Preparation of New Nitrogen-Bridged Heterocycles. 16.[1] Facile Synthesis of Thieno[2,3-*b*]indolizine Derivatives

Akikazu KAKEHI,* Suketaka ITO, Yasuhiro OHNO, Shouji SHIBA, and Sakashi KAMATA
Department of Industrial Chemistry, Faculty of Engineering, Shinshu University, Wakasato, Nagano 380
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2-Ethoxycarbonyl-3-methyl- and 3-phenylthieno[2,3-*b*]indolizine derivatives were first synthesized in moderate to good yields by the treatment of tricyclic 5,5a-dihydropyrido[2,1-*c*]thieno[3,2-*e*][1,4]thiazines with a dehydrogenating agent. In contrast to the cases of bicyclic 1,9a-dihydropyrido[2,1-*c*][1,4]thiazines, all of the thienoindolizines obtained here were rearranged products and no desulfurized product could be obtained.

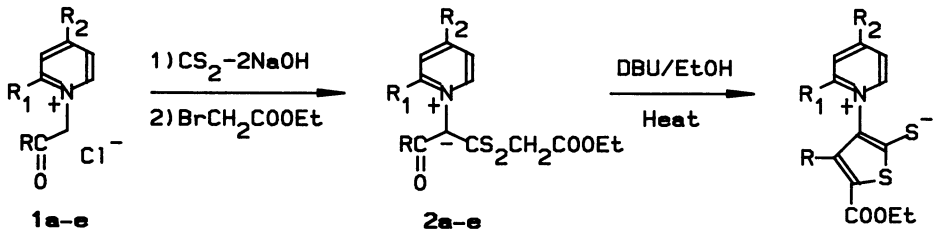
Our recent papers in this series have described the novel ring contraction reactions of pyrido[2,1-*c*]-[1,4]thiazines and pyrido[1,2-*d*][1,3,4]thiadiazines generated in situ from their dihydro compounds.[1,2] These reactions are not only convenient preparative methods for some indolizines and pyrazolo[1,5-*a*]-pyridines which are not obtainable by other methods but also good models for studying the behavior of the heterocyclic compounds having a $4n\pi$ electron system.[3] The wide versatility and the ready availability of starting materials and the synthetic and mechanistic interests prompted us to extend these reactions to a fused system with an aromatic ring in anticipation of the stabilization of reaction intermediates and of a new skeletal synthesis. In this paper we wish to report the isolations of some stable dihydropyridothiazines fused with a thiophene ring and their transformations to the corresponding thieno[2,3-*b*]indolizine derivatives and will also discuss about the effect of the fused aromatic ring on the reaction courses.

Results and Discussion

Preparations of 3-(1-Pyridinio)thiophene-2-thiolates. These pyridinium betaines **3a—e** bearing a thiophene ring were synthesized in 54—90% yields by the intramolecular condensations of pyridinium 1-methylides **2a—e**, readily obtainable from the reactions of 1-acetonyl- **1a** and **1b** and 1-phenacylpyridinium chlorides **1c—e**, carbon disulfide, and ethyl bromoacetate in the precence of base (Scheme 1).

The structures of pyridinium methylides **2a—e** and 3-(1-pyridinio)thiophene-2-thiolates **3a—e** were decided by their elemental analyses and by their spectral comparisons with those of analogous types of compounds.[4]

Preparations of 5,5a-Dihydropyrido[2,1-*c*]thieno-[3,2-*e*][1,4]thiazines. When the *S*-alkylations of pyridinium betaines **3a—d** with reagents such as bromoacetonitrile **4a**, methyl bromoacetate **4b**, ethyl bromoacetate **4c**, phenacyl bromide **4d**, *p*-chlorophenacyl bromide **4e**, and *p*-bromophenacyl bromide **4f** in chloroform followed by the treatment of the resulting pyridinium salts **5a—x** with 1,8-diazabicyclo[5.4.0]-undec-7-ene (DBU) in chloroform at 0 °C were carried out, the corresponding 2-ethoxycarbonyl-1-methyl- and 1-phenyl-5,5a-dihydropyrido[2,1-*c*]thieno[3,2-*e*]-[1,4]thiazines **6a—l** and **7a—x** were formed in considerable yields as crystalline compounds, respectively. On the other hand, the expected tricyclic adducts **6y**+**7y** and **6z**+**7z** could not be obtained by the alkaline treatment of pyridinium salts **5y** and **5z** which were



1	R	R_1	R_2
a	Me	H	H
b	Me	H	Me
c	Ph	H	H
d	Ph	H	Me
e	Ph	Me	H

2	R	R_1	R_2
a	Me	H	H
b	Me	H	Me
c	Ph	H	H
d	Ph	H	Me
e	Ph	Me	H

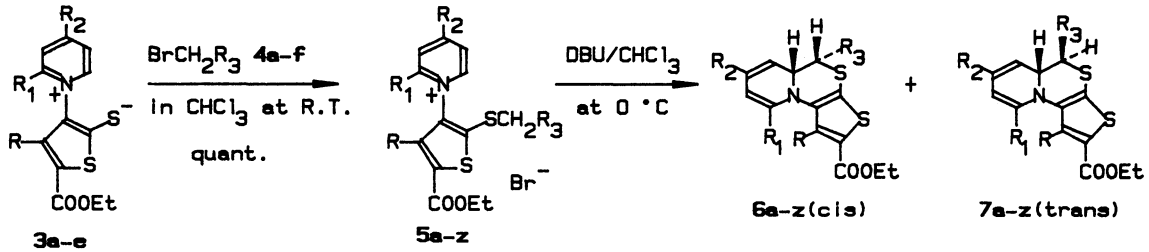
3	R	R_1	R_2
a	Me	H	H
b	Me	H	Me
c	Ph	H	H
d	Ph	H	Me
e	Ph	Me	H

Scheme 1.

similarly obtained from the reactions of pyridinium betaine **3e** bearing a methyl group at the 2-position with bromoacetonitrile **4a** and ethyl bromoacetate **4c**. (Scheme 2) The inaccessibility of adducts **6y+7y** and **6z+7z** from 2-methylpyridinium salts **5y** and **5z** suggested a large steric hinderance against the cyclization between the 2-methyl group and the bulky thiophene moiety.

