Preparation of New Nitrogen-Bridged Heterocycles. 29.[1] Reinvestigation on the Dehydrogenation Reaction of 5,5a-Dihydropyrido[2,1-*c*]thieno[3,2-*e*][1,4]thiazine Derivatives

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(Received November 12, 1991)

Reactions of the title compounds with 2,3-dichloro-4,5-dicyano-*p*-benzoquinone were reinvestigated; it was found that the corresponding products were not the ring-contracted and rearranged thieno[2,3-*b*]indolizines, as described previously by us, but were ordinary dehydrogenated compounds, pyrido[2,1-*c*]thieno[3,2-*e*][1,4]-thiazines. In contrast with pyrido[2,1-*c*]thieno[3,2-*e*][1,4]thiazine derivatives which have no substituent or only one methyl group on the pyridine ring, their 6,8-dimethyl compounds could be smoothly converted by keeping them at room temperature or heating their ethanolic solution to the corresponding desulfurized or rearranged 6,8-dimethylthieno[2,3-*b*]indolizine derivatives in moderately to good yields. The structures of these pyrido-[2,1-*c*]thieno[3,2-*e*][1,4]thiazines and thieno[2,3-*b*]indolizines were assigned mainly based on elemental analyses, and spectral inspections; X-ray analyses for two compounds finally confirmed the former structure, pyrido-[2,1-*c*]thieno[3,2-*e*][1,4]thiazine.

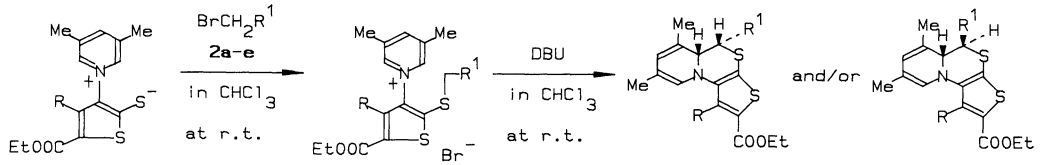
In a previous paper[2] we reported that the dehydrogenation of 5,5a-dihydropyrido[2,1-*c*]thieno[3,2-*e*][1,4]-thiazine derivatives bearing no substituent or the 7-methyl group on the pyridine ring with 2,3-dichloro-4,5-dicyano-*p*-benzoquinone (DDQ) directly gave ring-contracted and rearranged thieno[2,3-*b*]indolizines by way of their dehydrogenated intermediates. At that time these structures were assigned, based principally on the following reasons: 1) Its thiophene-free intermediate, pyrido[2,1-*c*][1,4]thiazine, was extremely unstable, and could not be isolated or detected even under the reaction conditions at 0 °C.[3] 2) The cyano absorption bands in some products were exhibited at an unusually lower region (near 2150 cm^{-1});[2] this value was in accord with that of thiocyanato group. 3) A smooth conversion from bicyclic pyrido[2,1-*c*][1,4]thiazine intermediates to the rearranged indolizines was actually observed.[3] However, a further examination of this reaction and our recent syntheses of authentic thieno[2,3-*b*]indolizine derivatives by another method[4] suggested to us the wrong structural assignment for the producuts, because, in contrast with those of authentic thieno[2,3-*b*]indolizines,[4] these dehydrogenated products had a deep color and decomposed easily upon heating. Furthermore, there was a mechanistic discrepancy in which only the rearrangement took place, regardless of the kind of 5-substituent of pyrido[2,1-*c*]thieno[3,2-*e*][1,4]thiazine intermediates in these reactions.[3,5] In this paper we wish primarily to describe the dehydrogenation reaction of some 6,8-dimethyl-5,5a-dihydropyrido[2,1-*c*]thieno[3,2-*e*][1,4]thiazine derivatives as well as the smooth transformation of the resulting products to the corresponding desulfurized or rearranged thieno[2,3-*b*]indolizines. On the basis of the above-mentioned results and X-ray structural analyses, we hope to correct our previous structural assignment[2] for dehydrogenated products.

Results and Discussion

Preparations and Reactions of Pyrido[2,1-*c*]thieno-[3,2-*e*][1,4]thiazines. In order to obtain definite information concerning the structure of pyrido[2,1-*c*]thieno[3,2-*e*][1,4]thiazine deivative, we first planned to convert compounds, which were formed earlier by us,[2] to the corresponding desulfurized or rearranged thieno[2,3-*b*]indolizine derivatives. However, these compounds did not afford any significant product upon keeping them at room temperature for a long time or by heating them in the presence or absence of desulfurizing reagents such as triphenylphosphine, triethyl phosphite, and methyl iodide. Therefore, this conversion reaction was examined for the 6,8-dimethyl derivatives in which the electron-donating effect of these methyl groups can be expected to make its pyridinium ion structure more stable (see **9a** in Fig. 3).

