Preparation of New Nitrogen-Bridged Heterocycles. 53.[1] Syntheses of 3-(Benzylthio)thieno[3,4-*b*]indolizine Derivatives and Their Intramolecular Arene–Arene Interactions

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Various ethyl 1-arylcarbonyl-3-[(un)substituted methylthio]thieno[3,4-*b*]indolizine-9-carboxylates were synthesized in good yields by a novel methodology in which the *S*-alkylation of 5-arylcarbonyl-4-ethoxycarbonylmethyl-3-(1-pyridinio)thiophene-2-thiolates with alkyl or benzyl halides, the 1,5-dipolar cyclization of the resulting pyridinium salts in the presence of a base, and the aromatization were performed. In the X-ray analyses of some 3-(benzylthio)thieno[3,4-*b*]indolizine-9-carboxylates, a gauche and two anti conformers in relation to the exocyclic sulfide linkage were found. Interestingly, all of the 3-(benzylthio)thieno[3,4-*b*]indolizine derivatives showed significant high-field shifts (δ up to 0.3 ppm) for the 5- and 6-proton signals compared with those of the 3-methylthio derivatives in the ^{1}H-NMR spectra and exhibited a definite absorption band near 425 nm in their UV spectra, indicating an intramolecular arene–arene interaction between the thieno[3,4-*b*]indolizine and the phenyl ring.

Key words thieno[3,4-*b*]indolizine; arene–arene interaction; gauche form; anti form; UV spectra; X-ray analysis

In our preliminary communication[1] we reported a new preparative method for 3-(benzylthio)thieno[3,4-*b*]indolizine derivatives having unique stacked structures due to the contribution of intramolecular arene–arene interactions. We also found that this method using 5-arylcarbonyl-4-ethoxycarbonylmethyl-3-(1-pyridinio)thiophene-2-thiolates as key intermediates is much more effective than those described earlier by us[2—4] and is widely applicable to the preparation of various 3-alkylthio- and 3-(benzylthio)thieno[3,4-*b*]indolizine derivatives. To the best of our knowledge, the intramolecular arene–arene interaction through a highly flexible spacer such as the sulfide bond is scarcely reported,[5,6] and if its conformational control is possible through such interaction, these molecules might be used as low energy molecular switches and chiral auxiliaries.[7,8]

For the staggered conformations in relation to the sulfide spacer in 3-(benzylthio)thieno[3,4-*b*]indolizine derivatives, there are two gauche (**G1**, **G2**) and one anti form. The latter is further subdivided into **A1**, **A2**, and **A3** (see Fig. 1). Only the **G1** form and the eclipse form (**E**) have the attractive arene–arene interactions. However, the **E** form has the greatest steric hindrance and is not a stable conformer. The title compounds, 3-(benzylthio)thieno[3,4-*b*]indolizine derivatives, with intramolecular arene–arene interactions (**G1** form) have the following structural features in comparison with the analogs with a ethylene spacer: 1) the sulfur atom does not have any substituent and hence the steric repulsion with the proton(s) and/or group(s) on the adjacent carbon atom is absent, 2) the long sulfide linkage decreases the energy difference between the anti (**A1**, **A2**, **A3**) and gauche conformers (**G1**, **G2**), 3) the narrow C–S–C bond angle (near 100°), in contrast with the C–C–C bond angle (109.5°), makes the through-space interaction between the two remote aromatic rings possible, 4) the 5- and 6-positions of the thieno[3,4-*b*]indolizine and the phenyl ring in the **G1** form are close and therefore an attractive interaction can be expected, while the other **G2** form has no arene–arene interaction and is considerably crowded, 5) the **A3** form is considerably hindered than the others (**A1**, **A2**). In addition, the electronic property of the indolizine skeleton in which the pyridine moiety has a cationic character may also assist this attractive interaction in the **G1** form. In this paper we report a novel and effective preparative method of ethyl 1-arylcarbonyl-3-[(un)substituted methylthio]thieno[3,4-*b*]indolizine-9-carboxylates starting from 1-(ethoxycarbonylacetonyl)pyridinium chlorides and also describe their structures involving the intramolecular arene–arene interactions.

Results and Discussion

Preparations of 5-Arylcarbonyl-4-ethoxycarbonylmethyl-3-(1-pyridinio)thiophene-2-thiolates When we found the unexpected formation of ethyl 3-(R-thio)-1-cynothieno[3,4-

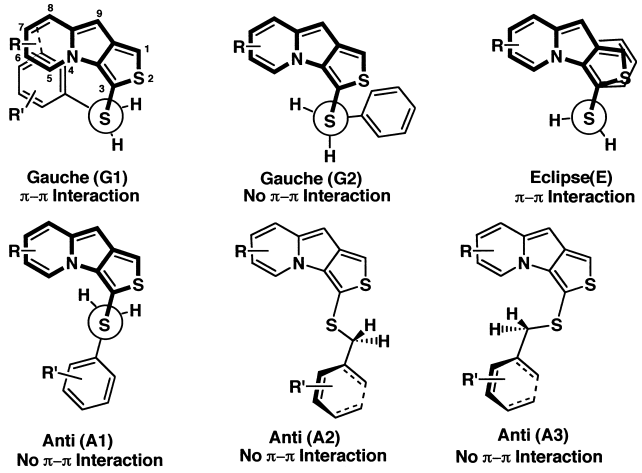

Fig. 1

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b]indolizine-9-carboxylates from the alkaline and dehydrogenative treatment of 1-[1-(R-thio)-1-cyanomethylthio-4-ethoxycarbonyl-1,3-butadien-2-yl]pyridinium halides,[2,3] we proposed 1,5-dipolar species, [2-(R-thio)-5-cyano-3-(1-pyridinio)thiophen-4-yl](ethoxycarbonyl)methanides, as the key intermediates in these reaction routes. The retro synthesis of the 1,5-dipolar intermediates lead to two potential materials: pyridinium [1-[R-thio(thiocarbonyl)](1-ethoxycarbonylacetyl)] methylides and its dehydrated 4-ethoxycarbonylmethyl-3-(1-pyridinio)thiophene-2-thiolates (see Chart 1). Recently, we developed a route to 3-(R-thio)thieno[3,4-*b*]indolizine derivatives starting from former methylides, but their yields were variable and generally low.[4] Therefore, we next examined the use of 4-ethoxycarbonylmethyl-3-(1-pyridinio)thiophene-2-thiolates for thieno[3,4-*b*]indolizine synthesis.

The desired compounds, 5-arylcarbonyl-4-ethoxycarbonylmethyl-3-(1-pyridinio)thiophene-2-thiolates (**4a**—**f**) were directly obtained in 30—66% yields from the treatment of a mixture of 1-(ethoxycarbonylacetonyl)pyridinium chloride (**1a**, **b**), carbon disulfide, and phenacyl bromide (**2a**—**c**) with triethylamine in chloroform at room temperature. In these reactions pyridinium 1-[(ethoxycarbonylacetyl)[phenacylthio-(thiocarbonyl)]]methylides (**3**) which were expected to be initially formed could not be detected at all (Chart 2).

Only one methylene proton singlet appeared at δ near 3.8 in the ^{1}H-NMR spectra of **4a**—**f**. This fact indicated that the products **4a**—**f** are not pyridinium methylides (**3**) before the intramolecular dehydration. The elementary analyses of **4a**—**f** were in good accord with our proposed compositions and the IR spectra showed characteristic absorption bands near 1730 and 1614—1636 cm^{-1} due to the saturated ester carbonyl and the largely delocalized carbonyl group, respectively, which were consistent well with the structures of **4a**—**f**.

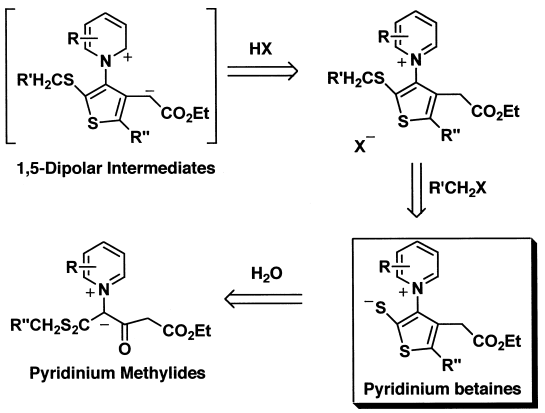
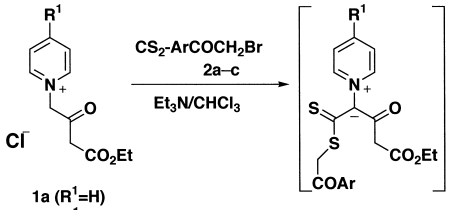


Chart 1

Preparations of Ethyl 3-(R-thio)-1-(arylcarbonyl)thieno-[3,4-*b*]indolizine-9-carboxylates To examine the utility of these pyridinium betaines (**4a**—**f**) in the synthesis of thieno[3,4-*b*]indolizine, we first investigated the reactions of **4a**—**f** with methyl iodide (**5a**). The *S*-alkylation of **4a**—**f** with excess **5a** in chloroform at room temperature, followed by treatment of the resulting pyridinium salts (**6a**—**c**, **8a**—**c**) with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as a base at 0 °C and then dehydrogenation using chloranil gave the expected ethyl 1-arylcarbonyl-3-(methylthio)thieno[3,4-*b*]indolizine-9-carboxylates (**7a**—**c**, **9a**—**c**) in good yields (62—88%). These yields are much higher than those using our previous methods.[2—4] Similar treatment of the corresponding pyridinium salts (**6d**—**z**, **8d**—**z**), readily obtainable from pyridinium betaines (**4a**—**f**) and a small excess of benzyl bromides (**5b**—**l**) or phenethyl bromide (**5m**), produced 3-benzylthio- (**7d**—**x**, **9d**—**x**) or 3-phenethylthiothieno[3,4-*b*]indolizine derivatives (**7y**, **z**, **9y**, **z**) in 62—93% yields. These results are shown in Charts 3 and 4.

