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# PREPARATION OF NEW NITROGEN-BRIDGED HETEROCYCLES. 50.[1] SYNTHESES OF SOME HETEROCYCLIC COMPOUNDS STARTING FROM PYRIDINIUM 1-(ETHOXYCARBONYLACETYL)METHYLIDES

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***Abstract*** - The reactions of the title methylides with dialkyl acetylene-dicarboxylates gave the corresponding 3-(ethoxycarbonylacetyl)-indolizine derivatives, whose 3-substituent was smoothly converted to a coumarin skeleton by Knoevenagel reaction with salicylaldehyde. The reactions of the methylides with carbon disulfide and alkylating agent in the presence of a base afforded pyridinium 1-[alkylthio-(thiocarbonyl)](ethoxycarbonylacetyl)methylides, and the *S*-alkylations of these ylides with phenacyl bromides and subsequent alkaline treatment of the resulting pyridinium salts gave ethyl 3-alkylthio-1-(arylcarbonyl)thieno[3,4-*b*]indolizine-9-carboxylates.

## INTRODUCTION

In our recent papers[1,2] we described the preparation of ethyl 1-cyanothieno[3,4-*b*]indolizine-9-carboxylates from the treatment of 1-(1-cyanomethylthio-4-ethoxycarbonyl-1,3-butadien-2-yl)pyridinium halides (see salt (**A**) in Figre 1) with a base and then a dehydrogenating agent. However, the yields of these tricyclic products were generally low and our several attempts to improve them were unsuccessful.[2] A principal reason for their low efficiency is that an alternative pyrido[1,2-*d*][1,4]thiazine pathway (Path B)[3] leading to ethyl 3-(1-cyanoindolizin-3-yl)acrylate from salt (**A**) is more favorable than the Michael addition one (Path A) to key intermediate (**C**) for thieno[3,4-*b*]indolizine.[1,2] The retrosynthesis of intermediate (**C**) disclosed also the possibility of its access from the intramolecular condensation route of 1-[1-(ethoxycarbonylacetyl)-2-(substituted methylthio)vinyl]pyridinium halide such as salt (**B**). In

† Dedicated to Professor Shô Itô in celebration of his 77th birthday.

tum, we assumed that salt (**B**) could be derived from pyridinium 1-[[alkylthio(thiocarbonyl)]-(ethoxycarbonylacetyl)]methylide, and the methylide from 1-(ethoxycarbonylacetonyl)- pyridinium halide. In order to confirm this assumption we first examined the reactivity of the title methylides, especially their cycloaddition reactions with acetylenic compounds, and then the independent synthesis of thieno[3,4-*b*]indolizine derivatives.

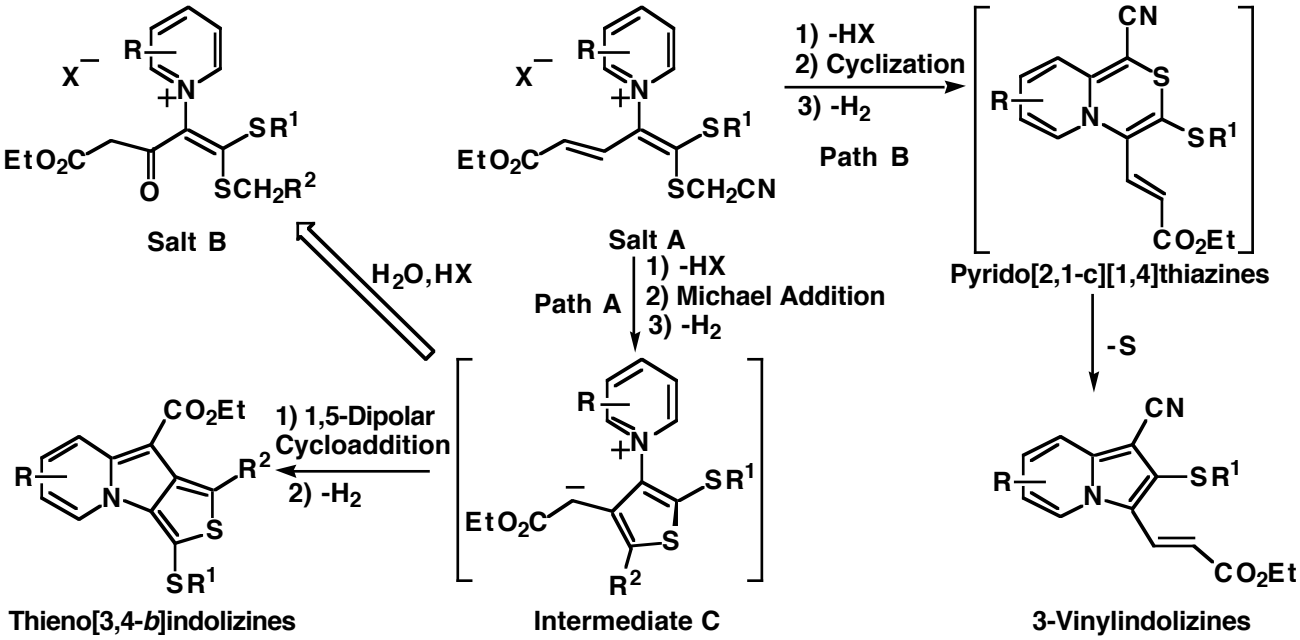
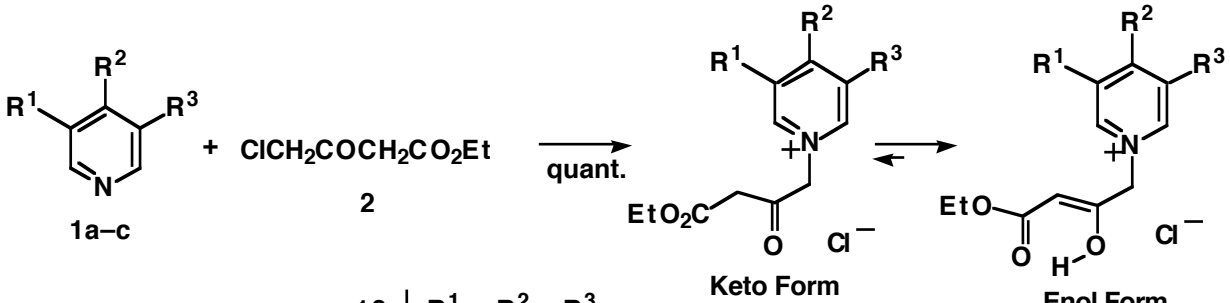