The compounds, 6,8-dimethyl-5,5a-dihydropyrido-[2,1-*c*]thieno[3,2-*e*][1,4]thiazines **4a**—**d** and **5a**—**j** were prepared by a route starting from 3-(3,5-dimethyl-1-pyridinio)thiophene-2-thiolates (**1a** and **1b**) according to our previous procedure (see Scheme 1).[2] The structures of these dihydropyridothienothiazines, **4** and **5**, were determined from their elemental analyses as well as by ^{1}H NMR (Table 1) and IR spectral comparisons with those of compounds reported earlier by us.[2]

Ethyl 5-cyano-1,6,8-trimethyl-5,5a-dihydropyrido-[2,1-*c*]thieno[3,2-*e*][1,4]thiazine-2-carboxylate (**4a**+**5a**), thus obtained, was treated with an equimolar amount of DDQ in chloroform at 0 °C for 15 min to afford product **6a** in 58% yield as dark-red prisms. Similarly, those of dihydropyridothienothiazines **4b**+**5b**, **5e**, **g**, **i** with the same reagent afforded the corresponding dehydrogenated compounds, **6b**, **e**, **g**, **i**, in 57, 56, 46, and 72% yields, respectively. On the other hand, although reactions of **4c**+**5c**, **4d**+**5d**, **5f**, **h**, **j** with DDQ yielded compounds **6c**,



2	R^1
a	CN
b	COOEt
c	COPh
d	COC_6H_4Cl-*p*
e	COC_6H_4Br-*p*

3	R	R^1
a	Me	CN
b	Ph	CN
c	Me	COOEt
d	Ph	COOEt
e	Me	COPh
f	Ph	COPh
g	Me	COC_6H_4Cl-*p*
h	Ph	COC_6H_4Cl-*p*
i	Me	COC_6H_4Br-*p*
j	Ph	COC_6H_4Br-*p*

4	R	R^1
a	Me	CN
b	Ph	CN
c	Me	COOEt
d	Ph	COOEt

5	R	R^1
a	Me	CN
b	Ph	CN
c	Me	COOEt
d	Ph	COOEt
e	Me	COPh
f	Ph	COPh
g	Me	COC_6H_4Cl-*p*
h	Ph	COC_6H_4Cl-*p*
i	Me	COC_6H_4Br-*p*
j	Ph	COC_6H_4Br-*p*

Scheme 1.

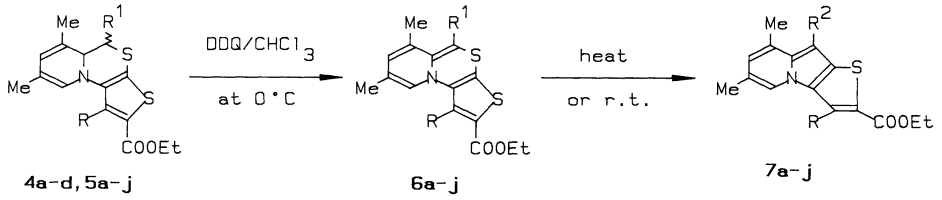
Table 1. ^{1}H NMR Spectra Data of Pyridothienothiazines

No.[a)]	C-5	C-5a	C-6	C-7	C-8	C-9	R	R^1	COOEt
4a	3.92 d	b)	1.91 s	5.95 br s	1.68 s	5.95 br s	2.48 s	—	1.35 t, 4.31 q
5a	c)	c)	1.91 s	5.67 br s	c)	5.67 br s	2.41 s	—	c) c)
4b	3.95 d	4.46 br s	1.78 s	5.39 br s	1.31 s	5.74 br s	7.40 s	—	1.15 t, 4.15 q
5b	c)	c)	c)	5.21 br s	c)	c)	c)	—	c) c)
4c	3.89 d	b)	1.92 s	5.81 br s	1.75 s	5.81 br s	2.47 s	1.19 t, 4.18 q	1.38 t, 4.30 q
5c	c)	c)	c)	c)	c)	c)	2.43 s	c) c)	c) c)
4d	b)	4.60 br s	1.97 s	5.28 br s	1.28 s	5.64 br s	7.48 s	1.24 t, 4.06 q	1.24 t, 4.20 q
5d	c)	c)	1.83 s	c)	c) s	c)	c)	c) c)	c) c)
5e	4.7—5.4 m		1.59 s	5.13 br s	1.59 s	5.43 br s	2.41 s	7.3—8.1 m	1.31 t, 4.27 q
5f	4.7—5.2 m		1.35 s	4.87 br s	1.35 s	5.19 br s	——7.1—8.0—— m		1.08 t, 4.10 q
5g	4.8—5.4 m		1.64 s	5.12 br s	1.64 s	5.51 br s	2.47 s	7.3—8.1 m	1.37 t, 4.33 q
5h	4.7—5.2 m		1.42 s	4.87 br s	1.42 s	5.26 br s	——7.1—8.0—— m		1.14 t, 4.14 q
5i	4.8—5.3 m		1.62 s	5.08 br s	1.62 s	5.48 br s	2.44 s	7.5—8.0 m	1.34 t, 4.30 q
5j	4.7—5.2 m		1.37 s	4.85 br s	1.37 s	5.25 br s	——7.2—7.9—— m		1.10 t, 4.12 q
6a	—	—	2.42 s	6.63 br s	2.08 s	7.09 br s	2.42 s	—	1.33 t, 4.31 q
6b	—	—	2.38 s	6.47 br s	1.42 s	6.39 br s	6.9—7.6 m	—	1.09 t, 4.11 q
6e	—	—	2.49 s	d)	2.34 s	d)	2.34 s	7.3—7.9 m	1.36 t, 4.25 q
6g	—	—	2.49 s	d)	2.38 s	d)	2.38 s	7.3—8.3 m	1.31 t, 4.24 q
6i	—	—	2.52 s	d)	2.39 s	d)	2.39 s	7.3—8.0 m	1.37 t, 4.25 q