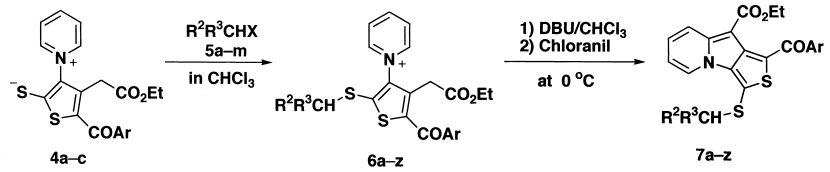
Elemental analyses of products **7a**—**z** and **9a**—**z** were in good accord with our proposed structures and their IR spectra showed the characteristic ester carbonyl band (1665—1688 cm^{-1}), and the cyano band (2220—2230 cm^{-1} for only **7m**—**r**, **9m**—**r**). Interestingly, the ^{1}H-NMR spectra (see Table 1 for **7a**—**z** and Table 2 for **9a**—**z**) showed significant high field shifts (δ <0.3 ppm) for the 5- and 6-protons in the 3-(benzylthio)thieno[3,4-*b*]indolizines (**7d**—**l**, **p**—**w**, **9d**—**l**, **p**—**w**) compared with those in the 3-methylthio derivatives (**7a**—**c**, **9a**—**c**). The high field shifts related to the 5-protons in 3-(2-cyanobenzylthio) (**7m**—**o**, **9m**—**o**) and 3-(diphenylmethylthio derivatives (**7x**, **9x**) were not observed, but this does not mean an absence of intramolecular arene–arene interactions in these compounds. This absence must be due to the anisotropic effect by an additional 2-cyano or phenyl group because the same effects is present on the adjacent 6-proton and the characteristic UV absorption band attributable to arene–arene interactions also appeared as described below. Similar high field shifts relative to the phenyl protons of the 3-substituent in compounds **7d**—**x** and **9d**—**x** were also observed. On the other hand, shielding effects were not exhib-



2	Ar
a	Ph
b	4-ClC$_6$H$_4$
c	4-BrC$_6$H$_4$

4	R^1	Ar	Yield (%)
a	H	Ph	38
b	H	4-ClC$_6$H$_4$	40
c	H	4-BrC$_6$H$_4$	66
d	Me	Ph	42
e	Me	4-ClC$_6$H$_4$	30
f	Me	4-BrC$_6$H$_4$	44

Chart 2



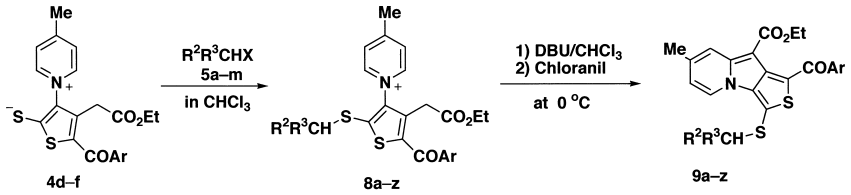
5	R^2	R^3	X
a	H	H	I
b	Ph	H	Br
c	2-MeC_6H_4	H	Br
d	4-MeC_6H_4	H	Br
e	2-NCC_6H_4	H	Br
f	4-NCC_6H_4	H	Br
g	2-ClC_6H_4	H	Br
h	4-ClC_6H_4	H	Br
i	4-BrC_6H_4	H	Br
j	4-FC_6H_4	H	Br
k	Ph	Me	Br
l	Ph	Ph	Br
m	$PhCH_2$	H	Br

6,7	Ar	R^2	R^3	Yield[a] (%)
a	Ph	H	H	80
b	4-ClC_6H_4	H	H	84
c	4-BrC_6H_4	H	H	88
d	Ph	Ph	H	74
e	4-ClC_6H_4	Ph	H	83
f	4-BrC_6H_4	Ph	H	91
g	Ph	2-MeC_6H_4	H	86
h	4-ClC_6H_4	2-MeC_6H_4	H	80
i	4-BrC_6H_4	2-MeC_6H_4	H	71
j	Ph	4-MeC_6H_4	H	83
k	4-ClC_6H_4	4-MeC_6H_4	H	90
l	4-BrC_6H_4	4-MeC_6H_4	H	73
m	Ph	2-NCC_6H_4	H	76

6,7	Ar	R^2	R^3	Yield[a] (%)
n	4-ClC_6H_4	2-NCC_6H_4	H	87
o	4-BrC_6H_4	2-NCC_6H_4	H	75
p	Ph	4-NCC_6H_4	H	66
q	4-ClC_6H_4	4-NCC_6H_4	H	62
r	4-BrC_6H_4	4-NCC_6H_4	H	75
s	Ph	2-ClC_6H_4	H	67
t	Ph	4-ClC_6H_4	H	76
u	Ph	4-BrC_6H_4	H	75
v	Ph	4-FC_6H_4	H	91
w	Ph	Ph	Me	75
x	Ph	Ph	Ph	79
y	Ph	$PhCH_2$	H	79
z	4-ClC_6H_4	$PhCH_2$	H	93

a) The yields from 4 to 7.

Chart 3



8,9	Ar	R^2	R^3	Yield[a] (%)
a	Ph	H	H	62
b	4-ClC_6H_4	H	H	74
c	4-BrC_6H_4	H	H	73
d	Ph	Ph	H	67
e	4-ClC_6H_4	Ph	H	75
f	4-BrC_6H_4	Ph	H	80
g	Ph	2-MeC_6H_4	H	65
h	4-ClC_6H_4	2-MeC_6H_4	H	77
i	4-BrC_6H_4	2-MeC_6H_4	H	70
j	Ph	4-MeC_6H_4	H	65
k	4-ClC_6H_4	4-MeC_6H_4	H	89
l	4-BrC_6H_4	4-MeC_6H_4	H	86
m	Ph	2-NCC_6H_4	H	62

8,9	Ar	R^2	R^3	Yield[a] (%)
n	4-ClC_6H_4	2-NCC_6H_4	H	90
o	4-BrC_6H_4	2-NCC_6H_4	H	82
p	Ph	4-NCC_6H_4	H	70
q	4-ClC_6H_4	4-NCC_6H_4	H	80
r	4-BrC_6H_4	4-NCC_6H_4	H	74
s	Ph	2-ClC_6H_4	H	66
t	Ph	4-ClC_6H_4	H	83
u	Ph	4-BrC_6H_4	H	74
v	Ph	4-FC_6H_4	H	65
w	Ph	Ph	Me	91
x	Ph	Ph	Ph	61
y	Ph	$PhCH_2$	H	83
z	4-ClC_6H_4	$PhCH_2$	H	77

a) The yields from 4 to 9.

Chart 4

ited in 3-phenethylthio derivatives (**7y**, **z**, **9y**, **z**), though the phenyl ring can approach much closer to the thieno[3,4-*b*]indolizine ring than those in 3-benzylthio derivatives (**7d**—**x**, **9d**—**x**). This fact suggests that the type(s) and number of atoms involved in the spacer are crucial for this type of arene–arene interaction. The other isomers of theino[3,4-*b*]indolizines including the conformers could not be detected in these ^{1}H-NMR spectra of **7a**—**z** and **9a**—**z** at room temperature and also in those of **7d**, **g** even at −50 °C. However, no nuclear Overhauser effect (NOE) between the 5- and 6-protons on the thieno[3,4-*b*]indolizine ring and the phenyl protons in these compounds was exhibited at all. The reason why the NOE effect could not be detected is not clear.

The UV spectra[9] of 3-(methylthio)thieno[3,4-*b*]indolizines (**7a**—**c**, **9a**—**c**) which have no arene–arene interactions exhibited characteristic absorption bands near 330, 480, and 515 (shoulder, **7a**—**c**) or 510 nm (shoulder, **9a**—**c**), which were very similar to those for 3-phenethylthio derivatives (**7y**, **z**, **9y**, **z**). On the other hand, all spectra[9] of 3-(benzylthio)thieno[3,4-*b*]indolizines (**7d**—**x**, **9d**—**x**) had a new band (421—429 nm) together with weak bands (near 480 and 515 (shoulder) or 510 nm (shoulder)). The spectra of some thieno[3,4-*b*]indolizines (**7a**, **d**, **m**, **x**) are shown in Fig. 2. As seen in Fig. 2, 3-(2-cyanobenzylthio)- (**7m**) and 3-(diphenylmethylthio)thieno[3,4-*b*]indolizine (**7x**) whose ^{1}H-NMR spectra did not show the high field shift for the 5-proton also had the characteristic absorption band due to the arene–arene interactions near 425 nm, and the 3-(diphenylmethylthio) derivative (**7x**) provided the largest molar extinction coefficient.

To obtain further structural information we carried out X-ray analyses for several thieno[3,4-*b*]indolizine derivatives and found three kinds of crystals (**G1**, **A1**, **A2**). As the repre-

Table 1. ^{1}H-NMR Spectral Data for 7-Unsubstituted Thieno[3,4-*b*]indolizines[a)]

