

Preparation of New Nitrogen-Bridged Heterocycles. 58.¹⁾ Syntheses and Intramolecular Arene- π Interactions of 3-(Allylthio)- and 3-(Propargylthio)thieno[3,4-*b*]indolizine Derivatives

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Various thieno[3,4-*b*]indolizine derivatives having an allylthio or propargylthio group at the 3-position were prepared and their intramolecular arene- π interactions were investigated. Their ¹H-NMR spectra showed significant low-field shifts (δ 0.10–0.34 ppm) to the 5-proton on the thieno[3,4-*b*]indolizine ring, and this effect was the reverse to that observed in 3-(arylmethylthio)thieno[3,4-*b*]indolizines. However, their UV spectra exhibited a characteristic absorption band due to the arene- π interaction near 430 nm and these values were almost similar to those for arene-arene interaction of 3-arylmethylthio derivatives though their molar extinction coefficients were largely varied by the 3-substituents. Furthermore, both types of *gauche* conformations in which the intramolecular arene- π interactions are possible in one form and impossible in the other were confirmed by X-ray analyses of some compounds.

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

In our recent papers we reported a convenient preparative method for 3-(arylmethylthio)thieno[3,4-*b*]indolizine derivatives and their intramolecular arene-arene interaction.^{2–4)} We also described that the magnitude of such interaction largely depends upon the type of aromatic ring in the 3-substituent. For example, the derivatives bearing a bicyclic or tricyclic aryl group exhibited larger high field shifts of the pyridine ring protons in the ¹H-NMR spectra, and showed stronger absorption bands near 420 nm in the UV spectra than those for the 3-benzylthio analogs.⁴⁾ In a continuation of this work, we next interested in the replacement of the 3-arylmethylthio group in this system with a 3-allylthio or 3-propargylthio group, because we realized that the terminal of the double or triple bond can sufficiently approach the thieno[3,4-*b*]indolizine ring in the *gauche* conformation required for the arene- π interaction. In addition, these unsaturated bonds are potential dipolarophiles, dienophiles, and nucleophiles^{5–8)} and, in particular, such reactions on the double bond in 3-(allylthio)thieno[3,4-*b*]indolizines may provide good models for confirming the face-selectivity by this type of intramolecular interaction. In this paper we report the syntheses of various 3-(allylthio)- and 3-(propargylthio)thieno[3,4-*b*]indolizine derivatives and their intramolecular arene- π interactions.

Results and Discussion

Preparations of Ethyl 3-(Allylthio)- and 3-(Propargylthio)thieno[3,4-*b*]indolizine-9-carboxylates The title compounds (**4a–x**) and (**6a–x**) were prepared in moderate to good yields (52–88%) from the reactions of 3-(1-pyridinio)thiophene-2-thiolates (**1a–f**) and various allyl or propargyl halides according to our previous procedure.^{2–4)} For example, the *S*-alkylation of 5-arylcarbonyl-4-ethoxycarbonylmethyl-3-(1-pyridinio)thiophene-2-thiolates (**1a–f**) with allyl bromide (**2a**) in acetone in the presence of excess sodium iodide, followed by the treatment of the resulting pyridinium salts (**3a–c**) and (**5a–c**) with DBU and then chloranil in an ice bath for 4–6 h afforded the corresponding

ethyl 3-allylthio-1-(arylcarbonyl)thieno[3,4-*b*]indolizine-9-carboxylates (**4a–c**) and (**6a–c**) in good yields (69–79%) as red prismatic crystals. Similar treatment of pyridinium betaines (**1a–f**) with (*E*)-1-bromo-2-butene (**2b**), 3-chloro-2-methylpropene (**2c**), 1-bromo-3-methyl-2-butene (**2d**), 3-bromocyclohexene (**2e**), cinnamyl bromide (**2f**), propargyl bromide (**2g**), and 1-bromo-2-butyne (**2h**) gave the corresponding products (**4d–x**) and (**6d–x**) in 52–88% yields. These results are summarized in Charts 1 and 2.

The elemental analyses for these products (**4a–x**) and (**6a–x**) were in good accord with our proposed structures. The IR spectra of **4a–x** and **6a–x** each showed a strong carbonyl absorption band at 1663–1692 cm⁻¹. Furthermore, the absorption bands of an acetylenic proton and a terminal triple bond for 3-propargylthio derivatives (**4s–u**) and (**6s–u**) appeared at 3268–3297 and near 2110 cm⁻¹, and a weak absorption band of an inner triple bond for 3-(2-butyne)thio derivatives (**4v–x**) and (**6v–x**) exhibited near 2230 cm⁻¹. The UV spectra have a characteristic absorption band in the range of 422–444 nm attributable to the arene- π interaction, and their absorption positions and patterns are similar to those recorded for 3-(arylmethylthio)thieno[3,4-*b*]indolizines reported previously by us.^{2–4)} In addition, those of 3-cinnamylthio derivatives (**4p–r**) and (**6p–r**) exhibited a significant increase in the molar extinction coefficients, which is most likely caused by the conjugation with the phenyl group.

In comparison with ethyl 1-benzoyl-3-(methylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7a**) and its 7-methyl derivative (**7b**)^{2,3,9)} which do not any arene- π or arene-arene interactions, the values of the 5-protons on the thieno[3,4-*b*]indolizine ring of **4a–x** and **6a–x** in ¹H-NMR spectra were shifted at the lower magnetic region, and the values (0.28–0.37 ppm) of the low-field shifts in 3-(propargylthio)thieno[3,4-*b*]indolizines (**4s–x**) and (**6s–x**) were larger than those (0.16–0.29 ppm) in 3-allylthio derivatives (**4a–r**) and (**6a–r**). This low-field shifts is reverse to the effects observed by intramolecular arene-arene interactions of 3-(arylmethylthio)thieno[3,4-*b*]indolizines.^{2–4)} However, this fact

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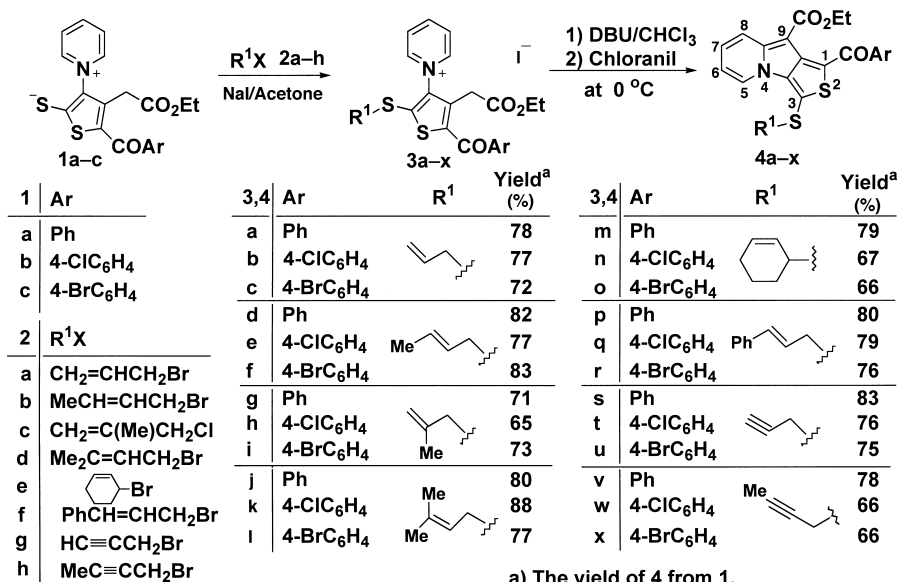


Chart 1

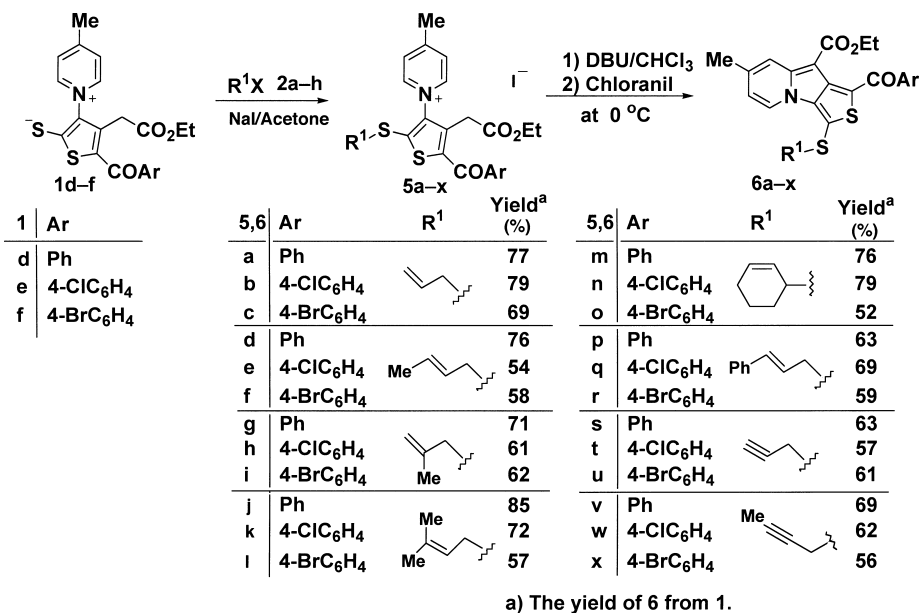


Chart 2

does not indicate the absence of arene- π interactions in these molecules (**4a-x**) and (**6a-x**) because an absorption band (near 430 nm) characteristic of such interactions is clearly present in their UV spectra and the appearance of the low field shifts implies some participation between the 5-proton and the 3-substituent. In addition, the ¹H-NMR spectra of 3-cinnamylthio derivatives (**4p-r**) and (**6p-r**) exhibited significant high-field shifts (0.06–0.13 ppm) on the 6- and 8-protons to suggest strongly the presence of such intramolecular interactions in this system. These ¹H-NMR spectral results are listed in Tables 1 and 2.