In contract to bicyclic dihydropyridothiazines[1] the adducts **6a—l** and **7a—x** were fairly stable compounds and scarcely decomposed at room temperature. The elemental analyses of adducts **6a—l** and **7a—x** were in good accord with the proposed compositions, and the chemical shifts and the signal patterns due to the dihydropyridothiazine moiety in their proton NMR (^{1}H NMR) spectra (see Table 1) were similar to those of bicyclic ones.[1] The latter also showed that adducts **6a—l** and **7a—l** were cis and trans mixtures with respect to the 8a and 9 positions and **7m—x** only trans isomers. The isomer ratios are shown in Scheme 2.

Preparations of 2-Ethoxycarbonyl-3-methyl- and 3-phenylthieno[2,3-*b*]indolizines. Although the reactions of dihydropyridothienothiazines **6a—l** and **7a—x** with lead tetraacetate did not afford the expected ring



4	R_3
a	CN
b	COOMe
c	COOEt
d	Bz
e	*p*-ClBz
f	*p*-BrBz

Bz=benzoyl

Prod.	Salt	R	R_1	R_2	R_3	6/7
6a+7a	5a	Me	H	H	CN	4/7
6b+7b	5b	Me	H	Me	CN	4/5
6c+7c	5c	Ph	H	H	CN	1/1
6d+7d	5d	Ph	H	Me	CN	2/1
6e+7e	5e	Me	H	H	COOMe	1/2
6f+7f	5f	Me	H	Me	COOMe	1/2
6g+7g	5g	Ph	H	H	COOMe	5/6
6h+7h	5h	Ph	H	Me	COOMe	5/7
6i+7i	5i	Me	H	H	COOEt	3/10
6j+7j	5j	Me	H	Me	COOEt	1/3
6k+7k	5k	Ph	H	H	COOEt	5/9
6l+7l	5l	Ph	H	Me	COOEt	2/5
7m	5m	Me	H	H	Bz	0/1

Prod.	Salt	R	R_1	R_2	R_3	6/7
7n	5n	Me	H	Me	Bz	0/1
7o	5o	Ph	H	H	Bz	0/1
7p	5p	Ph	H	Me	Bz	0/1
7q	5q	Me	H	H	*p*-ClBz	0/1
7r	5r	Me	H	Me	*p*-ClBz	0/1
7s	5s	Ph	H	H	*p*-ClBz	0/1
7t	5t	Ph	H	Me	*p*-ClBz	0/1
7u	5u	Me	H	H	*p*-BrBz	0/1
7v	5v	Me	H	Me	*p*-BrBz	0/1
7w	5w	Ph	H	H	*p*-BrBz	0/1
7x	5x	Ph	H	Me	*p*-BrBz	0/1
(6y+7y)	5y	Ph	Me	H	CN	
(6z+7z)	5z	Ph	Me	H	COOEt	

Scheme 2.

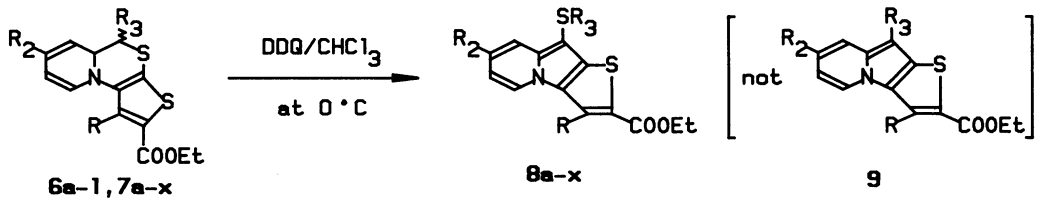
Table 1. ^{1}H NMR Spectral Data of Dihydropyridotienothiazines in $CDCl_3$

Compound[a] No.	C-5	C-6	C-7	C-8	C-8a	C-9	R	R_3	COOEt	
6a	6.44	b)	6.30	b)	c)	6.44	2.53	—	1.36	4.33
	d		br q			d	s		t	q
7a	6.13	b)	6.30	b)	c)	c)	2.47	—	1.36	4.33
	d		br q				s		t	q
6b	6.40	4.86	1.89	5.21	d)	3.60	2.52	—	1.36	4.33
	d	dd	s	br s		d	s		t	q
7b	6.08	5.04	1.89	5.43	d)	d)	2.46	—	1.36	4.33
	d	dd	d	br s			s		t	q
6c	5.80	e)	6.10	f)	e)	3.61	7.42	—	1.14	4.16
	d		m			d	s		t	q
7c	5.59	e)	6.10	f)	e)	e)	7.42	—	1.14	4.16
	d		m				s		t	q
6d	5.71	c)	1.71	5.00	c)	3.55	7.37	—	1.13	4.13
	d		s	br s		d	s		t	q
7d	5.50	c)	1.71	5.30	c)	c)	7.37	—	1.13	4.13
	d		s	br s			s		t	q

