Preparation of New Nitrogen-Bridged Heterocycles. 59.[1] Syntheses and Intramolecular Interactions of 3-(Acylmethylthio)- and 3-[(3-Ethoxycarbonyl-2-propenyl)thio]thieno[3,4-*b*]indolizine Derivatives

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Various thieno[3,4-*b*]indolizine derivatives having an acylmethylthio or (3-ethoxycarbonyl-2-propenyl)thio group at the 3-position which could not be obtained by a conventional method were prepared by a new procedure using cyanoethyl group as a protecting group and their intramolecular arene–π interactions were investigated. In the ^{1}H-NMR spectra of these thieno[3,4-*b*]indolizines, the low-field shifts (δ 0.10—0.33 ppm) for the 5-protons were observed in comparison with those of 3-(methylthio)thieno[3,4-*b*]indolizines as a standard. The UV spectra also exhibited a characteristic absorption band at 425—445 nm attributable to the arene–π interaction but their intensities were generally lower than those of 3-(arylmethylthio)thieno[3,4-*b*]indolizines. In their X-ray analyses, the anti conformation for 3-(acylmethylthio)thieno[3,4-*b*]indolizines and the gauche one for the 3-(3-ethoxycarbonyl-2-propenyl)thio derivatives were exhibited.

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

In our previous papers we described the syntheses of various 3-(arylmethylthio)- and 3-(allylthio- or propargylthio)-thieno[3,4-*b*]indolizine derivatives and their intramolecular arene–arene or arene–π interactions through a sulfide spacer.[2—5] From their ^{1}H-NMR and UV spectral analyses and the molecular calculations (Mopac PM3)[6] we deduced that a specific conformation (gauche 1 form (**G1**)) which makes such intramolecular interaction possible is more predominant than the other conformations (gauche 2 (**G2**), anti 1 (**A1**), anti 2 (**A2**), and so on) (see Fig. 1).[2—5,7] We initially thought that the conformational stability of sulfide derivatives have the same order (anti>gauche≫eclipse) as that of 1,2-disubstituted ethanes, but only in the **G1** form stabilized by such interaction its stability exceed that of the anti form (gauche>anti). However, the fact that even the crystals of the gauche 2 form (**G2**), in which the intramolecular interaction was impossible, were found by X-ray analysis[5] allowed us to suspect the conventional order for these conformations. The Mopac PM3[6] calculations for simple sulfides, which any attractive interaction is absent, such as ethyl methyl sulfide, benzyl methyl sulfide, and ethyl phenyl sulfide made clear our predicted order (gauche>anti≫eclipse), but the differences in the formation energies between the optimized gauche and anti forms were low (1—1.5 kcal/mol).[8] This fact means that all of 3-(*R*-methylthio)thieno[3,4-*b*]indolizine derivatives prefer inherently the gauche forms over the anti ones and its **G1** form with an intramolecular interaction should be naturally the most favorable. To verify this order (see Fig. 2) in the conformational stability of sulfide derivatives we planned to investigate further the conformation of other derivatives of this series. In this paper we report the syntheses of 3-(acylmethylthio)-, and 3-[(3-ethoxycarbonyl-2-propenyl)thio]thieno[3,4-*b*]indolizine derivatives, which were inaccessible from our conventional method,[2—5] and their intramolecular arene–π interactions.

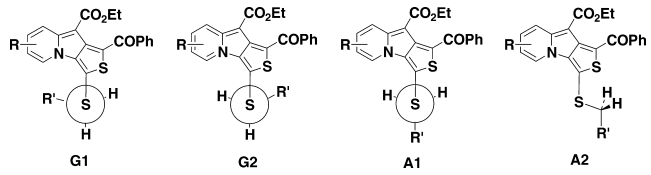

Fig. 1. Principal Conformations of 3-(*R*-Methylthio)thieno[3,4-*b*]indolizine

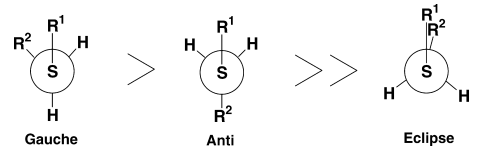

Fig. 2. Conformational Stability of Sulfides, $R^1SCH_2R^2$

Results and Discussion

Syntheses of 3-[(2-Cyanoethyl)thio]thieno[3,4-*b*]indolizine Derivatives We tried first to prepare the title compounds such as **4** from the procedures described earlier by us.[2—5] However, the *S*-alkylation of 3-(1-pyridinio)thiophene-2-thiolates (**1a**—**f**) with some acylmethyl halides such as chloroacetone (**2b**), phenacyl bromides (**2c**—**e**), ethyl bromoacetate (**2f**), and ethyl 4-bromocrotonate (**2g**), followed by the treatment of the resulting pyridinium salts (**3**) with a base and then dehydrogenating agent gave only complex mixtures involving small amounts of the expected products (**4**) (Chart 1). So we next examined the syntheses of thieno[3,4-*b*]indolizines bearing a protected thiol group at the 3-position. The *S*-alkylation of **1a**—**f** with 3-bromopropionitrile (**2a**) in acetone in the presence of excess sodium iodide and the treatment of the resulting pyridinium salts (**3a**—**f**) with 1,8-diazabicyclo[5.4.0]undec-2-ene (DBU) and then chloranil in chloroform at 0 °C provided the corresponding 3-[(2-cya-

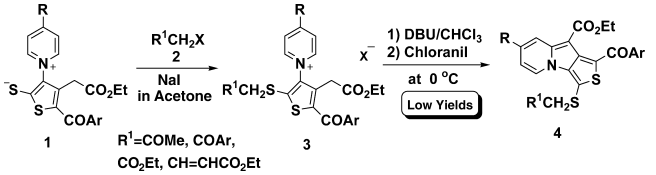

Chart 1

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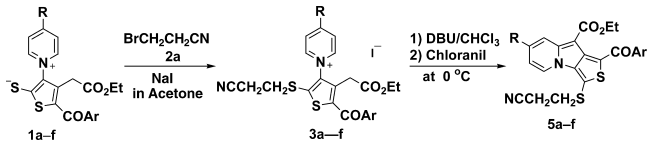


1,3	R	Ar
a	H	Ph
b	H	C_6H_4Cl-4
c	H	C_6H_4Br-4
d	Me	Ph
e	Me	C_6H_4Cl-4
f	Me	C_6H_4Br-4

5	R	Ar	Yield[a] (%)
a	H	Ph	65
b	H	C_6H_4Cl-4	69
c	H	C_6H_4Br-4	66
d	Me	Ph	60
e	Me	C_6H_4Cl-4	59
f	Me	C_6H_4Br-4	81

a) The yield is from 1 to 5.

Chart 2

noethyl)thio]thieno[3,4-*b*]indolizine derivatives (**5a**—**f**) in 59—81% yields respectively. These results are summarized in Chart 2.