**Figure 1**

## RESULTS AND DISCUSSION

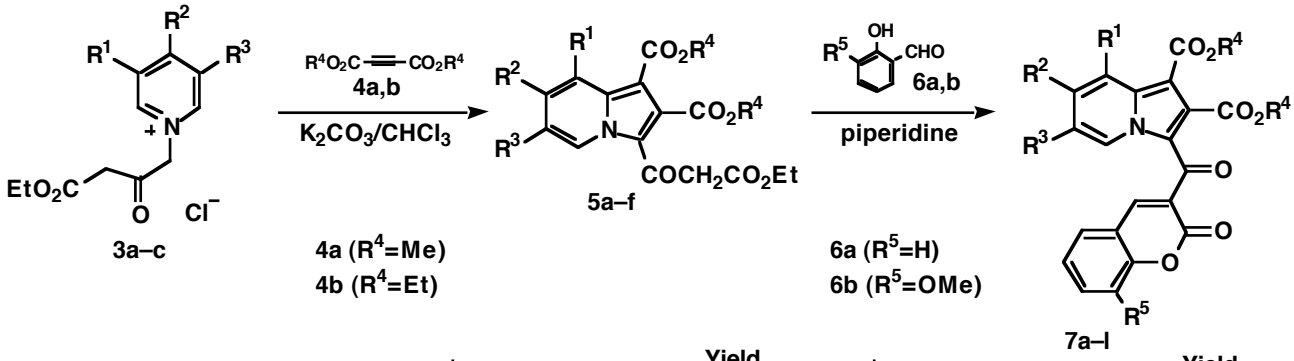
The corresponding pyridinium salts (**3a**—**c**) were quantitatively obtained from the reactions of pyridine derivatives (**1a**—**c**) with ethyl 4-chloroacetoacetate (**2**) without solvent (Scheme 1). The $^1$H-NMR spectra of **3a**—**c** were clearly showed that these salts are present as the enol form rather than the keto form, because an olefin proton and a hydroxy proton signal were appeared at near $\delta$ 6.6 and at $\delta$ 8.5—9.0, respectively, but no active methylene proton signal was detected.




| 1,3 | $R^1$ | $R^2$ | $R^3$ |
|---|---|---|---|
| a | H | H | H |
| b | H | Me | H |
| c | Me | H | Me |

**Scheme 1**

In order to investigate the reactivity of pyridinium salts (**3a**—**c**)[4] we first carried out the generation of pyridinium 1-(ethoxycarbonylacetyl)methylides from **3a**—**c** and the 1,3-dipolar cycloaddition with acetylenic compounds. When pyridinium salts (**3a**—**c**) were allowed to react with dimethyl acetylenedicarboxylate (**4a**) and chloranil in chloroform at room temperature, the expected dimethyl 3-(ethoxycarbonylacetyl)indolizine-1,2-dicarboxylates (**5a**—**c**) were obtained in 45, 46, 51% yields, respectively. Similar treatment of **3a**—**c**, diethyl acetylenedicarboxylate (**4b**), and chloranil afforded products (**5d**—**f**) in 52—79% yields. The structures of **5a**—**f** were simply determined by the analytical and spectral means. For example, these 1,3-dipolar bicycloadducts (**5a**—**f**) gave satisfactory analyses and a characteristic singlet signal due to the active methylene group in the 3-substituent exhibited at near δ 3.9 in their $^1$H-NMR spectra. Furthermore, the presence of an ethoxycarbonylacetyl group in the molecule was also indicated by its conversion to (3-coumarinyl)carbonyl group. The Knoevenagel reactions of **5a**—**f** with salicylaldehyde (**6a**) or orthovanillin (**6b**) in the presence of piperidine gave the corresponding dimethyl and diethyl 3-[(3-coumarinyl)carbonyl]indolizine-1,2-dicarboxylates (**7a**—**l**) in 16—88% yields. (Scheme 2) In the $^1$H-NMR spectra of **7a**—**l** a characteristic singlet signal attributable to the 4'-proton on the coumarin ring appeared at near δ 7.8, together with the other signals due to the familiar indolizine and phenyl protons.



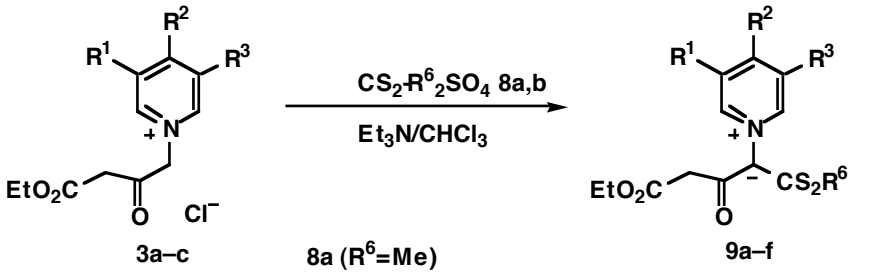

| 5 | $R^1$ | $R^2$ | $R^3$ | $R^4$ | Yield (%) |
|---|---|---|---|---|---|
| a | H | H | H | Me | 45 |
| b | H | Me | H | Me | 46 |
| c | Me | H | Me | Me | 51 |
| d | H | H | H | Et | 52 |
| e | H | Me | H | Et | 54 |
| f | Me | H | Me | Et | 79 |

| 7 | $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Yield (%) |
|---|---|---|---|---|---|---|
| a | H | H | H | Me | H | 73 |
| b | H | Me | H | Me | H | 54 |
| c | Me | H | Me | Me | H | 85 |
| d | H | H | H | Et | H | 30 |
| e | H | Me | H | Et | H | 25 |
| f | Me | H | Me | Et | H | 32 |
| g | H | H | H | Me | OMe | 88 |
| h | H | Me | H | Me | OMe | 49 |
| i | Me | H | Me | Me | OMe | 97 |
| j | H | H | H | Et | OMe | 41 |
| k | H | Me | H | Et | OMe | 16 |
| l | Me | H | Me | Et | OMe | 34 |

**Scheme 2**

We next examined the preparation of pyridinium 1-[[alkylthio(thiocarbonyl)](ethoxycarbonyl-acetyl)]methylide from 1-(ethoxycarbonylacetonyl)pyridinium chlorides (**3a**—**c**). However

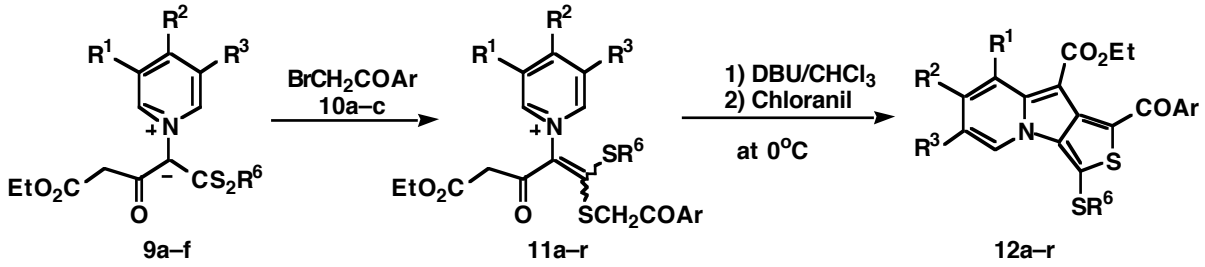
the reactions of **3a**—**c** with carbon disulfide and alkylating agent under usual basic conditions using a strong base such as sodium hydroxide and sodium ethoxide[5] gave only complex mixtures and the expected 1-[[alkylthio(thiocarbonyl)](ethoxycarbonylacetyl)]-methylides such as **9a**—**f** could not be obtained. After further exploration of the reaction conditions, we found that the use of a comparatively weak base gives good result for the preparation of **9a**—**f**. The reactions of salts (**3a**—**c**) with carbon disulfide and dimethyl (**8a**) or diethyl sulfate (**8b**) in the presence of excess triethylamine afforded the corresponding pyridinium methylides (**9a**—**f**) in moderate yields (26—47%, Scheme 3). In contrast with pyridinium salts (**3a**—**c**), the $^1$H-NMR spectra of **9a**—**f** exhibited a singlet signal (near $\delta$ 4.0) due to the active methylene group in the ethoxycarbonylacetyl moiety, but did not any enol proton signals. Perhaps, this group may be present only the keto form to stabilize the ylidic carbanion.




