Preparation of New Nitrogen-Bridged Heterocycles. 54.[1] Increased Arene–Arene Interactions of 3-(Bicyclic and Tricyclic Arylmethylthio)thieno[3,4-*b*]indolizine Derivatives

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Some thieno[3,4-*b*]indolizine derivatives having a 1-naphthylmethylthio, 2-methyl-1-naphthylmethylthio, 2-naphthylmethylthio, or 9-anthrylmethylthio group at the 3-position were prepared and their intramolecular arene–arene interactions were investigated. In comparison with 3-(methylthio)thieno[3,4-*b*]indolizines which have no such interactions, the ^{1}H-NMR spectra of title compounds showed large high-field shifts (δ 0.06—0.89 ppm) for the protons of the pyridine ring in the thieno[3,4-*b*]indolizine, and these values were considerably larger than those (δ <0.3 ppm) in 3-(benzylthio)thieno[3,4-*b*]indolizines. The UV spectra also exhibited a characteristic absorption band near 425 nm attributable to the arene–arene interaction. In the X-ray analyses of some compounds, however, the presence of both the gauche and the anti conformers at the sulfide spacer were confirmed.

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

In our recent papers we reported a new preparative method for 3-(benzylthio)thieno[3,4-*b*]indolizine derivatives and found that there is an arene–arene interaction between the two aromatic rings in the gauche conformation at the exocyclic sulfide linkage as a spacer.[1,2] In particular, these molecules exhibited a characteristic absorption band near 425 nm in the UV spectra and a moderate shielding effect on the aromatic protons in the NMR spectra due to the arene–arene interaction in the stacked structure. We were very interested in the smooth appearance of such through-space interaction in these molecules, and planned an extension to other thieno[3,4-*b*]indolizine derivatives bearing bicyclic and tricyclic benzenoid rings in the 3-substituent. These compounds can be also expected to have more effective arene–arene interactions between the aromatic ring and the thieno[3,4-*b*]indolizine ring, though the introduction of a bulkier aromatic group might give rise to a larger steric repulsion. In this paper we report the syntheses of ethyl 1-benzoyl-3-(1-naphthylmethylthio)-, 3-(2-methyl-1-naphthylmethylthio)-, 3-(2-naphthylmethylthio)-, and 3-(9-anthrylmethylthio)thieno[3,4-*b*]indolizine-9-carboxylates and their increased intramolecular arene–arene interactions.

Results and Discussion

Preparations of Ethyl 3-(Bicyclic and Tricyclic Arylmethylthio)thieno[3,4-*b*]indolizine-9-carboxylates The title compounds **4a**—**x** were prepared in low to moderate yields (16—69%) by a minor modification of our previous procedure[1,2] because of the slow and ineffective *S*-alkylations of the pyridinium betaines. For example, the *S*-alkylation of 5-arylcarbonyl-4-ethoxycarbonylmethyl-3-(1-pyridinio)thiophene-2-thiolates (**1a**—**f**) with 1-chloromethylnaphthalene (**2a**) in acetone in the presence of excess sodium iodide, followed by the treatment of the resulting pyridinium salts (**3a**—**c**, **m**—**o**) with DBU and then chloranil in an ice bath afforded the corresponding ethyl 1-arylcarbonyl-3-(1-naphthylmethylthio)thieno[3,4-*b*]indolizine-9-carboxylates (**4a**—**c**, **m**—**o**) in 22—63% yields as red or dark red prismatic crystals. Similar treatment of pyridinium betaines **1a**—**f** with 1-chloromethyl-2-methylnaphthalene (**2b**), 2-bromomethylnaphthalene (**2c**), and 9-chloromethylanthracene (**2d**) gave the expected products **4d**—**f**, **p**—**r**, **4g**—**i**, **s**—**u**, and **4j**—**l**, **v**—**x** in 16—69% yields, respectively. These results are summarized in Chart 1.

The elemental analyses for these products **4a**—**x** were in good accord with our proposed structures. The IR spectra of **4a**—**x** showed an ester carbonyl band at 1667—1690 cm^{-1} and a fairly shifted ketone carbonyl band[3,4] at 1582—1635 cm^{-1}, and the UV spectra of **4a**—**x** clearly exhibited an absorption band near 425 nm attributable to the arene–arene interaction. The molar extinction coefficients for these UV bands of thieno[3,4-*b*]indolizine derivatives **4a**—**c**, **g**—**o**, **s**—**x** except for 3-(2-methyl-1-naphthylmethylthio) analogs **4d**—**f**, **p**—**r** were generally larger than those observed for 3-benzylthio analogs,[1,2] indicating more effective arene–arene interactions by the bicyclic and tricyclic aromatic rings. The diminished absorption bands of **4d**—**f**, **p**—**r** must be attributable to the steric repulsion of the 2-methyl group. Next, the chemical shifts for the pyridine ring protons of **4a**—**x** in the ^{1}H-NMR spectra were compared with those of ethyl 1-benzoyl-3-(methylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**5a**) and its 7-methyl derivatives **5b**[2] (see Fig. 1) which have not any arene–arene interaction (see Table 1). The protons of **4a**—**x** appeared at higher magnetic fields than those of **5a**, **b**; the high field shifts for the 5- and 6-protons were in the range of δ 0.33—0.88 ppm and, even for the 7- and 8-protons, such effects (δ 0.08—0.32 ppm) were observed. These values of **4a**—**x** were also considerably higher than those (δ <0.3 ppm only for the 5- and 6-protons) in the 3-benzylthio derivatives. Similarly, significant high-field shifts (δ <0.63 ppm) for the naphthalene and anthracene ring protons in comparison with those[5] of **2a**—**d** were also observed. These facts strongly

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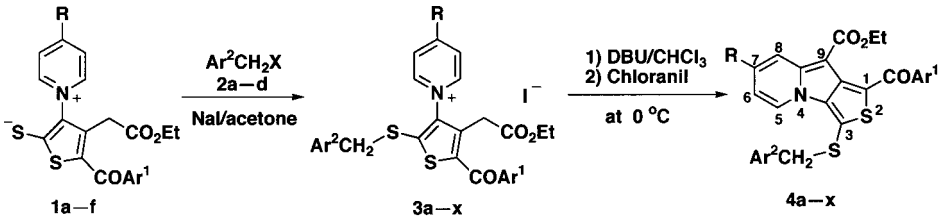


1	R	Ar^1
a	H	Ph
b	H	4-ClC_6H_4
c	H	4-BrC_6H_4
d	Me	Ph
e	Me	4-ClC_6H_4
f	Me	4-BrC_6H_4

2	Ar^2	X
a	1-Naphthyl	Cl
b	2-Me-1-naphthyl	Cl
c	2-Naphthyl	Br
d	9-Anthryl	Cl

3,4	R	Ar^1	Ar^2	Yield[a] (%)
a	H	Ph	1-Naphthyl	74
b	H	4-ClC_6H_4	1-Naphthyl	58
c	H	4-BrC_6H_4	1-Naphthyl	63
d	H	Ph	2-Me-1-naphthyl	54
e	H	4-ClC_6H_4	2-Me-1-naphthyl	82
f	H	4-BrC_6H_4	2-Me-1-naphthyl	80
g	H	Ph	2-Naphthyl	69
h	H	4-ClC_6H_4	2-Naphthyl	78
i	H	4-BrC_6H_4	2-Naphthyl	70
j	H	Ph	9-Anthryl	28
k	H	4-ClC_6H_4	9-Anthryl	31
l	H	4-BrC_6H_4	9-Anthryl	37

3,4	R	Ar^1	Ar^2	Yield[a] (%)
m	Me	Ph	1-Naphthyl	57
n	Me	4-ClC_6H_4	1-Naphthyl	74
o	Me	4-BrC_6H_4	1-Naphthyl	38
p	Me	Ph	2-Me-1-naphthyl	46
q	Me	4-ClC_6H_4	2-Me-1-naphthyl	64
r	Me	4-BrC_6H_4	2-Me-1-naphthyl	39
s	Me	Ph	2-Naphthyl	77
t	Me	4-ClC_6H_4	2-Naphthyl	69
u	Me	4-BrC_6H_4	2-Naphthyl	60
v	Me	Ph	9-Anthryl	16
w	Me	4-ClC_6H_4	9-Anthryl	40
x	Me	4-BrC_6H_4	9-Anthryl	31

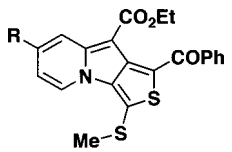
a) The yields from 1 to 4.