a) The coupling constants were as follows: $J_{5,5a}$(cis)=2.0, J_{Et}=7.0 Hz. b) Overlapped with the methylene proton signals of the ethoxycarbonyl group. c) Overlapped with the proton signals of the cis isomer. d) Overlapped with the phenyl proton signals.

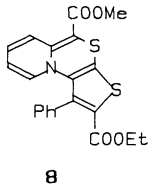
d, f, h, j, these products were very unstable; thus, during these reactions and their isolation they were smoothly converted to thieno[2,3-*b*]indolizines **7c, d, f, h, j** in moderately to good yields (30—81%). Of these pyridothienothiazines which could be isolated, compounds **6a, b** were very stable and could be stored at room temperature for a prolonged time, but compounds **6e, g ,i** were considerably unstable and slowly changed to the corresponding thienoindolizines **7e, g, i**, even at room temperature. Compounds **6a, b** were smoothly transformed to the corresponding thienoindolizines **7a, b** in good yields upon heating their ethanolic solutions for 5 h. These results and their ^{1}H NMR spectra are summarized in Scheme 2 and Tables 1 and 2.

Elemental analyses of these products **6a, b, e, g, i** coincided well with the proposed compositions of pyridothienothiazines; in their ^{1}H NMR spectra (see Table 1), the chemical shifts for skeletal protons and methyl protons were grossly similar to each other as well as with those of compounds synthesized earlier by us.[2] However, these chemical shifts were different to some extent from those (Table 2) for thieno[2,3-*b*]indolizines



6	R	R^1
a	Me	CN
b	Ph	CN
(c)	Me	COOEt
(d)	Ph	COOEt
e	Me	COPh
(f)	Ph	COPh
g	Me	COC_6H_4Cl-*p*
(h)	Ph	COC_6H_4Cl-*p*
i	Me	COC_6H_4Br-*p*
(j)	Ph	COC_6H_4Br-*p*

7	R	R^2
a	Me	CN
b	Ph	CN
c	Me	COOEt
d	Ph	COOEt
e	Me	SCOPh
f	Ph	SCOPh
g	Me	$SCOC_6H_4Cl$-*p*
h	Ph	$SCOC_6H_4Cl$-*p*
i	Me	$SCOC_6H_4Br$-*p*
j	Ph	$SCOC_6H_4Br$-*p*



8

Scheme 2.

Table 2. ^{1}H NMR Spectra Data of Thienoindolizines

No.[a]	C-5	C-6	C-7	C-8	R	R^1	COOEt
7a	8.19	2.36	6.88	2.67	2.94	—	1.42 4.38
	br s	s	br s	s	s		t q
7b	7.30	2.05	6.84	2.70	7.2—7.8	—	1.14 4.14
	br s	s	br s	s	m		t q
7c	8.18	2.31	6.87	2.87	2.96	1.44 1.49[b]	4.41 4.41[b]
	br s	s	br s	s	s	t t	q q
7d	7.26	1.99	6.82	2.83	7.2—7.7	1.48 4.40	1.13 4.15
	br s	s	br s	s	m	t q	t q
7e	8.22	2.19	6.65	2.53	2.91	7.4—8.4	1.32 4.23
	br s	s	br s	s	s	m	t q
7f	7.32	2.03	6.62	2.66	——7.3—8.3——		1.16 4.18
	br s	s	br s	s	m		t q
7g	8.29	2.21	6.63	2.56	2.94	7.4—8.3	1.32 4.28
	br s	s	br s	s	s	m	t q
7h	c)	2.00	6.62	2.60	——7.2—8.2——		1.15 4.12
	br s	s	br s	s	m		t q
7i	8.35	2.26	6.70	2.58	2.99	7.5—8.1	1.35 4.30
	br s	s	br s	s	s	m	t q
7j	7.26	1.94	6.58	2.54	——7.3—8.1——		1.08 4.12
	br s	s	br s	s	m		t q

a) The coupling constants for the ethoxy protons was 7.0 Hz. b) The signals due to these ethoxycarbonyl groups could not be definitely assigned. c) Overlapped with the phenyl proton signals.