| 9 | $R^1$ | $R^2$ | $R^3$ | $R^6$ | Yield (%) |
|---|---|---|---|---|---|
| a | H | H | H | Me | 44 |
| b | H | Me | H | Me | 37 |
| c | Me | H | Me | Me | 34 |
| d | H | H | H | Et | 47 |
| e | H | Me | H | Et | 35 |
| f | Me | H | Me | Et | 26 |

**Scheme 3**

As first expected, the *S*-alkylation of pyridinium 1-[[methylthio- and ethylthio(thiocarbonyl)]-(ethoxycarbonylacetyl)]methylides (**9a**—**f**) with phenacyl bromide (**10a**), followed by the treatment of the resulting pyridinium salts (**11a**—**f**) with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and chloranil at 0°C afforded the corresponding ethyl 1-benzoyl-3-methylthio- (**12a**—**c**) and (ethylthio)thieno[3,4-*b*]indolizine-9-carboxylates (**12d**—**f**) in 11—59% yields. Similar reactions of **9a**—**f** with *p*-chlorophenacyl bromide (**10b**) or *p*-bromophenacyl bromide (**10c**) gave 1-(*p*-chlorobenzoyl)- (**12g**—**l**) or 1-(*p*-bromobenzoyl)thieno[3,4-*b*]indolizine derivatives (**12m**—**r**) in 11—70% yields. These results are shown in Scheme 4. These products (**12a**—**r**) are strong fluorescent and somewhat unstable substances in comparison with those of thieno[2,3-*b*]indolizine derivatives.[6] Elemental analyses of **12a**—**r** were in good accord with the proposed compositions and IR and $^1$H-NMR spectra also supported these structures. In particular, the chemical shifts and signal patterns for the skeletal and methyl protons on the pyridine ring in $^1$H-NMR spectra were very similar to those for thieno[3,4-*b*]indolizines




| 10 | Ar |
|---|---|
| a | Ph |
| b | $C_6H_4Cl$-*p* |
| c | $C_6H_4Br$-*p* |

| 12 | $R^1$ | $R^2$ | $R^3$ | $R^6$ | Ar | Yield (%) |
|---|---|---|---|---|---|---|
| a | H | H | H | Me | Ph | 12 |
| b | H | Me | H | Me | Ph | 22 |
| c | Me | H | Me | Me | Ph | 36 |
| d | H | H | H | Et | Ph | 16 |
| e | H | Me | H | Et | Ph | 11 |
| f | Me | H | Me | Et | Ph | 59 |
| g | H | H | H | Me | $C_6H_4Cl$-*p* | 18 |
| h | H | Me | H | Me | $C_6H_4Cl$-*p* | 29 |
| i | Me | H | Me | Me | $C_6H_4Cl$-*p* | 28 |
| j | H | H | H | Et | $C_6H_4Cl$-*p* | 16 |
| k | H | Me | H | Et | $C_6H_4Cl$-*p* | 14 |
| l | Me | H | Me | Et | $C_6H_4Cl$-*p* | 70 |
| m | H | H | H | Me | $C_6H_4Br$-*p* | 11 |
| n | H | Me | H | Me | $C_6H_4Br$-*p* | 18 |
| o | Me | H | Me | Me | $C_6H_4Br$-*p* | 20 |
| p | H | H | H | Et | $C_6H_4Br$-*p* | 25 |
| q | H | Me | H | Et | $C_6H_4Br$-*p* | 17 |
| r | Me | H | Me | Et | $C_6H_4Br$-*p* | 65 |

**Scheme 4**

prepared earlier by us,[1,2] but considerable up-field shifts (δ 0.2—0.8) for the 9-ethoxycarbonyl proton signals were observed. The origin of this phenomenon seemed to be a shielding effect owing to the phenyl ring in the 1-substituent of **12a—r**, and this was confirmed by X-Ray analysis of compounds (**12g**). The ORTEP drawing[7] for **12g** is shown in Figure 2, and the dihedral angle between least-squares planes of the thieno[3,4-*b*]indolizine and the benzene ring was considerably large (49.8 °C).

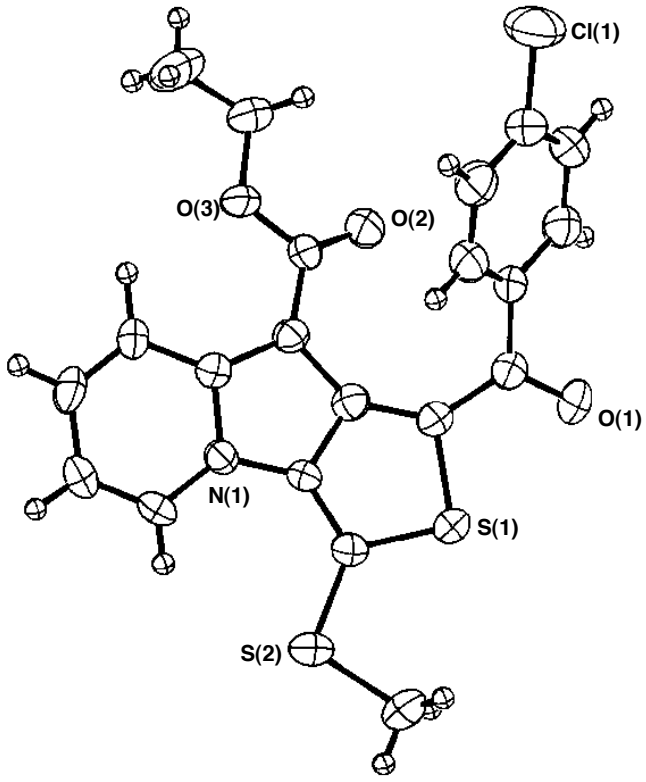



**Figure 2. ORTEP drawing of 12g**

## 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 as an internal standard; the chemical shifts are expressed in δ values. The IR spectra were taken with a JASCO FT/IR-5300 IR spectrophotometer.

**Preparations of 1-(ethoxycarbonylacetonyl)pyridinium chlorides. General method**: A mixture of pyridine derivatives (**1**, 0.1 mol) and ethyl 4-chloroacetoacetate (**2**, 16.5 g, 0.1 mol) was allowed to react at rt for 1 d. The corresponding pyridinium salts (**3a**–**c**) which were separated were washed with 3 portions of ether (150 mL) and dried under reduced pressure. These pyridinium salts (**3a**–**c**) were extremely hygroscopic substances and, hence, the preparation of pure samples for the analysis and the melting point measurement were unsuccessful. These salts (**3a**–**c**) were used for subsequent reactions without further purification.