No.	C-5	C-6	C-7	C-8	COOEt	COAr	SCHR^{2}R^3	δ (5-H)[b)]	δ (6-H)[b)]	δ (8-H)[b)]
7a	8.96	6.72	[c)]	8.21	0.96, 3.61	7.0—8.2	2.68	0.00	0.00	0.00
7b	8.97	6.75	7.27	8.21	1.02, 3.72	7.2—8.0	2.70	−0.01	−0.03	0.00
7c	8.96	6.75	7.32	8.21	1.02, 3.72	7.3—8.0	2.70	0.00	−0.03	0.00
7d	8.80	6.49	[c)]	8.15	0.96, 3.66	7.0—8.2	4.11, 7.11	0.16	0.23	0.06
7e	8.80	6.51	[c)]	8.13	1.01, 3.75	7.2—8.0	4.12, 7.12	0.16	0.21	0.08
7f	8.81	6.54	[c)]	8.14	1.02, 3.76	7.3—8.0	4.13, 7.12	0.15	0.18	0.07
7g	8.75	6.50	[c)]	8.15	0.97, 3.67	7.0—8.2	2.40, 4.15, 6.7—7.6	0.21	0.22	0.06
7h	8.79	6.54	[c)]	8.15	1.02, 3.76	7.2—8.0	2.41, 4.16, 6.7—7.6	0.17	0.18	0.06
7i	8.79	6.52	[c)]	8.15	1.02, 3.75	7.3—8.0	2.40, 4.16, 6.7—7.6	0.17	0.20	0.06
7j	8.77	6.49	7.26	8.15	0.97, 3.67	7.2—8.2	2.20, 4.09, 6.95	0.19	0.23	0.06
7k	8.79	6.53	7.27	8.17	1.03, 3.77	7.2—8.0	2.21, 4.11, 6.97	0.17	0.19	0.04
7l	8.78	6.51	7.27	8.14	1.02, 3.76	7.3—8.0	2.20, 4.10, 6.96	0.18	0.21	0.07
7m	8.93	6.59	[c)]	8.16	0.95, 3.67	6.8—8.0	4.26, 6.8—8.0	0.03	0.13	0.05
7n	8.93	6.61	[c)]	8.15	1.01, 3.76	7.0—8.0	4.26, 7.0—8.0	0.03	0.11	0.06
7o	8.93	6.61	[c)]	8.14	1.01, 3.76	7.0—8.0	4.26, 7.0—8.0	0.03	0.11	0.07
7p	8.73	6.52	[c)]	8.16	0.98, 3.69	7.0—8.0	4.11, 7.0—8.0	0.23	0.20	0.05
7q	8.74	6.55	[c)]	8.16	1.03, 3.79	7.0—8.0	4.13, 7.0—8.0	0.22	0.17	0.05
7r	8.73	6.56	[c)]	8.15	1.03, 3.78	7.0—8.0	4.12, 7.0—8.0	0.23	0.16	0.06
7s	8.83	6.51	[c)]	8.11	0.96, 3.67	6.7—8.1	4.19, 6.7—8.1	0.13	0.21	0.10
7t	8.74	6.52	[c)]	8.16	0.97, 3.68	6.8—8.1	4.06, 6.8—8.1	0.22	0.20	0.05
7u	8.71	6.52	[c)]	8.16	0.97, 3.68	6.8—8.1	4.03, 6.8—8.1	0.25	0.20	0.05
7v	8.80	6.54	[c)]	8.16	0.97, 3.68	6.7—8.0	4.09, 6.7—8.0	0.16	0.18	0.05
7w	8.86	6.53	[c)]	8.15	0.96, 3.67	7.0—8.1	1.77, 4.36, 7.14	0.10	0.19	0.06
7x	8.95	6.57	[c)]	8.17	0.95, 3.66	7.1—8.2	5.53, 7.1—7.7	0.01	0.15	0.04
7y	8.98	6.64	[c)]	8.21	0.97, 3.65	7.0—8.2	2.9—3.4, 7.21	−0.02	0.08	−0.01
7z	8.97	6.67	[c)]	8.22	1.02, 3.74	7.0—8.0	2.9—3.4, 7.20	−0.01	0.05	−0.02

a) The coupling constants are as follows; $J_{5,6}=J_{6,7}=7.0$ Hz, $J_{6,8}=2.0$ Hz, $J_{7,8}=9.0$ Hz, $J_{Et}=7.0$ Hz. *b*) The chemical shifts of compound **7a** are selected as the standards. *c*) Overlapped with the aromatic proton signals.

Table 2. ^{1}H-NMR Spectral Data for 7-Methylthieno[3,4-*b*]indolizines[a)]

No.	C-5	C-6	C-7	C-8	COOEt	COAr	SCHR^{2}R^3	δ (5-H)[b)]	δ (6-H)[b)]	δ (8-H)[b)]
9a	8.86	6.58	2.40	8.01	0.95, 3.59	7.3—8.2	2.66	0.00	0.00	0.00
9b	8.86	6.60	2.42	8.01	0.99, 3.68	7.3—8.1	2.68	0.00	−0.02	0.00
9c	8.83	6.59	2.42	7.99	1.00, 3.69	7.3—8.0	2.67	0.03	−0.01	0.02
9d	8.70	6.36	2.36	7.95	0.95, 3.62	7.3—8.2	4.11, 7.14	0.16	0.22	0.06
9e	8.67	6.39	2.37	7.93	0.99, 3.71	7.3—8.1	4.12, 7.13	0.19	0.19	0.08
9f	8.67	6.37	2.35	7.93	0.99, 3.71	7.3—8.0	4.11, 7.12	0.19	0.21	0.08
9g	8.68	6.38	2.38	7.95	0.95, 3.62	7.3—8.2	2.38, 4.16, 6.7—7.7	0.18	0.20	0.06
9h	8.67	6.39	2.38	7.93	0.99, 3.71	7.3—8.1	2.38, 4.15, 6.7—7.7	0.19	0.19	0.08
9i	8.65	6.38	2.37	7.93	0.99, 3.70	7.3—8.0	2.37, 4.13, 6.7—7.5	0.21	0.20	0.08
9j	8.65	6.35	2.37	7.96	0.95, 3.64	7.3—8.2	2.21, 4.09, 6.97	0.21	0.23	0.05
9k	8.64	6.37	2.36	7.94	1.00, 3.72	7.3—8.1	2.21, 4.08, 6.96	0.22	0.21	0.07
9l	8.66	6.38	2.38	7.95	1.00, 3.74	7.3—8.0	2.21, 4.11, 6.99	0.20	0.20	0.06
9m	8.86	6.49	2.40	[c)]	0.95, 3.66	7.0—8.1	4.28, 7.0—8.1	0.00	0.09	—
9n	8.84	6.49	2.39	7.94	0.99, 3.72	7.0—8.0	4.26, 7.0—8.0	0.02	0.09	0.07
9o	8.81	6.47	2.38	7.94	0.99, 3.72	7.0—8.0	4.25, 7.0—8.0	0.05	0.11	0.07
9p	8.57	6.37	2.38	7.95	0.95, 3.66	7.0—8.1	4.09, 7.0—8.1	0.29	0.21	0.06
9q	8.58	6.41	2.40	7.95	1.01, 3.75	7.0—8.1	4.11, 7.0—8.1	0.28	0.17	0.06
9r	8.57	6.37	2.38	7.93	1.01, 3.75	7.0—8.1	4.10, 7.0—8.1	0.29	0.21	0.08
9s	8.74	6.38	2.35	[c)]	0.94, 3.64	6.7—8.1	4.18, 6.7—8.1	0.12	0.20	—
9t	8.58	6.36	2.37	7.97	0.95, 3.64	6.8—8.1	4.04, 6.8—8.1	0.28	0.22	0.04
9u	8.54	6.35	2.38	7.97	0.96, 3.66	6.7—8.1	4.02, 6.7—8.1	0.32	0.23	0.04
9v	8.66	6.38	2.35	[c)]	0.95, 3.65	6.7—8.1	4.07, 6.7—8.1	0.20	0.20	—
9w	8.76	6.39	2.37	7.97	0.95, 3.64	7.1—8.1	1.77, 4.36, 7.13	0.10	0.19	0.04
9x	8.82	6.40	2.37	7.96	0.93, 3.61	7.1—8.1	5.51, 7.1—7.7	0.04	0.18	0.05
9y	8.86	6.50	2.40	8.01	0.95, 3.61	7.0—8.1	2.8—3.5, 7.20	0.00	0.08	0.00
9z	8.84	6.51	2.40	8.00	1.00, 3.70	7.3—8.0	2.8—3.5, 7.20	0.02	0.07	0.01

a) The coupling constants are as follows; $J_{5,6}=7.0$ Hz, $J_{6,8}=2.0$ Hz, $J_{Et}=7.0$ Hz. *b*) The chemical shifts of compound **9a** are selected as the standards. *c*) Overlapped with the aromatic proton signals.

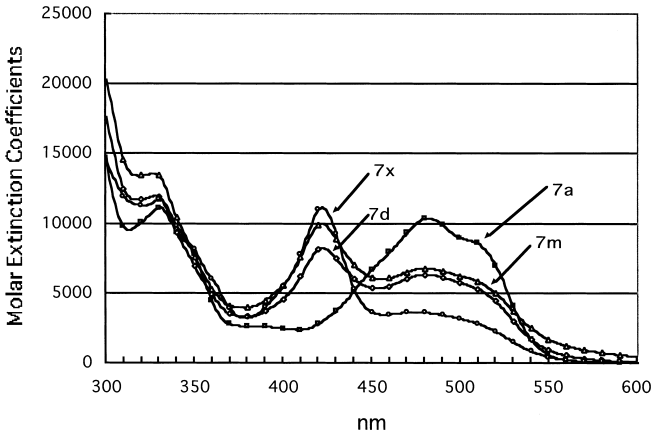


Fig. 2. UV Spectra of Some Thieno[3,4-*b*]indolizines **7a**, **d**, **m**, **x** in $CHCl_3$

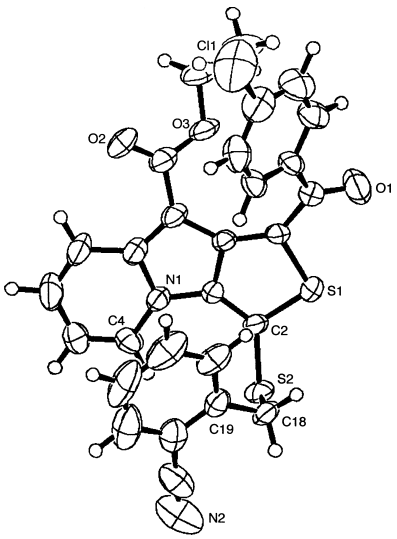


Fig. 3. ORTEP Drawing of Ethyl 1-(4-Chlorobenzoyl)-3-(2-cyanobenzylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7n**)

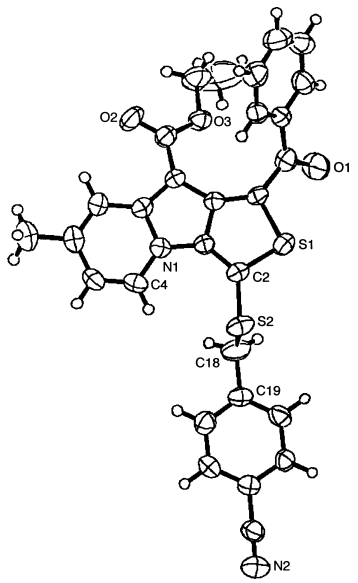


Fig. 4. ORTEP Drawing of Ethyl 1-Benzoyl-3-(4-cyanobenzylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**9p**)

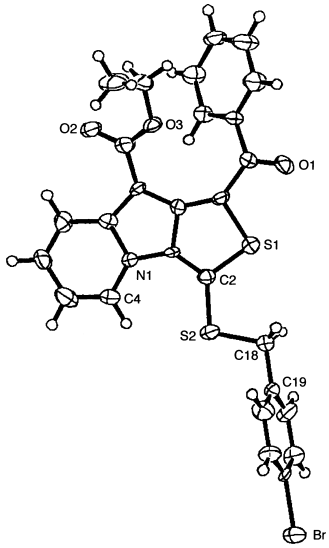


Fig. 5. ORTEP Drawing of Ethyl 1-Benzoyl-3-(4-bromobenzylthio)-thieno[3,4-*b*]indolizine-9-carboxylate (**7u**)