The structures of products (**5a**—**f**) were determined by their elemental analyses and the IR, UV, and ^{1}H-NMR spectral analyses. In particular, the IR spectra of **5a**—**f** showed a saturated cyano absorption band at 2247—2259 cm^{-1}, together with an ester carbonyl band (1669—1678 cm^{-1}) and a arylcarbonyl band (1611—1628 cm^{-1}). The absorption bands near 330, 485, and 505 nm (shoulder) in the UV spectra of **5a**—**f** were almost the same as those of 3-(alkylthio)-thieno[3,4-*b*]indolizines which do not have intramolecular arene–arene or arene–π interactions.[9] The chemical shifts and the signal patterns in the ^{1}H-NMR spectra (Tables 1, 2)

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

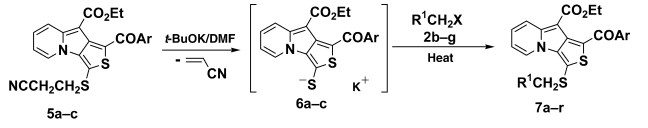
No[a,b]	C-5	C-6	C-7	C-8	R^{1}CH$_2$S	9-CO$_2$Et	δ (5-H)	δ (6-H)
7s[c]	8.96	6.73	7.31	8.20	2.68	0.97, 3.61	0.00	0.00
5a	9.19	6.77	[d]	8.23	2.72, 3.22	0.97, 3.68	−0.23	−0.04
5b	9.19	6.77	[d]	8.24	2.71, 3.20	0.98, 3.75	−0.23	−0.04
5c	9.17	6.77	7.39	8.23	2.73, 3.21	1.02, 3.76	−0.21	−0.04
7a	9.28	6.74	7.37	8.21	2.24, 3.90	0.95, 3.64	−0.32	−0.01
7b	9.27	6.76	7.36	8.20	2.25, 3.91	1.01, 3.74	−0.31	−0.03
7c	9.27	6.76	7.36	8.20	2.25, 3.91	1.01, 3.74	−0.31	−0.03
7d	9.15	6.67	[d]	8.18	4.46, 7.1—8.0	1.02, 3.75	−0.19	0.06
7e	9.14	6.66	[d]	8.18	4.46, 7.2—8.0	1.02, 3.75	−0.18	0.07
7f	9.14	6.68	[d]	8.17	4.44, 7.2—8.0	1.01, 3.75	−0.18	0.05
7g	9.07	6.66	[d]	8.18	4.36, 7.3—8.0	0.97, 3.67	−0.11	0.07
7h	9.08	6.67	[d]	8.17	4.37, 7.3—8.0	1.01, 3.73	−0.12	0.06
7i	9.08	6.66	[d]	8.18	4.37, 7.3—8.0	1.02, 3.74	−0.12	0.07
7j	9.07	6.66	[d]	8.19	4.38, 7.3—8.0	1.01, 3.63	−0.11	0.07
7k	9.08	6.67	[d]	8.20	4.37, 7.3—8.0	1.04, 3.76	−0.12	0.06
7l	9.09	6.67	[d]	8.20	4.37, 7.3—8.0	1.03, 3.76	−0.13	0.06
7m	9.26	6.74	[d]	8.22	1.12, 3.69, 4.07	0.96, 3.65	−0.30	−0.01
7n	9.26	6.76	[d]	8.21	1.12, 3.70, 4.08	1.01, 3.76	−0.30	−0.03
7o	9.27	6.76	[d]	8.24	1.14, 3.72, 4.07	1.02, 3.77	−0.31	−0.03
7p	9.14	6.71	[d]	8.22	1.17, 3.67, 4.05, 5.61, 6.93	0.96, 3.67	−0.18	0.02
7q	9.14	6.73	[d]	8.23	1.17, 3.67, 4.07, 5.61, 6.95	1.04, 3.78	−0.18	0.00
7r	9.14	6.72	[d]	8.22	1.17, 3.66, 4.07, 5.62, 6.95	1.03, 3.77	−0.18	0.01

a) The proton signals for the 1-arylcarbonyl group appeared in the range of δ 7.1—8.0 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*) Overlapped with the aromatic proton signals.

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

No[a,b]	C-5	C-6	C-7	C-8	R^{1}CH$_2$S	9-CO$_2$Et	δ (5-H)	δ (6-H)
8s[c]	8.84	6.58	2.40	8.00	2.67	0.95, 3.56	0.00	0.00
5d	9.05	6.60	2.41	8.02	2.70, 3.19	0.95, 3.64	−0.21	−0.02
5e	9.05	6.63	2.42	8.03	2.71, 3.20	1.00, 3.73	−0.21	−0.05
5f	9.04	6.61	2.41	8.02	2.70, 3.20	1.00, 3.72	−0.20	−0.03
8a	9.15	6.59	2.40	7.99	2.24, 3.89	0.94, 3.62	−0.31	−0.01
8b	9.15	6.61	2.41	7.99	2.24, 3.89	0.99, 3.70	−0.31	−0.03
8c	9.16	6.62	2.42	8.01	2.42, 3.90	1.00, 3.72	−0.32	−0.04
8d	9.01	6.49	2.39	[d]	4.42, 7.3—8.0	0.95, 3.61	−0.17	0.09
8e	9.01	6.51	2.39	[d]	4.42, 7.3—8.0	0.97, 3.65	−0.17	0.07
8f	9.02	6.52	2.40	[d]	4.43, 7.3—8.0	0.99, 3.71	−0.18	0.06
8g	8.96	6.50	2.40	7.97	4.34, 7.3—8.0	0.94, 3.60	−0.12	0.08
8h	8.96	6.51	2.41	7.95	4.37, 7.3—8.0	1.00, 3.72	−0.12	0.07
8i	8.97	6.54	2.42	7.97	4.36, 7.3—8.0	0.99, 3.70	−0.13	0.04
8j	8.94	6.50	2.40	7.97	4.35, 7.3—8.0	0.95, 3.61	−0.10	0.08
8k	8.94	6.50	2.40	[d]	4.34, 7.3—8.0	0.97, 3.69	−0.10	0.08
8l	8.94	6.51	2.42	[d]	4.35, 7.3—8.0	0.99, 3.71	−0.10	0.07
8m	9.17	6.60	2.42	8.04	1.14, 3.71, 4.09	0.96, 3.66	−0.33	−0.02
8n	9.13	6.59	2.42	8.00	1.12, 3.69, 4.07	0.99, 3.74	−0.29	−0.01
8o	9.15	6.60	2.42	8.02	1.00, 3.69, 4.07	1.00, 3.74	−0.31	−0.02
8p	9.00	6.56	2.39	8.00	1.16, 3.66, 4.06, 5.61, 6.94	0.96, 3.66	−0.16	0.02
8q	9.00	6.59	2.41	8.01	1.18, 3.65, 4.06, 5.63, 6.93	1.00, 3.73	−0.16	−0.01
8r	9.00	6.58	2.42	8.00	1.18, 3.66, 4.05, 5.64, 6.92	0.99, 3.70	−0.16	0.00

a) The proton signals for the 1-arylcarbonyl group appeared in the range of δ 7.1—8.0 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*) Overlapped with the aromatic proton signals.