Table 3. Crystal and Structure Analysis Data of Compounds **6a** and **8**

	6a	**8**
Formula	$C_{17}H_{16}N_2O_2S_2$	$C_{21}H_{17}NO_4S_2$
Formula weight	344.45	411.49
Crystal system	Orthorhombic	Monoclinic
Space group	$P2_12_12_1$; Z=4	$P2_1/c$;Z=4
Lattice parameters		
a/Å	12.598 (4)	10.090 (2)
b/Å	16.522 (1)	18.925 (3)
c/Å	8.039 (2)	10.244 (6)
α/°	90	90
β/°	90	92.84 (3)
γ/°	90	90
V/Å^3	1673.1 (6)	1954 (1)
D_{calcd}/g cm^{-3}	1.367	1.399
Crystal size/mm^3	0.24×0.18×0.60	0.06×0.16×0.80
Diffractometer	Rigaku AFC5S	Rigaku AFC5S
Radiation	Mo$K\alpha$ (λ=0.71069 Å)	Mo$K\alpha$ (λ=0.71069 Å)
Monochrometer	Graphite	Graphite
Scan type	ω–2θ	ω–2θ
2θ Max/°	55.0	54.9
Computer program	TEXSAN System[a)]	TEXSAN System[a)]
Structure solution	Direct method: SIR[b)]	Direct method; MITHRIL[c)]
Hydrogen atom treatment	Calculated, not refined	Calculated, not refined
Refinement	Full-matrix, anisotropic	Full-matrix, anisotropic
Least-squares weight	$4F_o^2/\sigma^2(F_o^2)$	$4F_o^2/\sigma^2(F_o^2)$
No. of measurement ref.	Total: 2230	Total: 4075
	Unique: 2230	Unique: 3824
No of observations[d)]	1147	1179
No. of variables	208	253
Residuals R; R_w	0.050; 0.055	0.059; 0.069
Max shift/error	0.04	0.03
$\Delta\rho_{max}$/e$^-$ Å^{-3}	0.29	0.29

a) See Ref 10. b) See Ref. 11. c) See Ref. 12. d) $I>3.00\sigma(I)$.

Table 4. Selected Bond Lengths and Bond Angles of Compounds **6a** and **8** (esd's, where given, are in parentheses)

	6a	**8**		**6a**	**8**
Bond lengths[a)]			Bond angles		
S1–C1	1.731(7)	1.735(9)	C3–N1–C8	119.2(6)	119.2(8)
S1–C10	1.710(7)	1.70(1)	C4–N1–C8	121.2(5)	120.0(9)
S2–C9	1.794(7)	1.81(1)	S1–C1–C2	112.7(5)	112.7(8)
S2–C10	1.738(7)	1.75(1)	C1–C2–C3	110.1(6)	109.7(8)
N1–C3	1.445(8)	1.44(1)	N1–C3–C2	126.0(6)	125.0(9)
N1–C4	1.369(8)	1.36(1)	N1–C3–C10	119.8(6)	120(1)
N1–C8	1.400(8)	1.40(1)	C2–C3–C10	114.0(6)	114(1)
C1–C2	1.385(8)	1.37(1)	N1–C4–C5	121.4(6)	123(1)
C2–C3	1.421(9)	1.42(1)	C4–C5–C6	117.5(7)	119(1)
C3–C10	1.353(9)	1.34(1)	C5–C6–C7	122.7(6)	121(1)
C4–C5	1.354(9)	1.32(1)	C6–C7–C8	119.1(7)	120(1)
C5–C6	1.40(1)	1.37(1)	N1–C8–C7	115.4(6)	115.2(9)
C6–C7	1.35(1)	1.36(1)	N1–C8–C9	118.2(6)	120.5(9)
C7–C8	1.43(1)	1.43(1)	C7–C8–C9	126.4(7)	124(1)
C8–C9	1.379(9)	1.41(1)	S2–C9–C8	119.3(5)	117.4(8)
C9–C13	1.42(1)	1.44(1)[b)]	S2–C9–C13	112.9(5)	117.2(8)[b)]
Bond angles			C8–C9–C13	127.6(7)	123(1)[d)]
C1–S1–C10	90.7(3)	90.7(5)	S1–C10–S2	126.3(4)	125.4(6)
C9–S2–C10	95.3(3)	96.0(5)	S1–C10–C3	112.5(5)	112.3(8)
C3–N1–C4	119.0(6)	120.1(9)	S2–C10–C3	121.0(5)	122.3(9)

a) For the numberings of compounds **6a** and **8** shown here, see their ORTEP drawings in Figs. 1 and 2. b) C9–C14. c) S2–C9–C14. d) C8–C9–C14.