In general, the main and subdivided conformers as shown in Figs. 1 and 2 can be drawn for 7-unsubstituted ethyl 1-benzoylthieno[3,4-*b*]indolizine-9-carboxylates (**4a, d, g, j, m, p, s, v**).^{3,4} So, the X-ray analyses for some products were performed to obtain the more detailed structural and conforma-

tional data of products (**4a-x**) and (**6a-x**). The X-ray analyses of 3-(allylthio)- (**4c**), 3-[(2-methyl-2-propenyl)thio]- (**4g**), 3-(cinnamylthio)- (**4p**), and 3-[(2-butynyl)thio]thieno[3,4-*b*]indolizine (**4v**) exhibited the *gauche* 1-*cis*-front (**G1CF**) or *gauche* 1-*trans*-front (**G1TF**) conformation in form **A** or **C** suitable to the arene- π interaction, while that of 3-(propargylthio)thieno[3,4-*b*]indolizine (**4s**) showed the *gauche* 2-*cis*-back (**G2CB**) conformation in form **C** inconvenient for such an interaction. The corresponding *anti* 1 (**A1**) conformation for these compounds could not be confirmed. The ORTEP drawings¹¹ of compounds (**4c, g, p, s, v**) are shown in Figs. 3–7. From these crystal structures the following relations between the 5-proton and the vinyl or the ethynyl terminal carbon in **G1CF** or **G1TF** conformation were given: 1) The dihedral angles between the least square planes of the thienoindolizine ring and the vinyl group in the

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

No ^{a,b}	C-5	C-6	C-7	C-8	COOEt	RS	δ (5-H)	δ (6-H)
7a ^{c,d}	8.96	6.73	7.31	8.20	0.97, 3.61	2.68	0.00	0.00
4a ^c	9.17	6.72	7.32	8.21	0.97, 3.63	3.60, 5.04, 5.05, 5.89	-0.21	0.01
4b	9.17	6.73	7.28	8.21	1.02, 3.75	3.61, 5.02, 5.07, 5.5—6.5	-0.21	0.00
4c	9.16	6.72	7.29	8.21	1.02, 3.76	3.63, 5.03, 5.07, 5.5—6.5	-0.20	0.01
4d ^c	9.17	6.71	7.31	8.20	0.96, 3.64	1.52, 3.54, 5.42, 5.55	-0.21	0.02
4e	9.17	6.72	7.28	8.21	1.02, 3.75	1.52, 3.53, 5.3—5.8	-0.21	0.01
4f	9.18	6.73	7.35	8.21	1.03, 3.75	1.53, 3.54, 5.3—5.8	-0.22	0.00
4g ^c	9.12	6.72	7.31	8.20	0.97, 3.63	1.89, 3.56, 4.68, 4.78	-0.16	0.01
4h	9.12	6.72	^e	8.21	1.01, 3.74	1.89, 3.58, 4.74	-0.16	0.01
4i	9.13	6.73	7.34	8.22	1.03, 3.75	1.89, 3.59, 4.75	-0.17	0.00
4j ^c	9.20	6.71	7.31	8.20	0.97, 3.63	1.36, 1.55, 3.60, 5.33	-0.24	0.02
4k	9.19	6.72	^e	8.20	1.03, 3.74	1.38, 1.56, 3.61, 5.34	-0.23	0.01
4l	9.21	6.73	7.31	8.23	1.02, 3.75	1.40, 1.57, 3.66, 5.36	-0.25	0.00
4m ^c	9.24	6.72	7.32	8.21	0.97, 3.63	1.6—2.3, 3.90, 5.80, 5.92	-0.28	0.01
4n	9.23	6.72	^e	8.22	1.02, 3.75	1.6—2.4, 3.86, 5.86	-0.27	0.01
4o	9.24	6.72	7.34	8.22	1.02, 3.74	1.6—2.4, 3.87, 5.87	-0.28	0.01
4p ^c	9.19	6.64	7.22	8.10	0.96, 3.63	3.73, 6.16, 6.19, 7.07, 7.17	-0.23	0.09
4q	9.21	6.66	^e	8.12	1.01, 3.75	3.75, 6.0—6.3, 7.15	-0.25	0.07
4r	9.21	6.67	^e	8.13	1.02, 3.76	3.76, 6.0—6.3, 7.15	-0.25	0.06
4s ^c	9.24	6.71	7.32	8.21	0.97, 3.66	2.21, 3.64	-0.28	0.02
4t	9.25	6.71	^e	8.22	0.97, 3.68	2.21, 3.65	-0.29	0.02
4u	9.25	6.72	^e	8.22	1.02, 3.77	2.22, 3.66	-0.29	0.01
4v ^c	9.33	6.72	7.32	8.21	0.97, 3.67	1.58, 3.61	-0.37	0.01
4w	9.33	6.73	^e	8.22	1.02, 3.77	1.58, 3.62	-0.37	0.00
4x	9.32	6.73	7.31	8.21	1.03, 3.78	1.58, 3.62	-0.36	0.00

a) The proton signals of the 1-arylcabonyl group appeared in the range of δ 7.1—8.1 as multiplets. b) The coupling constants are as follows; $J_{5,6}=J_{6,7}=7.0$ Hz, $J_{7,8}=9.0$ Hz, $J_{6,8}=2.0$ Hz, $J_{Et}=7.0$ Hz. c) Standard. d) 400 MHz. e) Overlapped with aromatic proton signals.

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

No ^{a,b}	C-5	C-6	C-7	C-8	COOEt	RS	δ (5-H)	δ (6-H)
7b ^{c,d}	8.84	6.58	2.40	8.00	0.95, 3.56	2.67	0.00	0.00
6a	9.04	6.54	2.40	8.00	0.95, 3.63	3.59, 5.01, 5.05, 5.5—6.5	-0.20	0.04
6b	9.03	6.58	2.42	7.99	1.00, 3.71	3.59, 5.02, 5.06, 5.5—6.5	-0.19	0.00
6c	9.02	6.56	2.40	7.99	1.01, 3.72	3.59, 5.02, 5.05, 5.5—6.5	-0.18	0.02
6d	9.06	6.55	2.41	8.02	0.95, 3.62	1.52, 3.51, 5.3—5.8	-0.22	0.03
6e	9.05	6.56	2.40	8.00	1.00, 3.71	1.52, 3.52, 5.3—5.8	-0.21	0.02
6f	9.05	6.58	2.42	8.02	1.01, 3.72	1.54, 3.53, 5.3—5.8	-0.21	0.00
6g	9.02	6.56	2.41	8.02	0.95, 3.64	1.89, 3.57, 4.75	-0.18	0.02
6h	9.01	6.59	2.42	8.02	1.00, 3.72	1.90, 3.58, 4.76	-0.17	-0.01
6i	9.01	6.59	2.42	8.02	1.00, 3.72	1.90, 3.58, 4.75	-0.17	-0.01
6j	9.08	6.57	2.40	8.01	0.95, 3.63	1.39, 1.56, 3.59, 5.32	-0.24	0.01
6k	9.07	6.58	2.42	8.01	1.00, 3.72	1.40, 1.58, 3.60, 5.34	-0.23	0.00
6l	9.07	6.56	2.42	8.01	1.00, 3.71	1.40, 1.57, 3.60, 5.34	-0.23	0.02
6m	9.12	6.55	2.40	8.00	0.95, 3.62	1.6—2.4, 3.85, 5.85	-0.28	0.03
6n	9.12	6.59	2.42	8.00	1.00, 3.72	1.6—2.4, 3.90, 5.85	-0.28	-0.01
6o	9.12	6.59	2.42	8.01	1.00, 3.72	1.6—2.4, 3.89, 5.87	-0.28	-0.01
6p	9.05	6.46	2.33	7.87	0.94, 3.62	3.68, 6.0—6.3, 7.14	-0.21	0.12
6q	9.05	6.48	2.34	7.88	0.99, 3.71	3.71, 6.0—6.3, 7.14	-0.21	0.10
6r	9.06	6.50	2.35	7.90	0.99, 3.71	3.71, 6.0—6.3, 7.15	-0.22	0.08
6s	9.12	6.55	2.41	8.02	0.95, 3.66	2.21, 3.62	-0.28	0.03
6t	9.15	6.60	2.43	8.01	1.00, 3.73	2.21, 3.60	-0.31	-0.02
6u	9.13	6.59	2.43	8.02	1.01, 3.74	2.21, 3.62	-0.29	-0.01
6v	9.18	6.55	2.40	8.01	0.96, 3.67	1.59, 3.60	-0.34	0.03
6w	9.20	6.58	2.42	8.02	1.01, 3.74	1.60, 3.61	-0.36	0.00
6x	9.21	6.59	2.42	8.03	1.01, 3.74	1.61, 3.62	-0.37	-0.01

a) The proton signals of the 1-arylcabonyl group appeared in the range of δ 7.1—8.1 as multiplets. b) The coupling constants are as follows; $J_{5,6}=7.0$ Hz, $J_{6,8}=2.0$ Hz, $J_{Et}=7.0$ Hz. c) Standard. d) 400 MHz.

crystal structures of **4c, g** are considerably larger (near 50°) than those (near 25°) between the thieno[3,4-*b*]indolizine and the phenyl rings in the same conformations of some ethyl 3-(arylmethylthio)thieno[3,4-*b*]indolizine-9-carboxylates^{2–4}); 2) The vinyl and ethynyl groups are considerably smaller

compared with aryl groups and, hence, the shielding of the 5-proton by the π-orbital of the vinyl or ethynyl terminal is less sufficient than the shielding by the larger and more effective aryl group of the corresponding 3-arylmethylthio derivatives. In other words, the 5-proton is not in the shielding re-