Chart 1

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

	C-5	C-6	C-7	C-8	SCH_2	CO_2Et		δ (5-H)[b)]	δ (6-H)[b)]	δ (7-R)[b)]	δ (8-H)[b)]
5a	8.96	6.73	7.31	8.20	2.68	0.97	3.60	0.00	0.00	0.00	0.00
4a	8.24	5.96	7.05	8.00	4.54	0.95	3.62	0.72	0.77	0.26	0.20
4b	8.26	6.00	7.09	8.00	4.56	1.01	3.72	0.70	0.73	0.22	0.20
4c	8.26	6.00	7.08	7.99	4.55	1.01	3.72	0.70	0.73	0.23	0.21
4d	8.54	6.23	7.15	8.06	4.68	0.95	3.60	0.42	0.50	0.16	0.14
4e	8.54	6.26	7.16	8.05	4.67	1.00	3.70	0.42	0.47	0.15	0.15
4f	8.54	6.26	7.16	8.05	4.67	1.01	3.71	0.42	0.47	0.15	0.15
4g	8.64	6.27	7.03	7.97	4.24	0.97	3.64	0.32	0.46	0.28	0.23
4h	8.64	6.29	7.06	7.96	4.24	1.02	3.73	0.32	0.44	0.25	0.24
4i	8.66	6.31	7.07	7.97	4.26	1.02	3.73	0.30	0.42	0.24	0.23
4j	8.09	5.84	7.00	7.89	5.14	0.93	3.54	0.87	0.89	0.31	0.31
4k	8.10	5.86	7.01	7.88	5.14	0.98	3.63	0.86	0.87	0.30	0.32
4l	8.09	5.84	7.02	7.88	5.14	0.98	3.63	0.87	0.89	0.29	0.32
5b	8.84	6.58	2.40	8.00	2.67	0.95	3.56	0.00	0.00	0.00	0.00
4m	8.15	5.82	2.26	7.81	4.54	0.93	3.58	0.69	0.76	0.14	0.19
4n	8.15	5.84	2.26	7.79	4.53	0.98	3.68	0.69	0.74	0.14	0.21
4o	8.16	5.86	2.27	7.80	4.54	0.99	3.68	0.68	0.72	0.13	0.20
4p	8.47	6.11	2.32	7.88	4.68	0.93	3.58	0.37	0.47	0.08	0.12
4q	8.46	6.13	2.32	7.87	4.67	0.98	3.67	0.38	0.45	0.08	0.13
4r	8.44	6.11	2.30	7.84	4.65	0.97	3.66	0.40	0.47	0.10	0.16
4s	8.44	6.03	2.18	7.75	4.22	0.95	3.60	0.40	0.55	0.22	0.25
4t	8.47	6.07	2.20	7.75	4.23	1.01	3.70	0.37	0.51	0.20	0.25
4u	8.46	6.07	2.20	7.75	4.23	1.00	3.70	0.38	0.51	0.20	0.25
4v	8.02	5.71	2.23	7.70	5.13	0.91	3.51	0.82	0.87	0.17	0.30
4w	7.99	5.71	2.23	7.68	5.11	0.96	3.60	0.85	0.87	0.17	0.32
4x	8.00	5.71	2.23	7.68	5.12	0.95	3.60	0.84	0.87	0.17	0.32

a) The coupling constants are as follows; $J_{5,6}$=6.8—7.1 Hz, $J_{6,7}$=6.6—6.8 Hz, $J_{6,8}$=1.6—1.8 Hz, $J_{7,8}$=9.3—9.5 Hz. *b*) The chemical shifts of 3-methylthio compounds **5a**, **b** are selected as the standards for **4a**—**l** and **4m**—**x**, respectively.



5a (R=H)
5b (R=Me)

Fig. 1

showed the increased contribution of these 3-(bicyclic and tricyclic arylmethylthio) systems for the arene–arene interactions. Very strangely, neither the nuclear Overhauser effect (NOE) between their interacting ring protons nor any other conformational isomers for products **4a**—**x** could be observed in their NMR spectra at ordinary temperature or at low temperature (−50 °C for **4j**) at all. Furthermore, the 9 protons and the14 carbons of the 9-anthryl ring in the ^{1}H-

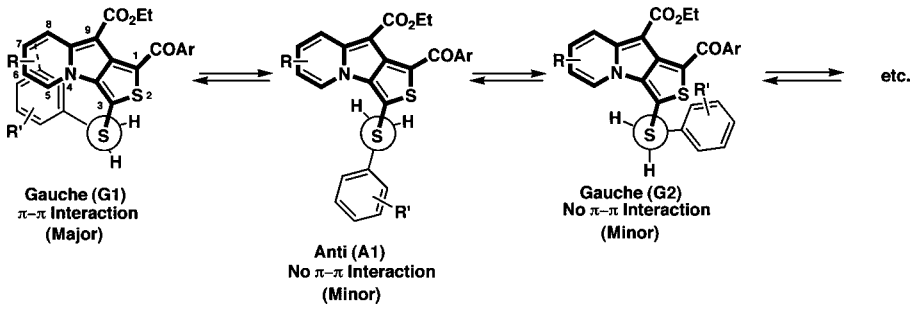


Chart 2

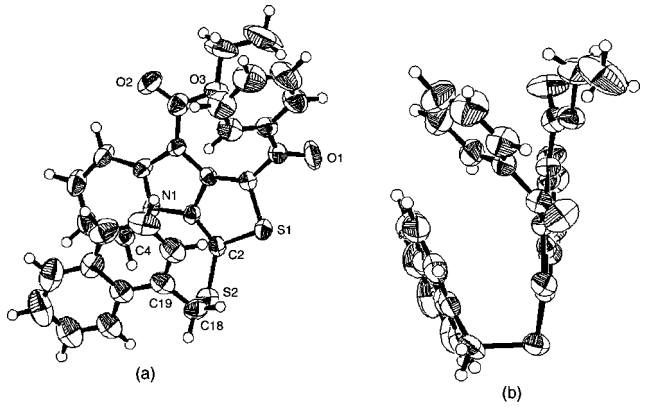


Fig. 2. ORTEP Drawings (the Over-View (a) and the Side-View (b)) of **4a**

and ^{13}C-NMR spectra of **4j**—**l**, **v**—**x** appeared as only 5 and 8 sets of the signals, respectively. This means that, in the NMR time scale, the 9-anthryl group still maintains magnetic symmetry in these molecules and the rotation about the axis of symmetry through the 9- and 10-positions of the anthracene ring is not restricted. Perhaps, all products **4a**—**x** involving 3-(9-anthrylmethylthio) derivatives in the solution state must be equilibrium mixtures of many possible conformers such as gauche (**G1**, **G2**), anti form (**A1**), and so on, as shown in Chart 2.