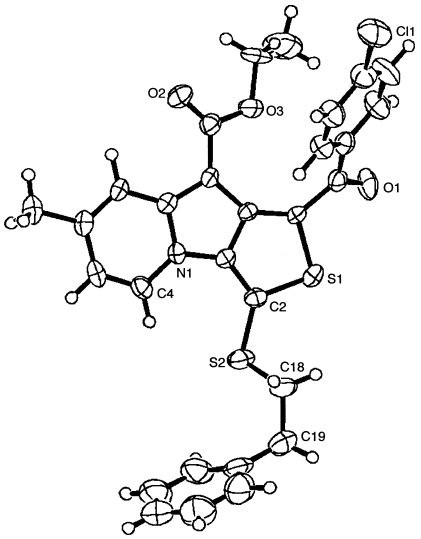


Fig. 6. ORTEP Drawing of Ethyl 1-(4-Chlorobenzoyl)-7-methyl-3-(phenethylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**9z**)

sentatives for **G1**, **A1**, and **A2** conformers thus confirmed, the ORTEP drawings[10] for **7n**, **9p**, and **7u** are shown in Figs. 3—5, and that for the 3-phenethylthio derivative **9z** is shown in Fig. 6. In general, the **G1** crystals were mainly obtained in the cases of 7-unsubstituted 3-(benzylthio)thieno[3,4-*b*]indolizines,[11] and the **A1** ones in those of the 7-methyl derivatives.[12] The **A2** form was only observed in **7u**. In the **G1** crystals found in thienoindolizines **7g**, **n** and **9n**, which have an unsymmetrically substituted 3-benzyl group such as a 2-methylbenzyl or 2-cyanobenzyl, the overlapping of the 2-substituent on the thienoindolizne ring was not observed. The distances (C4–C19) (see ORTEP drawings for its numbering) and the dihedral angles (C2–S2–C18–C19) for **7g**, **j**, **n** and **9n** (**G1** form) are 3.671—3.983 Å and 50.5—67.1° respectively, while those for **9p**, **z** (**A1** form) and **7u** (**A2** form) are over 5 Å and 168.3—176.2° respectively. As might be expected, the dihedral angles of the least-square planes of the thienoindolizine and the interacting phenyl ring

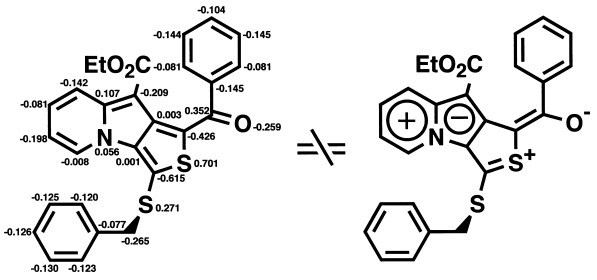


Fig. 7. Atomic Charges (Ground State) of Ethyl 1-Benzoyl-3-(benzylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7a**) and Its Initially Expected Ionic Structure

Table 3. Some Structural Data for Thieno[3,4-*b*]indolizines

No.	Form	C2–S2[a]	S2–C18[a]	N1–C19[a]	C2–S2–C18[b]	DA1[b,c]	DA2[b,d]
7g	G1	1.746(4)	1.844(5)	3.983	100.3(2)	53.3(4)	39.77
7j	G1	1.761(9)	1.85 (1)	3.671	99.8(4)	53.3(8)	24.75
7n	G1	1.756(5)	1.848(7)	3.686	97.7(3)	67.1(6)	26.07
7u	A2	1.75 (1)	1.83 (1)	5.993	103.4(5)	172.9(9)	103.18
9n	G1	1.747(4)	1.838(7)	3.762	100.8(3)	50.5(5)	25.22
9p	A1	1.746(5)	1.824(5)	5.044	100.4(2)	176.2(4)	8.93
9z	—	1.750(1)	1.793(8)	5.772	102.8(4)	168.3(7)	103.71

a) Å. *b*) °C. *c*) Dihedral angle for C2–S2–C18–C19. *d*) Dihedral angle of the least-square planes of thieno[3,4-*b*]indolizine and the interacting phenyl ring.

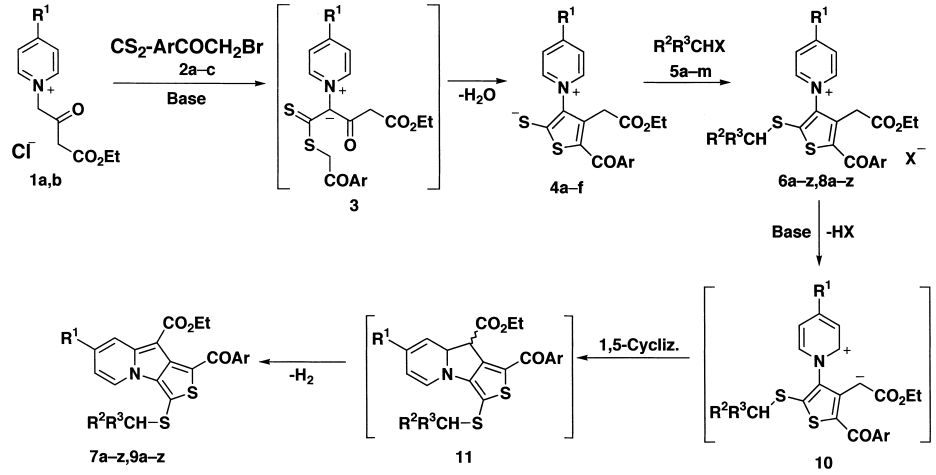


Chart 5

were fairly wide (24.75—39.44°). Some structural data for **7g**, **j**,[1] **n**, **u** and **9p**, **z** are listed in Table 3.

The atomic charges in the AM1 calculation[13] of compound **7d** showed the high electronic densities at the C-5, C-6, C-7, and C-8 carbons on the pyridine ring, indicating the low possibility of a cation-π like interaction in this ring system (see Fig. 7). Similarly, the HOMO–LUMO interaction of the same molecule did not exhibited any favorable effect between the pyridine and the phenyl rings.

Reaction Mechanisms The possible reaction mechanisms are shown in Chart 5. Except for the smooth dehydration of pyridinium (thiocarbonyl)methylides **3** to the corresponding pyridinium betaines (**4a**—**f**), these reactions proceeded well according to our initially proposed routes.

Experimental

Melting points were measured with a Yanagimoto micromelting point apparatus and are not corrected. Microanalyses were carried out on a Perkin-Elmer 2400 elemental analyzer. The ^{1}H-NMR spectra were determined with a Hitachi R-600 spectrometer (60 MHz) or JEOL JNM-LA400 (^{1}H and ^{13}C: 400 MHz) spectrometer in deuteriochloroform with tetramethylsilane used as the internal standard; the chemical shifts are expressed in δ values. The IR and UV spectra were taken with a JASCO FT/IR-5300 IR and a SHIMADZU UV-2500PC spectrophotometers, respectively.

Preparation of 3-(1-Pyridinio)thiophene-2-thiolates. General Method A chloroform solution (100 ml) of 1-(ethoxycarbonylacetonyl)pyridinium chloride (**1**, 10 mmol) and carbon disulfide (1.520 g, 20 mmol) was treated with triethylamine (3.0 g, 30 mmol) under stirring at rt for 1 h, and then phenacyl bromide (**2**, 10 mmol) was added to the reaction mixture and the resulting solution was allowed to react at rt for another 12 h. The solution was poured into water (300 ml) and extracted twice with 200 ml portions of chloroform. The combined extracts were dried over sodium sulfate and then filtered. The filtrate was concentrated at reduced pressure and the residue was separated by column chromatography on alumina using chloroform as an eluent. The chloroform layers of pyridinium betaines were combined and concentrated at reduced pressure. Recrystallization of the crude products from chloroform–ether afforded the corresponding 3-(1-pyridinio)thiophene-2-thiolates as yellow needles. In these reactions no pyridinium 1-[(ethoxycarbonylacetyl)[(phenacylthio)thiocarbonyl]]methylides (**3**) could be obtained.

Selected data for new products **4b**, **c**, **e**, **f** are as follows:

5-(4-Chlorobenzoyl)-4-ethoxycarbonylmethyl-3-(1-pyridinio)thiophene-3-thiolate (**4b**): 40% (from **1a**, carbon disulfide, and *p*-chlorophenacyl bromide (**2b**)), mp 221—223 °C. IR (KBr) cm^{-1}: 1728, 1635. ^{1}H-NMR (60 MHz, $CDCl_3$) δ: 1.23 (3H, t, J=7.0 Hz), 3.78 (2H, s), 4.18 (2H, q, J=7.0 Hz), 7.2—8.9 (9H, m). *Anal.* Calcd for $C_{20}H_{16}ClNO_3S_2$: C, 57.48; H, 3.86; N, 3.35. Found: C, 57.70; H, 3.75; N, 3.24.

5-(4-Bromobenzoyl)-4-ethoxycarbonylmethyl-3-(1-pyridinio)thiophene-3-thiolate (**4c**): 66% (from **1a**, carbon disulfide, and *p*-bromophenacyl bromide (**2c**)), mp 236—238 °C. IR (KBr) cm^{-1}: 1728, 1620. ^{1}H-NMR (60 MHz, $CDCl_3$) δ: 1.24 (3H, t, J=7.0 Hz), 3.77 (2H, s), 4.15 (2H, q, J=7.0 Hz), 7.2—9.0 (9H, m). *Anal.* Calcd for $C_{20}H_{16}BrNO_3S_2$: C, 51.95; H, 3.49; N, 3.03. Found: C, 51.89; H, 3.35; N, 2.89.

5-(4-Chlorobenzoyl)-4-ethoxycarbonylmethyl-3-(4-methyl-1-pyridinio)-thiophene-3-thiolate (**4e**): 30% (from **1a**, carbon disulfide, and *p*-chlorophenacyl bromide (**2b**)), mp 223—226 °C. IR (KBr) cm^{-1}: 1726, 1614. ^{1}H-NMR (60 MHz, $CDCl_3$) δ: 1.25 (3H, t, J=7.0 Hz), 2.75 (3H, s), 3.76 (2H, s), 4.15 (2H, q, J=7.0 Hz), 7.2—8.8 (8H, m). *Anal.* Calcd for $C_{21}H_{18}ClNO_3S_2$: C, 58.39; H, 4.20; N, 3.24. Found: C, 58.37; H, 4.12; N, 3.08.