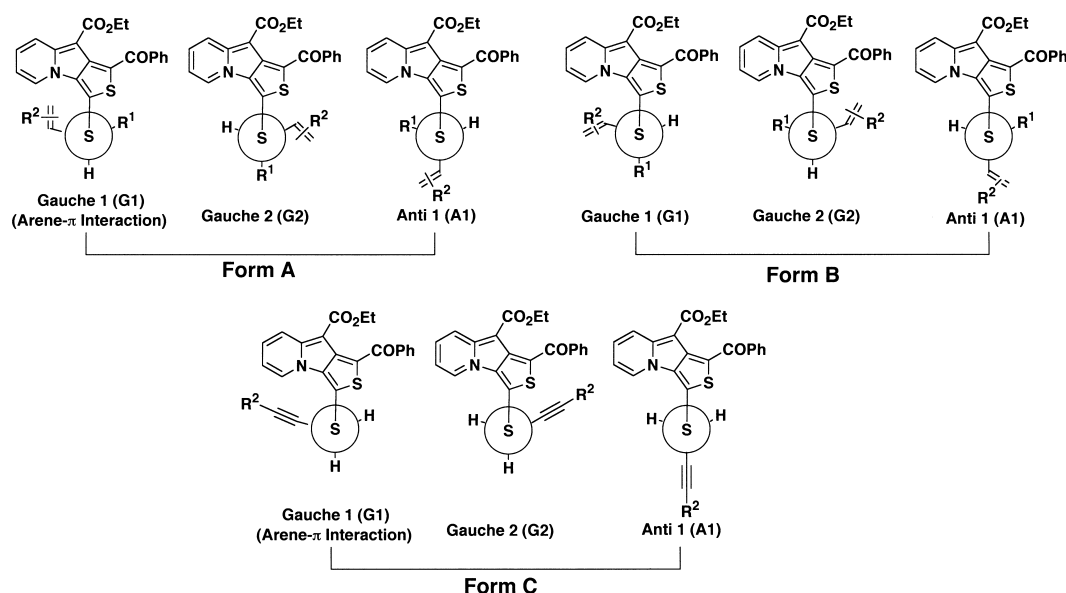


Fig. 1. Principal Conformers (Forms A and B) for 3-Allylthio Derivatives **4a**, **d**, **g**, **j**, **m**, **p** and that (Form C) for 3-Propargylthio Ones **4s**, **v**

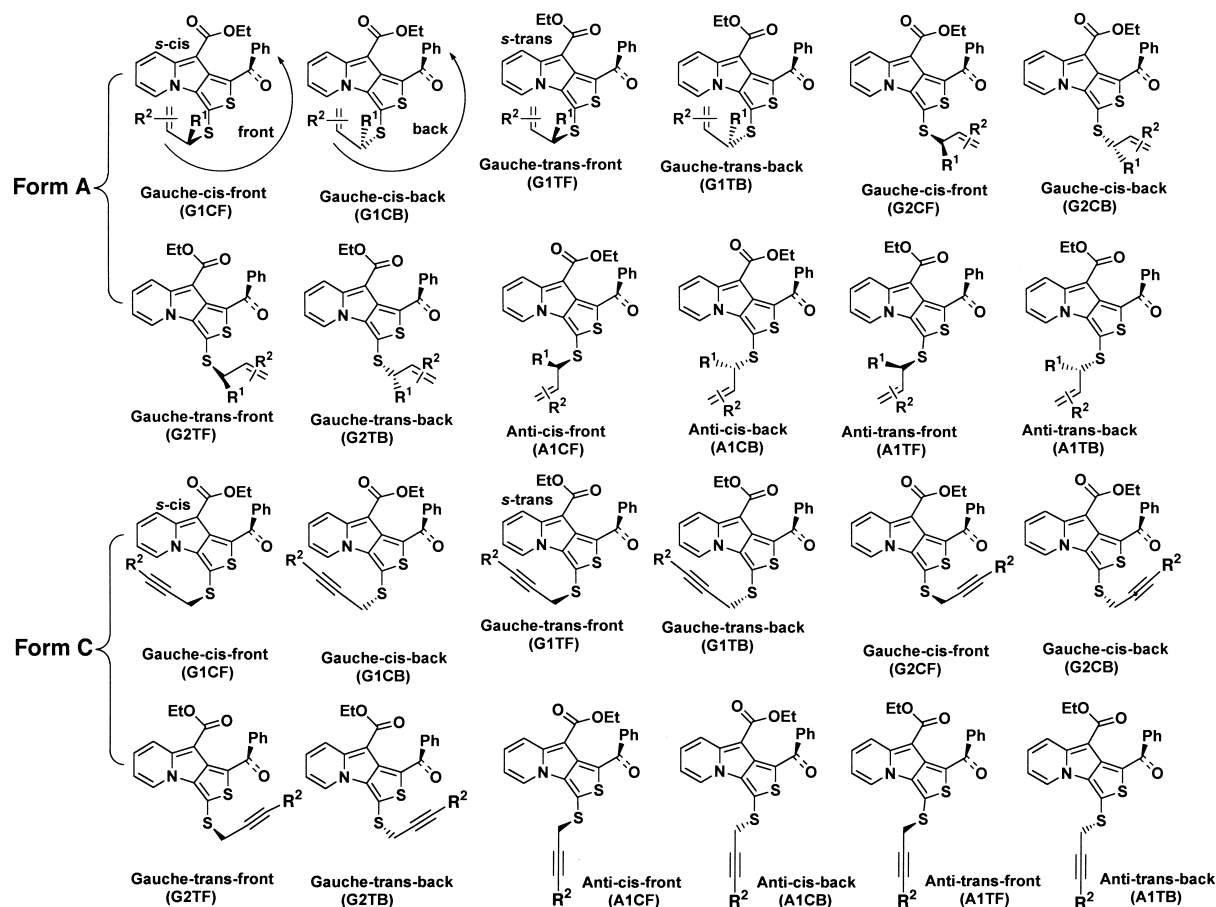


Fig. 2. Subdivided Conformations of Forms A and C and Their Abbreviations

gion, but in the deshielding region due to the wider dihedral angles of the two unsaturated systems and the smaller vinyl or ethynyl groups in these products. On the other hand, the presence of the **G2CB** conformation for **4s** indicates that the **G1CF** conformation in **4a**–**x** and **6a**–**x** is the most predominant both in solution and solid states but the **G1CF** con-

formation is still not fixed. Crystallization in the other conformers is also possible because of the small difference in the stability between them as described below.

Conformational Analyses by Mopac PM3 Calculations¹²⁾ To examine the stability of possible conformers for these molecules (**4a**–**x**) and (**6a**–**x**), we performed Mopac

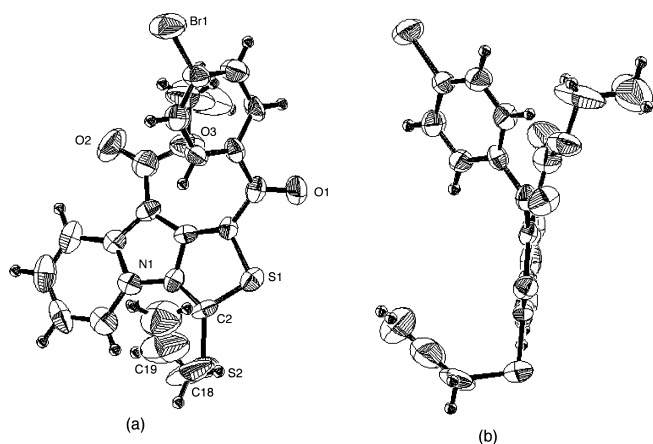


Fig. 3. ORTEP Drawings (the Over-view (a) and the Side-view (b)) of **4c**

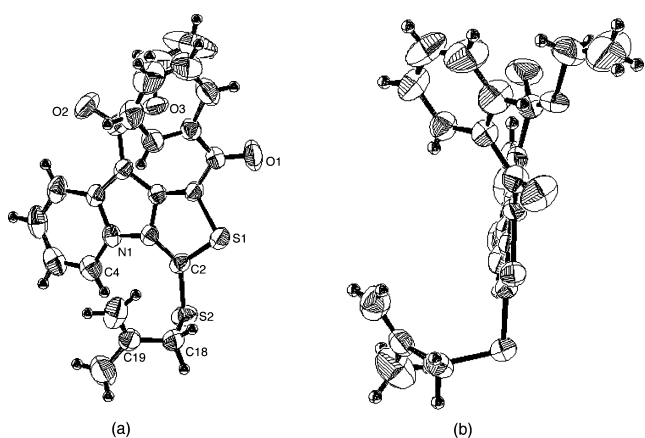


Fig. 4. ORTEP Drawings (the Over-view (a) and the Side-view (b)) of **4g**

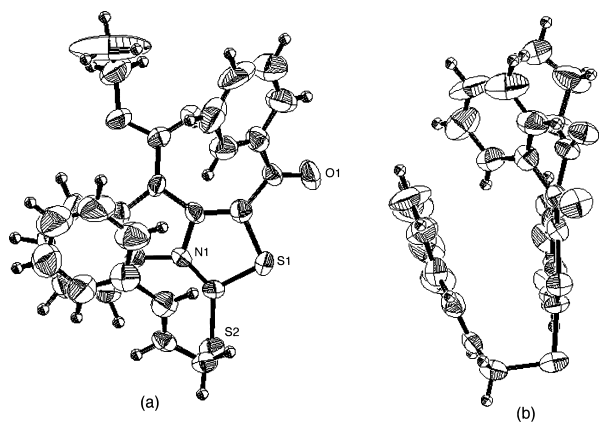


Fig. 5. ORTEP Drawings (the Over-view (a) and the Side-view (b)) of **4p**

PM3 (precise) calculations for the optimized geometry of each conformer of **4a**, **d**, **g**, **j**, **m**, **p**, **s**, **v** illustrated in Figs. 1 and 2. These results are summarized in Table 3. The results of the calculations for the conformers other than those described above were not involved in this table because all MOPAC calculations using them lead to the conformational conversion to the **A1** or **G1** form. Examination of these values indicates that form **A**, which is suitable to the intramolecular arene- π interaction, is more stable than form **B**, the rough stability for the main conformers is *gauche* 1 (**G1**) > *gauche* 2 (**G2**) > *anti* 1 (**A1**), and the *s-cis* conformation of