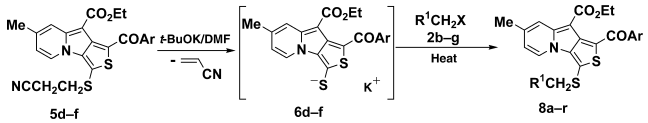


2	R'X
b	$ClCH_2COMe$
c	$BrCH_2COPh$
d	$BrCH_2COC_6H_4Cl$-4
e	$BrCH_2COC_6H_4Br$-4
f	$BrCH_2CO_2Et$
g	$BrCH_2CH{=}CHCO_2Et$

7	Ar	R^1	Yield[a] (%)
a	Ph	COMe	97
b	C_6H_4Cl-4	COMe	88
c	C_6H_4Br-4	COMe	85
d	Ph	COPh	78
e	C_6H_4Cl-4	COPh	84
f	C_6H_4Br-4	COPh	78
g	Ph	COC_6H_4Cl-4	77
h	C_6H_4Cl-4	COC_6H_4Cl-4	68
i	C_6H_4Br-4	COC_6H_4Cl-4	72
j	Ph	COC_6H_4Br-4	78
k	C_6H_4Cl-4	COC_6H_4Br-4	79
l	C_6H_4Br-4	COC_6H_4Br-4	80
m	Ph	CO_2Et	99
n	C_6H_4Cl-4	CO_2Et	88
o	C_6H_4Br-4	CO_2Et	82
p	Ph	$CH{=}CHCO_2Et$	63
q	C_6H_4Cl-4	$CH{=}CHCO_2Et$	65
r	C_6H_4Br-4	$CH{=}CHCO_2Et$	60

a) The yield is from 5 to 7.

Chart 3



8	Ar	R^1	Yield[a] (%)
a	Ph	COMe	96
b	C_6H_4Cl-4	COMe	80
c	C_6H_4Br-4	COMe	99
d	Ph	COPh	93
e	C_6H_4Cl-4	COPh	83
f	C_6H_4Br-4	COPh	78
g	Ph	COC_6H_4Cl-4	73
h	C_6H_4Cl-4	COC_6H_4Cl-4	78
i	C_6H_4Br-4	COC_6H_4Cl-4	61
j	Ph	COC_6H_4Br-4	78
k	C_6H_4Cl-4	COC_6H_4Br-4	61
l	C_6H_4Br-4	COC_6H_4Br-4	72
m	Ph	CO_2Et	96
n	C_6H_4Cl-4	CO_2Et	80
o	C_6H_4Br-4	CO_2Et	99
p	Ph	$CH{=}CHCO_2Et$	73
q	C_6H_4Cl-4	$CH{=}CHCO_2Et$	60
r	C_6H_4Br-4	$CH{=}CHCO_2Et$	74

a) The yield is from 5 to 8.

Chart 4

of **5a**—**f** are also very similar to those of thieno[3,4-*b*]indolizines prepared previously by us[2—5] except the signals of the 3-substituent, which appeared near δ 2.20 (2H, t, J=7.0 Hz, $C\underline{H}_2CN$) and 3.20 (2H, t, J=7.0 Hz, $SC\underline{H}_2$). Interestingly, a weak low field shift (δ 0.20—0.23 ppm) for the 5-proton in these molecules (**5a**—**f**) was observed, suggesting some participation of the **G1** conformation.

Syntheses of 3-(Acylmethylthio)-, and 3-[(3-Ethoxycarbonyl-2-propenyl)thio]thieno[3,4-*b*]indolizine Derivatives As might be expected, the deprotection of 3-[(2-cyanoethyl)thio]thieno[3,4-*b*]indolizine derivatives (**5a**—**c**) by treatment with potassium *tert*-butoxide in dimethylformamide (DMF) and the reactions of the resulting potassium thieno[3,4-*b*]indolizine-3-thiolate (**6a**—**c**) with chloroacetone (**2b**) afforded 3-(acetonylthio)thieno[3,4-*b*]indolizine derivatives (**7a**—**c**) in good yields. Similar reactions of **6a**—**c** with phenacyl bromide (**2c**), 4-chlorophenacyl bromide (**2d**), 4-bromophenacyl bromide (**2e**), ethyl bromoacetate (**2f**), and ethyl 4-bromocrotonate (**2g**) provided the corresponding 3-phenacylthio- (**7d**—**f**), 3-(4-chlorophenacylthio)- (**7g**—**i**), 3-(4-bromophenacylthio)- (**7j**—**l**), 3-(ethoxycarbonylmethylthio)- (**7m**—**o**), 3-[(3-ethoxycarbonyl-2-propenyl)thio]-thieno[3,4-*b*]indolizine derivatives (**7p**—**r**) in moderate to good yields respectively (Chart 3). Similarly, the deprotection of the 7-methyl compounds (**5e**—**f**), followed by the *S*-alkylations of the resulting potassium 7-methylthieno[3,4-*b*]indolizine-3-thiolates (**6d**—**f**) with **2b**—**g** gave the corresponding products (**8a**—**r**) in 61—99% yields (Chart 4).

The elemental analyses for these products (**7a**—**r**, **8a**—**r**) were in good accord with our proposed structures. The IR spectra of **7a**—**r** and **8a**—**r** showed an ester carbonyl band near 1680 cm^{-1} and a shifted ketone carbonyl band at