7a—j, both regarding a shielding effect due to the neighboring 1-phenyl group and the deshielding effect due to the 2-methylene-1,2-dihydropyridine structure. The IR spectra of **6a**, **b** again exhibited absorption bands (2150 cm^{-1} in **6a** and 2160 cm^{-1} in **6b**), which are attributable to the 5-cyano group. On the other hand, the structures of thieno[2,3-*b*]indolizines **7a—j** were determined by physical and spectral comparisons with those of authentic samples, including **7a**, **c**.[4] Since reaction products **6a—j** from dihydropyridothienothiazines **4** and **5** and DDQ actually afforded the corresponding desulfurized thieno[2,3-*b*]indolizines **7a—d** and rearranged ones **7e—j** and their physical and spectral data were different from those for thieno[2,3-*b*]indolizines **7a—j**, any other structure except thieno[2,3-*b*]-indolizines must be assigned to **6a—j**.

Crystallography of Pyrido[2,1-*c*]thieno[3,2-*e*][1,4]-thiazines. Finally, the structures of these dehydrogenated products **6a—j** were confirmed by single-crystal X-ray analyses of ethyl 5-cyano-1,6,8-trimethylpyrido-[2,1-*c*]thieno[3,2-*e*][1,4]thiazine-2-caboxylate (**6a**) and previously reported 2-ethyl 5-methyl 1-phenylpyrido-[2,1-*c*]thieno[3,2-*e*][1,4]thiazine-2,5-dicarboxylate (**8**)[2] (see Scheme 2). Crystal data and details of structure analyses are summarized in Tables 3 and 4, and the ORTEP drawings[6] of compounds **6a** and **8** are shown in Figs. 1 and 2, respectively.

These X-ray analyses of **6a** and **8** suggest some important facts: 1) The structural data for these pyridine and thiophene moieties are quite similar to those for usual and fused indolizines[2,4e,7] and thiophenes,[4e,8] and, though it might not be perfect, the aromatic character in both ring systems could be expected. 2) The bond length (1.794 Å in **6a** or 1.81 Å in **8**) for the S2–C9 bond

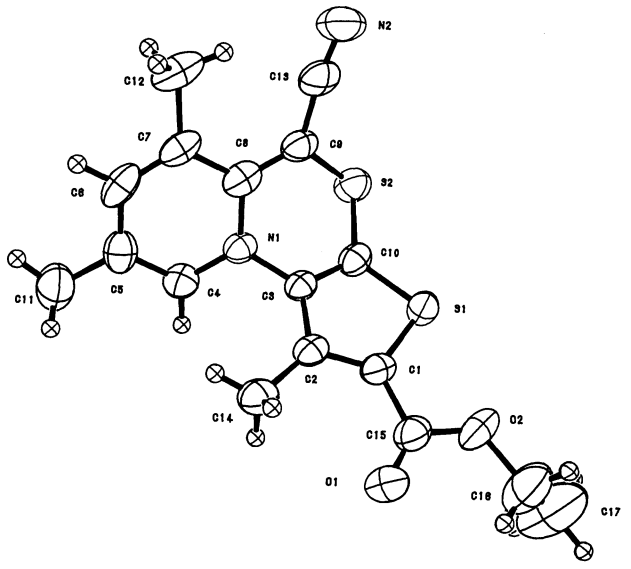


Fig. 1. ORTEP drawing of ethyl 5-cyano-1,6,8-trimethylpyrido[2,1-*c*]thieno[3,2-*e*][1,4]thiazine-2-carboxylate (**6a**) showing the atom labeling scheme and 50% probability thermal ellipsoids.

