20}H_{19}NO_3S_2$	62.31	4.97	3.63
									(62.38	4.91	3.58)

Table 4. (Continued)

Compd No.	React	Method(%)			Mp θ_m/°C	IR^{KBr} (cm^{-1})		Formula	Calcd% (Found%)		
		A	B	C					C	H	N
114	**64**	25	76		93	1667		$C_{19}H_{16}ClNO_3S_2$	56.22	3.97	3.45
									(56.27	3.88	3.49)
115	**65**	10	51		137—140	1679	1670	$C_{20}H_{18}ClNO_3S_2$	57.20	4.32	3.34
									(57.22	4.31	3.44)
116	**79**	0	39		147—148	2202		$C_{12}H_9N_3S$	63.41	3.99	18.49
									(63.75	3.92	18.22)
117	**80**	c)	56		59	2205	1705	$C_{14}H_{14}N_2O_2S$	61.29	5.14	10.21
									(61.37	5.13	10.14)
118	**81**	46			138—139	2206	1681	$C_{14}H_{14}N_2O_2S$	61.29	5.14	10.21
									(61.40	5.26	9.98)
119	**82**	18	53		Oil	1695$^{d)}$		$C_{16}H_{19}NO_4S$	59.79	5.96	4.36
									(59.70	5.99	4.42)
120	**83**	32	41		149	2195	1662	$C_{18}H_{14}N_2OS_2$	63.88	4.17	8.28
									(64.12	4.15	7.98)
121	**84**	20	24		75—76	1690	1667	$C_{20}H_{19}NO_3S_2$	62.31	4.97	3.63
									(62.03	4.92	3.86)
122	**85**	21	33		93—95	2200	1665	$C_{18}H_{13}ClN_2OS_2$	57.98	3.51	7.51
									(57.83	3.51	7.47)
123	**86**	25	26		113—114	1710	1670	$C_{20}H_{18}ClNO_3S_2$	57.20	4.32	3.34
									(57.05	4.37	3.56)
124	**87**	c)	31		125—127	2200	1670	$C_{18}H_{13}BrN_2OS_2$	51.80	3.14	6.71
									(51.86	3.13	6.53)
125	**88**	24	40		154—156	2190	1664	$C_{19}H_{16}N_2OS_2$	64.74	4.58	7.95
									(64.61	4.50	8.10)
126	**89**	18	42		187—190	2198	1668	$C_{24}H_{18}N_2OS_2$	69.54	4.38	6.76
									(69.28	4.30	6.47)
127	**79**	3			205—207	2218	2195$^{c)}$	$C_{14}H_{11}N_3O_2S$	58.93	3.89	14.73
									(58.67	3.89	14.45)

a) Mp 139 °C, see Ref. 5. b) Mp 138—139 °C, see Ref. 5. c) Trace. d) Neat.

the corresponding pyridinium chlorides, carbon disulfide, and dimethyl sulfate according to the procedure described in the literature.[10] Some properties of new compounds **2** and **66** are as follows: **2**, 76%, yellow needles, mp 180—181 °C (from EtOH-CHCl$_3$), IR (KBr) 2165 (CN) and 1399 cm^{-1}. Found: C, 54.27; H, 4.52; N, 12.65%. Calcd for $C_{10}H_{10}N_2S_2$: C, 54.02; H, 4.53; N, 12.60%. **66**, 68%, yellow prisms, mp 145—146 °C (from EtOH-CHCl$_3$), IR (KBr) 2160 (CN) and 1385 cm^{-1}. Found: C, 53.96; H, 4.54; N,12.65. Calcd for $C_{10}H_{10}N_2S_2$: C, 54.02; H, 4.53; N, 12.60.

Preparations of Pyridinium Bromides. General Method. These pyridinium salts **10—23**, **42—53**, and **68—78** (2 mmol) were prepared in quantitatively yields from the reactions of the corresponding pyridinium methylides **1**, **2**, **38—41**, **66**, and **67** (2 mmol) with small excess of alkyl bromides **3—9** (2.4 mmol) in chloroform at room temperature for 1—10 d. After the evaporation of the solvent followed by the removal of an unaltered alkylating agent by washing them three times with 30 ml portions of ether, they were used immediately to the next reactions without further purification.

Preparations of 1,9a-Dihydropyrido[2,1-*c*][1,4]thiazines. General Method. To a chloroform solution (20 ml) of pyridinium bromide (2 mmol) DBU (0.380 g, 2.5 mmol) was added dropwise under stirring in an ice bath. The resulting dark red solution was kept for further 10 min at the temperature, and then concentrated immediately at reduced pressure at below 40 °C. The residue was quickly separated by short pass column chromatography (alumina, 1.7 cm diameter×7 cm long) using chloroform as an eluent. The chloroform layer was concentrated at reduced pressure without heating. The same column separation was repeated further two times. Recrystallizations of the resulting 1,9a-dihydropyrido[2,1-*c*][1,4]thiazines from chloroform-hexane in a freezer afforded pure samples.

The preparations of pure samples of compounds **26**, **27**, **57**, **58**, **81**, **82**, and **89** for analyses and the separations of the cis and trans mixtures were unsuccessful because of their thermal instability, but pure **24a** was isolated by the repeated recrystallization. Compounds **26**, **27**, and **58** were decomposed in a freezer to give the aromatized indolizines **92**, **93**, and **98** in 76, 66, and 15% yields, respectively.