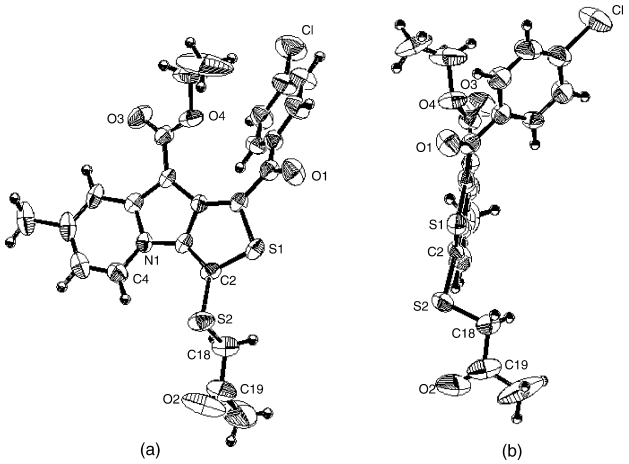


Fig. 3. ORTEP Drawings (the Over-View (a) and the Side-View (b)) of **8b**

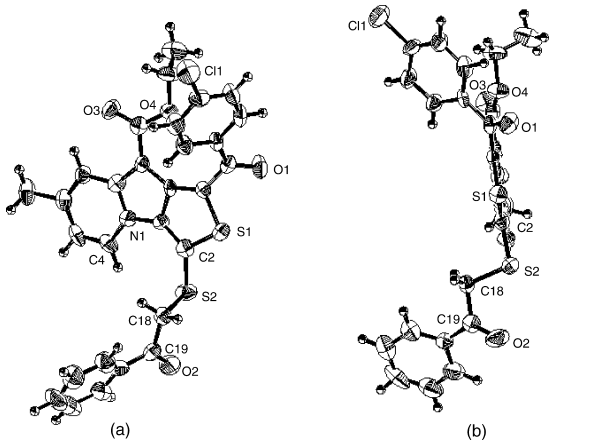


Fig. 4. ORTEP Drawings (the Over-View (a) and the Side-View (b)) of **8e**

1584—1638 cm^{-1}, together with a characteristic carbonyl band derived from the alkylating agents (**2b**—**g**) employed here. The UV spectra of **7a**—**r** and **8a**—**r** exhibited an absorption band near 440 nm attributable to the arene–π interaction, but their molar extinction coefficients were generally weaker than those observed for 3-(arylmethylthio)thieno[3,4-*b*]indolizines.[2—4] The characteristic bands of 3-acetonylthio (**7a**, **b**, **m**—**o**) and 3-ethoxycarbonylthio derivatives (**8m**, **n**) were particularly weak and only a shoulder was observed. The chemical shifts for the pyridine ring protons of **7a**—**r** and **8a**—**r** in the ^{1}H-NMR spectra were compared with those of ethyl 1-benzoyl-3-(methylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7s** (Ar=Ph, R^1=H)) and its 7-methyl derivatives **8s** (Ar=Ph, R^1=H)[2,3,9] which do not have any intramolecular interactions (see Tables 1, 2). As seen in these tables, the 5-protons in **7a**—**r** and **8a**—**r** appeared at lower magnetic fields than those of **7s** and **8s** respectively; the low field shifts for the 5-proton were in the range of δ 0.10—0.33 ppm and these values were comparable to those (δ 0.10—0.34) in 3-(allylthio)- and 3-(propargylthio)thieno[3,4-*b*]indolizines.[5] The X-ray analyses of 3-(acetonylthio)- (**8b**) and 3-(phenacylthio)thieno[3,4-*b*]indolizine (**8e**) showed only the **A1** form, while that of 3-[(3-ethoxycarbonyl-2-propenyl)-thio]thieno[3,4-*b*]indolizine (**7p**) exhibited the **G1** form. The ORTEP drawings[10] of compounds **8b**, **e** and **7p** are shown in Figs. 3—5. From the above results we could deduced the

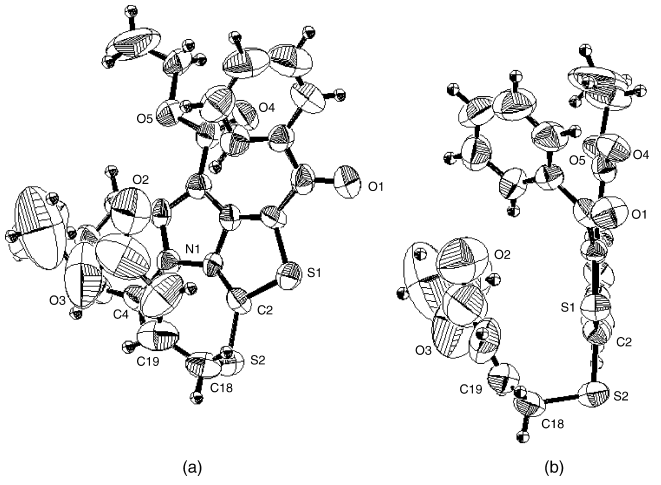


Fig. 5. ORTEP Drawings (the Over-View (a) and the Side-View (b)) of **7p**

small differences in the conformational stability of their gauche and anti forms.

Conformational Analyses by Mopac PM3 Calculations[6] Since molecular calculations for some 3-(2-propenylthio)thieno[3,4-*b*]indolizine derivatives were already described,[5] we performed the Mopac PM3 (precise) calculations for the optimized geometry of 3-(acylmethylthio)-thieno[3,4-*b*]indolizines (**7a**—**o**, **8a**—**o**) to obtain further conformational information. From theoretical consideration and the NMR spectral and X-ray analyses, we classified their possible conformers for compounds (**7a**, **d**, **m**) as seen in Fig. 6. As shown in this figure, there are 3 principal conformations for each Forms A and B. Furthermore, each principal form is subdivided into 4 conformations for a total of 12 conformations for both Forms, but only the subdivided ones for Form A were shown. In the Mopac calculations (Table 3) for these conformers the preferences of Form A over Form B and of the gauche form over the anti one were exhibited, but

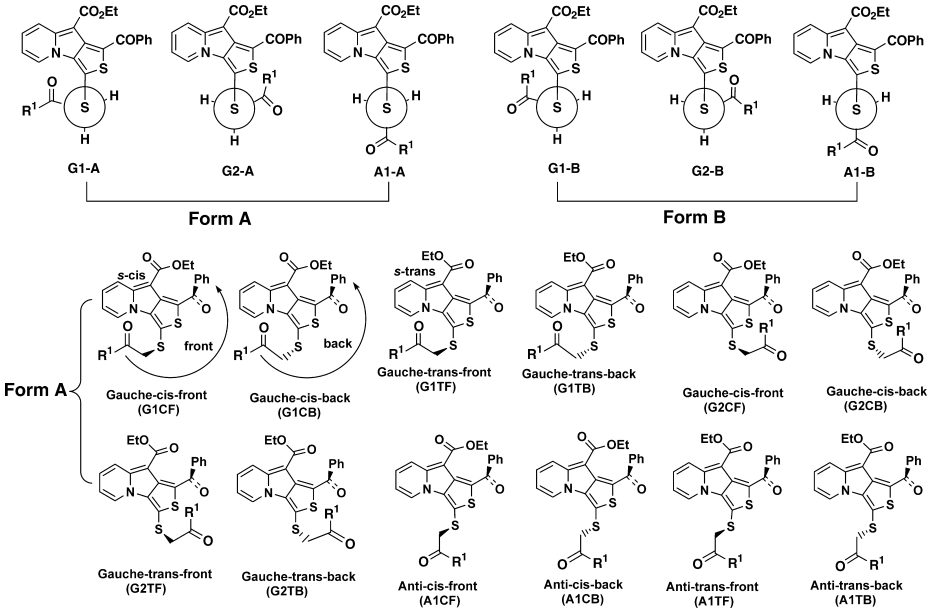


Fig. 6. Principal Conformations of **7a**, **d**, **m** and the Subdivided Comformations for Form A

Table 3. Mopac PM3 (Pricise) Calculation for 3-(Acylmethylthio)thieno[3,4-*b*]indolizines

No	Form	δ (G1CF-SV[a])	δ (G1CB-SV[a])	δ (G1TF-SV[a])	δ (G1TB-SV[a])	δ (G2CF-SV[a])	δ (G2CB-SV[a])
7a	A	0	−0.31616	0.61173	0.72023	0.57730	0.33898
	B	0.30446	0.10654	0.94197	0.83383	0.49503	0.25959
7d	A	0	−0.22287	0.61755	−0.32735	0.83979	0.84461
	B	0.56361	0.32223	1.18061	1.06583	0.79369	0.57246
7m	A	0	−0.23457	0.62409	0.51114	0.73079	0.46743
	B	0.32556	0.13561	0.97686	0.86542	0.09266	0.29681

No	Form	δ (G2TF-SV[a])	δ (G2TB-SV[a])	δ (A1CF-SV[a])	δ (A1CB-SV[a])	δ (A1TF-SV[a])	δ (A1TB-SV[a])
7a	A	1.24103	1.11019	to G1[b]	to G1[b]	to G1[b]	to G1[b]
	B	0.77756	0.72946	1.33927	1.06926	1.96084	1.85232
7d	A	1.28817	1.65032	to G1[b]	to G1[b]	to G1[b]	to G1[b]
	B	1.58782	1.03189	0.08601	1.16516	0.67672	0.59165
7m	A	1.20574	1.26289	to G1[b]	to G1[b]	to G1[b]	to G1[b]
	B	0.69800	0.76257	1.36884	1.09807	1.99289	1.88510

a) Optimized formation energy for G1CF conformation of form A: −44.17875 kcal/mol for **7a**; −8.71871 kcal/mol for **7d**; −89.20690 kcal/mol for **7m**. *b*) Conversion to G1 conformer.

the energy differences were expectedly small.