**1-(Ethoxycarbonylacetonyl)pyridinium chlorides (3a)**: yield 100% (from **1a** and **2**), colorless crystals; IR (KBr) 3418, 1743, 1637 cm$^{-1}$; $^1$H-NMR ($CDCl_3$) 1.25 (3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 4.03 (2H, s, $COCH_2$), 4.16 (2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 6.67 (1H, s, C=CH),7.8–8.8 (3H, m, 3, 4, 5-H), 8.91 (1H, br s, OH), 9.41 (2H, br d, *J*=7.0 Hz, 2, 6-H).

**1-Ethoxycarbonylacetonyl-4-methylpyridinium chlorides (3b)**: yield 100% (from **1b** and **2**), colorless crystals; IR (KBr) 3429, 1732, 1645 cm$^{-1}$; $^1$H-NMR ($CDCl_3$) 1.25 (3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 2.67 (3H, s, 4-$CH_3$), 3.99 (2H, s, $COCH_2$), 4.12 (2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 6.59 (1H, s, C=CH), 8.80 (2H, brd, *J*=7.0 Hz, 3, 5-H), 8.69 (1H, brs, OH), 9.21 (2H, brd, *J*=7.0 Hz, 2, 6-H).

**1-Ethoxycarbonylacetonyl-3,5-dimethylpyridinium chlorides (3c)**: yield 100% (from **1c** and **2**), colorless crystals; IR (KBr) 3387. 1730, 1633 cm$^{-1}$; $^1$H-NMR ($CDCl_3$) 1.28 (3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 2.57 (6H, s, 3, 5-$CH_3$), 4.02 (2H, s, $COCH_2$), 4.19 (2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 6.63 (1H, s, C=CH), 8.06 (1H, br s, 4-H), 8.50 (1H, br s, OH), 9.00 (2H, br s, 2, 6H).

**Reactions of 1-(ethoxycarbonylacetonyl)pyridinium chlorides with acetylenic compounds in the presence of a base. General method:** A chloroform solution (80 mL) of 1-(ethoxycarbonylacetonyl)pyridinium chlorides (**3**, 5 mmol) and dialkyl acetylenedicarboxylate (**4**, 6 mmol) was treated with triethylamine (0.606 g, 6 mmol) under stirring at rt for 3 h, and then chloranil (1.229g, 5 mmol) was added to the solution. The resulting mixture was stirred at rt for further 12 h. After the filtration of the mixture to remove

the insoluble substances, the filtrate was concentrated at reduced pressure and the residue was separated by column chromatography on alumina using chloroform. Recrystallization of the crude product from chloroform-hexane gave the corresponding dialkyl 3-(ethoxycarbonylacetyl)indolizine-1,2-dicarboxylate (**5**) as colorless needles.

**Dimethyl 3-(ethoxycarbonylacetyl)indolizine-1,2-dicarboxylate (5a)**: yield 45% (from **3a** and **4a**), mp 105—107°C; IR (KBr) 1732, 1645 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 1.29 (3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 3.89 (2H, s, $COCH_2$), 3.94, 4.05 (each 3H, s, $OCH_3$), 4.25 (2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 7.12 (1H, br t, *J*=7.0 Hz, 6-H), 7.53 (1H, br dd, *J*=7.0, 9.0 Hz, 7-H), 8.41 (1H, br d, *J*=9.0 Hz, 8-H), 10.09 (1H, br d, *J*=7.0 Hz, 5-H). *Anal.* Calcd for $C_{17}H_{17}NO_7$: C, 58.79; H, 4.93; N, 4.03. Found: C, 58.73; H, 4.97; N, 4.00.

**Dimethyl 3-ethoxycarbonylacetyl-7-methylindolizine-1,2-dicarboxylate (5b)**: yield 46% (from **3b** and **4a**), mp 137—139°C; IR (KBr) 1743, 1641 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 1.29 (3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 2.48 (3H, s, 7-$CH_3$), 3.85 (2H, s, $COCH_2$), 3.90, 4.03 (each 3H, s, $OCH_3$), 4.21 (2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 6.96 (1H, dd, *J*=7.0, 2.0 Hz, 6-H), 8.15 (1H, br s, 8-H), 9.88 (1H, d, *J*=7.0 Hz, 5-H). *Anal.* Calcd for $C_{18}H_{19}NO_7$: C, 59.83; H, 5.30; N, 3.88. Found: C, 59.79; H, 5.38; N, 3.96.

**Dimethyl 3-ethoxycarbonylacetyl-6,8-dimethylindolizine-1,2-dicarboxylate (5c)**: yield 51% (from **3c** and **4a**), mp 142—143°C; IR (KBr) 1739, 1628 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 1.28 (3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 2.36 (3H, s, 6-$CH_3$), 2.61 (3H, s, 8-$CH_3$), 3.88 (2H, s, $COCH_2$), 3.92, 4.00 (each 3H, s, $OCH_3$), 4.24 (2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 7.10 (1H, br s, 7-H), 9.80 (1H, br s, 5-H). *Anal.* Calcd for $C_{19}H_{21}NO_7$: C, 60.79; H, 5.64; N, 3.73. Found: C, 60.88; H, 5.67; N, 3.57.

**Diethyl 3-(ethoxycarbonylacetyl)indolizine-1,2-dicarboxylate (5d)**: yield 52% (from **3a** and **4b**), mp 104—106°C; IR (KBr) 1734, 1641 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 1.29, 1.39, 1.42 (each 3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 3.91 (2H, s, $COCH_2$), 4.24, 4.39, 4.53 (each 2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 7.13 (1H, br t, *J*=7.0 Hz, 6-H), 7.51 (1H, br dd, *J*=7.0, 9.0 Hz, 7-H), 8.45 (1H, br d, *J*=9.0 Hz, 8-H), 10.03 (1H, br d, *J*=7.0 Hz, 5-H). *Anal.* Calcd for $C_{19}H_{21}NO_7$: C, 60.79; H, 5.64; N, 3.73. Found: C, 60.92; H, 5.62; N, 3.63.

**Diethyl 3-ethoxycarbonylacetyl-7-methylindolizine-1,2-dicarboxylate (5e)**: yield 54% (from **3b** and **4b**), mp 119—121°C; IR (KBr) 1738, 1628 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 1.30, 1.40, 1.43 (each 3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 2.50 (3H, s, 7-$CH_3$), 3.90 (2H, s, $COCH_2$), 4.23, 4.38, 4.51 (each 2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 6.95 (1H, dd, *J*=7.0, 2.0 Hz, 6-H), 8.22 (1H, br s, 8-H), 9.92 (1H, d, *J*=7.0 Hz, 5-H). *Anal.* Calcd for $C_{20}H_{23}NO_7$: C, 61.69; H, 5.95; N, 3.60. Found: C, 61.87; H, 5.99; N, 3.55.

**Diethyl 3-ethoxycarbonylacetyl-6,8-dimethylindolizine-1,2-dicarboxylate (5f)**:

yield 79% (from **3c** and **4b**), mp 81—83°C; IR (KBr) 1745, 1630 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 1.28, 1.38, 1.40 (each 3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 2.33 (3H, s, 6-$CH_3$), 2.60 (3H, s, 8-$CH_3$), 3.93 (2H, s, $COCH_2$), 4.20, 4.37, 4.43 (each 2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 7.05 (1H, br s, 7-H), 9.77 (1H, br s, 5-H). *Anal.* Calcd for $C_{21}H_{25}NO_7$: C, 62.52; H, 6.25; N, 3.47. Found: C, 62.73; H, 6.24; N, 3.38.