Table 1. (Continued)

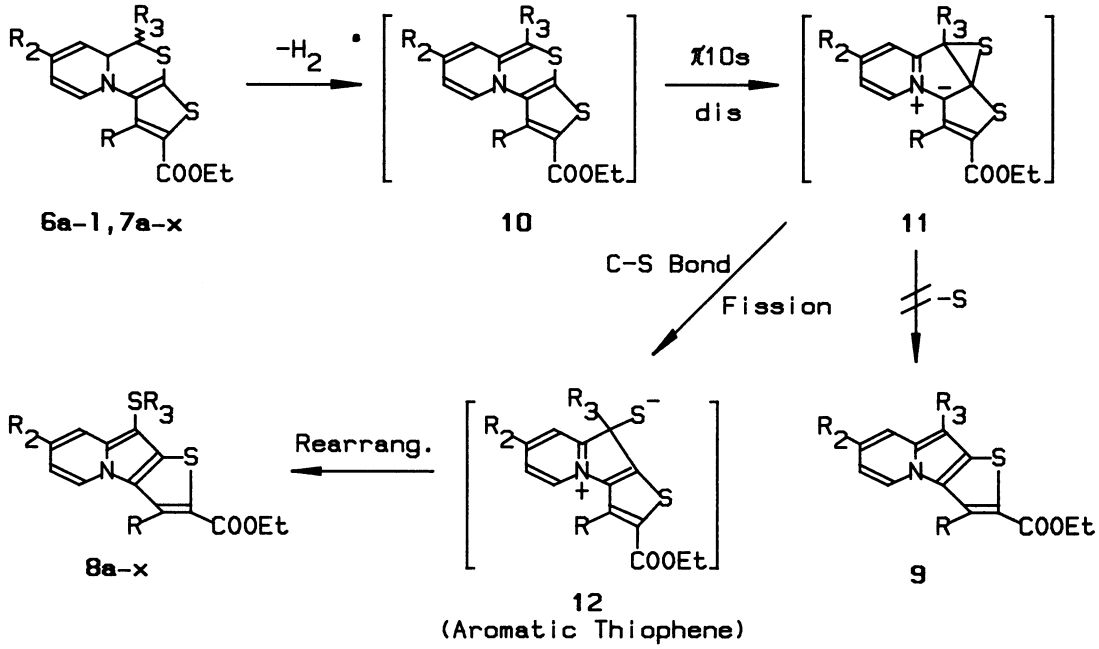
Compound[a] No.	C-5	C-6	C-7	C-8	C-8a	C-9	R	R_3		COOEt	
6e	g)	h)	g)	4.1—5.5 m		3.56 d	2.52 s	3.68 s		1.36 t	4.31 q
7e	g)	h)	g)	— 4.1—5.5 — m			2.47 s	3.81 s		1.36 t	4.31 q
6f	6.20 d	4.68 dd	1.79 s	5.07 br s	d)	3.50 d	2.50 s	3.64 s		1.34 t	4.32 q
7f	6.08 d	4.90 dd	1.79 s	5.07 br s	d)	d)	2.46 s	3.80 s		1.34 t	4.32 q
6g	5.59 d	c)	5.93 q	5.26 br q	c)	3.59 d	7.43 s	3.63 s		1.14 t	4.17 q
7g	5.59 d	c)	5.93 q	5.26 br q	c)	c)	7.43 s	3.80 s		1.14 t	4.17 q
6h	5.57 d	e)	1.65 s	5.00 br s	e)	3.52 d	7.42 s	3.61 s		1.13 t	4.16 q
7h	5.57 d	e)	1.65 s	5.00 br s	e)	e)	7.42 s	3.81 s		1.13 t	4.16 q
6i	g)	5.01 br t	g)	5.35 m	c)	3.53 d	2.50 s	1.30 t	4.30 q	1.34 t	4.31 q
7i	g)	5.01 br t	g)	5.35 m	c)	c)	2.46 s	1.30 t	4.30 q	1.34 t	4.31 q
6j	6.23 d	4.63 dd	1.79 s	5.10 br s	c)	3.52 d	2.52 s	1.31 t	4.27 q	1.36 t	4.32 q
7j	6.08 d	4.92 dd	1.81 s	5.10 br s	c)	c)	2.47 s	1.31 t	4.27 q	1.36 t	4.32 q
6k	5.60 d	e)	5.93 q	5.27 br q	e)	3.57 d	7.43 s	1.31 t	4.28 q	1.17 t	4.17 q
7k	5.60 d	e)	5.93 q	5.27 br q	e)	e)	7.43 s	1.31 t	4.28 q	1.17 t	4.17 q
6l	5.60 d	d)	1.67 s	5.04 br s	d)	3.53 d	7.43 s	1.31 t	4.28 q	1.15 t	4.17 q
7l	5.60 d	d)	1.67 s	5.04 br s	d)	d)	7.43 s	1.31 t	4.28 q	1.15 t	4.17 q
7m	6.21 d	5.02 br t	6.00 q	5.38 br q	4.63 br d	5.40 d	2.50 s	7.3—8.3 m		1.34 t	4.33 q
7n	6.07 br d	i)	1.57 s	— 4.3—5.5 — m			2.47 s	7.3—8.3 m		1.33 t	4.31 q
7o	5.67 br d	j)	5.67 br	5.25 br	j)	5.29 br d	7.45 s	7.3—8.3 m		1.17 t	4.18 q
7p	5.50 br d	k)	1.43 s	— 4.4—5.3 — m			7.45 s	7.3—8.2 m		1.16 t	4.17 q
7q	6.22 br d	5.05 br t	6.00 br q	l)	4.62 br d	5.32 br d	2.50 s	7.3—8.3 m		1.35 t	4.34 q
7r	5.90 br d	k)	1.57 s	— 4.4—5.3 — m			2.47 s	7.3—8.2 m		1.32 t	4.28 q
7s	5.67 br d	— 4.4—5.4 — m					7.39 s	7.3—8.1 m		1.34 t	4.13 q
7t	5.30 br d	m)	1.43 s	— 4.3—5.2 — m			7.44 s	7.3—8.2 m		1.14 t	4.15 q
7u	6.21 br d	5.06 br t	5.99 br q	l)	4.57 br d	5.30 br d	2.50 s	7.5—8.2 m		1.34 t	4.33 q
7v	5.93 br	k)	1.59 s	— 4.4—5.3 — m			2.49 s	7.5—8.1 m		1.35 t	4.32 q
7w	5.71 br d	n)	5.67 br	— 4.4—5.4 — m			7.43 s	7.5—8.1 m		1.16 t	4.17 q
7x	5.30 br	o)	1.43 s	— 4.4—5.2 — m			7.39 s	7.5—8.1 m		1.15 t	4.15 q