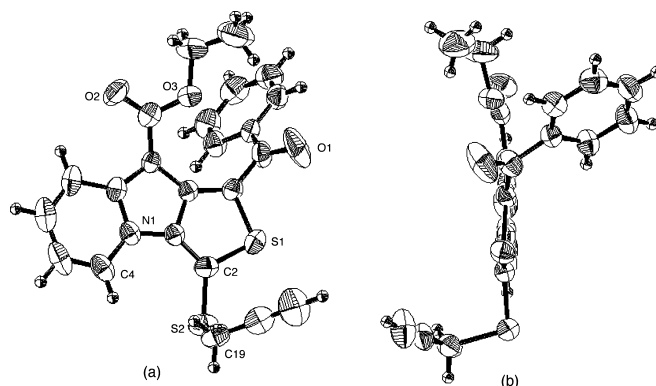


Fig. 6. ORTEP Drawings (the Over-view (a) and the Side-view (b)) of **4s**

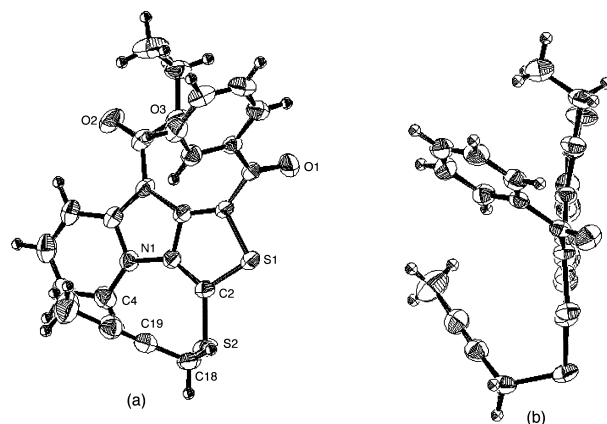


Fig. 7. ORTEP Drawings (the Over-view (a) and the Side-view (b)) of **4v**

the 9-ethoxycarbonyl group is more stable than the *s-trans* one. These trends are consistent with their spectral and X-ray analytical data shown above. In the **G1** form of the subdivided conformations, however, it was shown that the front (**F**) arrangement, in which both substituents on the 1 and 3-position are present on the same side, is not as stable as the back (**B**) one. This is inconsistent with the crystal structures for **4c**, **g**, **p**, **v** and some 3-(arylmethylthio)thieno[3,4-*b*]indolizines derivatives reported earlier by us.²⁻⁴⁾ The possibility of some attractive interaction between these substituents in the **G1CF** conformation of these molecules can also be considered, though it might be a minor event due to the small energy differences between their conformations.

In conclusion, we first synthesized some thieno[3,4-*b*]indolizines bearing an allylthio or propargylthio group at the 3-position, and could observe their arene- π 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 ¹H-NMR spectra were determined with a Hitachi R-600 spectrometer (60 MHz) or JEOL JNM-LA400 (¹H: 400 MHz and ¹³C: 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-(allylthio and propargylthio)thieno[3,4-*b*]indolizine-9-carboxylates. General Method A mixture of 1-(pyridinio)thiophene-2-thiolate (**1**, 1 mmol), alkyl halide (**2**, 1.2 mmol), and sodium iodide (2.0 g) in acetone (20 ml) was kept at rt or at 50 °C in a water bath under occasional stirring until the disappearance of pyridinium betaine (**1**) is detected by TLC monitoring (2-3 d). After *S*-alkylation was

Table 3. The Formation Energies (kcal/mol) in MOPAC PM3 (Precise) Calculation of Some Compounds

No.	Form	FE of standard ^{a)}	G1CF-G1CF ^{b)}	G1CB-G1CF ^{b)}	G1TF-G1CF ^{b)}	G1TB-G1CF ^{b)}	G2CF-G1CF ^{b)}	G2CB-G1CF ^{b)}
4a	A	12.72106	0.00000	-0.22908	0.61314	0.51762	0.64183	0.38305
	B		0.30446	0.10654	0.94197	0.83383	0.49503	0.25959
4d	A	3.77591	0.00000	-0.22287	0.61755	-0.32735	0.83979	0.84461
	B		0.56361	0.32223	1.18061	1.06583	0.79369	0.57246
4g	A	2.29274	0.00000	-0.23457	0.62409	0.51114	0.73079	0.46743
	B		0.32556	0.13561	0.97686	0.86542	0.09266	0.29681
4j	A	-7.27093	0.00000	-0.31413	-0.25850	0.49536	0.96106	0.34860
	B		0.34908	0.16905	0.90144	1.00845	0.60251	0.49541
4m	A	2.44256	0.00000	-0.25565	0.57436	0.52212	1.49963	1.25155
	B		1.33588	1.14176	1.96947	1.88121	0.89394	0.69420
4p	A	34.98862	0.00000	-0.28389	0.56255	1.19053	-0.88279	0.41981
	B		0.16935	-0.02051	0.82469	1.43613	-0.03310	0.36527
4s	C	47.66914	0.00000	-0.20057	0.59622	0.51936	0.60679	0.37770
4v	C	36.85892	0.00000	-0.13124	0.67730	0.58441	0.21192	0.42183

No.	G2TF-G1CF ^{b)}	G2TB-G1CF ^{b)}	A1CF-G1CF ^{b)}	A1CB-G1CF ^{b)}	A1TF-G1CF ^{b)}	A1TB-G1CF ^{b)}
4a	1.12137	1.17269	1.23096	0.97118	1.85963	1.74983
	0.77756	0.72946	1.33927	1.06926	1.96084	1.85232
4d	1.28817	1.65032	1.42247	-0.16740	2.03371	1.93490
	1.58782	1.03189	0.08601	1.16516	0.67672	0.59165
4g	1.20574	1.26289	1.28960	1.02924	1.92654	1.81566
	0.69800	0.76257	1.36884	1.09807	1.99289	1.88510
4j	1.38602	1.29837	0.58645	0.36497	1.13378	1.09394
	1.27900	1.15336	0.03923	1.11978	2.01899	1.91003
4m	2.11919	2.03234	1.25325	1.04749	1.89053	1.78508
	1.53995	1.44875	1.45296	1.19369	2.06194	1.96187
4p	-0.08741	1.08552	1.43493	0.98000	1.86887	1.75788
	1.70820	1.13309	1.59063	1.12244	2.01670	1.90873
4s	1.22703	1.14338	1.40976	1.13951	2.60179	to G1
4v	1.27819	1.19921	1.47325	1.78688	2.09172	1.98278

a) The formation energies (kcal/mol) for the G1CF conformers of form A or C were selected as a standard. b) The formation energy of the standard.

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 purification the resulting pyridinium salt (**3** or **5**) 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 a further 4–6 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-(allylthio or propargylthio)thieno[3,4-*b*]indolizine-9-carboxylate. Some ¹H-NMR spectral data for products (**4a–x**) and (**6a–x**) are listed in Tables 1 and 2, and the other data for them are as follows:

Ethyl 3-Allylthio-1-benzoylthieno[3,4-*b*]indolizine-9-carboxylate (**4a**): 78% (from **1a** and allyl bromide (**2a**)), red prisms, mp 114–115 °C. IR (KBr) cm⁻¹: 1684, 1591. ¹³C-NMR (CDCl₃) δ: 14.2, 42.6, 59.0, 93.5, 110.7, 116.8, 119.6, 120.1, 124.7, 127.1, 128.2, 129.3, 130.1, 132.0, 132.4, 134.7, 136.8, 139.0, 149.9, 164.0, 187.9. UV λ_{max} (CHCl₃) nm (log ε) 328 (4.06), 422 (3.89), 479 (3.79), ca. 510 (shoulder). Anal. Calcd for C₂₃H₁₉NO₃S₂: C, 65.53; H, 4.54; N, 3.32. Found: C, 65.65; H, 4.49; N, 3.25.

Ethyl 3-Allylthio-1-(4-chlorobenzoyl)thieno[3,4-*b*]indolizine-9-carboxylate (**4b**): 77% (from **1b** and **2a**), red prisms, mp 131–132 °C. IR (KBr) cm⁻¹: 1676, 1630. UV λ_{max} (CHCl₃) nm (log ε) 328 (shoulder), 429 (3.84), 476 (3.70), ca. 510 (shoulder). Anal. Calcd for C₂₃H₁₈ClNO₃S₂: C, 60.58; H, 3.98; N, 3.07. Found: C, 60.60; H, 4.19; N, 2.84.

Ethyl 3-Allylthio-1-(4-bromobenzoyl)thieno[3,4-*b*]indolizine-9-carboxylate (**4c**): 72% (from **1c** and **2a**), red prisms, mp 122–123 °C. IR (KBr) cm⁻¹: 1682, 1622. UV λ_{max} (CHCl₃) nm (log ε) 328 (shoulder), 428 (3.86), 479 (3.76), ca. 510 (shoulder). Anal. Calcd for C₂₃H₁₈BrNO₃S₂: C, 55.20; H, 3.63; N, 2.80. Found: C, 55.34; H, 3.60; N, 2.70.