**Reactions of 3-(ethoxycarbonylacetyl)indolizines with salicylaldehydes. General method:** An ethanolic solution (30 mL) of dimethyl or diethyl 3-(ethoxycarbonylacetyl)indolizine-1,2-dicarboxylate (**5**, 1 mmol), salicylaldehyde (**6a** 0.146 g 1.2 mmol) or orthovanillin (**6b**, 0.182 g, 1.2 mmol), and piperidine (0.1g) was heated under reflux for 20 min in a water bath. The crude product which was precipitated was filtered off by suction and purified by recrystallization from chloroform to provide the corresponding dialkyl 3-(3-coumarinylcarbonyl)indolizine-1,2-dicarboxylate (**7**) as colorless needles.

**Dimethyl 3-(3-coumarinylcarbonyl)indolizine-1,2-dicarboxylate (7a)**: yield 73% (from **5a** and **6a**), mp 256—257°C; IR (KBr) 1736, 1707, 1606 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 3.44, 3.89 (each 3H, s, $OCH_3$), 7.1—7.9 (6H, m, 6-, 7-H, phenyl-H), 7.87 (1H, s, 4'-H), 8.47 (1H, br d, *J*=9.0 Hz, 8-H), 10.05 (1H, br d, *J*=7.0 Hz, 5-H). *Anal.* Calcd for $C_{22}H_{15}NO_7$: C, 65.19; H, 3.73; N, 3.46. Found: C, 64.90; H, 3.71; N, 3.48.

**Dimethyl 3-(3-coumarinylcarbonyl)-7-methylindolizine-1,2-dicarboxylate (7b)**: yield 54% (from **5b** and **6a**), mp 243—244°C; IR (KBr) 1730, 1697, 1610 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 2.54 (3H, s, 7-$CH_3$), 3.38, 3.87 (each 3H, s, $OCH_3$), 7.06 (1H, dd, *J*=7.0, 2.0 Hz, 6-H), 7.2—7.9 (4H, m, phenyl-H), 7.82 (1H, s, 4'-H), 8.20 (1H, br s, 8-H), 9.94 (1H, d, *J*=7.0 Hz, 5-H). *Anal.* Calcd for $C_{23}H_{17}NO_7$: C, 65.87; H, 4.09; N, 3.34. Found: C, 65.89; H, 4.07; N, 3.22.

**Dimethyl 3-(3-coumarinylcarbonyl)-6,8-dimethylindolizine-1,2-dicarboxylate (7c)**: yield 85% (from **5c** and **6a**), mp 271—272°C; IR (KBr) 1736, 1697, 1608 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 2.40 (3H, s, 6-$CH_3$), 2.61 (3H, s, 8-$CH_3$), 3.44, 3.83 (each 3H, s, $OCH_3$), 7.13 (1H, br s, 7-H), 7.2—7.9 (4H, m, phenyl-H), 7.82 (1H, s, 4'-H), 9.76 (1H, br s, 5-H). *Anal.* Calcd for $C_{24}H_{19}NO_7$: C, 66.51; H, 4.42; N, 3.23. Found: C, 66.59; H, 4.42; N, 3.16.

**Diethyl 3-(3-coumarinylcarbonyl)indolizine-1,2-dicarboxylate (7d)**: yield 30% (from **5d** and **6a**), mp 217—218°C; IR (KBr) 1730, 1697, 1610 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 1.15, 1.34 (each 3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 3.80, 4.29 (each 2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 7.1—7.9 (6H, m, 6-, 7-H, phenyl-H), 7.84 (1H, s, 4'-H), 8.48 (1H, br d, *J*=9.0 Hz, 8-H), 10.00 (1H, br d, *J*=7.0 Hz, 5-H). *Anal.* Calcd for $C_{24}H_{19}NO_7$: C, 66.51; H, 4.42; N, 3.23. Found: C, 66.68; H, 4.37; N, 3.12.

**Diethyl 3-(3-coumarinylcarbonyl)-7-methylindolizine-1,2-dicarboxylate (7e)**: yield

25% (from **5e** and **6a**), mp 207—208°C; IR (KBr) 1736, 1697, 1608 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 1.14, 1.31 (each 3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 2.51 (3H, s, 7-$CH_3$), 3.76, 4.33 (each 2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 7.04 (1H, dd, *J*=7.0, 2.0 Hz, 6-H), 7.2—7.9 (4H, m, phenyl-H), 7.80 (1H, s, 4'-H), 8.24 (1H, br s, 8-H), 9.90 (1H, d, *J*=7.0 Hz, 5-H). *Anal.* Calcd for $C_{25}H_{21}NO_7$: C, 67.11; H, 4.73; N, 3.13. Found: C, 67.27; H, 4.70; N, 3.00.

**Diethyl 3-(3-coumarinylcarbonyl)-6,8-dimethylindolizine-1,2-dicarboxylate (7f)**: yield 32% (from **5f** and **6a**), mp 252—253°C; IR (KBr) 1724, 1608 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 1.13, 1.31 (each 3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 2.40 (3H, s, 6-$CH_3$), 2.64 (3H, s, 8-$CH_3$), 3.82, 4.32 (each 2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 7.12 (1H, br s, 7-H), 7.2—7.9 (4H, m, phenyl-H), 7.82 (1H, s, 4'-H), 9.74 (1H, br s, 5-H). *Anal.* Calcd for $C_{26}H_{23}NO_7$: C, 67.67; H, 5.02; N, 3.04. Found: C, 67.86; H, 4.95; N, 2.92.

**Dimethyl 3-(8-methoxycoumarin-3-ylcarbonyl)indolizine-1,2-dicarboxylate (7g)**: yield 88% (from **5a** and **6b**), mp 279—280°C; IR (KBr) 1736, 1702, 1624 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 3.46, 3.88 (3H, s, $OCH_3$), 4.01 (3H, s, 8'-$OCH_3$), 7.0—7.4 (4H, m, 6-H, phenyl-H), 7.83 (1H, s, 4'-H), 7.60 (1H, br dd, *J*=7.0, 9.0 Hz, 7-H), 8.47 (1H, br d, *J*=9.0 Hz, 8-H), 10.04 (1H, br d, *J*=7.0 Hz, 5-H). *Anal.* Calcd for $C_{23}H_{17}NO_8$: C, 63.45; H, 3.94; N, 3.22. Found: C, 63.47; H, 3.92; N, 3.22.

**Dimethyl 3-(8-methoxycoumarin-3-ylcarbonyl)-7-methylindolizine-1,2-dicarboxylate (7h)**: yield 49% (from **5b** and **6b**), mp 294—295°C; IR (KBr) 1724, 1699, 1608 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 2.53 (3H, s, 7-$CH_3$), 3.43, 3.86 (each 3H, s, $OCH_3$), 4.00 (3H, s, 8'-$OCH_3$), 6.9—7.4 (4H, m, 6-H, phenyl-H), 7.79 (1H, s, 4'-H), 8.20 (1H, br s, 8-H), 9.91 (1H, d, *J*=7.0 Hz, 5-H). *Anal.* Calcd for $C_{24}H_{19}NO_8$: C, 64.14; H, 4.26; N, 3.12. Found: C, 63.90; H, 4.34; N, 3.15.