a) The coupling constants are as follows: $J_{8a,9}$(cis)=2.0, $J_{8a,9}$(trans)=8.0, $J_{5,6}$=7.0, $J_{6,7}$=6.0, $J_{7,8}$=10.0, $J_{8,8a}$=4.0, $J_{5,7}$=2.0, and J_{Et}=7.0 Hz. b) Overlapped with the other signals at δ 4.8—5.9. c) Overlapped with the signals at δ 4.0—4.8. d) Overlapped with the other signals at δ 4.0—4.7. e) Overlapped with the other signals at δ 4.0—4.9. f) Overlapped with the other signals at δ 5.0—5.5. g) Overlapped with the other signals at δ 5.9—6.4. h) Overlapped with the other signals at δ 4.1—5.5. i) Overlapped with the other signals at δ 4.3—5.5. j) Overlapped with the other signals at δ 4.4—4.9. k) Overlapped with the other signals at δ 4.4—5.3. l) Overlapped with the other signals at δ 4.8—5.6. m) Overlapped with the other signals at δ 4.3—5.2. n) Overlapped with the other signals at δ 4.4—5.4. o) Overlapped with the other signals at δ 4.4—5.2.



Prod.	React.	R	R_2	R_3	Prod.	React.	R	R_2	R_3
8a	6a+7a	Me	H	CN	8m	7m	Me	H	Bz
8b	6b+7b	Me	Me	CN	8n	7n	Me	Me	Bz
8c	6c+7c	Ph	H	CN	8o	7o	Ph	H	Bz
8d	6d+7d	Ph	Me	CN	8p	7p	Ph	Me	Bz
8e	6e+7e	Me	H	COOMe	8q	7q	Me	H	*p*-ClBz
8f	6f+7f	Me	Me	COOMe	8r	7r	Me	Me	*p*-ClBz
8g	6g+7g	Ph	H	COOMe	8s	7s	Ph	H	*p*-ClBz
8h	6h+7h	Ph	Me	COOMe	8t	7t	Ph	Me	*p*-ClBz
8i	6i+7i	Me	H	COOEt	8u	7u	Me	H	*p*-BrBz
8j	6j+7j	Me	Me	COOEt	8v	7v	Me	Me	*p*-BrBz
8k	6k+7k	Ph	H	COOEt	8w	7w	Ph	H	*p*-BrBz
8l	6l+7l	Ph	Me	COOEt	8x	7x	Ph	Me	*p*-BrBz

Scheme 3.



Scheme 4.

contraction products, the treatment with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) in chloroform at 0 °C formed the corresponding thieno[2,3-*b*]indolizine derivatives **8a—z** as dark red or black crystals in 19—96% yields. Furthermore, the same products **8a—z** could be also obtained from adducts **6a—l** and **7a—x** by the action of palladium on carbon at room temperature, but their yields were low in compared with those using DDQ (Scheme 3).

Very interestingly, all of products **8a—x** were not the desulfurized thienoindolizines such as **9** but the rearranged ones regardless of the kinds of the substituent (R_3).[1,2]

The thienoindolizines, **8a—x**, were comparatively stable compounds at room temperature, but their 3-phenyl derivatives **8c**, **8d**, **8g**, **8h**, **8k**, **8l**, **8o**, **8p**, **8s**, **8t**, **8w**, and **8x**, in particular, were easily decomposed at the refluxing temperature of ethanol to give polymeric substances. The instability of these thienoindolizines **8a—x** must be caused by both the strained thiaazapenta-