In conclusion, we synthesized some 3-(acylmethylthio)- and 3-[(3-ethoxycarbonyl-2-propenyl)thio]thieno[3,4-*b*]indolizines by using a new procedure *via* the *S*-protected 3-thiol derivatives, 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 ^{1}H-NMR spectra were determined with a Hitachi R-600 spectrometer (60 MHz) in deuteriochloroform with tetramethylsilane used as the internal standard; the chemical shifts are expressed in d values. The IR and UV spectra were taken with JASCO FT/IR-5300 IR and SHIMADZU UV-2450 spectrophotometers, respectively.

Preparation of Ethyl 1-Arylcarbonyl-3-(2-cyanoethylthio)thieno[3,4-*b*]indolizine-9-carboxylates. General Method A mixture of 1-(pyridinio)thiophene-2-thiolate (**1**, 2 mmol), 3-bromopropanenitrile (**2**, 2.2 mmol), and sodium iodide (2 g) in acetone (30 ml) was kept at 40 °C in a water bath under occasional stirring until the spot of the material (**1**) disappeared by TLC monitoring (0.5—1 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 any unaltered alkylating agent. Without further purification the resulting mixture involving pyridinium salt (**3**) was dissolved in chloroform (30 ml) and the solution was treated with DBU (0.40 g, 2.6 mmol) under stirring in an ice bath for 10 min and then with chloranil (0.492 g, 2 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 (**5**) were combined and concentrated at reduced pressure. Recrystallization of the crude product from ethanol afforded the corresponding ethyl 1-arylcarbonyl-3-(2-cyanoethylthio)thieno[3,4-*b*]indolizine-9-carboxylate. The ^{1}H-NMR spectral data for these compounds (**5a**—**f**) are shown in Tables 1 and 2, and some other results and properties are as follows:

Ethyl 1-Benzoyl-3-(2-cyanoethylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**5a**): 65% (from **1a** and 3-bromopropanenitrile (**2a**)), orange needles, mp 156—157 °C. IR (KBr) cm^{-1}: 2253, 1672, 1628. UV λ_{max} ($CHCl_3$) nm (log ε): 329 (4.03), 485 (3.94), *ca.* 510 (shoulder). *Anal.* Calcd for $C_{23}H_{18}N_2O_3S_2$: C, 63.57; H, 4.18; N, 6.45. Found: C, 63.87; H, 3.92; N, 6.38.

Ethyl 1-(4-Chlorobenzoyl)-3-(2-cyanoethylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**5b**): 69% (from **1b**, **2a**), orange needles, mp 153—154 °C. IR (KBr) cm^{-1}: 2251, 1678, 1622. UV λ_{max} ($CHCl_3$) nm (log ε): 328 (3.97), 484 (3.89), *ca.* 509 (shoulder). *Anal.* Calcd for $C_{23}H_{17}ClN_2O_3S_2$: C, 58.90; H, 3.65; N, 5.97. Found: C, 59.04; H, 3.76; N, 5.72.

Ethyl 1-(4-Bromobenzoyl)-3-(2-cyanoethylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**5c**): 66% (from **1c**, **2a**), red needles, mp 153—154 °C. IR (KBr) cm^{-1}: 2259, 1672, 1626. UV λ_{max} ($CHCl_3$) nm (log ε): 329 (4.07), 485 (3.99), *ca.* 508 (shoulder). *Anal.* Calcd for $C_{23}H_{17}BrN_2O_3S_2$: C, 53.81; H, 3.34; N, 5.46. Found: C, 53.90; H, 3.34; N, 5.36.

Ethyl 1-Benzoyl-3-(2-cyanoethylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**5d**): 60% (from **1d**, **2a**), red prisms, mp 150—151 °C. IR (KBr) cm^{-1}: 2251, 1669, 1613. UV λ_{max} ($CHCl_3$) nm (log ε): 329 (4.13), 482 (4.01), *ca.* 504 (shoulder). *Anal.* Calcd for $C_{24}H_{20}N_2O_3S_2$: C, 64.26; H, 4.49; N, 6.25. Found: C, 64.45; H, 4.45; N, 6.10.

Ethyl 1-(4-Chlorobenzoyl)-3-(2-cyanoethylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**5e**): 59% (from **1e**, **2a**), red prisms, mp 164—165 °C. IR (KBr) cm^{-1}: 2247, 1671, 1611. UV λ_{max} ($CHCl_3$) nm (log ε): 319 (4.13), 329 (4.13), 484 (4.03), *ca.* 506 (shoulder). *Anal.* Calcd for $C_{24}H_{19}ClN_2O_3S_2$: C, 59.68; H, 3.97; N, 5.80. Found: C, 59.86; H, 3.99; N, 5.59.

Ethyl 1-(4-Bromobenzoyl)-3-(2-cyanoethylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**5f**): 81% (from **1f**, **2a**), red flakes, mp 160—163 °C. IR (KBr) cm^{-1}: 2247, 1671, 1611. UV λ_{max} ($CHCl_3$) nm (log ε): 329 (4.03), 485 (4.05), *ca.* 507 (shoulder). *Anal.* Calcd for $C_{24}H_{19}BrN_2O_3S_2$: C, 54.65; H, 3.63; N, 5.31. Found: C, 54.79; H, 3.70; N, 5.10.

Preparation of Ethyl 1-Arylcarbonyl-3-(*R*-thio)thieno[3,4-*b*]indolizine-9-carboxylates. General Method A mixture of 3-[(2-cyanoethyl)-thio]thieno[3,4-*b*]indolizine (**5**, 1 mmol), potassium *tert*-butoxide (168 mg, 1.5 mmol), and DMF (3 ml) was heated at 80 °C in a water bath for 15 min, and then the generated acrylonitrile was completely evaporated at reduced pressure. To the solution of potassium thieno[2,3-*b*]indolizine-3-thiolate (**6**) an equimolar amount of alkylating agent (**2**) was added and allowed to react for a further 5 h at room temperature. The reaction mixture was acidified with diluted hydrochloric acid and the precipitated substances were collected by suction. The crude product was purified by column chromatography on alumina using chloroform as an eluent. The solvent was evaporated and the recrystallization from chloroform–ethanol gave the corresponding products (**7a**—**r**, **8a**—**r**). The ^{1}H-NMR spectral data for compounds (**7a**—**r**, **8a**—**r**) listed in Tables 1 and 2, and other data are as follows:

Ethyl 3-Acetonylthio-1-benzoylthieno[3,4-*b*]indolizine-9-carboxylate (**7a**): 97% (from **5a** and chloroacetone (**2b**)), red flakes, mp 153—154 °C. IR (KBr) cm^{-1}: 1715, 1684, 1608. UV λ_{max} ($CHCl_3$) nm (log ε): 327 (shoulder), 443 (shoulder), 479 (3.84), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{23}H_{19}NO_4S_2$: C, 63.14; H, 4.38; N, 3.20. Found: C, 63.22; H, 4.27; N, 3.22.

Ethyl 3-Acetonylthio-1-(4-chlorobenzoyl)thieno[3,4-*b*]indolizine-9-carboxylate (**7b**): 88% (from **5b**, **2b**), red needles, mp 145—146 °C. IR (KBr) cm^{-1}: 1717, 1686, 1611. UV λ_{max} ($CHCl_3$) nm (log ε): 327 (shoulder), 445 (shoulder), 483 (3.90), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{23}H_{18}ClNO_4S_2$: C, 58.53; H, 3.84; N, 2.97. Found: C, 58.60; H, 3.78; N, 2.96.