On the other hand, the X-ray analyses for some products showed each sole conformer. For example, thieno[3,4-*b*]indolizines bearing the 3-(1-naphthylmethylthio) and a 3-(9-anthrylmethylthio) group were observed only in gauche form (**G1**) favorable to the arene–arene interaction,[6] while 3-(2-naphthylmethylthio)thieno[3,4-*b*]indolizines were seen as only in the anti form (**A1**),[7] but any other conformers involving the **G2** form could not be detected. The ORTEP drawings[8] of the representative compounds **4a**, **t**, **k** are shown in Figs. 2—4. The nearest distances (C4—C26 or C4—C24) (see ORTEP drawings for its numbering) between the 4-position of the thieno[3,4-*b*]indolizine ring and the naphtharene or anthracene ring, the dihedral angles (C2–S2–C18–C19 or C2–S2–C18–C32), and those of the least-square planes between the thienoindolizine and the naphthyl or anthryl rings in **4a**, **k** (gauche form) are 3.351 (7) and 3.76 (1) Å, ±54.8 (5) and ±68.9 (6)°, and ±26.29 (9) and ±25.1° (1), respectively. Both the distances and the dihedral angles of the least square planes between the thieno[3,4-*b*]indolizine ring and the interacting 1-naphthyl or 9-anthryl ring were slightly shorter and narrower than those for 3-(benzylthio)thieno[3,4-*b*]indolizines.[2]

Conformational Analyses by Mopac PM3 Calculations[9] In order to obtain further information for the conformation of molecules **4a**—**x**, we performed the Mopac PM3 (precise) calculations for their optimized geometry. From the theoretical consideration and the NMR spectral and X-ray analyses, we classified their possible conformers for products **4a**—**x** and its reference compound, 3-(benzylthio)thieno[3,4-*b*]indolizines as *gauche* 1 (**G1**), *gauche* 2 (**G2**), *anti* 1 (**A1**), *anti* 2 (**A2**), and *anti* 3 (**A3**), and further subdivide the **G1**, **G2** and **A1** conformers to *s-cis*–front (**CF**), *s-cis*–back (**CB**), *s-trans*–front (**TF**), and *s-trans*–back (**TB**), respectively, as shown in Fig. 5. Similar subdivision to the remaining **A2** and **A3** conformers was not exhibited because all MOPAC calculations using them lead to the confor-

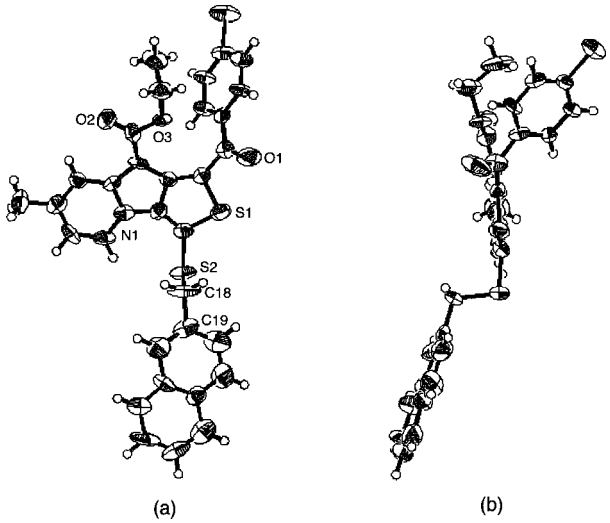


Fig. 3. ORTEP Drawings (the Over-View (a) and the Side-View (b)) of **4t**

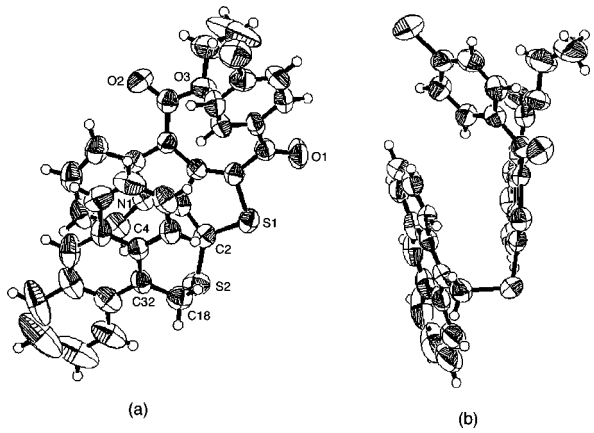


Fig. 4. ORTEP Drawings (the Over-View (a) and the Side-View (b)) of **4k**

mational conversion to the **A1** or **G1** form. The unsymmetrical 1-naphthyl, 2-methyl-1-naphthyl, and 2-naphthyl groups were also classified type **A** and type **B** depending upon their directions. Mopac calculations were carried out for representative 4 products **4a**, **d**, **g**, **j** and ethyl 1-benzoyl-3-(benzylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**6a**), and the formation energies at their optimized geometry and the energy differences between each formation energies and those of the **G1CF** conformers of **4a-B**, **4d-B**, **4g-B**, **4j**, and **6a** are summarized in Tables 2 and 3. As seen in these tables, the **G1** form with the arene–arene interaction was more stable than the other **G2** and **A1** ones without such interaction or

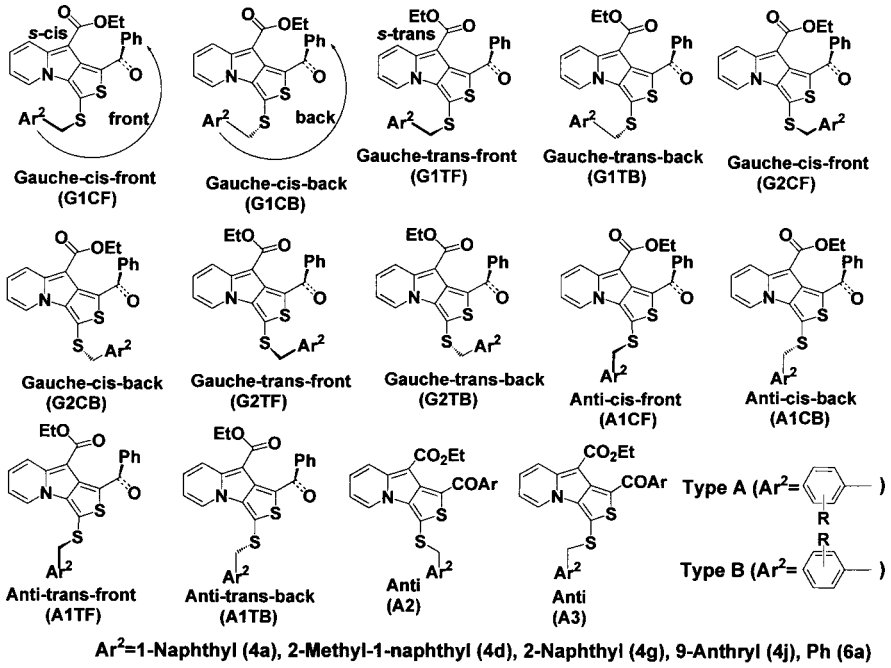


Fig. 5. Possible Comformers for Some Thieno[3,4-*b*]indoliziens

Table 2. The Formation Energies (kcal/mol) in MOPAC PM3 (Precise) Calculation of Some Compounds

	4a-A	4a-B	4d-A	4d-B	4g-A	4g-B	4j	5a
G1CF	39.81922	38.32194	31.75070	30.60892	38.50355	38.07728	61.44061	21.31802
G1CB	39.59324	39.36881	31.69808	31.65376	38.25233	38.14346	62.39548	21.06508
G1TF	40.45737	39.54283	32.18387	31.80025	39.11002	38.41256	62.88484	21.92356
G1TB	40.32566	40.13803	32.46401	32.44969	38.99358	38.90499	63.16975	21.81206
G2CF	40.21715	40.45077	32.52007	33.54331	38.66765	39.14417	63.58918	21.89240
G2CB	40.34758	40.56899	32.68465	33.52534	39.02356	39.12183	63.68283	21.83144
G2TF	41.19616	41.49763	33.56481	33.60144	40.01317	40.04132	64.54539	23.05197
G2TB	41.13489	41.36068	33.47771	33.88605	39.80915	39.90569	64.50345	22.61515
A1CF	39.78041	40.72040	31.85413	33.19413	38.70819	to G1CF	62.63155	22.43178
A1CB	39.49400	40.47634	31.60207	32.75575	39.35404	to G1CB	62.36472	22.16842
A1TF	40.35097	41.34376	32.44134	32.80829	39.28406	to G1TF	63.23776	23.05197
A1TB	40.26902	41.23950	32.35839	32.72772	39.80720	to G1TB	63.15194	22.94737

Table 3. The Energy Differences (kcal/mol) between Each Comformers and More Stable G1CF Ones