5-(4-Bromobenzoyl)-4-ethoxycarbonylmethyl-3-(4-methyl-1-pyridinio)-thiophene-3-thiolate (**4f**): 44% (from **1a**, carbon disulfide, and *p*-bromophenacyl bromide (**2c**)), mp 239—242 °C. IR (KBr) cm^{-1}: 1728, 1636. ^{1}H-NMR (60 MHz, $CDCl_3$) δ: 1.25 (3H, t, J=7.0 Hz), 2.75 (3H, s), 3.76 (2H, s), 4.16 (2H, q, J=7.0 Hz), 7.2—8.8 (8H, m). *Anal.* Calcd for $C_{21}H_{18}BrNO_3S_2$: C, 52.94; H, 3.81; N, 2.94. Found: C, 53.13; H, 3.73; N, 2.79.

Preparation of Ethyl 1-Arylcarbonyl-3-[(un)substituted methylthio]-thieno[3,4-*b*]indolizine-9-carboxylates. General Method A chloroform solution (30 ml) of 1-(pyridinio)thiophene-2-thiolate (**4**, 1 mmol) and methyl iodide (**5a**, 0.71 g, 5 mmol) or benzyl or phenethyl bromide (**2b**—**m**, 1.2 mmol) was kept at room temperature until the spot of the pyridinium betaine (**4**) disappeared by TLC monitoring (from 30 min to 12 h). After *S*-alkylation was completed, the resulting solution was concentrated at reduced pressure and the residue was washed three times with 20 ml portions of ether to remove any excess alkylating agent. Without further purification, pyridinium salt (**6** or **8**) was dissolved in chloroform (30 ml) and the solution was treated with DBU (0.20 g, 1.3 mmol) under stirring in an ice bath for 15 min and then with chloranil (0.499 g, 1 mmol) under the same conditions for another 12 h. The reaction mixture was concentrated at reduced pressure and the residue was separated by column chromatography on alumina using chloroform as an eluent. The reddish chloroform layers of product (**7** or **9**) were combined and concentrated at reduced pressure. Recrystallization of the crude products from chloroform–hexane afforded the corresponding ethyl 1-arylcarbonyl-3-[(un)substituted methylthio]thieno[3,4-*b*]indolizine-9-carboxylates.

The ^{1}H-NMR (60 MHz) spectral data for products **7a**—**z**, and **9a**—**z** are listed in Table 1, and the other data for them are as follows:

Ethyl 1-Benzoyl-3-(methylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7a**): 80% (from **4a** and methyl iodide (**5a**)), red needles, mp 128—129 °C (Lit.[2] 127—129 °C). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 0.97 (3H, t, J=7.1 Hz), 2.68 (3H, s), 3.60 (2H, q, J=7.1 Hz), 6.73 (1H, dt, J=6.8, 1.2 Hz), 7.31 (1H, ddd, J=9.2, 6.8, 1.0 Hz), 7.41 (2H, br t, J=7.3 Hz), 7.51 (1H, br t, J=7.3 Hz), 7.93 (2H, br d, J=7.3 Hz), 8.20 (1H, br d, J=9.2 Hz), 8.96 (1H, br d, J=6.8 Hz). ^{13}C-NMR ($CDCl_3$, 400 MHz) δ: 14.3, 21.8, 9.0, 93.8, 111.0, 120.1, 122.0, 122.8, 127.4, 128.2, 129.3, 130.1, 132.3, 135.0, 135.2, 139.3, 150.0, 164.1, 187.6. UV λ_{max} ($CHCl_3$) nm (log ε) 331 (4.05), 481 (4.02), *ca.* 515 (shoulder).

Ethyl 1-(4-Chlorobenzoyl)-3-(methylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7b**): 84% (from **4b** and methyl iodide (**5a**)), red needles, mp 154—155 °C (Lit.[2] 153—155 °C). UV λ_{max} ($CHCl_3$) nm (log ε) 331 (4.08), 483 (4.07), *ca.* 515 (shoulder).

Ethyl 1-(4-Bromobenzoyl)-3-(methylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7c**): 88% (from **4c** and methyl iodide (**5a**)), red needles, mp 140—142 °C (Lit.[2] 137—139 °C). UV λ_{max} ($CHCl_3$) nm (log ε) 331 (4.09), 484 (4.09), *ca.* 515 (shoulder).

Ethyl 1-Benzoyl-3-(benzylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7d**): 74% (from **4a** and benzyl bromide (**5b**)), red needles, mp 135—137 °C. IR (KBr) cm^{-1}: 1688, 1589. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 0.96 (3H, t, J=7.1 Hz), 3.64 (2H, q, J=7.1 Hz), 4.11 (2H, s), 6.50 (1H, dt, J=6.8, 1.2 Hz), 7.0—7.2 (5H, m), 7.22 (1H, ddd, J=9.2, 6.8, 1.0 Hz), 7.42 (2H, br t, J=7.3 Hz), 7.52 (1H, br t, J=7.3 Hz), 7.91 (2H, br d, J=7.3 Hz), 8.12 (1H, br d, J=9.2 Hz), 8.77 (1H, br d, J=6.8 Hz). ^{13}C-NMR ($CDCl_3$, 400 MHz) δ: 14.3, 44.7, 59.0, 93.3, 110.4, 116.1, 119.8, 125.1, 126.8, 127.9, 128.3, 128.6, 128.8, 129.4, 130.1, 132.5, 134.7, 136.3, 137.2, 139.0, 149.8, 164.0, 188.1. UV λ_{max} ($CHCl_3$) nm (log ε) 328 (4.08), 422 (3.91), 480 (3.80), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{27}H_{21}NO_3S_2$: C, 68.77; H, 4.99; N, 2.97. Found: C, 68.63; H, 4.37; N, 2.84.

Ethyl 3-Benzylthio-1-(4-chlorobenzoyl)thieno[3,4-*b*]indolizine-9-carboxylate (**7e**): 83% (from **4b** and benzyl bromide (**5b**)), red needles, mp 142—144 °C. IR (KBr) cm^{-1}: 1667, 1588. UV λ_{max} ($CHCl_3$) nm (log ε) 328 (4.09), 423 (3.93), 481 (3.78), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{27}H_{20}ClNO_3S_2$: C, 64.08; H, 3.98; N, 2.77. Found: C, 64.02; H, 4.02; N, 2.80.

Ethyl 3-Benzylthio-1-(4-bromobenzoyl)thieno[3,4-*b*]indolizine-9-carboxylate (**7f**): 91% (from **4c** and benzyl bromide (**5b**)), red needles, mp 141—143 °C. IR (KBr) cm^{-1}: 1682, 1586. UV λ_{max} ($CHCl_3$) nm (log ε) 328 (3.89), 422 (3.72), 481 (3.61), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{27}H_{20}BrNO_3S_2$: C, 58.91; H, 3.66; N, 2.54. Found: C, 58.77; H, 3.71; N, 2.62.

Ethyl 1-Benzoyl-3-(2-methylbenzylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7g**): 86% (from **4a** and 2-methylbenzyl bromide (**5c**)), red prisms, mp 120—122 °C. IR (KBr) cm^{-1}: 1678, 1595. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 0.96 (3H, t, J=7.1 Hz), 2.40 (3H, s), 3.64 (2H, q, J=7.1 Hz), 4.14 (2H, s), 6.51 (1H, dt, J=6.8, 1.2 Hz), 6.77 (1H, d, J=7.1 Hz), 6.88 (1H, t, J=7.5 Hz), 7.03 (1H, dt, J=7.6, 7.6, 1.2 Hz), 7.09 (1H, d, J=7.3 Hz), 7.22 (1H, ddd, J=9.3, 6.8, 1.0 Hz), 7.42 (2H, br t, J=7.3 Hz), 7.53 (1H, br t, J=7.6 Hz), 7.92 (2H, br d, J=7.1 Hz), 8.13 (1H, br d, J=9.3 Hz), 8.76 (1H, br d, J=7.1 Hz). ^{13}C-NMR ($CDCl_3$, 400 MHz) δ: 14.3, 19.2, 42.8, 59.0, 93.3, 110.4, 116.4, 119.8, 125.1, 125.9, 126.7, 128.2, 128.3, 129.4, 129.6, 130.1, 130.7, 132.5, 134.0, 134.7, 136.3, 137.2, 139.0, 149.8, 164.0, 188.1. UV λ_{max} ($CHCl_3$) nm (log ε) *ca.* 328 (shoulder), 422 (3.96), 476 (3.70), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{28}H_{23}NO_3S_2$: C, 69.25; H, 4.77; N, 2.88. Found: C, 69.15; H, 4.69; N, 3.06.

Ethyl 1-(4-Chlorobenzoyl)-3-(2-methylbenzylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7h**): 80% (from **4b** and 2-methylbenzyl bromide (**5c**)), red needles, mp 150—152 °C. IR (KBr) cm^{-1}: 1671, 1588. UV λ_{max} ($CHCl_3$) nm (log ε) *ca.* 322 (shoulder), 423 (3.90), 474 (3.77), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{28}H_{22}ClNO_3S_2$: C, 64.67; H, 4.26; N, 2.69. Found: C, 64.81; H, 4.42; N, 2.57.

Ethyl 1-(4-Bromobenzoyl)-3-(2-methylbenzylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7i**): 71% (from **4c** and 2-methylbenzyl bromide (**5c**)), red needles, mp 150—151 °C. IR (KBr) cm^{-1}: 1671, 1584. UV λ_{max} ($CHCl_3$) nm (log ε) *ca.* 324 (shoulder), 423 (3.93), 482 (3.79), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{28}H_{22}BrNO_3S_2$: C, 59.57; H, 3.93; N, 2.48. Found: C, 59.59; H, 3.94; N, 2.38.

Ethyl 1-Benzoyl-3-(4-methylbenzylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7j**): 83% (from **4a** and 4-methylbenzyl bromide (**5d**)), red prisms, mp 149—151 °C. IR (KBr) cm^{-1}: 1674, 1597. UV λ_{max} ($CHCl_3$) nm (log ε) 328 (4.09), 423 (3.90), 480 (3.84), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{28}H_{23}NO_3S_2$: C, 69.25; H, 4.77; N, 2.88. Found: C, 69.39; H, 4.68; N, 2.82.