Table 2. ^{1}H NMR Spectral Data of Thieno[2,3-*b*]indolizines in $CDCl_3$

Compound[a] No.	C-5	C-6	C-7	C-8	R	R_3	COOEt	
8a	7.28	6.11	6.6—7.2		2.49	—	1.35	4.34
	br d	m	m		s		t	q
8b	7.19	5.97	2.12	6.80	2.48	—	1.34	4.32
	d	dd	s	br s	s		t	q
8c	6.53	5.43	6.77	6.98	7.0—7.6	—	1.15	4.15
	br d	br t	br t	br d	m		t	q
8d	6.44	5.28	2.00	6.73	6.9—7.6	—	1.13	4.12
	d	dd	s	br s	m		t	q
8e	7.28	6.18	6.92	8.28	2.45	3.76	1.35	4.33
	br d	dt	br t	br d	s	s	t	q
8f	7.18	6.05	2.16	8.09	2.43	3.71	1.32	4.29
	d	dd	s	br s	s	s	t	q
8g	6.58	5.51	6.72	8.21	6.9—7.6	3.74	1.12	4.13
	br d	dt	br t	br d	m	s	t	q
8h	6.58	5.44	2.04	8.11	6.9—7.6	3.77	1.13	4.15
	d	dd	s	br s	m	s	t	q
8i	7.22	6.11	6.83	8.21	2.41	1.28 4.18	1.33	4.30
	br d	dt	br t	br d	s	t q	t	q
8j	7.21	6.06	2.17	8.11	2.43	1.29 4.20	1.34	4.31
	d	dd	s	br s	s	t q	t	q
8k	6.53	5.50	6.70	8.19	7.0—7.6	1.33 4.21	1.15	4.15
	br d	br t	br t	br d	m	t q	t	q
8l	6.55	5.42	2.03	8.10	7.0—7.6	1.32 4.21	1.14	4.15
	d	dd	s	br s	m	t q	t	q
8m	b)	6.48	7.08	7.98	2.52	7.3—7.8	1.35	4.34
		dt	br t	br d	s	m	t	q
8n	b)	6.39	2.22	8.03	2.50	7.3—7.7	1.34	4.30
		dd	s	br s	s	m	t	q
8o	6.92	5.82	b)	8.00	7.0—7.8	7.0—7.8	1.16	4.15
		dt		br d	m	m	t	q
8p	6.91	5.82	2.09	8.09	7.0—7.9	7.0—7.9	1.13	4.17
	d	dd	s	br s	m	m	t	q
8q	b)	6.57	7.19	8.10	2.53	7.3—7.8	1.37	4.35
		dt	br t	br d	s	m	t	q
8r	b)	6.51	2.27	8.16	2.51	7.2—7.7	1.34	4.32
		dd	s	br s	s	m	t	q
8s	6.94	5.92	b)	8.13	7.0—7.8	7.0—7.8	1.15	4.17
	br d	br t		br d	m	m	t	q
8t	6.99	5.92	2.18	8.26	7.0—8.0	7.0—8.0	1.16	4.19
	d	dd	s	br s	m	m	t	q
8u	b)	6.57	7.19	8.13	2.51	7.3—7.8	1.34	4.33
		dt	br t	br d	s	m	t	q
8v	b)	6.47	2.27	8.17	2.49	7.2—7.7	1.33	4.30
		dd	s	br d	s	m	t	q
8w	6.94	5.93	b)	8.13	7.0—7.7	7.0—7.7	1.15	4.17
	br d	br t		br d	m	m	t	q
8x	7.00	5.93	2.17	8.27	7.0—7.9	7.0—7.9	1.14	4.18
	d	dd	s	br s	m	m	t	q

a) The coupling constants are as follows: $J_{5,6}=J_{6,7}=7.0$, $J_{7,8}=10.0$, $J_{6,8}=2.0$ Hz, and $J_{Et}=7.0$ Hz.
b) Overlapped with the phenyl proton signals.

lene skeleton and the steric repulsion between the 3-substituent (R) and the 5-proton.

The elementary analyses of these products **8a—x** were in accord with the compositions of the thieno[2,3-*b*]indolizines carrying a thio group at the 9-position. The IR spectra of thienoindolizines **8a—d** exhibited also clearly the precence of a thiocyanato group (2141—2151 cm^{-1}). The proton signals (Table 2) on the pyridine ring in compounds **8a—x** appeared in the range of δ 5.28—8.28, and the values (δ 5.97—8.28) except those (δ 5.28—5.93) due to the 5- and 6-protons of 3-phenyl derivatives **8c**, **8d**, **8g**, **8h**, **8k**, **8l**, **8o**, **8p**, **8s**, **8t**, **8w**, and **8x** are not contradictory to those of aromatic indolizine derivatives.[1,5] These high field shifts observed largely for the 5- and 6-protons in 3-phenyl derivatives must be caused by the shielding effect of the 3-phenyl group whose resonance-stabilized planar conformation is prevented owing to the proximity of great extent between the 3-phenyl group and the 5-proton. From these data, the products