	4a-A[a)]	4a-B	4d-A[a)]	4d-B	4g-A[a)]	4g-B	4j	5a
Standard	1.49728	0.00000	1.14178	0.00000	0.42627	0.00000	0.00000	0.00000
δ (G1CB–G1CF)	1.27130	1.04687	1.08916	1.04484	0.17505	0.06618	0.95487	−0.25294
δ (G1TF–G1CF)	2.13543	1.22089	1.57495	1.19133	1.03274	0.33528	1.44423	0.60554
δ (G1TB–G1CF)	2.00372	1.81609	1.85509	1.84077	0.91630	0.82771	1.72914	0.49404
δ (G2CF–G1CF)	1.89521	2.12883	1.91115	2.93439	0.59037	1.06689	2.14857	0.57438
δ (G2CB–G1CF)	2.02564	2.24705	2.07573	2.91642	0.94628	1.04455	2.24222	0.51342
δ (G2TF–G1CF)	2.87422	3.17569	2.95589	2.99252	1.93589	1.96404	3.10478	1.73395
δ (G2TB–G1CF)	2.81295	3.03874	2.86879	3.27713	1.73187	1.82841	3.06284	1.29713
δ (A1CF–G1CF)	1.45847	2.39846	1.24521	2.58521	0.63091	No Calc.	1.19094	1.11376
δ (A1CB–G1CF)	1.17206	2.15440	0.99315	2.14683	1.27676	No Calc.	0.92411	0.85040
δ (A1TF–G1CF)	2.02903	3.02182	1.83242	2.19937	1.20678	No Calc.	1.79715	1.73395
δ (A1TB–G1CF)	1.94708	2.91756	1.74947	2.11880	1.72992	No Calc.	1.71133	1.62935

a) Smaller values of the G1CF conformer of type B were used as standard.

with weaker one, and more stacked form (type **B**) of the two aromatic rings in the cases (**4a**, **d**, **g**) with unsymmetrical benzenoid substituents was more stable than the other (type **A**). However, this stability order for these conformers was not necessarily consistent with the results obtained from their X-ray analyses. That the energy differences between them are very small may explain the conformations of **4a**—**x** in the solid state.

In conclusion, we first synthesized some thieno[3,4-*b*]indolizines bearing a bicyclic and tricyclic arylmethylthio group at the 3-position, and could observe their increased arene–arene interactions.

Experimental

Melting points were measured with a Yanagimoto micromelting point apparatus and were not corrected. Microanalyses were carried out on a Perkin-Elmer 2400 elemental analyzer. The ^{1}H-NMR spectra were determined with a JEOL JNM-LA300 (^{1}H: 300 MHz, ^{13}C: 75 MHz), or JEOL JNM-LA400 (^{1}H: 400 MHz, ^{13}C: 100 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 JASCO FT/IR-5300 IR and SHIMADZU UV-2500PC spectrophotometers, respectively.

Preparation of Ethyl 1-Arylcarbonyl-3-(arylmethylthio)thieno[3,4-*b*]indolizine-9-carboxylates. General Method A mixture of 1-(pyridinio)thiophene-2-thiolate (**1**, 1 mmol), alkyl halide (**2**, 1 mmol), and sodium iodide (1 g) in acetone (20 ml) was kept at 50 °C in a water bath under occasional stirring until the spot of the pyridinium betaine (**1**) disappeared by TLC monitoring (2—3 d). After *S*-alkylation was completed, the resulting solution was concentrated at reduced pressure and the residue was washed three times with 10 ml portions of ether to remove unaltered alkylating agent. Without further isolation and purification of the resulting pyridinium salt (**3**) the mixture 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 10 min and then with chloranil (0.499 g, 1 mmol) under the same conditions for another 5 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 (**4**) were combined and concentrated at reduced pressure. Recrystallization of the crude product from chloroform–ethanol afforded the corresponding ethyl 1-arylcarbonyl-3-(bicyclic or tricyclic arylmethylthio]thieno[3,4-*b*]indolizine-9-carboxylate. Some ^{1}H-NMR spectral data for products **4a**—**x**, are listed in Table 1, and the other data for them are as follows:

Ethyl 1-Benzoyl-3-(1-naphthylmethylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**4a**): 74% (from **1a** and 1-chloromethylnaphthalene (**2a**)), red prisms, mp 178—180 °C. IR (KBr) cm^{-1}: 1676, 1628. ^{1}H-NMR ($CDCl_3$) δ: 6.86 (1H, dd, J=7.1, 1.0 Hz), 7.03 (1H, t, J=7.8 Hz), 7.38—7.58 (6H, m), 7.75 (1H, d, J=8.1 Hz), 7.88—7.94 (2H, m), 8.06 (1H, d, J=8.5 Hz). ^{13}C-NMR ($CDCl_3$) δ: 14.3, 42.8, 58.9, 93.0, 109.8, 115.6, 119.5, 123.1, 124.7, 125.5, 126.0, 126.2, 126.5, 127.4, 128.3, 128.9, 129.0, 129.4, 129.9, 130.9, 131.7, 132.5, 134.0, 134.6, 137.8, 139.0, 149.7, 164.0, 188.2. UV λ_{max} ($CHCl_3$) nm (log ε) 325 (shoulder), 423 (3.98), 477 (3.74), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{31}H_{23}NO_3S_2$: C, 71.38; H, 4.44; N, 2.69. Found: C, 71.50; H, 4.37; N, 2.57.

Ethyl 1-(4-Chlorobenzoyl)-3-(1-naphthylmethylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**4b**): 58% (from **1b** and **2a**), red prisms, mp 151—152 °C. IR (KBr) cm^{-1}: 1669, 1628. ^{1}H-NMR ($CDCl_3$) δ: 6.87 (1H, d, J=6.8 Hz), 7.04 (1H, t, J=8.1 Hz), 7.38—7.43 (2H, m), 7.49 (1H, t, J=7.8 Hz), 7.52—7.59 (2H, m), 7.76 (1H, d, J=8.3 Hz), 7.80—7.86 (2H, m), 8.05 (1H, d, J=8.3 Hz). ^{13}C-NMR ($CDCl_3$) δ: 14.4, 42.8, 59.1, 92.9, 110.0, 116.6, 119.5, 123.1, 124.7, 126.0, 126.3, 126.6, 127.4, 128.5, 128.9, 129.1, 130.2, 130.7, 130.9, 131.6, 134.0, 134.8, 137.5, 137.7, 138.7, 149.8, 163.8, 186.9 (one carbon is overlapping). UV λ_{max} ($CHCl_3$) nm (log ε) 325 (shoulder), 423 (3.94), 483 (3.78), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{31}H_{22}ClNO_3S_2$: C, 66.96; H, 3.99; N, 2.52. Found: C, 67.04; H, 3.98; N, 2.45.

Ethyl 1-(4-Bromobenzoyl)-3-(1-naphthylmethylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**4c**): 63% (from **1c** and **2a**), red prisms, mp 143—144 °C. IR (KBr) cm^{-1}: 1669, 1624. ^{1}H-NMR ($CDCl_3$) δ: 6.87 (1H, d, J=6.8 Hz), 7.03 (1H, t, J=8.1 Hz), 7.48 (1H, t, J=7.1 Hz), 7.51—7.60 (4H, m), 7.72—7.79 (3H, m), 8.05 (1H, d, J=8.3 Hz). ^{13}C-NMR ($CDCl_3$) δ: 14.4, 42.7, 59.1, 93.0, 110.0, 116.7, 119.5, 123.1, 124.7, 124.7, 126.0, 126.3, 126.6, 127.4, 127.4, 128.9, 129.1, 130.2, 130.8, 130.9, 131.5, 131.6, 134.0, 134.8, 137.7, 138.0, 149.8, 163.7, 187.0. IR (KBr) cm^{-1}: 1669, 1624. UV λ_{max} ($CHCl_3$) nm (log ε) 327 (shoulder), 423 (4.01), 484 (3.82), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{31}H_{22}BrNO_3S_2$: C, 62.00; H, 3.69; N, 2.33. Found: C, 62.01; H, 3.71; N, 2.14.

Ethyl 1-Benzoyl-3-[(2-methyl-1-naphthyl)methylthio]thieno[3,4-*b*]indolizine-9-carboxylate (**4d**): 54% (from **1a** and 1-chloromethyl-2-methylnaphthalene (**2b**)), red prisms, mp 139—141 °C. IR (KBr) cm^{-1}: 1674, 1622. ^{1}H-NMR ($CDCl_3$) δ: 2.35 (3H, s), 7.15 (1H, d, J=8.1 Hz), 7.34—7.46 (4H, m), 7.51—7.57 (2H, m), 7.72 (1H, m), 7.87—7.91 (3H, m). ^{13}C-NMR ($CDCl_3$) δ: 14.3, 20.0, 37.9, 58.9, 93.2, 110.2, 116.5, 119.6, 122.6, 125.0, 125.4, 126.5, 128.2, 128.3, 128.6, 128.7, 128.8, 129.4, 130.0, 131.7, 132.5, 134.6, 135.0, 137.2, 139.0, 149.7, 163.9, 188.0 (two carbons are overlapping). UV λ_{max} ($CHCl_3$) nm (log ε) 324 (4.10), 422 (3.91), 480 (3.76), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{32}H_{25}NO_3S_2$: C, 71.75; H, 4.70; N, 2.61. Found: C, 71.85; H, 4.49; N, 2.31.