Ethyl 1-Benzoyl-3-(2-butenylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**4d**): 82% (from **1a** and (*E*)-1-bromo-2-butene (**2b**)), red prisms, mp 116–118 °C. IR (KBr) cm⁻¹: 1687, 1624. ¹³C-NMR (CDCl₃) δ: 14.3, 17.6, 42.2, 59.0, 93.5, 110.6, 117.5, 120.1, 123.8, 124.8, 127.2, 128.3, 129.4, 130.1,

131.3, 132.4, 134.7, 139.2, 149.9, 164.0, 188.0 (two carbons are overlapping). UV λ_{max} (CHCl₃) nm (log ε) 327 (4.06), 421 (3.92), 474 (3.70), ca. 510 (shoulder). Anal. Calcd for C₂₄H₂₁NO₃S₂: C, 66.18; H, 4.86; N, 3.22. Found: C, 66.35; H, 4.81; N, 3.15.

Ethyl 3-(2-Butenylthio)-1-(4-chlorobenzoyl)thieno[3,4-*b*]indolizine-9-carboxylate (**4e**): 77% (from **1b** and **2b**), red prisms, mp 116–118 °C. IR (KBr) cm⁻¹: 1680, 1626. UV λ_{max} (CHCl₃) nm (log ε) 327 (4.08), 423 (3.90), 481 (3.79), ca. 510 (shoulder). Anal. Calcd for C₂₄H₂₀ClNO₃S₂: C, 61.33; H, 4.29; N, 2.98. Found: C, 61.37; H, 4.28; N, 2.95.

Ethyl 1-(4-Bromobenzoyl)-3-(2-butenylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**4f**): 83% (from **1c** and **2b**), red needles, mp 127–129 °C. IR (KBr) cm⁻¹: 1686, 1624. UV λ_{max} (CHCl₃) nm (log ε) 326 (4.08), 423 (3.90), 482 (3.80), ca. 510 (shoulder). Anal. Calcd for C₂₄H₂₀BrNO₃S₂: C, 56.03; H, 3.92; N, 2.72. Found: C, 55.76; H, 3.83; N, 2.64.

Ethyl 1-Benzoyl-3-[(2-methyl-2-propenyl)thio]thieno[3,4-*b*]indolizine-9-carboxylate (**4g**): 71% (from **1a** and 3-chloro-2-methyl-1-propene (**2c**)), red prisms, mp 112–114 °C. IR (KBr) cm⁻¹: 1688, 1622. ¹³C-NMR (CDCl₃) δ: 14.3, 21.0, 47.4, 59.0, 93.6, 110.7, 116.0, 117.6, 120.2, 124.6, 127.1, 128.3, 129.4, 130.1, 132.4, 134.7, 136.7, 139.2, 149.9, 164.0, 188.0 (one carbon is overlapping). UV λ_{max} (CHCl₃) nm (log ε) 328 (4.07), 422 (3.87), 479 (3.82), ca. 510 (shoulder). Anal. Calcd for C₂₄H₂₁NO₃S₂: C, 66.18; H, 4.86; N, 3.22. Found: C, 66.24; H, 4.86; N, 3.18.

Ethyl 1-(4-Chlorobenzoyl)-3-[(2-methyl-2-propenyl)thio]thieno[3,4-*b*]indolizine-9-carboxylate (**4h**): 65% (from **1b** and **2c**), red prisms, mp 130–133 °C. IR (KBr) cm⁻¹: 1684, 1622. UV λ_{max} (CHCl₃) nm (log ε) 328 (4.08), 425 (3.80), 482 (3.83), ca. 510 (shoulder). Anal. Calcd for C₂₄H₂₀ClNO₃S₂: C, 61.33; H, 4.29; N, 2.98. Found: C, 61.34; H, 4.29; N, 2.96.

Ethyl 1-(4-Bromobenzoyl)-3-[(2-methyl-2-propenyl)thio]thieno[3,4-*b*]indolizine-9-carboxylate (**4i**): 82% (from **1c** and **2c**), red prisms, mp 119–121 °C. IR (KBr) cm⁻¹: 1684, 1622. UV λ_{max} (CHCl₃) nm (log ε) 325 (4.06), 424 (3.81), 4.82 (3.83), ca. 510 (shoulder). Anal. Calcd for C₂₄H₂₀BrNO₃S₂: C, 56.03; H, 3.92; N, 2.72. Found: C, 56.03; H, 3.93; N, 2.71.

Ethyl 1-Benzoyl-3-[(3-methyl-2-butenyl)thio]thieno[3,4-*b*]indolizine-9-carboxylate (**4j**): 80% (from **1a** and 1-bromo-3-methyl-2-butene (**2d**)), red

prisms, mp 151—153 °C. IR (KBr) cm^{-1} : 1682, 1616. ^{13}C -NMR (CDCl_3) δ : 14.3, 17.5, 25.6, 37.9, 59.0, 93.5, 110.5, 118.2, 120.0, 124.8, 127.2, 128.3, 129.4, 130.1, 132.4, 134.7, 136.8, 138.8, 139.2, 149.9, 164.0, 187.9 (one carbon is overlapping). UV λ_{max} (CHCl_3) nm (log ϵ) 327 (4.06), 421 (3.85), 475 (3.73), *ca.* 510 (shoulder). *Anal.* Calcd for $\text{C}_{25}\text{H}_{23}\text{NO}_3\text{S}_2$: C, 66.79; H, 5.16; N, 3.12. Found: C, 66.80; H, 5.16; N, 3.11.

Ethyl 1-(4-Chlorobenzoyl)-3-[(3-methyl-2-butenyl)thio]thieno[3,4-*b*]indolizine-9-carboxylate (**4k**): 88% (from **1b** and **2d**), red prisms, mp 117—118 °C. IR (KBr) cm^{-1} : 1678, 1615. UV λ_{max} (CHCl_3) nm (log ϵ) 307 (shoulder), 437 (3.68), 476 (3.76), *ca.* 510 (shoulder). *Anal.* Calcd for $\text{C}_{25}\text{H}_{22}\text{ClNO}_3\text{S}_2$: C, 62.04; H, 4.58; N, 2.89. Found: C, 62.11; H, 4.56; N, 2.84.

Ethyl 1-(4-Bromobenzoyl)-3-[(3-methyl-2-butenyl)thio]thieno[3,4-*b*]indolizine-9-carboxylate (**4l**): 77% (from **1c** and **2d**), red prisms, mp 118—120 °C. IR (KBr) cm^{-1} : 1684, 1626. UV λ_{max} (CHCl_3) nm (log ϵ) 326 (shoulder), 443 (3.69), 479 (3.80), *ca.* 510 (shoulder). *Anal.* Calcd for $\text{C}_{25}\text{H}_{22}\text{BrNO}_3\text{S}_2$: C, 56.82; H, 4.20; N, 2.65. Found: C, 56.89; H, 4.18; N, 2.59.

Ethyl 1-Benzoyl-3-(2-cyclohexenylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**4m**): 79% (from **1a** and 3-bromocyclohexene (**2e**)), red needles, mp 128—130 °C. IR (KBr) cm^{-1} : 1682, 1591. ^{13}C -NMR (CDCl_3) δ : 14.3, 19.2, 24.9, 28.7, 49.8, 59.0, 93.6, 110.7, 117.7, 120.1, 124.6, 125.5, 127.2, 128.3, 129.4, 130.2, 132.4, 132.5, 134.8, 136.9, 139.1, 150.0, 164.1, 188.0. UV λ_{max} (CHCl_3) nm (log ϵ) 328 (4.08), 422 (3.91), 476 (3.76), *ca.* 510 (shoulder). *Anal.* Calcd for $\text{C}_{26}\text{H}_{23}\text{NO}_3\text{S}_2$: C, 67.65; H, 5.02; N, 3.03. Found: C, 67.64; H, 5.02; N, 3.00.

Ethyl 1-(4-Chlorobenzoyl)-3-(2-cyclohexenylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**4n**): 67% (from **1b** and **2e**), red prisms, mp 106—109 °C. IR (KBr) cm^{-1} : 1686, 1614. UV λ_{max} (CHCl_3) nm (log ϵ) 327 (shoulder), 438 (3.69), 476 (3.73), *ca.* 510 (shoulder). *Anal.* Calcd for $\text{C}_{26}\text{H}_{22}\text{ClNO}_3\text{S}_2$: C, 62.95; H, 4.47; N, 2.82. Found: C, 62.99; H, 4.42; N, 2.82.

Ethyl 1-(4-Bromobenzoyl)-3-(2-cyclohexenylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**4o**): 66% (from **1c** and **2e**), red prisms, mp 130—132 °C. IR (KBr) cm^{-1} : 1680, 1587. UV λ_{max} (CHCl_3) nm (log ϵ) 328 (shoulder), 440 (3.70), 477 (3.75), *ca.* 510 (shoulder). *Anal.* Calcd for $\text{C}_{26}\text{H}_{22}\text{BrNO}_3\text{S}_2$: C, 57.78; H, 4.10; N, 2.59. Found: C, 57.80; H, 4.09; N, 2.54.

Ethyl 1-Benzoyl-3-(cinnamylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**4p**): 80% (from **1a** and cinnamyl bromide (**2f**)), red prisms, mp 122—125 °C. IR (KBr) cm^{-1} : 1678, 1615. ^{13}C -NMR (CDCl_3) δ : 14.3, 43.0, 58.9, 93.5, 110.6, 116.3, 120.1, 122.9, 125.0, 126.2, 126.9, 128.0, 128.2, 128.5, 129.4, 130.0, 132.4, 134.7, 134.8, 135.8, 137.4, 139.0, 149.9, 163.9, 188.0. UV λ_{max} (CHCl_3) nm (log ϵ) 327 (4.12), 421 (4.07), 475 (3.72), *ca.* 510 (shoulder). *Anal.* Calcd for $\text{C}_{29}\text{H}_{23}\text{NO}_3\text{S}_2$: C, 69.99; H, 4.66; N, 2.81. Found: C, 70.05; H, 4.62; N, 2.79.