Table 3. Some Data of Dihydropyridothienothiazines

Compd. No.	Salt(S.M.)[a]	Yield %	Mp θ_m/°C	IR^{KBr}/cm^{-1}	Formula	Calcd/% (Found/%) C	H	N
6a+7a	5a(**3a**, **4a**)	71	b)	2235 1709	$C_{15}H_{14}N_2O_2S_2$	56.58 (56.40)	4.43 4.46	8.80 9.08)
6b+7b	**5b**(**3b**, **4a**)	64	b)	2239 1690	$C_{16}H_{16}N_2O_2S_2$	57.81 (57.98)	4.85 4.86	8.43 8.40)
6c+7c	**5c**(**3c**, **4a**)	77	b)	2215 1710	$C_{20}H_{16}N_2O_2S_2$	63.13 (63.10)	4.24 4.31	7.36 7.33)
6d+7d	**5d**(**3d**, **4a**)	74	b)	2210 1710	$C_{21}H_{18}N_2O_2S_2$	63.93 (63.72)	4.60 4.55	7.10 7.12)
6e+7e	**5e**(**3a**, **4b**)	56	b)	1720 1695	$C_{16}H_{17}NO_4S_2$	54.68 (54.86)	4.88 4.89	3.99 3.94)
6f+7f	**5f**(**3b**, **4b**)	44	b)	1716 1690	$C_{17}H_{19}NO_4S_2$	55.87 (55.89)	5.24 5.11	3.83 3.94)
6g+7g	**5g**(**3c**, **4b**)	97	b)	1733 1675	$C_{21}H_{19}NO_4S_2$	61.00 (61.07)	4.63 4.62	3.39 3.33)
6h+7h	**5h**(**3d**, **4b**)	88	b)	1735 1680	$C_{22}H_{21}NO_4S_2$	61.81 (62.08)	4.95 4.87	3.28 2.99)
6i+7i	**5i**(**3a**, **4c**)	54	b)	1728 1680	$C_{17}H_{19}NO_4S_2$	55.87 (55.90)	5.24 5.21	3.83 3.69)
6j+7j	**5j**(**3b**, **4c**)	26	b)	1723 1700	$C_{18}H_{21}NO_4S_2$	56.97 (57.18)	5.58 5.31	3.69 3.83)
6k+7k	**5k**(**3c**, **4c**)	83	b)	1732 1702	$C_{22}H_{21}NO_4S_2$	61.81 (61.77)	4.95 4.91	3.28 3.24)
6l+7l	**5l**(**3d**, **4c**)	80	b)	1732 1682	$C_{23}H_{23}NO_4S_2$	62.56 (62.68)	5.25 5.29	3.17 3.00)
7m	**5m**(**3a**, **4b**)	80	108—110	1703 1680	$C_{21}H_{19}NO_3S_2$	63.45 (63.45)	4.82 4.82	3.52 3.43)
7n	**5n**(**3b**, **4d**)	54	107—109	1704 1675	$C_{22}H_{21}NO_3S_2$	64.21 (64.20)	5.14 5.15	3.40 3.23)
7o	**5o**(**3c**, **4d**)	89	178—180	1681 1670	$C_{26}H_{21}NO_3S_2$	67.95 (67.92)	4.61 4.67	3.05 2.86)
7p	**5p**(**3d**, **4d**)	89	170—172	1710 1662	$C_{27}H_{23}NO_3S_2$	68.47 (68.57)	4.90 5.09	2.96 2.67)
7q	**5q**(**3a**, **4e**)	91	152—155	1680 1665	$C_{21}H_{18}ClNO_3S_2$	58.39 (58.09)	4.20 4.16	3.24 3.54)
7r	**5r**(**3b**, **4e**)	51	147—150	1701 1679	$C_{22}H_{20}ClNO_3S_2$	59.25 (59.16)	4.52 4.47	3.14 3.42)
7s	**5s**(**3c**, **4e**)	66	142—144	1720 1683	$C_{26}H_{20}ClNO_3S_2$	63.21 (63.32)	4.08 4.07	2.84 2.80)
7t	**5t**(**3d**, **4e**)	54	147—149	1720 1680	$C_{27}H_{22}ClNO_3S_2$	63.83 (63.54)	4.36 4.27	2.76 3.04)
7u	**5u**(**3a**, **4f**)	70	157—159	1690 1663	$C_{21}H_{18}BrNO_3S_2$	52.94 (52.92)	3.81 3.83	2.94 3.11)
7v	**5v**(**3b**, **4f**)	46	152—154	1703 1679	$C_{22}H_{20}BrNO_3S_2$	53.88 (53.87)	4.11 3.95	2.86 3.03)
7w	**5w**(**3c**, **4f**)	77	161—163	1710 1679	$C_{26}H_{20}BrNO_3S_2$	57.99 (57.80)	3.74 3.72	2.60 2.77)
7x	**5x**(**3d**, **4f**)	89	168—170	1720 1666	$C_{27}H_{22}BrNO_3S_2$	58.70 (58.51)	4.01 3.97	2.54 2.77)
(**6y+7y**)	**5y**(**3e**, **4a**)	0						
(**6z+7z**)	**5z**(**3e**, **4c**)	0						

a) Starting materials. b) This compound is a cis and trans mixture.

were concluded to be 5-thiocyanato- **8a—d**, 9-(alkoxycarbonylthio)-**8e—l**, and 9-(aroylthio)thieno-[2,3-*b*]indolizine derivatives **8m—x**, respectively.

Reaction Mechanisms. Possible mechanisms for the formation of the rearranged thienoindolizines **8a—x** from the corresponding dihydropyridothienothiazines **6a—l** and **7a—x** are shown in Scheme 4. The most remarkable feature in these ring contraction reactions is that only the rearranged tricyclic indolizines were formed regardless of the kinds of the R_3 group and the desulfurized compounds as described in similar reactions of bicyclic dihydropyridothiazines were not at all.[1] The reason why the desulfurized indolizines were not afforded in this tricyclic system is still uncertain, but, perhaps, the rapid ring opening from tetracyclic thiirane **11** to indolizinium 9-thiolate **12** possessing an aromatic thiophene ring may take place prior to the desulfurization to **9**.