Ethyl 1-(4-Chlorobenzoyl)-3-[(2-methyl-1-naphthyl)methylthio]thieno-[3,4-*b*]indolizine-9-carboxylate (**4e**): 82% (from **1b** and **2b**), red prisms, mp 161—163 °C. IR (KBr) cm^{-1}: 1667, 1628. ^{1}H-NMR ($CDCl_3$) δ: 2.35 (3H, s), 7.15 (1H, d, J=8.3 Hz), 7.34—7.44 (4H, m), 7.54 (1H, d, J=8.3 Hz), 7.70 (1H, m), 7.78—7.83 (2H, br d, J=6.6 Hz), 7.86 (1H, m). ^{13}C-NMR ($CDCl_3$) δ: 14.4, 20.0, 37.8, 59.0, 93.1, 110.4, 117.4, 119.7, 122.6, 124.6, 125.0, 126.5, 126.5, 128.4, 128.5, 128.6, 128.7, 128.9, 130.2, 130.7, 131.7, 132.4, 134.8, 135.1, 137.1, 137.6, 138.7, 149.7, 163.7, 186.7. UV λ_{max} ($CHCl_3$) nm (log ε) 323 (4.14), 424 (3.89), 484 (3.83), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{32}H_{24}ClNO_3S_2$: C, 67.41; H, 4.24; N, 2.46. Found: C, 67.40; H, 4.15; N, 2.30.

Ethyl 1-(4-Bromobenzoyl)-3-[(2-methyl-1-naphthyl)methylthio]thieno-[3,4-*b*]indolizine-9-carboxylate (**4f**): 80% (from **1c** and **2b**), red prisms, mp 157—158 °C. IR (KBr) cm^{-1}: 1667, 1628. ^{1}H-NMR ($CDCl_3$,) δ: 2.35 (3H, s), 7.15 (1H, d, J=8.5 Hz), 7.33—7.40 (2H, m), 7.50—7.60 (3H, m), 7.67—7.75 (3H, m), 7.86 (1H, m). ^{13}C-NMR ($CDCl_3$) δ: 14.4, 20.0, 37.8, 59.1, 93.2, 110.4, 117.6, 119.7, 122.6, 124.6, 125.0, 126.5, 126.6, 127.3, 128.4, 128.5, 128.7, 128.9, 130.2, 130.8, 131.5, 131.7, 132.4, 134.9, 135.1, 137.1, 138.0, 149.7, 163.7, 186.8. UV λ_{max} ($CHCl_3$) nm (log ε) 322 (4.15), 423 (3.89), 484 (3.83), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{32}H_{24}BrNO_3S_2$: C, 62.54; H, 3.94; N, 2.28. Found: C, 62.35; H, 3.78; N, 1.99.

Ethyl 1-Benzoyl-3-(2-naphthylmethylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**4g**): 69% (from **1a** and 2-chloromethylnaphthalene (**2c**)), red prisms, mp 139—140 °C. IR (KBr) cm^{-1}: 1690, 1589. ^{1}H-NMR ($CDCl_3$) δ: 7.24 (1H, dd, J=8.3, 1.7 Hz), 7.34 (1H, br s), 7.35—7.43 (4H, m), 7.48—7.57 (2H, m), 7.62 (1H, d, J=8.6 Hz), 7.66 (1H, d, J=7.2 Hz), 7.86—7.92 (2H, br d, J=7.1 Hz). ^{13}C-NMR ($CDCl_3$) δ: 14.3, 45.3, 58.9, 93.2, 110.2, 119.6, 125.1, 126.1, 126.3, 126.5, 126.5, 127.5, 127.5, 127.6, 128.2, 128.5, 129.4, 129.9, 132.4, 132.7, 133.0, 133.6, 134.7, 137.4, 139.0, 149.7, 163.9, 188.0 (one carbon is overlapping). UV λ_{max} ($CHCl_3$) nm (log ε) 328 (4.11), 423 (4.04), 476 (3.77), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{31}H_{23}NO_3S_2$: C, 71.38; H, 4.44; N, 2.69. Found: C, 71.16; H, 4.26; N, 2.39.

Ethyl 1-(4-Chlorobenzoyl)-3-(2-naphthylmethylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**4h**): 78% (from **1b** and **2c**), red prisms, mp 145—147 °C. IR (KBr) cm^{-1}: 1676, 1586. ^{1}H-NMR ($CDCl_3$) δ: 7.24 (1H, dd, J=8.3, 1.7 Hz), 7.30—7.42 (5H, m), 7.52 (1H, br d, J=7.2 Hz), 7.61 (1H, d, J=8.3 Hz), 7.66 (1H, br d, J=7.2 Hz), 7.76—7.83 (2H, m). ^{13}C-NMR ($CDCl_3$) δ: 14.4, 45.2, 59.0, 93.2, 110.4, 116.8, 119.6, 124.3, 126.2, 126.4, 126.5, 126.6, 127.5, 127.5, 127.6, 128.5, 128.5, 130.1, 130.6, 132.7, 132.9, 133.5, 134.9, 137.3, 137.5, 138.6, 149.8, 163.7, 186.7. UV λ_{max} ($CHCl_3$) nm (log ε) 329 (4.12), 423 (4.02), 483 (3.83), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{31}H_{22}ClNO_3S_2$: C, 66.96; H, 3.99; N, 2.52. Found: C, 66.75; H, 3.93; N, 2.44.

Ethyl 1-(4-Bromobenzoyl)-3-(2-naphthylmethylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**4i**): 70% (from **1c** and **2c**), red prisms, mp 147—148 °C. IR (KBr) cm^{-1}: 1669, 1582. ^{1}H-NMR ($CDCl_3$) δ: 7.25 (1H, dd, J=8.3 1.7 Hz), 7.34 (1H, br s), 7.36—7.42 (2H, m), 7.49—7.55 (3H, m), 7.63 (1H, d, J=8.5 Hz), 7.64—7.73 (3H, m). ^{13}C-NMR ($CDCl_3$) δ: 14.4, 45.2, 59.0, 93.2, 110.4, 116.9, 119.6, 124.3, 126.2, 126.4, 126.4, 126.6, 127.3, 127.5, 127.5, 127.6, 128.6, 130.1, 130.8, 131.5, 132.7, 132.9, 133.5, 134.9, 137.3, 137.9, 149.8, 163.7, 186.8. UV λ_{max} ($CHCl_3$) nm (log ε) 328 (4.30), 423 (4.11), 482 (4.01), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{31}H_{22}BrNO_3S_2$: C, 62.00; H, 3.69; N, 2.33. Found: C, 61.75; H, 3.75; N, 2.14.

Ethyl 3-(9-Anthrylmethylthio)-1-benzoylthieno[3,4-*b*]indolizine-9-carboxylate (**4j**): 28% (from **1a** and 9-chloromethylanthracene (**2d**)), red prisms, mp 174—176 °C. IR (KBr) cm^{-1}: 1669, 1620. ^{1}H-NMR ($CDCl_3$) δ: 7.33—7.43 (6H, m), 7.52 (1H, br t, J=7.4 Hz), 7.79—7.86 (4H, m), 7.96—

8.04 (2H, m), 8.16 (1H, s). ^{13}C-NMR ($CDCl_3$) δ: 14.3, 36.9, 58.8, 92.9, 109.8, 115.5, 119.3, 123.0, 125.0, 125.8, 126.0, 126.4, 127.1, 128.1, 128.2, 129.1, 129.5, 129.7, 129.9, 131.1, 132.5, 134.4, 137.8, 138.9, 149.4, 163.8, 188.0. UV λ_{max} ($CHCl_3$) nm (log ε) 329 (4.11), *ca.* 350 (shoulder), *ca.* 365 (shoulder), 389 (3.90), 420 (4.04), 466 (3.63), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{35}H_{25}NO_3S_2$: C, 73.53; H, 4.41; N, 2.45. Found: C, 73.81; H, 4.37; N, 2.23.