Ethyl 1-(4-Chlorobenzoyl)-3-(cinnamylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**4q**): 79% (from **1b** and **2f**), red prisms, mp 131—132 °C. IR (KBr) cm^{-1} : 1674, 1612. UV λ_{max} (CHCl_3) nm (log ϵ) 326 (4.12), 422 (4.00), 479 (3.78), *ca.* 510 (shoulder). *Anal.* Calcd for $\text{C}_{29}\text{H}_{22}\text{ClNO}_3\text{S}_2$: C, 65.46; H, 4.17; N, 2.63. Found: C, 65.61; H, 4.08; N, 2.57.

Ethyl 1-(4-Bromobenzoyl)-3-(cinnamylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**4r**): 76% (from **1c** and **2f**), red prisms, mp 127—129 °C. IR (KBr) cm^{-1} : 1676, 1613. UV λ_{max} (CHCl_3) nm (log ϵ) 326 (4.12), 422 (4.00), 481 (3.82), *ca.* 510 (shoulder). *Anal.* Calcd for $\text{C}_{29}\text{H}_{22}\text{BrNO}_3\text{S}_2$: C, 60.42; H, 3.85; N, 2.43. Found: C, 60.53; H, 3.79; N, 2.37.

Ethyl 1-Benzoyl-3-(propargylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**4s**): 83% (from **1a** and propargyl bromide (**2g**)), red prisms, mp 124—125 °C. IR (KBr) cm^{-1} : 3277, 2116, 1663, 1630. ^{13}C -NMR (CDCl_3) δ : 14.3, 28.4, 59.0, 73.8, 78.2, 93.5, 110.6, 113.5, 120.1, 126.5, 127.4, 128.3, 129.5, 130.3, 132.7, 134.7, 137.7, 138.8, 150.0, 164.0, 188.2. UV λ_{max} (CHCl_3) nm (log ϵ) 328 (4.06), 434 (3.77), 480 (3.84), *ca.* 510 (shoulder). *Anal.* Calcd for $\text{C}_{25}\text{H}_{17}\text{NO}_3\text{S}_2$: C, 65.85; H, 4.08; N, 3.34. Found: C, 65.79; H, 4.13; N, 3.35.

Ethyl 1-(4-Chlorobenzoyl)-3-(propargylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**4t**): 76% (from **1b** and **2g**), red needles, mp 161—164 °C. IR (KBr) cm^{-1} : 3297, 2114, 1674, 1630. UV λ_{max} (CHCl_3) nm (log ϵ) 329 (shoulder), 441 (3.82), 476 (3.80), *ca.* 510 (shoulder). *Anal.* Calcd for $\text{C}_{25}\text{H}_{16}\text{ClNO}_3\text{S}_2$: C, 60.85; H, 3.55; N, 3.09. Found: C, 60.79; H, 3.79; N, 2.91.

Ethyl 1-(4-Bromobenzoyl)-3-(propargylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**4u**): 75% (from **1c** and **2g**), red prisms, mp 138—140 °C. IR (KBr) cm^{-1} : 3268, 2112, 1680, 1620. UV λ_{max} (CHCl_3) nm (log ϵ) 328 (shoulder), 435 (3.54), 475 (3.53), *ca.* 510 (shoulder). *Anal.* Calcd for $\text{C}_{25}\text{H}_{16}\text{BrNO}_3\text{S}_2$: C, 55.43; H, 3.24; N, 2.81. Found: C, 55.42; H, 3.29; N, 2.77.

Ethyl 1-Benzoyl-3-(2-butenylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**4v**): 78% (from **1a** and 1-bromo-2-butyne (**2h**)), red prisms, mp 130—131 °C. IR (KBr) cm^{-1} : 2236, 1676, 1630. ^{13}C -NMR (CDCl_3) δ : 3.5, 14.3, 29.2, 59.0, 73.6, 82.2, 93.4, 110.4, 114.6, 120.0, 126.1, 127.4, 128.3, 129.5, 130.1, 132.6, 134.7, 137.7, 138.9, 149.9, 164.0, 188.2. UV λ_{max} (CHCl_3) nm (log ϵ) 327 (4.07), 423 (3.90), 477 (3.79), *ca.* 510 (shoulder). *Anal.* Calcd for $\text{C}_{24}\text{H}_{19}\text{NO}_3\text{S}_2$: C, 66.49; H, 4.42; N, 3.23. Found: C, 66.50; H, 4.41; N, 3.23.

Ethyl 3-(2-Butenylthio)-1-(4-chlorobenzoyl)thieno[3,4-*b*]indolizine-9-carboxylate (**4w**): 66% (from **1b** and **2h**), red needles, mp 118—119 °C. IR (KBr) cm^{-1} : 2226, 1692, 1609. UV λ_{max} (CHCl_3) nm (log ϵ) 328 (shoulder), 436 (3.74), 474 (3.70), *ca.* 510 (shoulder). *Anal.* Calcd for $\text{C}_{24}\text{H}_{18}\text{ClNO}_3\text{S}_2$: C, 61.60; H, 3.88; N, 2.99. Found: C, 61.62; H, 3.90; N, 2.96.

Ethyl 1-(4-Bromobenzoyl)-3-(2-butenylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**4x**): 66% (from **1c** and **2h**), red needles, mp 142—144 °C. IR (KBr) cm^{-1} : 2232, 1690, 1615. UV λ_{max} (CHCl_3) nm (log ϵ) 328 (shoulder), 436 (3.78), 475 (3.74), *ca.* 510 (shoulder). *Anal.* Calcd for $\text{C}_{24}\text{H}_{18}\text{BrNO}_3\text{S}_2$: C, 56.25; H, 3.54; N, 2.73. Found: C, 56.27; H, 3.54; N, 2.70.

Ethyl 3-Allylthio-1-benzoyl-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**6a**): 77% (from **1d** and **2a**), red prisms, mp 123—124 °C. IR (KBr) cm^{-1} : 1671, 1624. UV λ_{max} (CHCl_3) nm (log ϵ) 327 (shoulder), 425 (4.03), 478 (3.75), *ca.* 505 (shoulder). *Anal.* Calcd for $\text{C}_{24}\text{H}_{21}\text{NO}_3\text{S}_2$: C, 66.18; H, 4.86; N, 3.22. Found: C, 66.37; H, 4.77; N, 3.02.

Ethyl 3-Allylthio-1-(4-chlorobenzoyl)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**6b**): 79% (from **1e** and **2a**), red prisms, mp 136—138 °C. IR (KBr) cm^{-1} : 1676, 1632. UV λ_{max} (CHCl_3) nm (log ϵ) 329 (shoulder), 427 (3.98), 478 (3.78), *ca.* 505 (shoulder). *Anal.* Calcd for $\text{C}_{24}\text{H}_{20}\text{ClNO}_3\text{S}_2$: C, 61.33; H, 4.29; N, 2.98. Found: C, 61.50; H, 4.28; N, 2.81.

Ethyl 3-Allylthio-1-(4-bromobenzoyl)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**6c**): 69% (from **1f** and **2a**), red prisms, mp 117—119 °C. IR (KBr) cm^{-1} : 1674, 1630. UV λ_{max} (CHCl_3) nm (log ϵ) 326 (4.13), 422 (3.94), 479 (3.75), *ca.* 505 (shoulder). *Anal.* Calcd for $\text{C}_{24}\text{H}_{20}\text{BrNO}_3\text{S}_2$: C, 56.03; H, 3.92; N, 2.72. Found: C, 56.17; H, 3.71; N, 2.79.

Ethyl 1-Benzoyl-3-(2-butenylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**6d**): 76% (from **1d** and **2b**), red prisms, mp 116—118 °C. IR (KBr) cm^{-1} : 1671, 1632. UV λ_{max} (CHCl_3) nm (log ϵ) 320 (shoulder), 428 (3.99), 479 (3.75), *ca.* 505 (shoulder). *Anal.* Calcd for $\text{C}_{25}\text{H}_{23}\text{NO}_3\text{S}_2$: C, 66.79; H, 5.16; N, 3.12. Found: C, 66.97; H, 5.10; N, 3.04.

Ethyl 3-(2-Butenylthio)-1-(4-chlorobenzoyl)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**6e**): 54% (from **1e** and **2b**), red needles, mp 116—118 °C. IR (KBr) cm^{-1} : 1680, 1639. UV λ_{max} (CHCl_3) nm (log ϵ) 328 (shoulder), 441 (3.76), 475 (3.74), *ca.* 505 (shoulder). *Anal.* Calcd for $\text{C}_{25}\text{H}_{22}\text{ClNO}_3\text{S}_2$: C, 62.04; H, 4.58; N, 2.89. Found: C, 62.04; H, 4.60; N, 2.83.

Ethyl 1-(4-Bromobenzoyl)-3-(2-butenylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**6f**): 58% (from **1f** and **2b**), red prisms, mp 127—129 °C. IR (KBr) cm^{-1} : 1672, 1636. UV λ_{max} (CHCl_3) nm (log ϵ) 327 (shoulder), 430 (3.95), 478 (3.79), *ca.* 505 (shoulder). *Anal.* Calcd for $\text{C}_{25}\text{H}_{22}\text{BrNO}_3\text{S}_2$: C, 56.82; H, 4.20; N, 2.65. Found: C, 56.84; H, 4.19; N, 2.64.