Some data of these products are listed in Tables 1 and 3.

Preparations of Indolizines. General Method A. To a tetrahydrofuran solution (30 ml) of dihydropyridothiazine (1 mmol) LTA (0.443 g, 1 mmol) was added under stirring in an ice bath and the solution was stirred for further 6 h at the temperature. The resulting solution was filtered to remove insoluble substances and the filtrate was concentrated at reduced pressure. The residue was separated by column chromatography (alumina) using ether and then chloroform as eluents. The combined chloroform layer was concentrated and the recrystallization of the residue from chloroform-hexane gave the corresponding indolizine derivatives.

General Method B. DDQ (0.227 g, 1 mmol) as a dehydrogenating agent and chloroform as a solvent were employed here instead of LTA and tetrahydrofuran in Method A. The same work-ups yielded the corresponding indolizines.

General Method C. To a chloroform solution (30 ml) of pyridinium bromide (2 mmol) DBU (0.380 g, 2.5 mmol) was added dropwise under stirring in an ice bath and the resulting dark red solution was stirred for further 10 min at the temperature. An equimolar amount of DDQ was added to the reaction mixture and the resulting solution was stirred for 6 h in an ice bath. The same work-ups described in Method A gave indolizine derivatives.

The treatment of dihydropyridothiazines with LTA or DDQ at over 0°C gave always polymeric tars, and those at below 0 °C required more prolonged reaction time (a week to a month). When LTA was used as a dehydrogenating agent in the preparations of indolizines **92—95**, **98—101**, **117—119**, **121**, and **123** possessing an ethoxycarbonyl groups, the isolations of their indolizines from the reaction mixtures were considerably troublesome due to the formation of polymeric tars with similar solubility.

These data were summarized in Tables 2 and 4.

Preparations of Disulfides. General Method. An ethanolic solution (30 ml) of 1-benzoylthioindolizine (1 mmol) and piperidine **128** (0.50 g, 5.9 mmol) was heated under reflux for 6 h, the resulting solution was cooled overnight in a freezer, the separated crystals were collected by filtration, and the recrystallization from ethanol afforded the corresponding disulfide. The concentration of the filtrate, followed by its column separation (alumina) gave 1-benzoylpiperidine **133** in very good yields (88—96%). The structure of compound **133** was determined by comparison with the authentic sample.[11]

Some data of these disulfides are as follows: **129**, 90%, yellow prisms, mp 190—193 °C, IR (KBr) 2199 cm^{-1} (CN), ^{1}H NMR (CDCl$_3$) δ=2.62 (6H, s, 2×SMe), 6.6—7.1 (6H, m, 6, 7, 8, 6′, 7′, and 8′-H), and 8.11 (2H, br d, *J*=7.0 Hz, 5 and 5′-H). Found: C, 54.54; H, 3.19; N, 13.03%. Calcd for $C_{20}H_{14}N_4S_4$: C, 54.77; H, 3.22; N, 12.77%. **130**, 90%, yellow needles, mp 206—207 °C, IR (KBr) 2190 cm^{-1} (CN), ^{1}H NMR, (CDCl$_3$) δ=2.24 (6H, s, 2×Me), 2.66 (6H, s, 2×SMe), 6.5—6.9 (4H, m, 6, 8, 6′, and 8′-H), and 7.99 (2H, d, *J*=7.0 Hz, 5 and 5′-H). Found: C, 56.54; H, 3.86; N, 12.28%. Calcd for $C_{22}H_{18}N_4S_4$: C, 56.62; H, 3.89; N, 12.01%. **131**, 73%, yellow needles, mp 120—121 °C, IR (KBr) 1681 cm^{-1} (CO), ^{1}H NMR (CDCl$_3$) δ=1.46 (6H, t, *J*=7.0 Hz, 2×$\underline{CH_3}$CH$_2$O), 2.59 (6H, s, 2×SMe), 4.47 (4H, q, *J*=7.0Hz, 2×CH$_3$$\underline{CH_2}$O), 6.5—7.1 (6H, m, 6, 7, 8, 6′, 7′, and 8′-H), and 9.31 (2H, m, 5 and 5′-H). Found: C, 54.10; H, 4.53; N, 5.43%. Calcd for $C_{24}H_{24}N_2O_4S_4$: C, 54.11; H, 4.54; N, 5.26%. **132**, 86%, yellow prisms, mp 141 °C, IR (KBr) 1664 cm^{-1} (CO), ^{1}H NMR (CDCl$_3$) δ=1.45 (6H, t, *J*=7.0 Hz, 2×$\underline{CH}_3$CH$_2$O), 2.01 (6H, s, 2×Me), 2.64 (6H, s, 2×SMe), 4.47 (4H, q, *J*=7.0 Hz, 2×CH$_3$$\underline{CH_2}$O), 6.47 (2H, br d, *J*=7.0 Hz, 6 and 6′-H), 6.51 (2H, br s, 8 and 8′-H), and 9.20 (2H, d, *J*=7.0 Hz, 5 and 5′-H). Found: C, 55.67; H, 4.92; N, 4.80%. Calcd for $C_{26}H_{28}N_2O_4S_4$: C, 55.69; H, 5.03; N, 5.00%.

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