Ethyl 3-(9-Anthrylmethylthio)-1-(4-Chlorobenzoyl)thieno[3,4-*b*]indolizine-9-carboxylate (**4k**): 31% (from **1b** and **2d**), red prisms, mp 172—174 °C. IR (KBr) cm^{-1}: 1672, 1620. ^{1}H-NMR ($CDCl_3$) δ: 7.28—7.41 (6H, m), 7.65—7.75 (2H, m), 7.78—7.80 (2H, m), 7.95—8.03 (2H, m), 8.15 (1H, s). ^{13}C-NMR ($CDCl_3$) δ: 14.4, 36.8, 58.9, 92.8, 109.9, 116.1, 119.4, 122.9, 125.0, 125.2, 125.3, 125.9, 126.4, 127.0, 128.1, 128.4, 129.2, 129.9, 130.7, 131.1, 134.6, 137.4, 137.7, 138.7, 149.5, 163.6, 186.7. UV λ_{max} ($CHCl_3$) nm (log ε) 329 (4.12), *ca.* 350 (shoulder), *ca.* 365 (shoulder), 389 (3.88), 420 (4.00), 474 (3.71), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{35}H_{24}ClNO_3S_2$: C, 69.35; H, 3.99; N, 2.31. Found: C, 69.51; H, 3.93; N, 2.21.

Ethyl 3-(9-Anthrylmethylthio)-1-(4-bromobenzoyl)thieno[3,4-*b*]indolizine-9-carboxylate (**4l**): 37% (from **1c** and **2d**), red prisms, mp 179—181 °C. IR (KBr) cm^{-1}: 1672, 1618. ^{1}H-NMR ($CDCl_3$) δ: 7.34—7.39 (4H, m), 7.52—7.56 (2H, m), 7.63—7.72 (2H, m), 7.82—7.86 (2H, m), 7.98—8.02 (2H, m), 8.15 (1H, s). ^{13}C-NMR ($CDCl_3$) δ: 14.4, 36.8, 58.9, 92.8, 109.9, 116.2, 119.3, 122.9, 125.0, 125.3, 125.9, 126.4, 127.0, 127.3, 128.1, 129.2, 129.9, 130.0, 130.9, 131.1, 131.4, 134.6, 137.8, 137.9, 149.5, 163.5, 186.9. UV λ_{max} ($CHCl_3$) nm (log ε) 328 (4.13), *ca.* 350 (shoulder), *ca.* 365 (shoulder), 389 (3.90), 421 (4.01), 478 (3.74), *ca.* 515 (shoulder). *Anal.* Calcd for $C_{35}H_{24}BrNO_3S_2$: C, 64.61; H, 3.72; N, 2.15. Found: C, 64.87; H, 3.65; N, 2.05.

Ethyl 1-Benzoyl-7-methyl-3-(1-naphthylmethylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**4m**): 57% (from **1d** and 1-chloromethylnaphthalene (**2a**)), red prisms, mp 184—185 °C. IR (KBr) cm^{-1}: 1672, 1618. ^{1}H-NMR ($CDCl_3$) δ: 6.88 (1H, d, J=7.1 Hz), 7.05 (1H, q, J=8.0, 1.0 Hz), 7.39—7.61 (7H, m), 7.76 (1H, d, J=8.0 Hz), 7.89—7.94 (2H, m), 8.07 (1H, d, J=8.0 Hz). ^{13}C-NMR ($CDCl_3$) δ: 14.3, 22.0, 42.7, 58.8, 91.8, 112.6, 115.3, 117.6, 123.2, 124.8, 124.9, 125.5, 125.9, 126.5, 127.4, 128.2, 128.8, 128.9, 129.4, 130.9, 131.6, 132.4, 134.0, 134.9, 137.7, 139.0, 142.0, 150.4, 164.2, 188.2. UV λ_{max} ($CHCl_3$) nm (log ε) 326 (shoulder), 427 (4.04), 476 (3.73), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{32}H_{25}NO_3S_2$: C, 71.75; H, 4.70; N, 2.61. Found: C, 72.01; H, 4.63; N, 2.34.

Ethyl 1-(4-Chlorobenzoyl)-7-methyl-3-(1-naphthylmethylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**4n**): 74% (from **1e** and **2a**), dark red prisms, mp 176—178 °C. IR (KBr) cm^{-1}: 1672, 1635. ^{1}H-NMR ($CDCl_3$) δ: 6.87 (1H, d, J=7.1 Hz), 7.03 (1H, q, J=8.3, 1.2 Hz), 7.35—7.41 (2H, m), 7.45—7.60 (3H, m), 7.74 (1H, d, J=8.1 Hz), 7.80—7.87 (2H, m), 8.04 (1H, d, J=7.8 Hz). ^{13}C-NMR ($CDCl_3$) δ: 14.4, 22.0, 42.6, 58.9, 91.8, 112.8, 116.1, 117.6, 123.2, 124.2, 124.8, 125.6, 126.9, 126.5, 127.5, 128.5, 128.9, 129.0, 130.7, 130.9, 131.6, 134.0, 135.1, 137.6, 137.6, 138.6, 142.3, 150.4, 163.9, 186.9. UV λ_{max} ($CHCl_3$) nm (log ε) 325 (shoulder), 427 (4.03), 476 (3.80), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{32}H_{24}ClNO_3S_2$: C, 67.41; H, 4.24; N, 2.46. Found: C, 67.64; H, 4.21; N, 2.26.

Ethyl 1-(4-Bromobenzoyl)-7-methyl-3-(1-naphthylmethylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**4o**): 38% (from **1f** and **2a**), dark red prisms, mp 183—184 °C. IR (KBr) cm^{-1}: 1676, 1607. ^{1}H-NMR ($CDCl_3$) δ: 6.89 (1H, d, J=7.1 Hz), 7.04 (1H, t, J=7.6 Hz), 7.49 (1H, br t, J=8.1 Hz), 7.52—7.59 (4H, m), 7.73—7.79 (3H, m), 8.05 (1H, d, J=8.3 Hz). ^{13}C-NMR ($CDCl_3$) δ: 14.4, 22.1, 42.6, 58.9, 91.8, 112.8, 116.4, 117.7, 123.2, 124.1, 124.8, 125.6, 126.0, 126.5, 127.3, 127.5, 128.9, 129.0, 130.8, 130.9, 131.5, 131.6, 134.0, 135.2, 137.6, 138.0, 142.4, 150.4, 164.0, 187.0. UV λ_{max} ($CHCl_3$) nm (log ε) 326 (shoulder), 427 (4.06), 478 (3.84), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{32}H_{24}BrNO_3S_2$: C, 62.54; H, 3.94; N, 2.28. Found: C, 62.35; H, 3.71; N, 2.06.

Ethyl 1-Benzoyl-7-methyl-3-[(2-methyl-1-naphthyl)methylthio]thieno-[3,4-*b*]indolizine-9-carboxylate (**4p**): 46% (from **1d** and **2b**), dark red prisms, mp 193—195 °C. IR (KBr) cm^{-1}: 1671, 1622. ^{1}H-NMR ($CDCl_3$) δ: 2.37 (3H, s), 7.18 (1H, d, J=8.6 Hz), 7.37—7.47 (4H, m), 7.53 (1H, br t, J=7.4 Hz) 7.58 (1H, d, J=8.3 Hz), 7.74 (1H, br d, J=7.5 Hz), 7.88—7.94 (3H, m). ^{13}C-NMR ($CDCl_3$) δ: 14.3, 20.0, 22.1, 37.9, 58.8, 92.1, 113.0, 117.8, 122.8, 124.8, 125.0, 125.8, 126.5, 128.2, 128.3, 128.4, 128.7, 128.7, 128.9, 129.4, 131.8, 132.4, 132.5, 135.0, 135.1, 137.1, 139.1, 142.1, 150.4, 164.2, 188.0. UV λ_{max} ($CHCl_3$) nm (log ε) 323 (4.14), 426 (4.00), 475 (3.72), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{33}H_{27}NO_3S_2$: C, 72.10; H, 4.95; N, 2.55. Found: C, 72.35; H, 4.98; N, 2.27.