Ethyl 1-(4-Chlorobenzoyl)-3-(4-methylbenzylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7k**): 90% (from **4b** and 4-methylbenzyl bromide (**5d**)), red needles, mp 148—149 °C. IR (KBr) cm^{-1}: 1682, 1589. UV λ_{max} ($CHCl_3$) nm (log ε) 325 (4.09), 423 (3.90), 482 (3.81), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{28}H_{22}ClNO_3S_2$: C, 64.67; H, 4.26; N, 2.69. Found: C, 64.41; H, 3.27; N, 2.50.

Ethyl 1-(4-Bromobenzoyl)-3-(4-methylbenzylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7l**): 71% (from **4c** and 4-methylbenzyl bromide (**5d**)), red needles, mp 147—149 °C. IR (KBr) cm^{-1}: 1682, 1588. UV λ_{max} ($CHCl_3$) nm (log ε) 325 (4.09), 423 (3.94), 485 (3.81), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{28}H_{22}BrNO_3S_2$: C, 59.57; H, 3.93; N, 2.48. Found: C, 59.78; H, 3.83; N, 2.37.

Ethyl 1-Benzoyl-3-(2-cyanobenzylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7m**): 76% (from **4a** and 2-cyanobenzyl bromide (**5e**)), brown prisms, mp 119—120 °C. IR (KBr) cm^{-1}: 2226, 1688, 1630. UV λ_{max} ($CHCl_3$) nm (log ε) 322 (4.13), 422 (4.00), 480 (3.83), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{28}H_{20}N_2O_3S_2$: C, 67.72; H, 4.06; N, 5.64. Found: C, 67.77; H, 4.01; N, 5.54.

Ethyl 1-(4-Chlorobenzoyl)-3-(2-cyanobenzylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7n**): 87% (from **4b** and 2-cyanobenzyl bromide (**5e**)), brown prisms, mp 121—122 °C. IR (KBr) cm^{-1}: 2220, 1684, 1614. UV λ_{max} ($CHCl_3$) nm (log ε) 323 (4.12), 422 (4.00), 484 (3.82), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{28}H_{19}ClN_2O_3S_2$: C, 63.33; H, 3.61; N, 5.28. Found: C, 63.51; H, 3.55; N, 5.16.

Ethyl 1-(4-Bromobenzoyl)-3-(2-cyanobenzylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7o**): 75% (from **4c** and 2-cyanobenzyl bromide (**5e**)), brown prisms, mp 128—130 °C. IR (KBr) cm^{-1}: 2220, 1682, 1611. UV λ_{max} ($CHCl_3$) nm (log ε) 323 (4.14), 422 (4.03), 485 (3.84), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{28}H_{19}BrN_2O_3S_2$: C, 58.44; H, 3.33; N, 4.87. Found: C, 58.47; H, 3.24; N, 4.67.

Ethyl 1-Benzoyl-3-(4-cyanobenzylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7p**): 66% (from **4a** and 4-cyanobenzyl bromide (**5f**)), red needles, mp 172—173 °C. IR (KBr) cm^{-1}: 2222, 1674, 1593. UV λ_{max} ($CHCl_3$) nm (log ε) 327 (4.10), 421 (4.06), 477 (3.70), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{28}H_{20}N_2O_3S_2$: C, 67.72; H, 4.06; N, 5.64. Found: C, 67.89; H, 4.02; N, 5.50.

Ethyl 1-(4-Chlorobenzoyl)-3-(4-cyanobenzylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7q**): 62% (from **4b** and 4-cyanobenzyl bromide (**5f**)), brown prisms, mp 152—153 °C. IR (KBr) cm^{-1}: 2226, 1674, 1587. UV λ_{max} ($CHCl_3$) nm (log ε) 328 (4.01), 422 (4.03), 483 (3.73), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{28}H_{19}ClN_2O_3S_2$: C, 63.33; H, 3.61; N, 5.28. Found: C, 63.37; H, 3.85; N, 5.00.

Ethyl 1-(4-Bromobenzoyl)-3-(4-cyanobenzylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7r**): 75% (from **4c** and 4-cyanobenzyl bromide (**5f**)), brown prisms, mp 125—127 °C. IR (KBr) cm^{-1}: 2230, 1670, 1583. UV λ_{max} ($CHCl_3$) nm (log ε) 326 (4.09), 421 (3.82), 485 (3.82), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{28}H_{19}BrN_2O_3S_2$: C, 58.44; H, 3.33; N, 4.87. Found: C, 58.47; H, 3.54; N, 4.60.

Ethyl 1-Benzoyl-3-(2-chlorobenzylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7s**): 67% (from **4a** and 2-chlorobenzyl bromide (**5g**)), orange needles, mp 127—129 °C. IR (KBr) cm^{-1}: 1678, 1630. UV λ_{max} ($CHCl_3$) nm (log ε) 328 (4.07), 423 (3.83), 478 (3.72), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{27}H_{20}ClNO_3S_2$: C, 64.08; H, 3.98; N, 2.77. Found: C, 64.20; H, 3.95; N, 2.69.

Ethyl 1-Benzoyl-3-(4-chlorobenzylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7t**): 76% (from **4a** and 4-chlorobenzyl bromide (**5h**)), orange flakes, mp 150—152 °C. IR (KBr) cm^{-1}: 1674, 1595. UV λ_{max} ($CHCl_3$ nm (log ε) 328 (4.09), 422 (3.96), 481 (3.81), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{27}H_{20}ClNO_3S_2$: C, 64.08; H, 3.98; N, 2.77. Found: C, 64.25; H, 4.01; N, 2.58.

Ethyl 1-Benzoyl-3-(4-bromobenzylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7u**): 75% (from **4a** and 4-bromobenzyl bromide (**5i**)), red prisms, mp 123—125 °C. IR (KBr) cm^{-1}: 1672, 1608. UV λ_{max} ($CHCl_3$) nm (log ε) 327 (4.07), 421 (3.98), 479 (3.75), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{27}H_{20}BrNO_3S_2$: C, 58.91; H, 3.66; N, 2.54. Found: C, 59.14; H, 3.56; N, 2.41.

Ethyl 1-Benzoyl-3-(4-fluorobenzylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7v**): 91% (from **4a** and 4-fluorobenzyl bromide (**5j**)), red prisms, mp 148—150 °C. IR (KBr) cm^{-1}: 1682, 1603. UV λ_{max} ($CHCl_3$) nm (log ε) 328 (4.08), 423 (3.83), 481 (3.89), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{27}H_{20}FNO_3S_2$: C, 66.78; H, 4.40; N, 2.78. Found: C, 66.73; H, 4.30; N, 2.65.

Ethyl 1-Benzoyl-3-(1-phenylethylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7w**): 75% (from **4a** and 1-phenylethyl bromide (**5k**)), red prisms, mp 110—111 °C. IR (KBr) cm^{-1}: 1669, 1620. UV λ_{max} ($CHCl_3$) nm (log ε) 319 (4.05), 422 (3.91), 478 (3.74), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{28}H_{23}NO_3S_2$: C, 69.25; H, 4.77; N, 2.88. Found: C, 69.39; H, 4.70; N, 2.81.

Ethyl 1-Benzoyl-3-(diphenylmethylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7x**): 79% (from **4a** and diphenylmethyl bromide (**5l**)), orange needles, mp 177—179 °C. IR (KBr) cm^{-1}: 1667, 1633. UV λ_{max} ($CHCl_3$) nm (log ε) 330 (4.07), 422 (4.05), 475 (3.56), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{33}H_{25}NO_3S_2$: C, 72.37; H, 4.60; N, 2.56. Found: C, 72.08; H, 4.69; N, 2.76.

Ethyl 1-Benzoyl-3-(2-phenylethylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7y**): 79% (from **4a** and 2-phenethyl bromide (**5m**)), red needles, mp 147—149 °C. IR (KBr) cm^{-1}: 1672, 1624. UV λ_{max} ($CHCl_3$) nm (log ε) 330 (4.08), 483 (4.01), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{28}H_{23}NO_3S_2$: C, 69.25; H, 4.77; N, 2.88. Found: C, 69.39; H, 4.74; N, 2.78.

Ethyl 1-(4-chlorobenzoyl-3-(2-phenylethylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7z**): 93% (from **4b** and 2-phenethyl bromide (**5m**)), red needles, mp 111—112 °C. IR (KBr) cm^{-1}: 1672, 1620. UV λ_{max} ($CHCl_3$) nm (log ε) 331 (4.03), 485 (3.99), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{28}H_{22}ClNO_3S_2$: C, 64.67; H, 4.26; N, 2.69. Found: C, 64.68; H, 4.27 N, 2.53.

Ethyl 1-Benzoyl-7-methyl-3-(methylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**9a**): 62% (from **4d** and methyl iodide (**5a**)), red needles, mp 116—118 °C (Lit.[2] 113—115 °C). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 0.95 (3H, t, J=7.1 Hz), 2.40 (3H, s), 2.67 (3H, s), 3.56 (2H, q, J=7.1 Hz), 6.68 (1H, dd, J=7.1, 1.7 Hz), 7.40 (2H, br t, J=7.3 Hz), 7.50 (1H, br t, J=7.3 Hz), 7.94 (2H, br d, J=7.1 Hz), 8.00 (1H, br s), 8.84 (1H, d, J=7.1 Hz). ^{13}C-NMR ($CDCl_3$, 400 MHz) δ: 14.3, 21.7, 22.1, 58.9, 92.7, 113.8, 118.2, 121.5, 122.4, 126.7, 128.2, 129.2, 132.2, 135.1, 135.4, 139.3, 142.3, 150.6, 164.3, 187.7. UV λ_{max} ($CHCl_3$) nm (log ε) 331 (4.18), 478 (4.11), *ca.* 510 (shoulder).

Ethyl 1-(4-Chlorobenzoyl)-7-methyl-3-(methylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**9b**): 74% (from **4e** and methyl iodide (**5a**)), red needles, mp 167—169 °C (Lit.[2] 163—165 °C). UV λ_{max} ($CHCl_3$) nm (log ε) 332 (4.13), 480 (4.10), *ca.* 510 (shoulder).

Ethyl 1-(4-Bromobenzoyl)-7-methyl-3-(methylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**9c**): 73% (from **4f** and methyl iodide (**5a**)), red needles, mp 173—175 °C (Lit.[2] 169—171 °C). UV λ_{max} ($CHCl_3$) nm (log ε) 332 (4.12), 481 (4.09), *ca.* 510 (shoulder).