**Dimethyl 3-(8-methoxycoumarin-3-ylcarbonyl)-6,8-dimethylindolizine-1,2-dicarboxylate (7i)**: yield 97% (from **5c** and **6b**), mp 272—273°C; IR (KBr) 1722, 1610 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 2.39 (3H, s, 6-$CH_3$), 2.61 (3H, s, 8-$CH_3$), 3.45, 3.81 (each 3H, s, $OCH_3$), 4.00 (3H, s, 8'-$OCH_3$), 7.0—7.4 (4H, m, 7-H, phenyl-H), 7.80 (1H, s, 4'-H), 9.73 (1H, br s, 5-H). *Anal.* Calcd for $C_{25}H_{21}NO_8$: C, 64.79; H, 4.57; N, 3.02. Found: C, 64.61; H, 4.59; N, 3.02.

**Diethyl 3-(8-methoxycoumarin-3-ylcarbonyl)indolizine-1,2-dicarboxylate (7j)**: yield 41% (from **5d** and **6b**), mp 243—244°C; IR (KBr) 1730, 1697, 1604 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 1.13, 1.32 (each 3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 4.00 (3H, s, 8'-$OCH_3$), 3.80, 4.347 (each 2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 7.13 (1H, br t, *J*=7.0 Hz, 6-H), 7.0—7.4 (4H, m, 6-H, phenyl-H), 7.59 (1H, br dd, *J*=7.0, 9.0 Hz, 7-H), 7.81 (1H, s, 4'-H), 8.47 (1H, br d, *J*=9.0 Hz, 8-H), 10.02

64.98; H, 4.53 N, 2.88.

**Diethyl 3-(8-methoxycoumarin-3-ylcarbonyl)-7-methylindolizine-1,2-dicarboxylate (7k)**: yield 16% (from **5e** and **6b**), mp 223—224°C; IR (KBr) 1734, 1699, 1622 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 1.15, 1.31 (each 3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 2.52 (3H, s, 7-$CH_3$), 4.01 (3H, s, 8'-$OCH_3$), 3.67, 4.32 (each 2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 6.9—7.4 (4H, m, 7-H, phenyl-H), 7.80 (1H, s, 4'-H), 8.26 (1H, br s, 8-H), 9.90 (1H, d, *J*=7.0 Hz, 5-H). *Anal.* Calcd for $C_{26}H_{23}NO_8$: C, 65.40; H, 4.86; N, 2.93. Found: C, 65.65; H, 4.84; N, 2.70.

**Diethyl 3-(8-methoxycoumarin-3-ylcarbonyl)-6,8-dimethylindolizine-1,2-dicarboxylate (7l)**: yield 34% (from **5f** and **6b**), mp 272—273°C; IR (KBr) 1716, 1693, 1606 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 1.15, 1.30 (each 3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 2.39 (3H, s, 6-$CH_3$), 2.61 (3H, s, 8-$CH_3$), 4.00 (3H, s, 8'-$OCH_3$), 3.82, 4.30 (each 2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 6.9—7.4 (4H, m, 7-H, phenyl-H), 7.81 (1H, s, 4'-H), 9.73 (1H, br s, 5-H). *Anal.* Calcd for $C_{27}H_{25}NO_8$: C, 65.98; H, 5.13; N, 2.85. Found: C, 66.02; H, 5.13; N, 2.81.

**Preparations of pyridinium 1-[(ethoxycarbonylacetyl)[alkylthio(thiocarbonyl)]]-methylides. General method**: A chloroform solution (80 mL) of 1-(ethoxycarbonyl-acetonyl)pyridinium chloride (**3**, 5 mmol) and carbon disulfide (0.532 g, 7 mmol) was treated with triethylamine (1.515 g, 15 mmol) under stirring at rt for 1 h, and then alkylating agent (**8**, 6 mmol) was added to the reaction mixture and the resulting solution was allowed to react at rt for further 12 h. The solution was concentrated at reduced pressure and the residue was separated by column chromatography on alumina using chloroform as an eluent. The chloroform layers involving pyridinium methylide were combined and concentrated at reduced pressure. Recrystallization of the crude products from chloroform-ether afforded the corresponding pyridinium 1-[(ethoxycarbonylacetyl)-[alkylthio-(thiocarbonyl)]]methylide (**9a**—**f**) as yellow needles.

In the syntheses of pyridinium methylides (**9a**—**f**), the uses of other strong bases such as sodium hydroxide and sodium ethoxide did not provide good results.

**Pyridinium 1-[(ethoxycarbonylacetyl)[methylthio(thiocarbonyl)]]methylide (9a)**: yield 44% (from **3a** and **8a**), mp 131—133°C; IR (KBr) 1724, 1626 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 1.28 (3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 2.52 (3H, s, $SCH_3$), 3.99 (2H, br s, $COCH_2$), 4.22 (2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 7.7—8.7 (5H, m, pyridine-H). *Anal.* Calcd for $C_{13}H_{15}NO_3S_2$: C, 52.50; H, 5.08; N, 4.71. Found: C, 52.49; H, 5.11; N, 4.69.

**4-Methylpyridinium 1-[(ethoxycarbonylacetyl)[methylthio(thiocarbonyl)]]-methylide (9b)**: yield 37% (from **3b** and **8a**), mp 127—129°C; IR (KBr) 1711, 1635 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 1.26 (3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 2.57 (3H, s, $SCH_3$), 2.68 (3H, s, 4-$CH_3$), 3.97

(2H, br s, $COCH_2$), 4.17 (2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 7.68 (2H, br d, *J*=6.0 Hz, 3-, 5-H), 8.31 (2H, br d, *J*=6.0 Hz, 2-, 6-H). *Anal.* Calcd for $C_{14}H_{17}NO_3S_2$: C, 53.99; H, 5.50; N, 4.50. Found: C, 53.98; H, 5.62; N, 4.60.

**3,5-Dimethylpyridinium 1-[(ethoxycarbonylacetyl)[methylthio(thiocarbonyl)]]-methylide (9c)**: yield 34% (from **3c** and **8a**), mp 125—127°C; IR (KBr) 1738, 1624 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 1.25 (3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 2.50 (6H, s, 3-, 5-$CH_3$), 2.58 (3H, s, $OCH_3$), 4.02 (2H, br s, $COCH_2$), 4.18 (2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 8.00 (1H, br s, 4-H), 8.12 (1H, br s, 2-, 6-H). *Anal.* Calcd for $C_{15}H_{19}NO_3S_2$: C, 55.36; H, 5.88; N, 4.30. Found: C, 55.36; H, 5.90; N, 4.35.

**Pyridinium 1-[(ethoxycarbonylacetyl)[ethylthio(thiocarbonyl)]]methylide (9d**: yield 47% (from **3a** and **8b**), mp 126—128°C; IR (KBr) 1730, 1624 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 1.27 (6H, t, *J*=7.0 Hz, $OCH_2CH_3$, $SCH_2CH_3$), 3.27 (2H, q, *J*=7.0 Hz, $SCH_2CH_3$), 4.04 (2H, br s, $COCH_2$), 4.18 (2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 7.7—8.6 (5H, m, pyridine-H). *Anal.* Calcd for $C_{14}H_{17}NO_3S_2$: C, 53.99; H, 5.50; N, 4.50. Found: C, 53.71; H, 5.42; N, 4.53.