Ethyl 3-Acetonylthio-1-(4-bromobenzoyl)thieno[3,4-*b*]indolizine-9-carboxylate (**7c**): 85% (from **5c**, **2b**), red needles, mp 166—167 °C. IR (KBr) cm^{-1}: 1727, 1676, 1620. UV λ_{max} ($CHCl_3$) nm (log ε): 328 (shoulder), 443 (3.73), 483 (3.81), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{23}H_{18}BrNO_4S_2$: C, 53.49; H, 3.51; N, 2.71. Found: C, 53.55; H, 3.30; N, 2.86.

Ethyl 1-Benzoyl-3-(phenacylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7d**): 78% (from **5a** and phenacyl bromide (**2c**)), red needles, mp 162—163 °C. IR (KBr) cm^{-1}: 1690, 1665, 1607. UV λ_{max} ($CHCl_3$) nm (log ε): 328 (shoulder), 425 (3.74), 470 (3.63), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{28}H_{21}NO_4S_2$: C, 67.31; H, 4.24; N, 2.80. Found: C, 67.37; H, 4.21; N, 2.77.

Ethyl 1-(4-Chlorobenzoyl)-3-(phenacylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7e**): 84% (from **5b**, **2c**), red needles, mp 148—149 °C. IR (KBr) cm^{-1}: 1684, 1624. UV λ_{max} ($CHCl_3$) nm (log ε): 328 (shoulder), 431 (3.73), 472 (3.63), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{28}H_{20}ClNO_4S_2$: C, 62.97; H, 3.77; N, 2.62. Found: C, 63.04; H, 3.74; N, 2.58.

Ethyl 1-(4-Bromobenzoyl)-3-(phenacylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7f**): 78% (from **5c**, **2c**), red needles, mp 163—165 °C. IR (KBr) cm^{-1}: 1676, 1612. UV λ_{max} ($CHCl_3$) nm (log ε): 327 (shoulder), 431 (3.77), 472 (3.67), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{28}H_{20}BrNO_4S_2$: C, 58.13; H, 3.48; N, 2.42. Found: C, 58.23; H, 3.47; N, 2.33.

Ethyl 1-Benzoyl-3-(4-chlorophenacylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7g**): 77% (from **5a** and 4-chlorophenacyl bromide (**2d**)), red needles, mp 144—145 °C. IR (KBr) cm^{-1}: 1688, 1667, 1624. UV λ_{max} ($CHCl_3$) nm (log ε): 327 (shoulder), 427 (3.74), 471 (3.63), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{28}H_{20}ClNO_4S_2$: C, 62.97; H, 3.77; N, 2.62. Found: C, 62.94; H, 3.78; N, 2.65.

Ethyl 1-(4-Chlorobenzoyl)-3-(4-chlorophenacylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7h**): 68% (from **5b**, **2d**), red needles, mp 205—207 °C. IR (KBr) cm^{-1}: 1680, 1613. UV λ_{max} ($CHCl_3$) nm (log ε): 327 (shoulder), 431 (3.76), 471 (3.64), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{28}H_{19}Cl_2NO_4S_2$: C, 59.16; H, 3.37; N, 2.46. Found: C, 59.26; H, 3.30; N, 2.43.

Ethyl 1-(4-Bromobenzoyl)-3-(4-chlorophenacylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7i**): 72% (from **5c**, **2d**), red needles, mp 202—203 °C. IR (KBr) cm^{-1}: 1682, 1611. UV λ_{max} ($CHCl_3$) nm (log ε): 327 (shoulder), 432 (3.75), 473 (3.65), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{28}H_{19}BrClNO_4S_2$: C, 54.87; H, 3.12; N, 2.29. Found: C, 54.64; H, 2.98; N, 2.29.

Ethyl 1-Benzoyl-3-(4-bromophenacylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7j**): 78% (from **5a** and 4-bromophenacyl bromide (**2e**)), red flakes, mp 140—141 °C. IR (KBr) cm^{-1}: 1689, 1667, 1624. UV λ_{max} ($CHCl_3$) nm (log ε): 327 (shoulder), 434 (3.72), 477 (3.66), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{28}H_{20}BrNO_4S_2$: C, 58.13; H, 3.48; N, 2.42. Found: C, 58.16; H, 3.40; N, 2.47.

Ethyl 3-(4-Bromophenacylthio)-1-(4-chlorobenzoyl)thieno[3,4-*b*]indolizine-9-carboxylate (**7k**): 79% (from **5b**, **2e**), red needles, mp 214—215 °C. IR (KBr) cm^{-1}: 1680, 1613. UV λ_{max} ($CHCl_3$) nm (log ε): 328 (shoulder), 434 (3.74), 478 (3.67), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{28}H_{19}BrClNO_4S_2$: C, 54.87; H, 3.12; N, 2.29. Found: C, 54.97; H, 3.02; N, 2.29.

Ethyl 1-(4-Bromobenzoyl)-3-(4-bromophenacylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7l**): 80% (from **5c**, **2e**), red needles, mp 212—214 °C. IR (KBr) cm^{-1}: 1680, 1613. UV λ_{max} ($CHCl_3$) nm (log ε): 328 (shoulder), 434 (3.79), 477 (3.72), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{28}H_{19}Br_2NO_4S_2$: C, 51.16; H, 2.91; N, 2.13. Found: C, 51.14; H, 2.83; N, 2.22.

Ethyl 1-Benzoyl-3-(ethoxycarbonylmethylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7m**): 99% (from **5a** and ethyl bromoacetate (**2f**)), red prisms, mp 102—103 °C. IR (KBr) cm^{-1}: 1730, 1676, 1622. UV λ_{max} ($CHCl_3$) nm (log ε): 318 (4.06), 328 (4.05), 440 (shoulder), 480 (3.92), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{24}H_{21}NO_5S_2$: C, 61.65; H, 4.53; N, 3.00. Found: C, 61.68; H, 4.49; N, 3.01.

Ethyl 1-(4-Chlorobenzoyl)-3-(ethoxycarbonylmethylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7n**): 88% (from **5b**, **2f**), red needles, mp 122—124 °C. IR (KBr) cm^{-1}: 1723, 1665, 1630. UV λ_{max} ($CHCl_3$) nm (log ε): 328 (shoulder), 438 (shoulder), 482 (3.94), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{24}H_{20}ClNO_5S_2$: C, 57.42; H, 4.02; N, 2.79. Found: C, 57.71; H, 3.93; N, 2.50.

Ethyl 1-(4-Bromobenzoyl)-3-(ethoxycarbonylmethylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**7o**): 82% (from **5c**, **2f**), red flakes, mp 84—85 °C. IR (KBr) cm^{-1}: 1713, 1688, 1626. UV λ_{max} ($CHCl_3$) nm (log ε): 327 (shoulder), 440 (shoulder), 483 (3.94), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{24}H_{20}BrNO_5S_2$: C, 52.75; H, 3.69; N, 2.56. Found: C, 52.86; H, 3.65; N, 2.49.

Ethyl 1-Benzoyl-3-[(3-ethoxycarbonyl-2-propenyl)thio]thieno[3,4-*b*]indolizine-9-carboxylate (**7p**): 63% (from **5a** and ethyl 4-bromocrotonate (**2g**)), red prisms, mp 96—97 °C. IR (KBr) cm^{-1}: 1715, 1678, 1622. UV λ_{max} ($CHCl_3$) nm (log ε): 326 (shoulder), 437 (3.80), 477 (3.82), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{26}H_{23}NO_5S_2$: C, 63.27; H, 4.70; N, 2.84. Found: C, 63.17; H, 4.70; N, 2.94.