Ethyl 1-Benzoyl-7-methyl-3-[(2-methyl-2-propenyl)thio]thieno[3,4-*b*]indolizine-9-carboxylate (**6g**): 71% (from **1d** and **2c**), red prisms, mp 139—141 °C. IR (KBr) cm^{-1} : 1668, 1633. UV λ_{max} (CHCl_3) nm (log ϵ) 328 (shoulder), 439 (3.84), 482 (3.73), *ca.* 505 (shoulder). *Anal.* Calcd for $\text{C}_{25}\text{H}_{23}\text{NO}_3\text{S}_2$: C, 66.79; H, 5.16; N, 3.12. Found: C, 66.95; H, 5.12; N, 3.01.

Ethyl 1-(4-Chlorobenzoyl)-7-methyl-3-[(2-methyl-2-propenyl)thio]thieno[3,4-*b*]indolizine-9-carboxylate (**6h**): 61% (from **1e** and **2c**), red prisms, mp 133—136 °C. UV λ_{max} (CHCl_3) nm (log ϵ) 328 (shoulder), 440 (3.88), 476 (shoulder), *ca.* 505 (shoulder). *Anal.* Calcd for $\text{C}_{25}\text{H}_{22}\text{ClNO}_3\text{S}_2$: C, 62.04; H, 4.58; N, 2.89. Found: C, 62.00; H, 4.58; N, 2.80.

Ethyl 1-(4-Bromobenzoyl)-7-methyl-3-[(2-methyl-2-propenyl)thio]thieno[3,4-*b*]indolizine-9-carboxylate (**4i**): 62% (from **1f** and **2c**), red prisms, mp 133—136 °C. IR (KBr) cm^{-1} : 1668, 1628. UV λ_{max} (CHCl_3) nm (log ϵ) 329 (shoulder), 441 (3.87), 484 (shoulder), *ca.* 505 (shoulder). *Anal.* Calcd for $\text{C}_{25}\text{H}_{22}\text{BrNO}_3\text{S}_2$: C, 56.82; H, 4.20; N, 2.65. Found: C, 56.65; H, 4.18; N, 2.61.

Ethyl 1-Benzoyl-7-methyl-3-[(3-methyl-2-butenyl)thio]thieno[3,4-*b*]indolizine-9-carboxylate (**6j**): 85% (from **1d** and **2d**), red prisms, mp 116—118 °C. IR (KBr) cm^{-1} : 1676, 1638. UV λ_{max} (CHCl_3) nm (log ϵ) 328 (shoulder), 441 (3.74), 474 (3.79), *ca.* 505 (shoulder). *Anal.* Calcd for $\text{C}_{26}\text{H}_{25}\text{NO}_3\text{S}_2$: C, 67.36; H, 5.44; N, 3.02. Found: C, 67.37; H, 5.45; N, 3.00.

Ethyl 1-(4-Chlorobenzoyl)-7-methyl-[(3-methyl-2-butenyl)thio]thieno[3,4-*b*]indolizine-9-carboxylate (**6k**): 72% (from **1e** and **2d**), red needles, mp

118–121 °C. IR (KBr) cm^{-1} : 1676, 1636. UV λ_{max} (CHCl_3) nm (log ϵ) 327 (shoulder), 433 (3.84), 478 (3.83), *ca.* 505 (shoulder). *Anal.* Calcd for $\text{C}_{26}\text{H}_{24}\text{ClNO}_3\text{S}_2$: C, 62.70; H, 4.86; N, 2.81. Found: C, 62.70; H, 4.85; N, 2.81.

Ethyl 1-(4-Bromobenzoyl)-7-methyl-3-[(3-methyl-2-butenyl)thio]thieno[3,4-*b*]indolizine-9-carboxylate (**6i**): 57% (from **1f** and **2d**), red needles, mp 131–133 °C. IR (KBr) cm^{-1} : 1684, 1636. UV λ_{max} (CHCl_3) nm (log ϵ) 327 (shoulder), 444 (3.73), 479 (3.77), *ca.* 505 (shoulder). *Anal.* Calcd for $\text{C}_{26}\text{H}_{24}\text{BrNO}_3\text{S}_2$: C, 57.56; H, 4.46; N, 2.58. Found: C, 57.53; H, 4.53; N, 2.55.

Ethyl 1-Benzoyl-3-(2-cyclohexenylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**6m**): 76% (from **1d** and **2e**), red prisms, mp 164–166 °C. IR (KBr) cm^{-1} : 1680, 1631. UV λ_{max} (CHCl_3) nm (log ϵ) 329 (shoulder), 441 (3.77), 470 (3.76), *ca.* 505 (shoulder). *Anal.* Calcd for $\text{C}_{27}\text{H}_{25}\text{NO}_3\text{S}_2$: C, 68.18; H, 5.30; N, 2.94. Found: C, 68.15; H, 5.32; N, 2.95.

Ethyl 1-(4-Chlorobenzoyl)-3-(2-cyclohexenylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**6n**): 79% (from **1e** and **2e**), red prisms, mp 140–142 °C. IR (KBr) cm^{-1} : 1671, 1622. UV λ_{max} (CHCl_3) nm (log ϵ) 329 (shoulder), 431 (3.86), 472 (3.68), *ca.* 505 (shoulder). *Anal.* Calcd for $\text{C}_{27}\text{H}_{24}\text{ClNO}_3\text{S}_2$: C, 63.58; H, 4.74; N, 2.75. Found: C, 63.51; H, 4.83; N, 2.75.

Ethyl 1-(4-Bromobenzoyl)-3-(2-cyclohexenylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**6o**): 52% (from **1f** and **2e**), red prisms, mp 147–150 °C. IR (KBr) cm^{-1} : 1671, 1624. UV λ_{max} (CHCl_3) nm (log ϵ) 328 (shoulder), 442 (3.76), 476 (3.76), *ca.* 505 (shoulder). *Anal.* Calcd for $\text{C}_{27}\text{H}_{24}\text{BrNO}_3\text{S}_2$: C, 58.48; H, 4.36; N, 2.53. Found: C, 58.48; H, 4.33; N, 2.50.

Ethyl 1-Benzoyl-3-(cinnamylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**6p**): 63% (from **1d** and **2f**), red prisms, mp 130–132 °C. IR (KBr) cm^{-1} : 1672, 1611. UV λ_{max} (CHCl_3) nm (log ϵ) 329 (shoulder), 430 (3.95), 472 (3.76), *ca.* 505 (shoulder). *Anal.* Calcd for $\text{C}_{30}\text{H}_{25}\text{NO}_3\text{S}_2$: C, 70.42; H, 4.93; N, 2.74. Found: C, 70.36; H, 5.02; N, 2.71.

Ethyl 1-(4-Chlorobenzoyl)-3-(cinnamylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**6q**): 69% (from **1e** and **2f**), red prisms, mp 141–144 °C. IR (KBr) cm^{-1} : 1667, 1634. UV λ_{max} (CHCl_3) nm (log ϵ) 328 (shoulder), 428 (3.94), 477 (3.79), *ca.* 505 (shoulder). *Anal.* Calcd for $\text{C}_{30}\text{H}_{24}\text{ClNO}_3\text{S}_2$: C, 65.98; H, 4.43; N, 2.56. Found: C, 66.02; H, 4.43; N, 2.52.

Ethyl 1-(4-Bromobenzoyl)-3-(cinnamylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**6r**): 59% (from **1f** and **2f**), red needles, mp 142–144 °C. IR (KBr) cm^{-1} : 1667, 1630. UV λ_{max} (CHCl_3) nm (log ϵ) 329 (4.15), 437 (3.93), 474 (shoulder), *ca.* 505 (shoulder). *Anal.* Calcd for $\text{C}_{30}\text{H}_{24}\text{BrNO}_3\text{S}_2$: C, 61.02; H, 4.10; N, 2.37. Found: C, 61.12; H, 4.09; N, 2.28.

Ethyl 1-Benzoyl-7-methyl-3-(propargylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**6s**): 72% (from **1d** and **2g**), red needles, mp 133–135 °C. IR (KBr) cm^{-1} : 3246, 2114, 1669, 1638. UV λ_{max} (CHCl_3) nm (log ϵ) 329 (shoulder), 439 (3.80), 471 (shoulder), *ca.* 505 (shoulder). *Anal.* Calcd for $\text{C}_{26}\text{H}_{19}\text{NO}_3\text{S}_2$: C, 66.49; H, 4.42; N, 3.23. Found: C, 66.51; H, 4.41; N, 3.22.

Ethyl 1-(4-Chlorobenzoyl)-7-methyl-3-(propargylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**6t**): 69% (from **1e** and **2g**), red needles, mp 130–132 °C. IR (KBr) cm^{-1} : 3277, 2116, 1671, 1634. UV λ_{max} (CHCl_3) nm (log ϵ) 328 (shoulder), 440 (3.86), 471 (shoulder), *ca.* 505 (shoulder). *Anal.* Calcd for $\text{C}_{24}\text{H}_{18}\text{ClNO}_3\text{S}_2$: C, 61.60; H, 3.88; N, 2.99. Found: C, 61.41; H, 4.09; N, 2.99.

Ethyl 1-(4-Bromobenzoyl)-7-methyl-3-(propargylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**6u**): 61% (from **1f** and **2g**), red prisms, mp 177–179 °C. IR (KBr) cm^{-1} : 3294, 2114, 1676, 1634. UV λ_{max} (CHCl_3) nm (log ϵ) 329 (shoulder), 439 (3.87), 477 (shoulder), *ca.* 505 (shoulder). *Anal.* Calcd for $\text{C}_{24}\text{H}_{18}\text{BrNO}_3\text{S}_2$: C, 56.25; H, 3.54; N, 2.73. Found: C, 56.24; H, 3.56; N, 2.70.