Ethyl 1-(4-Chlorobenzoyl)-7-methyl-3-[(2-methyl-1-naphthyl)methylthio]thieno[3,4-*b*]indolizine-9-carboxylate (**4q**): 64% (from **1e** and **2b**), red prisms, mp 186—188 °C. IR (KBr) cm^{-1}: 1667, 1624. ^{1}H-NMR ($CDCl_3$) δ: 2.37 (3H, s), 7.17 (1H, d, J=8.6 Hz), 7.36—7.44 (4H, m), 7.57 (1H, d, J=8.6 Hz), 7.72 (1H, m), 7.79—7.85 (2H, m), 7.88 (1H, overlapped with the 8-proton signal). ^{13}C-NMR ($CDCl_3$) δ: 14.4, 20.0, 22.1, 37.8, 58.9, 92.0, 113.2, 117.1, 117.9, 122.7, 124.1, 125.0, 125.9, 126.5, 128.4, 128.5, 128.6, 128.6, 128.9, 130.7, 131.8, 132.5, 135.1, 135.2, 137.0, 137.6, 138.6, 142.4, 150.4, 164.0, 186.8. UV λ_{max} ($CHCl_3$) nm (log ε) 322 (4.16), 428 (3.92), 479 (3.80), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{33}H_{26}ClNO_3S_2$: C, 67.85; H, 4.49; N, 2.40. Found: C, 68.02; H, 4.49; N, 2.23.

Ethyl 1-(4-Bromobenzoyl)-7-methyl-3-[(2-methyl-1-naphthyl)methylthio]thieno[3,4-*b*]indolizine-9-carboxylate (**4r**): 39% (from **1f** and **2b**), dark red prisms, mp 178—179 °C. IR (KBr) cm^{-1}: 1665, 1624. ^{1}H-NMR ($CDCl_3$) δ: 2.35 (3H, s), 7.15 (1H, d, J=8.6 Hz), 7.33—7.41 (2H, m), 7.49—7.58 (3H, m), 7.67—7.74 (3H, m), 7.86 (1H, overlapped with the 8-proton signal). ^{13}C-NMR ($CDCl_3$) δ: 14.4, 20.0, 22.1, 37.7, 58.9, 92.0, 113.2, 117.2, 117.9, 122.6, 124.0, 125.0, 125.8, 126.4, 127.2, 128.3, 128.5, 128.6, 128.8, 130.8, 131.4, 131.7, 132,4, 135.1, 135.2, 137.0, 138.0, 142.3, 150.4, 163.9, 186.9. UV λ_{max} ($CHCl_3$) nm (log ε) 322 (4.18), 428 (4.05), 483 (3.82), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{33}H_{26}BrNO_3S_2$: C, 63.05; H, 4.17; N, 2.23. Found: C, 63.30; H, 4.05; N, 2.00.

Ethyl 1-Benzoyl-7-methyl-3-(2-naphthylmethylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**4s**): 77% (from **1d** and **2c**), dark red prisms, mp 188—190 °C. IR (KBr) cm^{-1}: 1669, 1616. ^{1}H-NMR ($CDCl_3$) δ: 7.20 (1H, dd, J=8.3 1.4 Hz), 7.34 (1H, br s), 7.33—7.41 (4H, m), 7.48—7.55 (2H, m), 7.60 (1H, d, J=8.6 Hz), 7.65 (1H, br d, J=9.0 Hz), 7.87—7.92 (2H, m). ^{13}C-NMR ($CDCl_3$) δ: 14.3, 21.9, 45.3, 58.7, 92.0, 112.9, 115.5, 117.6, 124.6, 125.6, 126.0, 126.2, 126.5, 127.4, 127.5, 128.2, 128.4, 129.3, 132.4, 132.7, 133.0, 133.8, 135.1, 137.4, 139.0, 142.0, 150.3, 164.1, 188.1 (one carbon is overlapping). UV λ_{max} ($CHCl_3$) nm (log ε) 327 (4.13), 426 (4.08), 476 (3.80), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{32}H_{25}NO_3S_2$: C, 71.75; H, 4.70; N, 2.61. Found: C, 71.98; H, 4.62; N, 2.47.

Ethyl 1-(4-Chlorobenzoyl)-7-methyl-3-(2-naphthylmethylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**4t**): 69% (from **1e** and **2c**), dark red prisms, mp 165—167 °C. IR (KBr) cm^{-1}: 1667, 1624. ^{1}H-NMR ($CDCl_3$) δ: 7.21 (1H, dd, J=8.5, 1.7 Hz), 7.34 (1H, br s), 7.34—7.42 (2H, m), 7.48—7.55 (3H, m), 7.60 (1H, d, J=8.6 Hz), 7.66 (1H, br d, J=7.2 Hz), 7.70—7.75 (2H, m). ^{13}C-NMR ($CDCl_3$) δ: 14.4, 22.0, 45.2, 58.9, 92.0, 113.2, 116.4, 117.7, 123.9, 125.8, 126.1, 126.3, 126.5, 127.3, 127.4, 127.5, 127.6, 128.5, 130.8, 131.5, 132.8, 133.0, 133.7, 135.3, 137.4, 138.0, 142.3, 150.4, 163.9, 186.9. UV λ_{max} ($CHCl_3$) nm (log ε) 327 (4.12), 427 (4.04), 479 (3.83), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{32}H_{24}ClNO_3S_2$: C, 67.41; H, 4.24; N, 2.46. Found: C, 67.27; H, 4.02; N, 2.19.

Ethyl 1-(4-Bromobenzoyl)-7-methyl-3-(2-naphthylmethylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**4u**): 60% (from **1f** and **2c**), dark red prisms, mp 177—178 °C. IR (KBr) cm^{-1}: 1667, 1614. ^{1}H-NMR ($CDCl_3$) δ: 7.21 (1H, dd, J=8.3, 1.7 Hz), 7.34 (1H, br s), 7.34—7.41 (2H, m), 7.49—7.58 (3H, m), 7.60 (1H, d, J=8.3 Hz), 7.66 (1H, br d, J=7.2 Hz), 7.70—7.78 (2H, m). ^{13}C-NMR ($CDCl_3$) δ: 14.4, 22.0, 45.2, 58.9, 92.0, 113.1, 116.4, 117.7, 123.8, 125.7, 126.1, 126.3, 126.5, 127.2, 127.4, 127.5, 127.6, 128.5, 130.8, 131.4, 132.7, 133.0, 133.7, 135.3, 137.4, 138.0, 142.3. 150.4, 163.9, 186.9. UV λ_{max} ($CHCl_3$) nm (log ε) 326 (4.15), 428 (4.05), 479 (3.86), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{32}H_{24}BrNO_3S_2$: C, 62.54; H, 3.94; N, 2.28. Found: C, 62.46; H, 3.72; N, 2.03.

Ethyl 3-(9-Anthrylmethylthio)-1-benzoyl-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**4v**): 16% (from **1d** and **2d**), dark red prisms, mp 189—190 °C. IR (KBr) cm^{-1}: 1667, 1622. ^{1}H-NMR ($CDCl_3$) δ: 7.34—7.42 (6H, m), 7.52 (1H, br t, J=7.4 Hz), 7.79—7.89 (4H, m), 8.00—8.04 (2H, m), 8.17 (1H, s). ^{13}C-NMR ($CDCl_3$) δ: 14.3, 22.0, 36.8, 58.6, 91.8, 112.6, 115.2, 117.4, 123.0, 125.0, 125.2, 125.4, 126.4, 127.1, 128.0, 128.1, 129.1, 129.4, 129.9, 131.2, 132.4, 134.8, 137.7, 138.9, 141.9, 150.1, 164.0, 188.1. UV λ_{max} ($CHCl_3$) nm (log ε) 329 (4.14), *ca.* 350 (shoulder), *ca.* 365 (shoulder), 389 (3.88), 425 (4.13), 471 (3.64), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{36}H_{27}NO_3S_2$: C, 73.82; H, 4.65; N, 2.39. Found: C, 74.10; H, 4.53; N, 2.18.