Ethyl 1-(4-Chlorobenzoyl)-3-[(3-ethoxycarbonyl-2-propenyl)thio]thieno-[3,4-*b*]indolizine-9-carboxylate (**7q**): 65% (from **5b**, **2g**), red needles, mp 127—128 °C. IR (KBr) cm^{-1}: 1715, 1672, 1622. UV λ_{max} ($CHCl_3$) nm (log ε): 326 (shoulder), 435 (3.84), 477 (3.78), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{26}H_{22}ClNO_5S_2$: C, 59.14; H, 4.20; N, 2.65. Found: C, 58.98; H, 4.12; N, 2.56.

Ethyl 1-(4-Bromobenzoyl)-3-[(3-ethoxycarbonyl-2-propenyl)thio]thieno-[3,4-*b*]indolizine-9-carboxylate (**7r**): 60% (from **5c**, **2f**), red needles, mp 117—118 °C. IR (KBr) cm^{-1}: 1717, 1674, 1622. UV λ_{max} ($CHCl_3$) nm (log ε): 326 (shoulder), 434 (3.83), 476 (3.78), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{26}H_{22}BrNO_5S_2$: C, 54.55; H, 3.87; N, 2.45. Found: C, 54.71; H, 3.73; N, 2.43.

Ethyl 3-Acetonylthio-1-benzoyl-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**8a**): 96% (from **5d**, **2b**), red prisms, mp 144—145 °C. IR (KBr) cm^{-1}: 1719, 1678, 1638. UV λ_{max} ($CHCl_3$) nm (log ε): 328 (shoulder), 438 (3.75), 474 (shoulder), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{24}H_{21}NO_4S_2$: C, 63.84; H, 4.69; N, 3.10. Found: C, 63.84; H, 4.66; N, 3.13.

Ethyl 3-Acetonylthio-1-(4-chlorobenzoyl)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**8b**): 80% (from **5e**, **2b**), red prisms, mp 160—161 °C. IR (KBr) cm^{-1}: 1719, 1680, 1637. UV λ_{max} ($CHCl_3$) nm (log ε): 329 (shoulder), 439 (3.81), 474 (shoulder), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{24}H_{20}ClNO_4S_2$: C, 59.31; H, 4.15; N, 2.88. Found: C, 59.30; H, 4.00; N, 3.04.

Ethyl 3-Acetonylthio-1-(4-bromobenzoyl)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**8c**): 99% (from **5f**, **2b**), red prisms, mp 148—149 °C. IR (KBr) cm^{-1}: 1719, 1678, 1637. UV λ_{max} ($CHCl_3$) nm (log ε): 330 (shoulder), 439 (3.82), 473 (shoulder), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{24}H_{20}BrNO_4S_2$: C, 54.34; H, 3.80; N, 2.64. Found: C, 54.41; H, 3.72; N, 2.65.

Ethyl 1-Benzoyl-7-methyl-3-(phenacylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**8d**): 93% (from **5d**, **2c**), red needles, mp 141—142 °C. IR (KBr) cm^{-1}: 1694, 1674, 1612. UV λ_{max} ($CHCl_3$) nm (log ε): 329 (shoulder), 432 (3.80), 477 (shoulder), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{29}H_{23}NO_4S_2$: C, 67.81; H, 4.51; N, 2.73. Found: C, 67.87; H, 4.53; N, 2.64.

Ethyl 1-(4-Chlorobenzoyl)-7-methyl-3-(phenacylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**8e**): 83% (from **5e**, **2c**), red prisms, mp 165—167 °C. IR (KBr) cm^{-1}: 1680, 1671, 1638. UV λ_{max} ($CHCl_3$) nm (log ε): 328 (shoulder), 432 (3.84), 478 (shoulder), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{29}H_{22}ClNO_4S_2$: C, 63.55; H, 4.05; N, 2.56. Found: C, 63.52; H, 4.24; N, 2.39.

Ethyl 1-(4-Bromobenzoyl)-7-methyl-3-(phenacylthio)thieno[3,4-*b*]indolizine-9-carboxylate (**8f**): 78% (from **5f**, **2c**), red needles, mp 170—171 °C. IR (KBr) cm^{-1}: 1694, 1674, 1618. UV λ_{max} ($CHCl_3$) nm (log ε): 328 (shoulder), 437 (3.81), 479 (shoulder), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{29}H_{22}BrNO_4S_2$: C, 58.79; H, 3.74; N, 2.36. Found: C, 59.00; H, 3.55; N, 2.34.

Ethyl 1-Benzoyl-3-(4-chlorophenacylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**8g**): 73% (from **5d**, **2d**), red needles, mp 144—145 °C. IR (KBr) cm^{-1}: 1674, 1636. UV λ_{max} ($CHCl_3$) nm (log ε): 328 (shoulder), 437 (3.80), 478 (shoulder), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{29}H_{22}ClNO_4S_2$: C, 63.55; H, 4.05; N, 2.56. Found: C, 63.65; H, 3.88; N, 2.43.

Ethyl 1-(4-Chlorobenzoyl)-3-(4-chlorophenacylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**8h**): 78% (from **5e**, **2d**), red needles, mp 201—202 °C. IR (KBr) cm^{-1}: 1676, 1638. UV λ_{max} ($CHCl_3$) nm (log ε): 329 (shoulder), 437 (3.80), 479 (shoulder), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{29}H_{21}Cl_2NO_4S_2$: C, 59.79; H, 3.63; N, 2.40. Found: C, 59.93; H, 3.52; N, 2.37.

Ethyl 1-(4-Bromobenzoyl)-3-(4-chlorophenacylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**8i**): 61% (from **5f**, **2d**), red needles, mp 196—197 °C. IR (KBr) cm^{-1}: 1676, 1638. UV λ_{max} ($CHCl_3$) nm (log ε): 329 (shoulder), 437 (3.81), 479 (shoulder), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{29}H_{21}BrClNO_4S_2$: C, 55.56; H, 3.38; N, 2.23. Found: C, 55.66; H, 3.28; N, 2.23.

Ethyl 1-Benzoyl-3-(4-bromophenacylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**8j**): 78% (from **5d**, **2e**), red prisms, mp 148—150 °C. IR (KBr) cm^{-1}: 1671, 1637. UV λ_{max} ($CHCl_3$) nm (log ε): 328 (shoulder), 433 (3.90), 476 (shoulder), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{29}H_{22}BrNO_4S_2$: C, 58.79; H, 3.74; N, 2.36. Found: C, 58.78; H, 3.73; N, 2.38.

Ethyl 3-(4-Bromophenacylthio)-1-(4-chlorobenzoyl)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**8k**): 61% (from **5e**, **2e**), red needles, mp 212—213 °C. IR (KBr) cm^{-1}: 1676, 1638. UV λ_{max} ($CHCl_3$) nm (log ε): 329 (shoulder), 438 (3.81), 479 (shoulder), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{29}H_{21}BrClNO_4S_2$: C, 55.56; H, 3.38; N, 2.23. Found: C, 55.61; H, 3.29; N, 2.26.