**4-Methylpyridinium 1-[(ethoxycarbonylacetyl)[methylthio(thiocarbonyl)]]-methylide (9e)**: yield 35% (from **3b** and **8b**), mp 117—119°C; IR (KBr) 1739, 1633 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 1.27 (6H, t, *J*=7.0 Hz, $OCH_2CH_3$, $SCH_2CH_3$), 2.69 (3H, s, 4-$CH_3$), 3.26 (2H, q, *J*=7.0 Hz, $SCH_2CH_3$), 4.04 (2H, br s, $COCH_2$), 4.18 (2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 7.71 (2H, br d, *J*=6.0 Hz, 3-, 5-H), 8.30 (2H, br d, *J*=6.0 Hz, 2-, 6-H). *Anal.* Calcd for $C_{15}H_{19}NO_3S_2$: C, 55.36; H, 5.88; N, 4.30. Found: C, 55.23; H, 5.93; N, 4.38.

**3,5-Dimethylpyridinium 1-[(ethoxycarbonylacetyl)[methylthio(thiocarbonyl)]]-methylide (9f)**: yield 26% (from **3c** and **8b**), mp 150—152°C; IR (KBr) 1732, 1624 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 1.29 (6H, t, *J*=7.0 Hz, $OCH_2CH_3$, $SCH_2CH_3$), 2.54 (6H, s, 3-, 5-$CH_3$), 3.27 (2H, q, *J*=7.0 Hz, $SCH_2CH_3$), 4.14 (2H, br s, $COCH_2$), 4.21 (2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 8.00 (1H, br s, 4-H), 8.14 (1H, br s, 2-, 6-H). *Anal.* Calcd for $C_{16}H_{21}NO_3S_2$: C, 56.61; H, 6.24; N, 4.13. Found: C, 56.73; H, 6.24; N, 4.19.

**Preparations of thieno[3,4-*b*]indolizines. General method:** A chloroform solution (30 mL) of pyridinium 1-[(ethoxycarbonylacetyl)[alkylthio(thiocarbonyl)]]methylide (**9**, 2 mmol) and phenacyl bromide (**10**, 2.2 mmol) was kept at rt until the disappearance of **9** was confirmed by the TLC monitoring (12 h—1 d). The resulting solution was concentrated at reduced pressure and the residual oil was washed well with three portions of ether (90 mL) to remove excess alkylating agent (**9**). Pyridinium salt (**11**) thus obtained was again dissolved in chloroform (30 mL). The resulting solution was treated with DBU (0.365 g, 2.4 mmol) under stirring at 0°C for 1 h and then with chloranil (0.492 g, 2 mmol) under the same conditions for 3 h. The solution was concentrated at reduced pressure and the residue was

separated by column chromatography on alumina using chloroform as an eluent. The chloroform layers involving thieno[3,4-*b*]indolizine (**12**) were combined and concentrated at reduced pressure. Recrystallization of the crude products from ether-hexane afforded the corresponding ethyl 3-alkylthio-1-(arylcarbonyl)thieno[3,4-*b*]indolizine-9-carboxylates (**12a**—**r**).

**Ethyl 1-benzoyl-3-(methylthio)thieno[3,4-*b*]indolizine-9-carboxylates (12a)**: yield 12% (from **9a** and **10a**), orange prisms, mp 127—129°C; IR (KBr) 1672, 1595 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 0.96 (3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 2.67 (3H, s, $SCH_3$), 3.64 (2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 6.77 (1H, br t, *J*=7.0 Hz, 6-H), 7.2—8.2(6H, m, 7-H, phenyl-H), 8.27 (1H, br d, *J*=9.0 Hz, 8-H), 9.04 (1H, br d, *J*=7.0 Hz, 5-H). *Anal.* Calcd for $C_{21}H_{17}NO_3S_2$: C, 63.78; H, 4.33; N, 3.54. Found: C, 63.49; H, 4.62; N, 3.57.

**Ethyl 1-benzoyl-7-methyl-3-(methylthio)thieno[3,4-*b*]indolizine-9-carboxylates (12b)**: yield 22% (from **9b** and **10a**), orange prisms, mp 113—115°C; IR (KBr) 1668, 1597 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 0.95 (3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 2.43 (3H, s, 7-$CH_3$), 2.70 (3H, s, $SCH_3$), 3.62 (2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 6.67 (1H, dd, *J*=7.0, 2.0 Hz, 6-H), 7.3—8.3 (5H, m, phenyl-H), 8.12 (1H, br s, 8-H), 8.99 (1H, d, *J*=7.0 Hz, 5-H). *Anal.* Calcd for $C_{22}H_{19}NO_3S_2$: C, 64.52; H, 4.68; N, 3.42. Found: C, 64.35; H, 4.72; N, 3.41.

**Ethyl 1-benzoyl-6,8-dimethyl-3-(methylthio)thieno[3,4-*b*]indolizine-9-carboxylates (12c)**: yield 36% (from **9c** and **10a**), red prisms, mp 173—175°C; IR (KBr) 1699, 1593 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 1.19 (3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 2.32 (3H, s, 6-$CH_3$), 2.55 (3H, s, 8-$CH_3$), 2.67 (3H, s, $SCH_3$), 4.03 (2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 6.97 (1H, br s, 7-H), 7.3—8.3 (5H, m, phenyl-H), 8.75 (1H, br s, 5-H). *Anal.* Calcd for $C_{23}H_{21}NO_3S_2$: C, 65.22; H, 5.00; N, 3.31. Found: C, 65.34; H, 4.94; N, 3.25.

**Ethyl 1-benzoyl-3-(ethylthio)thieno[3,4-*b*]indolizine-9-carboxylates (12d)**: yield 16% (from **9d** and **10a**), orange prisms, mp 84—86°C; IR (KBr) 1684, 1589 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 0.99 (3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 1.40 (3H, t, *J*=7.0 Hz, $SCH_2CH_3$), 3.07 (2H, q, *J*=7.0 Hz, $SCH_2CH_3$), 3.70 (2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 6.81 (1H, br t, *J*=7.0 Hz, 6-H), 7.3—8.2 (6H, m, 7-H, phenyl-H), 8.34 (1H, br d, *J*=9.0 Hz, 8-H), 9.29 (1H, br d, *J*=7.0 Hz, 5-H). *Anal.* Calcd for $C_{22}H_{19}NO_3S_2$: C, 64.52; H, 4.68; N, 3.42. Found: C, 64.58; H, 4.82; N, 3.23.

**Ethyl 1-benzoyl-7-methyl-3-(methylthio)thieno[3,4-*b*]indolizine-9-carboxylates (12e)**: yield 11% (from **9e** and **10a**), orange prisms, mp 110—112°C; IR (KBr) 1678, 1597 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 0.96 (3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 1.39 (3H, t, *J*=7.0 Hz, $SCH_2CH_3$), 2.43 (3H, s, 7-$CH_3$), 3.07 (2H, q, *J*=7.0 Hz, $SCH_2CH_3$), 3.66 (2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 6.67 (1H, dd, *J*=7.0, 2.0 Hz, 6-H), 7.3—8.2 (6H, m, 8-H, phenyl-H), 9.16 (1H, d, *J*=7.0 Hz, 5-H). *Anal.*

Calcd for $C_{23}H_{21}NO_3S_2$: C, 65.22; H, 5.00; N, 3.31. Found: C, 65.26; H, 5.02; N, 3.32.