Table 4. Some Data of Thieno[2,3-*b*]indolizines

Compd. No.	React.	Yield %	Mp θ_m/°C	IR^{KBr}/cm^{-1}	Formula	Calcd/% (Found/%) C	H	N
8a	**6a+7a**	81	159—162	2151 1680	$C_{15}H_{12}N_2O_2S_2$	56.94 (57.00	3.82 3.67	8.85 8.94)
8b	**6b+7b**	49	157—159	2144 1702	$C_{16}H_{14}N_2O_2S_2$	58.16 (58.21	4.27 3.97	8.48 8.73)
8c	**6c+7c**	94	146—148	2141 1711	$C_{20}H_{14}N_2O_2S_2$	63.47 (63.35	3.73 3.94	7.40 7.31)
8d	**6d+7d**	56	131—132	2150 1674	$C_{21}H_{16}N_2O_2S_2$	64.26 (64.42	4.11 4.14	7.14 6.95)
8e	**6e+7e**	77	125—127	1701 1670	$C_{16}H_{15}NO_4S_2$	55.00 (55.03	4.33 4.14	4.01 4.13)
8f	**6f+7f**	37	133—135	1695	$C_{17}H_{17}NO_4S_2$	56.18 (56.24	4.71 4.68	3.85 3.83)
8g	**6g+7g**	54	122—124	1678	$C_{21}H_{17}NO_4S_2$	61.30 (61.35	4.16 4.05	3.40 3.46)
8h	**6h+7h**	51	144—146	1690	$C_{22}H_{19}NO_4S_2$	62.10 (61.98	4.50 4.46	3.29 3.44)
8i	**6i+7i**	72	124—126	1700	$C_{17}H_{17}NO_4S_2$	56.18 (56.41	4.71 4.68	3.85 3.82)
8j	**6j+7j**	38	132—134	1690	$C_{18}H_{19}NO_4S_2$	57.27 (57.47	5.07 4.82	3.71 3.69)
8k	**6k+7k**	84	132—135	1709	$C_{22}H_{19}NO_4S_2$	62.10 (61.87	4.50 4.52	3.29 3.51)
8l	**6l+7l**	68	126—128	1689	$C_{23}H_{21}NO_4S_2$	62.85 (62.66	4.82 5.01	3.19 3.19)
8m	**7m**	43	141—142	1690	$C_{21}H_{17}NO_3S_2$	63.78 (63.91	4.33 4.07	3.54 3.67)
8n	**7n**	38	144—146	1683	$C_{22}H_{19}NO_3S_2$	64.52 (64.59	4.68 4.88	3.42 3.16)
8o	**7o**	66	104—106	1705	$C_{26}H_{19}NO_3S_2$	68.25 (68.25	4.19 4.28	3.06 2.97)
8p	**7p**	56	133—135	1710	$C_{27}H_{21}NO_3S_2$	68.77 (68.92	4.49 4.53	2.97 2.78)
8q	**7q**	29	139—141	1691	$C_{21}H_{16}ClNO_3S_2$	58.67 (58.54	3.75 3.74	3.26 3.07)
8r	**7r**	35	143—145	1705	$C_{22}H_{18}ClNO_3S_2$	59.52 (59.53	4.09 4.05	3.15 3.18)
8s	**7s**	78	136—138	1710	$C_{26}H_{18}ClNO_3S_2$	63.47 (63.24	3.69 3.82	2.85 2.96)
8t	**7t**	71	152—155	1713	$C_{27}H_{20}ClNO_3S_2$	64.09 (64.12	3.98 3.98	2.77 2.74)
8u	**7u**	19	149—151	1685	$C_{21}H_{16}BrNO_3S_2$	53.17 (53.04	3.40 3.32	2.95 3.17)
8v	**7v**	27	146—148	1685	$C_{22}H_{18}BrNO_3S_2$	54.10 (54.17	3.71 3.58	2.87 2.93)
8w	**7w**	96	151—153	1708	$C_{26}H_{18}BrNO_3S_2$	58.21 (58.02	3.38 3.39	2.61 2.79)
8x	**7x**	62	141—143	1710 1686	$C_{27}H_{20}BrNO_3S_2$	58.91 (59.04	3.66 3.79	2.54 2.56)

In contract to the observations obtained by other investigators,[3,6] a strong trend toward the rearrangement was found in our pyrido[2,1-*c*][1,4]thiazine system, and further efforts to explain this phenomenon will be done.

Experimental

Melting points were measured with a Yanagimoto micro-melting 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.

Preparations of Pyridinium Methylides 2a—e. These pyridinium 1-(dithiocarboxy)methylides **2a—e** were prepared from the reactions of 1-acetonyl- **1a** and **1b** and 1-phenacylpyridinium chlorides **1c—e**, carbon disulfide, and ethyl bromoacetate in the presence of base according to the procedure described in the literature.[4] Some data of compounds **2a—e** are as follows: **2a**, 90%, yellow flakes (from ethanol), mp 162—164 °C, IR (KBr) 1730 cm^{-1} (CO). Found: C, 52.48; H, 5.06; N, 4.76%. Calcd for $C_{13}H_{15}NO_3S_2$: C, 52.50; H, 5.08; N, 4.71%. **2b**, 76%, yellow flakes (from ethanol), mp

170—172 °C, IR (KBr) 1730 cm^{-1} (CO). Found: C, 53.77; H, 5.47; N, 4.76%. Calcd for $C_{14}H_{17}NO_3S_2$: C, 54.00; H, 5.50; N, 4.50%. **2c**, 73%, yellow needles (from ethanol), mp 190—192 °C, IR (KBr) 1720 cm^{-1} (CO). Found: C, 59.98; H, 4.93; N, 3.90%. Calcd for $C_{18}H_{17}NO_3S_2$: C, 60.14; H, 4.77; N, 3.90%. **2d**, 84%, yellow needles (from ethanol), mp 191—193 °C, IR (KBr) 1730 cm^{-1} (CO). Found: C, 61.26; H, 4.79; N, 3.93%. Calcd for $C_{19}H_{19}NO_3S_2$: C, 61.10; H, 5.13; N, 3.75%. **2e**, 54%, yellow prisms (from ethanol), mp 183—185 °C, IR (KBr) 1720 cm^{-1} (CO). Found: C, 60.93; H, 5.11; N, 3.95%. Calcd for $C_{19}H_{19}NO_3S_2$: C, 61.10; H, 5.13; N, 3.75%.