Ethyl 1-Benzoyl-3-benzylthio-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**9d**): 67% (from **4d** and benzyl bromide (**5b**)), red needles, mp 144—147 °C. IR (KBr) cm^{-1}: 1669, 1595. UV λ_{max} ($CHCl_3$) nm (log ε) 329 (4.12), 425 (4.18), 479 (3.58), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{28}H_{23}NO_3S_2$: C, 69.25; H, 4.77; N, 2.88. Found: C, 69.37; H, 4.77; N, 2.77.

Ethyl 3-Benzylthio-1-(4-chlorobenzoyl)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**9e**): 75% (from **4e** and benzyl bromide (**5b**)), red needles, mp 153—155 °C. IR (KBr) cm^{-1}: 1671, 1586. UV λ_{max} ($CHCl_3$) nm (log ε) 326 (4.09), 428 (3.99), 476 (3.74), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{28}H_{22}ClNO_3S_2$: C, 64.67; H, 4.26; N, 2.69. Found: C, 64.77; H, 4.23; N, 2.62.

Ethyl 3-Benzylthio-1-(4-bromobenzoyl)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**9f**): 80% (from **4f** and benzyl bromide (**5b**)), orange needles, mp 163—165 °C. IR (KBr) cm^{-1}: 1667, 1584. UV λ_{max} ($CHCl_3$) nm (log ε) 326 (4.11), 429 (3.96), 477 (3.76), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{28}H_{22}BrNO_3S_2$: C, 59.57; H, 3.93; N, 2.48. Found: C, 59.49; H, 4.21; N, 2.28.

Ethyl 1-Benzoyl-7-methyl-3-(2-methylbenzylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**9g**): 65% (from **4d** and 2-methylbenzyl bromide (**5c**)), orange flakes, mp 180—183 °C. IR (KBr) cm^{-1}: 1671, 1595. UV λ_{max} ($CHCl_3$) nm (log ε) *ca.* 326 (shoulder), 427 (3.97), 473 (3.73), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{29}H_{25}NO_3S_2$: C, 69.71; H, 5.04; N, 2.80. Found: C, 69.87; H, 5.01; N, 2.67.

Ethyl 1-(4-Chlorobenzoyl)-7-methyl-3-(2-methylbenzylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**9h**): 77% (from **4e** and 2-methylbenzyl bromide (**5c**)), orange needles, mp 180—181 °C. UV λ_{max} ($CHCl_3$) nm (log ε) *ca.* 326 (shoulder), 427 (3.97), 477 (3.77), *ca.* 510 (shoulder). IR (KBr) cm^{-1}: 1674, 1588. UV λ_{max} ($CHCl_3$) nm (log ε) *ca.* 326 (shoulder), 427 (3.97), 477 (3.77), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{29}H_{24}ClNO_3S_2$: C, 65.22; H, 4.53; N, 2.62. Found: C, 65.33; H, 4.51; N, 2.52.

Ethyl 1-(4-Bromobenzoyl)-7-methyl-3-(2-methylbenzylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**9i**): 70% (from **4f** and 2-methylbenzyl bromide (**5c**)), brown prisms, mp 133—135 °C. IR (KBr) cm^{-1}: 1674, 1586. UV λ_{max} ($CHCl_3$) nm (log ε) *ca.* 325 (shoulder), 428 (4.05), 473 (3.78), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{29}H_{24}BrNO_3S_2$: C, 60.21; H, 4.18; N, 2.42. Found: C, 60.31; H, 4.15; N, 2.35.

Ethyl 1-Benzoyl-7-methyl-3-(4-methylbenzylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**9j**): 65% (from **4d** and 4-methylbenzyl bromide (**5d**)), red needles, mp 110—111 °C. IR (KBr) cm^{-1}: 1674, 1591. UV λ_{max} ($CHCl_3$) nm (log ε) 327 (4.09), 428 (3.98), 474 (3.78), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{29}H_{25}NO_3S_2$: C, 69.71; H, 5.04; N, 2.80. Found: C, 69.81; H, 5.04; N, 2.67.

Ethyl 1-(4-Chlorobenzoyl)-7-methyl-3-(4-methylbenzylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**9k**): 89% (from **4e** and 4-methylbenzyl bromide (**5d**)), brown prisms, mp 179—182 °C. IR (KBr) cm^{-1}: 1667, 1586. UV λ_{max} ($CHCl_3$) nm (log ε) 325 (4.12), 428 (4.02), 478 (3.80), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{29}H_{24}ClNO_3S_2$: C, 65.22; H, 4.53; N, 2.62. Found: C, 65.09; H, 4.50; N, 2.54..

Ethyl 1-(4-Bromobenzoyl)-7-methyl-3-(4-methylbenzylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**9l**): 71% (from **4f** and 4-methylbenzyl bromide (**5d**)), brown prisms, mp 177—180 °C. IR (KBr) cm^{-1}: 1667, 1584. UV λ_{max} ($CHCl_3$) nm (log ε) *ca.* 326 (shoulder), 427 (3.96), 482 (3.89), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{29}H_{24}BrNO_3S_2$: C, 60.21; H, 4.18; N, 2.42. Found: C, 60.35; H, 4.16; N, 2.32.

Ethyl 1-Benzoyl-3-(2-cyanobenzylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**9m**): 62% (from **4d** and 2-cyanobenzyl bromide (**5e**)), orange needles, mp 186—188 °C. IR (KBr) cm^{-1}: 2224, 1662, 1624. UV λ_{max} ($CHCl_3$) nm (log ε) 322 (4.07), 426 (4.03), 471 (3.70), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{29}H_{22}N_2O_3S_2$: C, 68.21; H, 4.34; N, 5.49. Found: C, 68.31; H, 4.18; N, 5.55.

Ethyl 1-(4-Chlorobenzoyl)-3-(2-cyanobenzylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**9n**): 90% (from **4e** and 2-cyanobenzyl bromide (**5e**)), red prisms, mp 167—169 °C. IR (KBr) cm^{-1}: 2226, 1676, 1633. UV λ_{max} ($CHCl_3$) nm (log ε) 321 (4.13), 426 (4.06), 479 (3.79), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{29}H_{21}ClN_2O_3S_2$: C, 63.90; H, 3.88; N, 5.14. Found: C, 64.12; H, 3.79; N, 5.01.

Ethyl 1-(4-Bromobenzoyl)-3-(2-cyanobenzylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**9o**): 82% (from **4c** and 2-cyanobenzyl bromide (**5e**)), brown prisms, mp 169—170 °C. IR (KBr) cm^{-1}: 2226, 1676, 1635. UV λ_{max} ($CHCl_3$) nm (log ε) 323 (3.99), 426 (3.93), 478 (3.65), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{29}H_{21}BrN_2O_3S_2$: C, 59.08; H, 3.59; N, 4.75. Found: C, 59.32; H, 3.54; N, 4.57.

Ethyl 1-Benzoyl-3-(4-cyanobenzylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**9p**): 70% (from **4d** and 4-cyanobenzyl bromide (**5f**)), brown prisms, mp 202—204 °C. IR (KBr) cm^{-1}: 2226, 1666, 1595. UV λ_{max} ($CHCl_3$) nm (log ε) 322 (4.20), 426 (4.20), 472 (3.79), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{29}H_{22}N_2O_3S_2$: C, 68.21; H, 4.34; N, 5.49. Found: C, 68.23; H, 4.34; N, 5.26.

Ethyl 1-(4-Chlorobenzoyl)-3-(4-cyanobenzylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**9q**): 80% (from **4e** and 4-cyanobenzyl bromide (**5f**)), orange needles, mp 171—173 °C. IR (KBr) cm^{-1}: 2228, 1670, 1601. UV λ_{max} ($CHCl_3$) nm (log ε) *ca.* 325 (shoulder), 426 (4.07), 478 (3.73), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{29}H_{21}ClN_2O_3S_2$: C, 63.90; H, 3.88; N, 5.14. Found: C, 63.93; H, 4.15; N, 4.84.

Ethyl 1-(4-Bromobenzoyl)-3-(4-cyanobenzylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**9r**): 74% (from **4f** and 4-cyanobenzyl bromide (**5f**)), brown prisms, mp 173—174 °C. IR (KBr) cm^{-1}: 2228, 1670, 1585. UV λ_{max} ($CHCl_3$) nm (log ε) *ca.* 326 (shoulder), 427 (3.99), 484 (3.87), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{29}H_{21}BrN_2O_3S_2$: C, 59.08; H, 3.59; N, 4.75. Found: C, 59.20; H, 3.78; N, 4.47.

Ethyl 1-Benzoyl-3-(2-chlorobenzylthio)-7-methylthieno[3,4-*b*]indolizine-

9-carboxylate (**9s**): 66% (from **4d** and 2-chlorobenzyl bromide (**5g**)), red flakes, mp 194—195 °C. IR (KBr) cm^{-1}: 1667, 1620. UV λ_{max} ($CHCl_3$) nm (log ε) 325 (4.09), 425 (4.07), 476 (3.71), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{28}H_{22}ClNO_3S_2$: C, 64.67; H, 4.26; N, 2.69. Found: C, 64.69; H, 4.29; N, 2.65.

Ethyl 1-Benzoyl-3-(4-chlorobenzylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**9t**): 83% (from **4d** and 4-chlorobenzyl bromide (**5h**)), red needles, mp 156—157 °C. IR (KBr) cm^{-1}: 1667, 1630. UV λ_{max} ($CHCl_3$) nm (log ε) 327 (4.10), 426 (4.06), 473 (3.76), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{28}H_{22}ClNO_3S_2$: C, 64.67; H, 4.26; N, 2.69. Found: C, 64.78; H, 4.25; N, 2.59.

Ethyl 1-Benzoyl-3-(4-bromobenzylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**9u**): 74% (from **4d** and 4-bromobenzyl bromide (**5i**)), orange flakes, mp 138—139 °C. IR (KBr) cm^{-1}: 1669, 1622. UV λ_{max} ($CHCl_3$) nm (log ε) 323 (4.09), 426 (4.05), 474 (3.73), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{28}H_{22}BrNO_3S_2$: C, 59.57; H, 3.93; N, 2.48. Found: C, 59.68; H, 3.96; N, 2.35.

Ethyl 1-Benzoyl-3-(4-fluorobenzylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**9v**): 65% (from **4d** and 4-fluorobenzyl bromide (**5j**)), orange flakes, mp 145—147 °C. IR (KBr) cm^{-1}: 1669, 1597. UV λ_{max} ($CHCl_3$) nm (log ε) 327 (4.10), 426 (4.00), 476 (3.81), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{28}H_{22}FNO_3S_2$: C, 66.78; H, 4.40; N, 2.78. Found: C, 66.73; H, 4.30; N, 2.65.