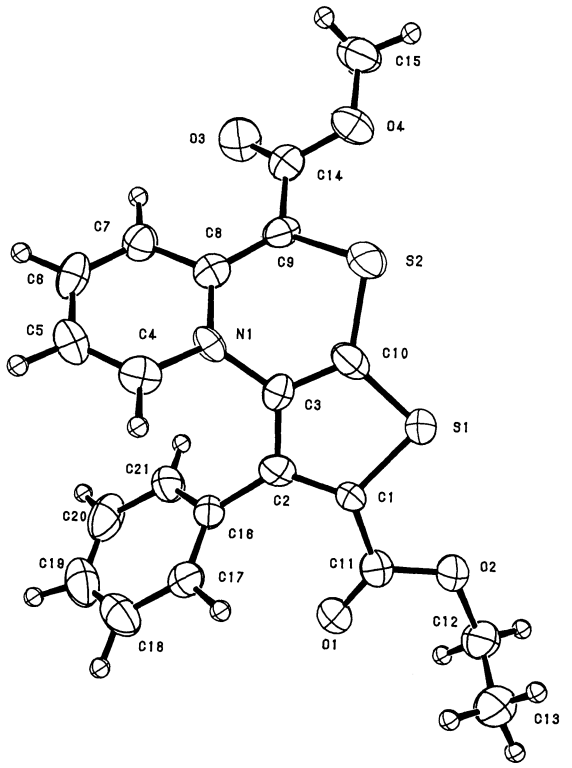


Fig. 2. ORTEP drawing of 2-ethyl 5-methyl 6,8-dimethyl-1-phenylpyrido[2,1-*c*]thieno[3,2-*e*][1,4]-thiazine-2,5-dicarboxylate (**8**) showing the atom labeling scheme and 50% probability thermal ellipsoids.

(see Figs. 1 and 2 and Table 4) in the 4*H*-1,4-thiazine ring is nearly parallel to that (1.813 Å) for the sulfur–carbon single bond in ethyl methyl sulfide;[9] and these values are apparently unusual for the bond length in such an unsaturated ring system. The abnormality of the S2–C9 bond length in this pyrido[2,1-*c*]thieno[3,2-*e*][1,4]-thiazine structure (**9**, see Fig. 3) may reflect an interesting situation against the unstable antiaromatic π electron system, because this molecule **9** has total 16π electrons if the resonance contributors such as **9b**, **c** are considered.

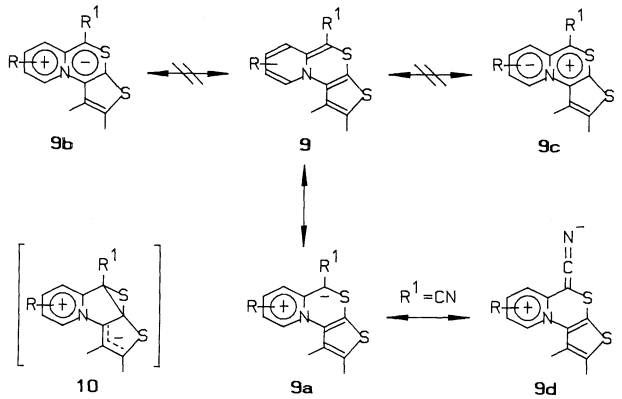


Fig. 3. Possible resonance structures of pyrido[2,1-*c*]-thieno[3,2-*e*][1,4]thiazine (**9**) and tetracyclic thiirane intermediate (**10**).

Eventually, the entire conjugated system in such molecule **9** is cut off at that bond position and the localized structure of the anion at the 5-position such as **9a** must be a main contributor. The lowered absorption band near 2150 cm^{-1} is attributable to the 5-cyano group, and can be explained better by considering a resonance structure such as the **9d** derived from this **9a**.

Mechanistic Consideration. The reason why thermolyses of 6,8-dimethyl-5,5a-dihydropyrido[2,1-*c*]thieno-[3,2-*e*][1,4]thiazines **6a**—**j** smoothly gave the corresponding thieno[2,3-*b*]indolizines **7a**—**j** but those of compounds bearing no substituent or only the 7-methyl group on the pyridine ring did not afford any significant product is still unclear. In general, these transformation reactions from pyridothienothiazines **6** to thienoindolizines **7** seem to be energetically unfavorable. This is because a tetracyclic thiirane intermediate such as **10** (see Fig. 3), which should be involved in this reaction, has no aromatic stabilization of the thiophene ring, in contrast with that in starting material **6**. However, such a conversion for 6,8-dimethylpyridothienothiazine derivatives **6a**—**j** was actually found, and the influence of the 5-substituent on the thermal stabilities of **6a**—**j** was also observed. Pyridothienothiazines **6a**, **b** having a less steric cyano group at the 5-position are more stable than the others, and their conversions to thienoindolizines **7a**, **b** were carried out under more severe conditions. Eventually, stabilization of the intermediate **10** by the electron-donating property of the 6,8-dimethyl groups and acceleration for ring-closure from pyridothienothiazine **6** to thiirane **10** by relief of the peri interaction between the 5-R^1 and the 6-methyl group in **6** must be the major driving forces for this reaction.