Preparations of 3-(1-Pyridinio)thiophene-2-thiolates 3a—e. General Method: An ethanolic solution (100 ml) of pyridinium 1-methylide (10 mmol) and DBU (1.82 g, 12 mmol) was heated under the reflux temperature on a water bath until the disappearance of yellow spot of pyridinium 1-methylide was confirmed by the TLC monitoring of the reaction solution. (2—5 h) The resulting red solution was cooled to room temperature and then the product crystallized was collected by filtration. Recrystallizations from ethanol gave 3-(1-pyridinio)thiophen-2-thiolates **3a—e** as red needles. Some data of compounds **3a—e** are shown below. **3a**, 68%, mp 205—207 °C, IR (KBr) 1685 cm^{-1} (CO). Found: C, 55.80; H, 4.70; N, 5.09%. Calcd for $C_{13}H_{13}NO_2S_2$: C, 55.89; H, 4.69; N, 5.01%. **3b**, 83%, mp 202—205 °C, IR (KBr) 1670 cm^{-1} (CO). Found: C, 57.47; H, 5.08; N, 4.68%. Calcd for $C_{14}H_{15}NO_2S_2$: C, 57.31; H, 5.15; N, 4.77%. **3c**, 87%, mp 244—246 °C, IR (KBr) 1675 cm^{-1} (CO). Found: C, 63.09; H, 4.44; N, 4.16%. Calcd for $C_{18}H_{15}NO_2S_2$: C, 63.32; H, 4.43; N, 4.10%. **3d**, 76%, mp 242—244 °C, IR (KBr) 1685 cm^{-1} (CO). Found: C, 64.32; H, 4.69; N, 3.95%. Calcd for $C_{19}H_{17}NO_2S_2$: C, 64.20; H, 4.82; N, 3.94%. **3e**, 60%, mp 217—221 °C, IR (KBr) 1690 cm^{-1} (CO). Found: C, 63.99; H, 4.93; N, 4.04%. Calcd for $C_{19}H_{17}NO_2S_2$: C, 64.20; H, 4.82; N, 3.94%.

Preparations of 5,5a-Dihydropyrido[2,1-*c*]thieno[3,2-*e*]-[1,4]thiazines 6a—l and 7a—x. General Method. A mixture of pyridinium betaine (2 mmol) and alkyl bromide (2.2 mmol) was dissolved in chloroform (20 ml) and the resulting solution was kept at room temperature until the spot of pyridinium betaine disappeared (1—7 d, by TLC monitoring). The solution was concentrated under reduced pressure and the residue was washed three times with ether to remove the unaltered alkylating agent. To the chloroform solution (50 ml) of the pyridinium salt prepared above DBU (0.38 g, 2.5 mmol) was added dropwise at 0 °C in an ice bath, and then stirred for further 10 min at the temperature. The resulting solution was concentrated under reduced pressure and the residue was separated by column chromatography (alumina) using chloroform as an eluent. The chloroform layer was concentrated under reduced pressure. Recrystallizations from chloroform-hexane or ether-hexane gave pure products as pale yellow prisms (**6a+7a** and **6f+7f**). pale yellow needles (**6b+7b—6e+7e**, **6g+7g—6i+7i**, and **7m**), yellow prisms (**6j+7j** and **7v**), yellow needles (**6k+7k**, **6l+71**, **7n—7s**, and **7u**), or orange needles (**7t**, **7w**, and **7x**).

On the other hand, similar treatment of pyridinium salts **5y** and **5z** gave complex mixtures and any significant product could not be isolated.

There results and some physical and spectral data are summarized in Tables 1 and 3.

Preparations of Thieno[2,3-*b*]indolizines 8a—x. General Method. To a chloroform solution (50 ml) of dihydropyridothienothiazine (0.2—0.5 g) an equimolar amount of DDQ was added under stirring at 0 °C in an ice bath and the resulting mixture was stirred at the temperature until the material was disappeared (TLC monitoring). (about 2—4 h) The solution was filtered to remove insoluble substances and then the filtrate was concentrated under reduced pressure at below 40 °C. The residual oil was separated by column chromatography (alumina) using chloroform as an eluent. The evaporation of the solvent and recrystallization of the residue from chloroform-hexane gave the corresponding thieno[2,3-*b*]indolizine derivatives as dark red needles (**8a—c**, **8j**, **8n**, **8t**, and **8v**) or black needles (**8d—i**, **8k—m**, **8o—s**, **8u**, **8w**, and **8x**).

These thienoindolizines could be also obtained in moderate yields from the reactions of dihydropyridothienothiazines with palladium on carbon (5%) in dry benzene at room temperature.

These results and some data are listed in Tables 2 and 4.

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