Ethyl 1-Benzoyl-7-methyl-3-(1-phenylethylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**9w**): 91% (from **4d** and 1-phenylethyl bromide (**5k**)), red prisms, mp 151—153 °C. IR (KBr) cm^{-1}: 1672, 1620. UV λ_{max} ($CHCl_3$) nm (log ε) 325 (4.08), 426 (3.99), 472 (3.74), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{29}H_{25}NO_3S_2$: C, 69.71; H, 5.04; N, 2.80. Found: C, 69.82; H, 4.99; N, 2.75.

Ethyl 1-Benzoyl-3-(diphenylmethylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**9x**): 61% (from **4d** and diphenylmethyl bromide (**5l**)), orange needles, mp 205—207 °C. IR (KBr) cm^{-1}: 1665, 1631. UV λ_{max} ($CHCl_3$) nm (log ε) 330 (4.10), 427 (4.14), 473 (3.65), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{34}H_{27}NO_3S_2$: C, 72.70; H, 4.85; N, 2.49. Found: C, 72.82; H, 4.83; N, 2.39.

Ethyl 1-Benzoyl-7-methyl-3-(2-phenylethylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**9y**): 83% (from **4d** and 2-phenethyl bromide (**5m**)), orange needles, mp 178—179 °C. IR (KBr) cm^{-1}: 1672, 1589. UV λ_{max} ($CHCl_3$) nm (log ε) 332 (4.13), 481 (4.05), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{29}H_{25}NO_3S_2$: C, 69.71; H, 5.04; N, 2.80. Found: C, 69.71; H, 4.96; N, 2.88.

Ethyl 1-Benzoyl-7-methyl-3-(2-phenylethylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**9z**): 77% (from **4e** and 2-phenethyl bromide (**5m**)), red prisms, mp 127—128 °C. IR (KBr) cm^{-1}: 1672, 1635. UV λ_{max} ($CHCl_3$) nm (log ε) 332 (4.13), 485 (4.07), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{29}H_{24}ClNO_3S_2$: C, 65.22; H, 4.53; N, 2.62. Found: C, 65.32; H, 4.48; N, 2.52.

Crystallography of Ethyl 1-Benzoyl-3-(2-methylbenzylthio)thieno[3,4-*b*]indolizine-9-carboxylate (7g) A single crystal (0.12×0.46×0.68 mm) grown from $CHCl_3$–hexane was used for the unit-cell determinations and data collection by a Rigaku AFC5S four-circle diffractometer with graphite-monochromated Mo$K\alpha$ radiation (λ=0.71069 Å). The crystal data of these compounds are as follows: **7g**: $C_{28}H_{23}NO_3S_2$; M=485.61; triclinic, space group $P\bar{1}$ (#2), Z=2 with a=11.736 (3)Å, b=12.268 (4)Å, c=9.437 (3)Å, α=109.31 (2)°, β=105.68° (3), γ=73.98° (3); V=1208.2 (8)Å^3 and $D_{calc.}$=1.335 g/cm^3. All calculations were performed using the teXsan program.[14] The structure was solved by a direct method (SIR).[15] The non-hydrogen atoms were refined anisotropically, and the hydrogen atoms were attached at the idealized position and not refined. The final R- and R_w-factors after full-matrix least-squares refinements were 0.062 and 0.053 for 2857 (I>2.00σ(I)) observed reflections, respectively.

Crystallography of Ethyl 1-(4-Chlorobenzoyl)-3-(2-cyanobenzylthio)-thieno[3,4-*b*]indolizine-9-carboxylate (7n) A single crystal (0.42×0.48×0.82 mm) grown from $CHCl_3$–hexane was used for the unit-cell determinations and data collection by a Rigaku AFC5S four-circle diffractometer with graphite-monochromated Mo$K\alpha$ radiation (λ=0.71069Å). The crystal data of these compounds are as follows: **7n**: $C_{28}H_{19}ClN_2O_3S_2$; M=517.04; monoclinic, space group $C2/c$ (#15), Z=8 with a=15.497 (3)Å, b=15.378 (4)Å, c=22.152 (4)Å, β=102.94° (2); V=5145 (2)Å^3 and $D_{calc.}$= 1.335 g/cm^3. All calculations were performed using the teXsan program.[14] The structure was solved by a direct method (SIR).[15] The non-hydrogen atoms were refined anisotropically, and the hydrogen atoms were attached at the idealized position and not refined. The final R- and R_w-factors after full-matrix least-squares refinements were 0.068 and 0.055 for 2422 (I>2.00σ(I)) observed reflections, respectively.

Crystallography of Ethyl 1-Benzoyl-3-(4-bromobenzylthio)thieno[3,4-*b*]indolizine-9-carboxylate (7u) A single crystal (0.18×0.18×0.64 mm) grown from $CHCl_3$–hexane was used for the unit-cell determinations and data collection by a Rigaku AFC5S four-circle diffractometer with graphite-monochromated Mo$K\alpha$ radiation (λ=0.71069Å). Crystal data of these compounds are as follows: **7u**: $C_{27}H_{20}BrNO_3S_2$; M=550.48; monoclinic, space group $P2_1/a$ (#14), Z=4 with a=8.700 (3)Å, b=16.442 (2)Å, c= 16.865 (3)Å, β=99.68° (2); V=2378.1 (8)Å^3 and $D_{calc.}$=1.537 g/cm^3. All calculations were performed using the teXsan program.[14] The structure was solved by a direct method (SIR).[15] The non-hydrogen atoms were refined anisotropically, and the hydrogen atoms were attached at the idealized position and not refined. The final R- and R_w-factors after full-matrix least-squares refinements were 0.064 and 0.055 for 1850 (I>2.00σ(I)) observed reflections, respectively.

Crystallography of Ethyl 1-(4-Chlorobenzoyl-3-(2-cyanobenzylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (9n) A single crystal (0.42×0.54×0.68 mm) grown from $CHCl_3$–hexane was used for the unit-cell determinations and data collection by a Rigaku AFC5S four-circle diffractometer with graphite-monochromated Mo$K\alpha$ radiation (λ=0.71069Å). The crystal data of these compounds are as follows: **9n**: $C_{29}H_{21}N_2O_3S_2Cl$; M=531.06; triclinic, space group $P\bar{1}$ (#2), Z=2 with a=11.224 (2)Å, b=12.752 (3)Å, c=10.709 (3)Å, α=109.93 (2)°, β=108.20° (3), γ= 101.93° (2); V=1281.9 (7)Å^3 and $D_{calc.}$=1.376 g/cm^3. All calculations were performed using the teXsan program.[14] The structure was solved by a direct method (SIR).[15] The non-hydrogen atoms were refined anisotropically, and the hydrogen atoms were attached at the idealized position and not refined. The final R- and R_w-factors after full-matrix least-squares refinements were 0.056 and 0.045 for 2873 (I>2.00σ(I)) observed reflections, respectively.

Crystallography of Ethyl 1-Benzoyl-3-(4-cyanobenzylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (9p) A single crystal (0.08×0.42×1.00 mm) grown from $CHCl_3$–hexane was used for the unit-cell determinations and data collection by a Rigaku AFC5S four-circle diffractometer with graphite-monochromated Mo$K\alpha$ radiation (λ=0.71069Å). The crystal data of these compounds are as follows: **9p**: $C_{29}H_{22}N_2O_3S_2$; M=510.62; triclinic, space group $P\bar{1}$ (#2), Z=2 with a=11.824 (2)Å, b=13.586 (2)Å, c= 8.902 (2)Å, α=108.89 (1)°, β=103.38° (1), γ=100.29° (1); V=1265.3 (5)Å^3 and $D_{calc.}$=1.340 g/cm^3. All calculations were performed using the teXsan program.[14] The structure was solved by a direct method (SIR).[15] The non-hydrogen atoms were refined anisotropically, and the hydrogen atoms were attached at the idealized position and not refined. The final R- and R_w-factors after full-matrix least-squares refinements were 0.063 and 0.051 for 2598 (I>2.00σ(I)) observed reflections, respectively.

Crystallography of Ethyl 1-(4-Cyanobenzoyl)-7-methyl-3-(phenethylthio)thieno[3,4-*b*]indolizine-9-carboxylate (9z) A single crystal (0.24×0.64×0.86 mm) grown from $CHCl_3$–hexane was used for the unit-cell determinations and data collections by a Rigaku AFC5S four-circle diffractometer with graphite-monochromated Mo$K\alpha$ radiation (λ=0.71069Å). The crystal data of **9z** are as follows: $C_{29}H_{24}ClNO_3S_2$; M=534.09; monoclinic, space group $P2_1/a$ (#14), Z=4 with a=14.650 (3)Å, b=11.055 (3)Å, c=15.963 (2)Å, β=96.23° (1); V=2570.1 (9)Å^3 and $D_{calc.}$=1.380 g/cm^3. All calculations were performed using the teXsan program.[14] The structure was solved by a direct method (MITHRIL).[15] The non-hydrogen atoms were refined anisotropically, and the hydrogen atoms were attached at the idealized position and not refined. The final R- and R_w-factors after full-matrix least-squares refinements were 0.073 and 0.078 for 2705 (I>2.00σI)) observed reflections, respectively.

References and Notes

1) For part 52 of this series, see Kakehi A., Ito S., Suga H., Miwa T., Mori T., Kobayashi T., *Heterocycles*, **57**, 17—20 (2002).
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9) These UV spectra were measured in chloroform with a drop of triethylamine in order to avoid the influence of the hydrogen chloride generated.
10) Johnson C. K., "ORTEP II, Report ORNL-5138," Oak Ridge National

Laboratory, Oak Ridge, Tennessee, 1976.
11) The single crystals of compounds **7i**, **o**, **s** and **9i**, **n** were shown to have the corresponding **G1** form by the X-ray analyses.
12) The single crystals of compounds **7k** and **9k**, **l**, **t** were shown to have the corresponding **A1** form by the X-ray analyses.
13) "WinMOPAC (Version 3.0)", Fujitsu Corporation.
14) teXsan for Windows version 1.06: Crystal Structure Analysis Package, Molecular Structure Corporation (1997-9).
15) SIR92: Altomare A., Cascarano G., Giacovazzo C., Guagliardi A., *J. Appl. Cryst.*, **26**, 343—350 (1993).