Experimental

The meltings points were measured with a Yanagimoto micromelting point apparatus and were not corrected. Microanalyses were carried out using a Perkin-Elmer 2400 elemental analyzer. The ^1H NMR spectra were determined with a Varian EM360A spectrometer in deuteriochloroform with tetramethylsilane used 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. 3-(3,5-Dimethyl-1-pyridinio)thiophene-2-thiolate derivatives (**1a**, **b**) were prepared according to our previous procedure.[2] They were synthesized by heating the corresponding 3,5-dimethylpyridinium methylides, readily available from the reactions of 1-acetonyl- and 1-phenacyl-3,5-dimethylpyridinium chloride, carbon disulfide, and ethyl bromoacetate in the presence of a base, with DBU in ethanol for 5 h. These results, as well as some of the properties of a new ylide and **1a**, **b** are as follows: 2-Benzoyl-2-(3,5-dimethylpyridino)-1-(ethoxycarbonylmethylthio)ethylene-1-thiolate, 73%, yellow needles (chloroform–ether), mp 173—176 °C, ν (KBr) 1725 cm^{-1} (CO), Anal. ($C_{20}H_{21}NO_3S_2$) C, H, N. **1a**, 86% dark red prisms (ethanol), mp 228—229 °C, ν (KBr) 1670 cm^{-1} (CO), Anal. ($C_{15}H_{17}NO_2S_2$) C, H, N. **1b**, 54%, dark red prisms, mp 227—228 °C, ν (KBr) 1689 cm^{-1} (CO), Anal. ($C_{20}H_{19}NO_2S_2$) C, H, N.

Preparations of 5,5a-Dihydropyrido[2,1-*c*]thieno[3,2-*e*]-[1,4]thiazines. General Method. A chloroform solution (10 ml) of 3-(3,5-dimethyl-1-pyridinio)thiophene-2-thiolate derivatives (**1**, 2 mmol) and an alkylating agent (2.2 mmol), such as bromoacetonitrile (**2a**), ethyl bromoacetate (**2b**), phenacyl bromide (**2c**), *p*-chlorophenacyl bromide (**2d**), and *p*-bromophenacyl bromide (**2e**), was kept at room temperature until the disappearance of the ylide **1** was confirmed by thin-layer chromatographic (TLC) monitoring (ca. 1 d). After the resulting reaction mixture was concentrated at reduced pressure, the residue was washed three times with ether to remove any excess alkylating agent. To the thus obtained pyridinium salt **3** chloroform (30 ml) was added, and the resulting solution was treated with 1,8-diazabicyclo[5.4.0]-undec-7-ene (DBU) at room temperature for 15 min. The solvent was removed from the reaction mixture at reduced pressure and the residual oil was separated by column chromatography on activated alumina using chloroform as an eluent. The chloroform layer was concentrated and crude products **4** and/or **5** were purified by recrystallization from chloroform–hexane.

In these reactions 6,8-dimethyl-5,5a-dihydropyrido[2,1-*c*]-thieno[3,2-*e*][1,4]thiazines were obtained as cis–trans mixtures

Table 5. Some Data for Dihydropyridothienothiazines

No.[a]	React	Yield %	Mp °C	ν (KBr) cm^{-1}	Formula[b]
4a+5a	**1a** **2a**	95	Mixture[c]	2239 1692	$C_{17}H_{18}N_2O_2S_2$
4b+5b	**1b** **2a**	75	Mixture[d]	2225 1690	$C_{22}H_{20}N_2O_2S_2$
4c+5c	**1a** **2b**	92	Mixture[e]	1732 1690	$C_{19}H_{23}NO_4S_2$
4d+5d	**1b** **2b**	71	Mixture[f]	1742 1673	$C_{24}H_{25}NO_4S_2$
5e	**1a** **2c**	94	200—202	1695 1675	$C_{23}H_{23}NO_3S_2$
5f	**1b** **2c**	80	141—144	1710 1685	$C_{28}H_{25}NO_3S_2$
5g	**1a** **2d**	92	152—155	1692	$C_{23}H_{22}ClNO_3S_2$
5h	**1b** **2d**	93	139—141	1708 1663	$C_{28}H_{24}ClNO_3S_2$
5i	**1a** **2e**	91	151—152	1688	$C_{23}H_{22}BrNO_3S_2$
5j	**1b** **2e**	97	137—139	1710 1667	$C_{28}H_{24}BrNO_3S_2$

a) These compounds **4a**—**d**, **5a**—**j** were obtained as orange prisms. b) The satisfactory analytical data (within 0.3% for C. H. and N) were obtained for all compounds. c) The ratio of **4a** to **5a** was 2:1. d) The ratio of **4b** to **5b** was 6:1. e) The ratio of **4c** to **5c** was 14:3. f) The ratio of **4d** to **5d** was 10:3.