Ethyl 3-(9-Anthrylmethylthio)-1-(4-chlorobenzoyl)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**4w**): 40% (from **1e** and **2d**), dark red prisms, mp 192—194 °C. IR (KBr) cm^{-1}: 1667, 1620. ^{1}H-NMR ($CDCl_3$) δ: 7.33—7.38 (6H, m), 7.52 (1H, br t, J=7.4 Hz), 7.68—7.73 (2H, m), 7.80—7.86 (2H, m), 7.97—8.02 (2H, m), 8.15 (1H, s). ^{13}C-NMR ($CDCl_3$) δ: 14.4, 22.0, 36.6, 58.7, 91.7, 112.7, 115.9, 117.5, 123.0, 124.7, 125.0, 125.2, 126.3, 126.9, 128.0, 128.4, 129.1, 129.9, 130.7, 131.1, 134.9, 137.5, 137.6, 138.6, 142.1, 150.1, 163.8, 186.8. UV λ_{max} ($CHCl_3$) nm (log ε) 329 (4.10), *ca.* 350 (shoulder), *ca.* 365 (shoulder), 389 (3.81), 426 (4.02), 467 (shoulder), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{36}H_{26}ClNO_3S_2$: C, 69.72; H, 4.33; N, 2.26. Found: C, 69.59; H, 4.09; N, 2.10.

Ethyl 3-(9-Anthrylmethylthio)-1-(4-bromobenzoyl)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**4x**): 31% (from **1f** and **2d**), dark red prisms, mp 185—186 °C. IR (KBr) cm^{-1}: 1669, 1618. ^{1}H-NMR ($CDCl_3$) δ: 7.33—7.38 (4H, m), 7.50—7.55 (2H, m), 7.61—7.66 (2H, m), 7.81—7.86 (2H, m), 7.97—8.03 (2H, m), 8.15 (1H, s). ^{13}C-NMR ($CDCl_3$) δ: 14.4, 22.0, 36.6, 58.7, 91.7, 112.7, 115.9, 117.5, 123.0, 124.7, 125.0, 125.2, 126.3, 126.9, 127.2, 128.0, 129.1, 129.9, 130.8, 131.1, 131.3, 134.9, 137.6, 137.9, 142.1, 150.1, 163.7, 186.9. UV λ_{max} ($CHCl_3$) nm (log ε) 329 (4.22), *ca.* 350 (shoulder), *ca.* 365 (shoulder), 389 (3.93), 426 (4.13), 471 (3.81), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{36}H_{26}BrNO_3S_2$: C, 65.06; H, 3.94; N, 2.11. Found: C, 65.33; H, 3.83; N, 1.95.

Crystallography of Ethyl 1-Benzoyl-3-(2-naphthylmethylthio)thieno-[3,4-*b*]indolizine-9-carboxylate (4a) A red prismatic single crystal (0.24×0.68×0.68 mm) grown from $CHCl_3$–ethanol 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: **4a**: $C_{31}H_{23}NO_3S_2$; M=521.65; monoclinic, space group $P2_1/n$ (#14), Z=4 with a=8.896 (3) Å, b=22.340 (3) Å, c=13.898 (3) Å, β=106.93° (2), V=2642 (1) Å^3 and $D_{calc.}$=1.311 g/cm^3. All calculations were performed using the teXsan package.[10] The structure was solved by a direct method (SIR).[11] 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 0.070 and 0.08.5 for 2571 ($I>2.00\sigma(I)$ observed reflections, respectively.

Crystallography of Ethyl 3-(9-Anthranylmethylthio)-1-(4-chlorobenzoyl)thieno[3,4-*b*]indolizine-9-carboxylate (4k) A red prismatic single crystal (0.52×0.88×0.96 mm) grown from $CHCl_3$–ethanol 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). Crystal data of these compounds are as follows: **4k**: $C_{35}H_{24}ClNO_3S_2$; M=606.15; monoclinic, space group $P2_1/n$ (#14), Z=4 with a=12.238 (1) Å, b=11.024 (2) Å, c=21.763 (1) Å, β=101.227° (7); V=2879.9 (5) Å^3 and $D_{calc.}$=1.398 g/cm^3. All calculations were performed using the teXsan package.[10] The structure was solved by a direct method (SIR).[11] 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 0.050 for 2098 ($I>2.00\sigma(I)$ observed reflections, respectively.

Crystallography of Ethyl 1-(4-Chlorobenzoyl)-7-methyl-3-(2-naphthylmethylthio)thieno[3,4-*b*]indolizine-9-carboxylate (4t) A dark red prismatic single crystal (0.22×0.34×0.62 mm) grown from $CHCl_3$–ethanol 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: **4t**: $C_{32}H_{24}ClN_2O_3S_2$; M=570.12; monoclinic, space group $P2_1/c$ (#14), Z=4 with a=11.223 (5) Å, b=20.994 (4) Å, c=11.999 (5) Å, β=101.86° (3), V=2767 (2) Å^3 and $D_{calc.}$=1.368 g/cm^3. All calculations were performed using the teXsan package.[10] The structure was solved by a direct method (SIR).[11] 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 0.075 and 0.080 for 1356 ($I>2.00\sigma(I)$ observed reflections, respectively.

References and Notes

1) For part 53 of this series, see: Kakehi A., Ito S., Suga H., Miwa T., Mori T., Fujii T., Tanaka N., Kobayashi T., *Chem. Pharm. Bull.*, **51**, 75—84 (2003).
2) Kakehi A., Ito S., Suga H., Miwa T., Mori T., Kobayashi T., *Heterocycles*, **57**, 17—20 (2002).
3) It is well known that the carbonyl absorption bands of the 2-arylcarbonyl group on the thiophene ring in some thiophene-fused heterocycles appear at considerably low region. See: Kakehi A., Ito S., Suga H., Sakurai T., Urushido K., Isawa H., Takashima T., *Chem. Pharm. Bull.*, **38**, 2667—2675 (1990).
4) It is well known that the carbonyl absorption bands of the 2-arylcarbonyl group on the thiophene ring in some thiophene-fused heterocycles appear at considerably low region. See: Kakehi A., Ito S., Ueda T., Takano S., *Chem. Pharm. Bull.*, **41**, 1753—1756 (1993).
5) These ^{1}H-NMR spectra ($CDCl_3$, 300 MHz) are as follows: **2a**, δ: 5.02 (2H, s), 7.39 (1H, q, J=7.1, 8.3 Hz), 7.49 (1H, br d, J=7.1 Hz), 7.50 (1H, m), 7.57 (1H, m), 7.82 (1H, br d, J=8.3 Hz), 7.86 (1H, d, J=7.3 Hz), 8.12 (1H, d, J=8.8 Hz); **2b**, 2.56 (3H, s), 5.04 (2H, s), 7.28 (1H, d, J=8.4 Hz), 7.42 (1H, m), 7.54 (1H, m), 7.71 (1H, d, J=8.2 Hz), 7.79 (1H, br d, J=8.1 Hz), 8.06 (1H, d, J=8.6 Hz); **2c**, 4.64 (2H, s), 7.44—7.52 (3H, m), 7.76—7.84 (4H, m); **2d**, 5.55 (2H, s), 7.46 (2H, m), 7.57 (2H, m), 7.97 (2H, br d, J=8.4 Hz), 8.26 (2H, d, J=9.0 Hz), 8.42 (1H, s).
6) The single crystals of compounds **4e**, **n**, **o**, **v**, **x** were shown to have the corresponding **G1** form by the X-ray analyses.
7) The single crystals of compound **4u** was shown to have the corresponding **A1** form by the X-ray analyses.
8) Johnson C. K., "ORTEP II, Report ORNL-5138," Oak Ridge National Laboratory, Tennessee, 1976.
9) "WinMOPAC (Version 3.0)," Fujitsu Corporation.
10) teXsan for Windows version 1.06: Crystal Structure Analysis Package, Molecular Structure Corporation (1997-9).
11) SIR92: Altomare A., Cascarano G., Giacovazzo C., Guagliardi A., *J. Appl. Cryst.*, **26**, 343—350 (1993).