Ethyl 1-(4-Bromobenzoyl)-3-(4-bromophenacylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**8l**): 72% (from **5f**, **2e**), red needles, mp 210—211 °C. IR (KBr) cm^{-1}: 1676, 1638. UV λ_{max} ($CHCl_3$) nm (log ε): 329 (shoulder), 437 (3.80), 480 (shoulder), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{29}H_{21}Br_2NO_4S_2$: C, 51.88; H, 3.15; N, 2.09. Found: C, 51.90; H, 3.11; N, 2.11.

Ethyl 1-Benzoyl-3-(ethoxycarbonylmethylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**8m**): 96% (from **5d**, **2f**), red needles, mp 101—102 °C. IR (KBr) cm^{-1}: 1734, 1674, 1613. UV λ_{max} ($CHCl_3$) nm (log ε): 328 (shoulder), 445 (shoulder), 482 (3.90), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{25}H_{23}NO_5S_2$: C, 62.35; H, 4.81; N, 2.91. Found: C, 62.58; H, 4.80; N, 2.68.

Ethyl 1-(4-Chlorobenzoyl)-3-(ethoxycarbonylmethylthio)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**8n**): 80% (from **5e**, **2f**), red needles, mp 135—136 °C. IR (KBr) cm^{-1}: 1721, 1676, 1632. UV λ_{max} ($CHCl_3$) nm (log ε): 328 (shoulder), 448 (shoulder), 482 (3.90), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{25}H_{22}ClNO_5S_2$: C, 58.19; H, 4.30; N, 2.71. Found: C, 58.13; H, 4.41; N, 2.75.

Ethyl 1-(4-Bromobenzoyl)-3-(ethoxycarbonylmethylthio)-7-methylthieno-[3,4-*b*]indolizine-9-carboxylate (**8o**): 99% (from **5f**, **2f**), red needles, mp 134—135 °C. IR (KBr) cm^{-1}: 1719, 1674, 1632. UV λ_{max} ($CHCl_3$) nm (log ε): 329 (shoulder), 445 (3.83), 481 (3.86), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{25}H_{22}BrNO_5S_2$: C, 53.57; H, 3.96; N, 2.50. Found: C, 53.84; H, 3.94; N, 2.43.

Ethyl 1-Benzoyl-3-[(3-ethoxycarbonyl-2-propenyl)thio]-7-methylthieno-[3,4-*b*]indolizine-9-carboxylate (**8p**): 73% (from **5d**, **2g**), red prisms, mp 141—142 °C. IR (KBr) cm^{-1}: 1715, 1676, 1622. UV λ_{max} ($CHCl_3$) nm (log ε): 327 (shoulder), 435 (3.89), 474 (shoulder), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{27}H_{25}NO_5S_2$: C, 63.88; H, 4.96; N, 2.76. Found: C, 64.07; H, 4.92; N, 2.61.

Ethyl 1-(4-Chlorobenzoyl)-3-[(3-ethoxycarbonyl-2-propenyl)thio]-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**8q**): 60% (from **5e**, **2g**), red prisms, mp 138—139 °C. IR (KBr) cm^{-1}: 1715, 1672, 1622. UV λ_{max} ($CHCl_3$) nm (log ε): 328 (shoulder), 439 (3.91), 474 (shoulder), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{27}H_{24}ClNO_5S_2$: C, 59.83; H, 4.46; N, 2.52. Found: C, 59.91; H, 4.45; N, 2.51.

Ethyl 1-(4-Bromobenzoyl)-3-[(3-ethoxycarbonyl-2-propenyl)thio]-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (**8r**): 74% (from **5f**, **2f**), red prisms, mp 104—106 °C. IR (KBr) cm^{-1}: 1715, 1674, 1622. UV λ_{max} ($CHCl_3$) nm (log ε): 327 (shoulder), 440 (3.88), 474 (shoulder), *ca.* 500 (shoulder). *Anal.* Calcd for $C_{27}H_{24}BrNO_5S_2$: C, 55.29; H, 4.12; N, 2.39. Found: C, 55.42; H, 3.98; N, 2.40.

Crystallography of Ethyl 1-Benzoyl-3-[(3-ethoxycarbonyl-2-propenyl)thio]thieno[3,4-*b*]indolizine-9-carboxylate (7p) A red prismatic single crystal (0.12×0.36×0.42 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: **7p**: $C_{26}H_{23}NO_5S_2$; M=493.59; monoclinic, space group $P2_1/n$ (#14), Z=4

with $a=14.455(4)$ Å, $b=11.811(5)$ Å, $c=15.705(3)$ Å, $\beta=115.00(1)°$; $V=2430(1)$ Å^3 and $D_{calc.}=1.349$ g/cm^3. All calculations were performed using the teXsan package.[11] The structure was solved by a direct method (SIR).[12] 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 0.082 and 0.075 for 1808 ($I>2.00\sigma(I)$) observed reflections, respectively.

Crystallography of Ethyl 3-Acetonylthio-1-(4-chlorobenzoyl)-7-methylthieno[3,4-*b*]indolizine-9-carboxylate (8b) A red prismatic single crystal (0.06×0.42×0.84 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 ($\lambda=0.71069$ Å). Crystal data of these compounds are as follows: **8b**: $C_{24}H_{20}ClNO_4S_2$; $M=486.00$; monoclinic, space group $P2_1/a$ (#14), $Z=4$ with $a=14.31(1)$ Å, $b=11.13(1)$ Å, $c=15.06(1)$ Å, $\beta=100.80(6)°$; $V=2355(3)$ Å^3 and $D_{calc.}=1.371$ g/cm^3. All calculations were performed using the teXsan package.[11] The structure was solved by a direct method (SIR).[12] 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 0.071 and 0.071 for 2192 ($I>2.00\sigma(I)$) observed reflections, respectively.

Crystallography of Ethyl 1-(4-Chlorobenzoyl)-7-methyl-3-(phenacylthio)thieno[3,4-*b*]indolizine-9-carboxylate (8e) A red dark prismatic single crystal (0.20×0.62×0.62 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 ($\lambda=0.71069$ Å). The crystal data of these compounds are as follows: **8e**: $C_{29}H_{22}ClNO_4S_2$; $M=548.07$; orthorohmbic, space group $Pbca$ (#61), $Z=8$ with $a=14.11(1)$ Å, $b=31.64(1)$ Å, $c=11.34(1)$ Å; $V=5066(6)$ Å^3 and $D_{calc.}=1.437$ g/cm^3. All calculations were performed using the teXsan package.[11] The structure was solved by a direct method (SIR).[12] 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 0.074 and 0.066 for 2058 ($I>2.00\sigma(I)$) observed reflections, respectively.

References and Notes

1) For part 58 of this series, see Kakehi A., Suga H., Kaneko Y., Fujii T., Tanaka N., *Chem. Pharm. Bull.*, **53**, 1430—1438 (2005).
2) Kakehi A., Ito S., Suga H., Miwa T., Mori T., Kobayashi T., *Heterocycles*, **57**, 17—20 (2002).
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6) "WinMOPAC (Version 3.0)," Fujitsu Corporation.
7) The presentation of each conformation is for the sulfide bond in these molecules.
8) The formation energies (FEg and FEa) for the opitimized gauche and anti conformations are as follows: ethyl methyl sulfide (FEg=−15.1451 kcal/mol and FEa=−14.1033 kcal/mol); benzyl methyl sulfide (FEg=17.9939 kcal/mol and FEa=19.4272 kcal/mol); ethyl phenyl sulfide (FEg=18.8116 kcal/mol and FEa=20.2082).
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