Table 6. Some Data for Pyridothienothiazines and Thienoindolizines

No.[a]	React	Yield %	Mp °C	ν (KBr) cm⁻¹	Formula[b]
6a	**4a+5a**	58	153—155	2150 1705	$C_{17}H_{16}N_2O_2S_2$
6b	**4b+5b**	57	135—137	2160 1695	$C_{22}H_{18}N_2O_2S_2$
6e	**5e**	56	123—125	1703 1685	$C_{23}H_{21}NO_3S_2$
6g	**5g**	46	109—111	1708	$C_{23}H_{20}ClNO_3S_2$
6i	**5i**	72	102—104	1705	$C_{23}H_{20}BrNO_3S_2$
7a	**6a**	71	258—260 (Lit,[c,d] mp 257—260 °C)		
7b	**6b**	80	230—232	2201 1683	$C_{22}H_{18}N_2O_2S$
7c	**4c+5c**	30	127—128 (Lit,[c] mp 127—128 °C)		
7d	**4d+5d**	55	173—175	1699	$C_{24}H_{23}NO_4S$
7e	**6e**	77	205—208	1685 1675	$C_{23}H_{21}NO_3S_2$
7f	**5f**	45	193—195	1700 1675	$C_{28}H_{23}NO_3S_2$
7g	**6g**	84	187—188	1693 1680	$C_{23}H_{20}ClNO_3S_2$
7h	**5h**	58	189—192	1708 1677	$C_{28}H_{22}ClNO_3S_2$
7i	**6i**	59	200—202	1688 1672	$C_{23}H_{20}BrNO_3S_2$
7j	**5j**	81	195—196	1706 1670	$C_{28}H_{22}BrNO_3S_2$

a) Compounds **6a, b** were obtained as dark red prisms, **6e, g,i** as dark brown needles, **7a—d** as pale yellow needles, and **7e—j** as orange needles. b) Satisfactory analytical data (within 0.3% for C, H, and N) were obtained for all compounds. c) See Ref. 3b. d) See Ref. 13.

(**4+5**) at the 5- and 5a-positions when R^1 is a cyano or ethoxycarbonyl group and only as trans isomers (**5**) when the group is an aroyl (Scheme 1); however, separations of these cis–trans mixtures were unsuccessful, because of their similar solubilities. These results and some data are summarized in Tables 1 and 5.

Dehydrogenation Reactions of 5,5a-Dihydropyrido[2,1-*c*]-thieno[3,2-*e*][1,4]thiazines. General Method. After a chloroform solution (30 ml) of **4** and/or **5** (1 mmol) was chilled to 0 °C in an ice bath, an equimolar amount of DDQ (0.227 g) was added under stirring. After 15 min the reaction mixture was concentrated under reduced pressure and the residue was separated by column chromatography (alumina) using chloroform as an eluent. Removal of the solvent and recrystallization from chloroform or chloroform–hexane gave the corresponding pyrido[2,1-*c*]thieno[3,2-*e*][1,4]thiazine derivatives (**6a, b, e, g ,i**). On the other hand, although the formation of compounds **6c, d, f, h, j** could be confirmed by TLC monitoring, they were very unstable and isomerized to the corresponding thieno[2,3-*b*]indolizine derivatives **7c, d, f, h, j** during these reactions and purifications.

The use of chloranil as a dehydrogenating agent in this reaction or the prolonged reaction time caused diminished yields of the expected products **6** or **7**. These results are given in Tables 1, 2, and 6.

Thermolyses of Pyrido[2,1-*c*]thieno[3,2-*e*][1,4]thiazines. General Mothod A. Compounds **6e, g, i** were smoothly transformed to the corresponding thieno[2,3-*b*]indolizines **7e, g, i** by only keeping their chloroform solution at room temperature for 1 d.

General Method B. An ethanolic solution (20 ml) of 5-cyano derivatives (**6a** or **6b**, 0.5 mmol) was heated under reflux in a water bath for 5 h. The solution was then chilled to under 0 °C in a freezer. The precipitates which separated were collected by suction and the crude product was recrystallized from ethanol.

These results are listed in Tables 2 and 6.

Crystallography of Pyrido[2,1-*c*]thieno[3,2-*e*][1,4]thiazines. The crystals of ethyl 5-cyano-1,6,8-trimethylpyrido[2,1-*c*]-thieno[3,2-*e*][1,4]thiazine-2-caboxylate **6** and 2-ethyl 5-methyl 1-phenylpyrido[2,1-*c*]thieno[3,2-*e*][1,4]thiazine-2,5-dicarboxylate **8** were grown from their chloroform solution. A dark-red orthorhombic crystal for **6a** and a black monoclinic crystal for **8** were used for structure determinations. Crystal data and details concerning structure analyses are shown in Tables 3 and 4. The bond lengths, bond and torsion angles, atomic coordinates and equivalent temperature factors, and F_c-F_o tables are deposited as Document No. 8989 at the Office of the Editor of Bull. Chem. Soc. Jpn.

The authors are grateful to the Ministry of Education, Science and Culture for the financial support to this work [Grant-in-Aids for Scientific Research Nos. 02453085 and 03650669].

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