Ethyl 1-Benzoyl-3-(2-butenylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**6v**): 69% (from **1d** and **2h**), red prisms, mp 153–154 °C. IR (KBr) cm^{-1} : 2232, 1678, 1636. UV λ_{max} (CHCl_3) nm (log ϵ) 328 (shoulder), 437 (3.85), 474 (shoulder), *ca.* 505 (shoulder). *Anal.* Calcd for $\text{C}_{25}\text{H}_{21}\text{NO}_3\text{S}_2$: C, 67.09; H, 4.73; N, 3.13. Found: C, 67.08; H, 4.73; N, 3.10.

Ethyl 3-(2-Butenylthio)-1-(4-Chlorobenzoyl)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**6w**): 62% (from **1e** and **2h**), red needles, mp 174–175 °C. IR (KBr) cm^{-1} : 2232, 1674, 1640. UV λ_{max} (CHCl_3) nm (log ϵ) 328 (shoulder), 439 (3.85), 476 (shoulder), *ca.* 505 (shoulder). *Anal.* Calcd for $\text{C}_{25}\text{H}_{20}\text{ClNO}_3\text{S}_2$: C, 62.30; H, 4.18; N, 2.91. Found: C, 62.38; H, 4.21; N, 2.77.

Ethyl 1-(4-Bromobenzoyl)-3-(2-butenylthio)-7-methylthieno[3,4-*b*]indo-

lazine-9-carboxylate (**6x**): 56% (from **1f** and **2h**), red needles, mp 180–181 °C. IR (KBr) cm^{-1} : 2234, 1674, 1642. UV λ_{max} (CHCl_3) nm (log ϵ) 328 (shoulder), 441 (3.88), 475 (shoulder), *ca.* 505 (shoulder). *Anal.* Calcd for $\text{C}_{25}\text{H}_{20}\text{BrNO}_3\text{S}_2$: C, 57.04; H, 3.83; N, 2.66. Found: C, 57.18; H, 3.77; N, 2.58.

Crystallography of Ethyl 1-(4-Bromobenzoyl)-3-(allylthio)thieno[3,4-*b*]indolizine-9-carboxylate (4c**)** A red prismatic single crystal (0.04 × 0.24 × 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 $\text{MoK}\alpha$ radiation ($\lambda = 0.71069 \text{ \AA}$). The crystal data of this compound are as follows: **4c**: $\text{C}_{23}\text{H}_{18}\text{BrNO}_3\text{S}_2$; $M = 500.42$; monoclinic, space group $P2_1/a$ (#14), $Z = 4$ with $a = 11.306(4) \text{ \AA}$, $b = 26.419(4) \text{ \AA}$, $c = 7.575(3) \text{ \AA}$, $\beta = 94.03(2)^\circ$; $V = 2257(1) \text{ \AA}^3$ and $D_{\text{calc}} = 1.473 \text{ g/cm}^3$. All calculations were performed using the teXsan package.¹³ The structure was solved by a direct method (SIR).¹⁴ 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 0.067 and 0.050 for 1618 ($I > 2.00\sigma(I)$) observed reflections, respectively.

Crystallography of Ethyl 1-Benzoyl-3-(2-methyl-2-propenylthio)thieno[3,4-*b*]indolizine-9-carboxylate (4g**)** A red prismatic single crystal (0.14 × 0.46 × 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 $\text{MoK}\alpha$ radiation ($\lambda = 0.71069 \text{ \AA}$). Crystal data of this compound are as follows: **4g**: $\text{C}_{24}\text{H}_{21}\text{NO}_3\text{S}_2$; $M = 435.55$; triclinic, space group $P\bar{1}$ (#2), $Z = 2$ with $a = 11.221(3) \text{ \AA}$, $b = 13.451(2) \text{ \AA}$, $c = 7.555(2) \text{ \AA}$, $\alpha = 103.45(2)^\circ$, $\beta = 100.46(2)^\circ$, $\gamma = 83.24(2)^\circ$; $V = 1087.1(4) \text{ \AA}^3$ and $D_{\text{calc}} = 1.331 \text{ g/cm}^3$. All calculations were performed using the teXsan package.¹³ The structure was solved by a direct method (SIR).¹⁴ 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 0.060 and 0.048 for 2098 ($I > 2.00\sigma(I)$) observed reflections, respectively.

Crystallography of Ethyl 1-Benzoyl-3-(cinnamylthio)thieno[3,4-*b*]indolizine-9-carboxylate (4p**)** A dark red prismatic single crystal (0.12 × 0.42 × 0.88 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 $\text{MoK}\alpha$ radiation ($\lambda = 0.71069 \text{ \AA}$). The crystal data of this compound are as follows: **4p**: $\text{C}_{29}\text{H}_{23}\text{NO}_3\text{S}_2$; $M = 497.63$; monoclinic, space group $P2_1/a$ (#14), $Z = 4$ with $a = 15.263(4) \text{ \AA}$, $b = 11.360(4) \text{ \AA}$, $c = 15.487(3) \text{ \AA}$, $\beta = 110.46(2)^\circ$; $V = 2767(2) \text{ \AA}^3$ and $D_{\text{calc}} = 1.314 \text{ g/cm}^3$. All calculations were performed using the teXsan package.¹³ The structure was solved by a direct method (SIR).¹⁴ 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 0.072 and 0.077 for 1625 ($I > 2.00\sigma(I)$) observed reflections, respectively.

Crystallography of Ethyl 1-Benzoyl-3-(propargylthio)thieno[3,4-*b*]indolizine-9-carboxylate (4s**)** A dark red prismatic single crystal (0.34 × 0.88 × 1.00 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 $\text{MoK}\alpha$ radiation ($\lambda = 0.71069 \text{ \AA}$). The crystal data of this compound are as follows: **4s**: $\text{C}_{23}\text{H}_{17}\text{NO}_3\text{S}_2$; $M = 419.51$; triclinic, space group $P\bar{1}$ (#2), $Z = 2$ with $a = 11.744(3) \text{ \AA}$, $b = 11.298(3) \text{ \AA}$, $c = 8.848(2) \text{ \AA}$, $\alpha = 90.51(2)^\circ$, $\beta = 80.62(2)^\circ$, $\gamma = 118.51(2)^\circ$; $V = 1014.6(5) \text{ \AA}^3$ and $D_{\text{calc}} = 1.373 \text{ g/cm}^3$. All calculations were performed using the teXsan package.¹³ The structure was solved by a direct method (SIR).¹⁴ 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 0.057 and 0.057 for 2841 ($I > 2.00\sigma(I)$) observed reflections, respectively.

Crystallography of Ethyl 1-Benzoyl-3-(2-butenylthio)thieno[3,4-*b*]indolizine-9-carboxylate (4v**)** A dark red prismatic single crystal (0.22 × 0.68 × 0.72 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 $\text{MoK}\alpha$ radiation ($\lambda = 0.71069 \text{ \AA}$). The crystal data of this compound are as follows: **4v**: $\text{C}_{24}\text{H}_{19}\text{NO}_3\text{S}_2$; $M = 433.54$; triclinic, space group $P\bar{1}$ (#2), $Z = 2$ with $a = 10.682(4) \text{ \AA}$, $b = 12.131(4) \text{ \AA}$, $c = 10.091(2) \text{ \AA}$, $\alpha = 98.40(2)^\circ$, $\beta = 110.07(2)^\circ$, $\gamma = 115.75(2)^\circ$; $V = 1036.7(9) \text{ \AA}^3$ and $D_{\text{calc}} = 1.389 \text{ g/cm}^3$. All calculations were performed using the teXsan package.¹³ The structure was solved by a direct method (SIR).¹⁴ 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 0.052 and 0.054 for 3381 ($I > 2.00\sigma(I)$) observed reflections, respectively.

References and Notes

- 1) For part 57 of this series, see Kakehi A., Suga H., Hatayama S., Kubo D., *Heterocycles*, **65**, 1557–1560 (2005).
- 2) Kakehi A., Ito S., Suga H., Miwa T., Mori T., Kobayashi T., *Heterocycles*, **57**, 17–20 (2002).
- 3) Kakehi A., Ito S., Suga H., Miwa T., Mori T., Fujii T., Tanaka N., Kobayashi T., *Chem. Pharm. Bull.*, **51**, 75–84 (2003).
- 4) Kakehi A., Suga H., Kako T., Fujii T., Tanaka N., Kobayashi T., *Chem. Pharm. Bull.*, **51**, 1246–1252 (2003).
- 5) Many reactions involving carbon–carbon double and triple bonds are well known. See, ref. 6–8.
- 6) “The Chemistry of Alkenes,” ed. by Patai S., Interscience Publishers, London, 1964.
- 7) “The Chemistry of Alkenes,” Vol. 2, ed. by Zabicky J., Interscience Publishers, London, 1970.
- 8) “The Chemistry of the Carbon–Carbon Triple Bond,” Part 1 and 2, ed. by Patai S., John-Wiley & Sons, Chichester, 1978.
- 9) Kakehi A., Ito S., Suga H., Yasuraoka K., *Heterocycles*, **54**, 185–200 (2001).
- 10) The subdivided conformers of form B are abbreviated.
- 11) Johnson C. K., “ORTEP II, Report ORNL-5138,” Oak Ridge National Laboratory, Oak Ridge, Tennessee, 1976.
- 12) “WinMOPAC (Version 3.0),” Fujitsu Corporation.
- 13) teXsan for Windows version 1.06: Crystal Structure Analysis Package, Molecular Structure Corporation (1997–9).
- 14) SIR92: Altomare A., Cascarano G., Giacovazzo C., Guagliardi A., *J. Appl. Cryst.*, **26**, 343–350 (1993).