**Ethyl 1-benzoyl-6,8-dimethyl-3-(ethylthio)thieno[3,4-*b*]indolizine-9-carboxylates (12f)**: yield 59% (from **9f** and **10a**), red prisms, mp 148—150°C; IR (KBr) 1699, 1591 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 1.21 (3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 1.36 (3H, t, *J*=7.0 Hz, $SCH_2CH_3$), 2.31 (3H, s, 6-$CH_3$), 2.53 (3H, s, 8-$CH_3$), 3.08 (2H, q, *J*=7.0 Hz, $SCH_2CH_3$), 4.08 (2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 6.97 (1H, br s, 7-H), 7.3—8.2 (5H, m, phenyl-H), 8.92 (1H, br s, 5-H). *Anal.* Calcd for $C_{24}H_{23}NO_3S_2$: C, 65.88; H, 5.30; N, 3.20. Found: C, 65.65; H, 5.17; N, 3.10.

**Ethyl 1-(*p*-chlorobenzoyl)-3-(methylthio)thieno[3,4-*b*]indolizine-9-carboxylates (12g)**: yield 18% (from **9a** and **10b**), orange needles, mp 153—155°C; IR (KBr) 1687, 1589 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 1.02 (3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 2.76 (3H, s, $SCH_3$), 3.76 (2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 6.86 (1H, br t, *J*=7.0 Hz, 6-H), 7.3—8.2(5H, m, 7-H, phenyl-H), 8.33 (1H, br d, *J*=9.0 Hz, 8-H), 9.11 (1H, br d, *J*=7.0 Hz, 5-H). *Anal.* Calcd for $C_{21}H_{16}NO_3ClS_2$: C, 58.66; H, 3.75; N, 3.26. Found: C, 58.96; H, 3.45; N, 3.26.

**Ethyl 1-(*p*-chlorobenzoyl)-7-methyl-3-(methylthio)thieno[3,4-*b*]indolizine-9-carboxylates (12h)**: yield 29% (from **9b** and **10b**), orange prisms, mp 163—165°C; IR (KBr) 1682, 1606 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 1.06 (3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 2.42 (3H, s, 7-$CH_3$), 2.69 (3H, s, $SCH_3$), 3.73 (2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 6.66 (1H, dd, *J*=7.0, 2.0 Hz, 6-H), 7.3—8.2 (4H, m, phenyl-H), 8.07 (1H, br s, 8-H), 8.94 (1H, d, *J*=7.0 Hz, 5-H). *Anal.* Calcd for $C_{22}H_{18}NO_3ClS_2$: C, 59.52; H, 4.09; N, 3.15. Found: C, 59.50; H, 4.09; N, 3.14.

**Ethyl 1-(*p*-chlorobenzoyl)-6,8-dimethyl-3-(methylthio)thieno[3,4-*b*]indolizine-9-carboxylates (12i)**: yield 28% (from **9c** and **10b**), red prisms, mp 164—166°C; IR (KBr) 1718, 1608 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 1.21 (3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 2.30 (3H, s, 6-$CH_3$), 2.51 (3H, s, 8-$CH_3$), 2.68 (3H, s, $SCH_3$), 4.06 (2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 6.96 (1H, br s, 7-H), 7.3—8.2 (4H, m, phenyl-H), 8.70 (1H, br s, 5-H). *Anal.* Calcd for $C_{23}H_{20}NO_3ClS_2$: C, 60.32; H, 4.40; N, 3.06. Found: C, 60.19; H, 4.51; N, 3.08.

**Ethyl 1-(*p*-chlorobenzoyl)-3-(ethylthio)thieno[3,4-*b*]indolizine-9-carboxylates (12j)**: yield 16% (from **9d** and **10b**), orange prisms, mp 142—144°C; IR (KBr) 1693, 1595 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 1.03 (3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 1.41 (3H, t, *J*=7.0 Hz, $SCH_2CH_3$), 3.11 (2H, q, *J*=7.0 Hz, $SCH_2CH_3$), 3.81 (2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 6.89 (1H, br t, *J*=7.0 Hz, 6-H), 7.3—8.2 (5H, m, 7-H, phenyl-H), 8.39 (1H, br d, *J*=9.0 Hz, 8-H), 9.34 (1H, br d, *J*=7.0 Hz, 5-H). *Anal.* Calcd for $C_{22}H_{18}NO_3ClS_2$: C, 59.52; H, 4.09; N, 3.15. Found: C, 59.27; H, 3.97; N, 3.05.

**Ethyl 1-(*p*-chlorobenzoyl)-3-ethylthio-7-methylthieno[3,4-*b*]indolizine-9-carboxylates (12k)**: yield 14% (from **9e** and **10b**), orange prisms, mp 111—113°C; IR (KBr)

1676, 1585 cm$^{-1}$; $^1$H-NMR ($CDCl_3$) 1.01 (3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 1.40 (3H, t, *J*=7.0 Hz, $SCH_2CH_3$), 2.44 (3H, s, 7-$CH_3$), 3.08 (2H, q, *J*=7.0 Hz, $SCH_2CH_3$), 3.74 (2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 6.67 (1H, dd, *J*=7.0, 2.0 Hz, 6-H), 7.3—8.2 (4H, m, phenyl-H), 8.12 (1H, br s, 8-H), 9.14 (1H, d, *J*=7.0 Hz, 5-H). *Anal.* Calcd for $C_{23}H_{20}NO_3ClS_2$: C, 60.32; H, 4.40; N, 3.06. Found: C, 60.21; H, 4.32; N, 2.87.

**Ethyl 1-(*p*-chlorobenzoyl)-3-ethylthio-6,8-dimethylthieno[3,4-*b*]indolizine-9-carboxylates (12l)**: yield 70% (from **9f** and **10b**), red prisms, mp 158—160°C; IR (KBr) 1707, 1593 cm$^{-1}$; $^1$H-NMR ($CDCl_3$) 1.23 (3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 1.37 (3H, t, *J*=7.0 Hz, $SCH_2CH_3$), 2.33 (3H, s, 6-$CH_3$), 2.55 (3H, s, 8-$CH_3$), 3.09 (2H, q, *J*=7.0 Hz, $SCH_2CH_3$), 4.12 (2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 7.04 (1H, br s, 7-H), 7.3—8.2 (4H, m, phenyl-H), 9.01 (1H, br s, 5-H). *Anal.* Calcd for $C_{24}H_{22}NO_3ClS_2$: C, 61.07; H, 4.70; N, 2.97. Found: C, 61.06; H, 4.65; N, 2.96.

**Ethyl 1-(*p*-bromobenzoyl)-3-(methylthio)thieno[3,4-*b*]indolizine-9-carboxylates (12m)**: yield 11% (from **9a** and **10c**), orange prisms, mp 137—139°C; IR (KBr) 1685, 1585 cm$^{-1}$; $^1$H-NMR ($CDCl_3$) 1.02 (3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 2.72 (3H, s, $SCH_3$), 3.77 (2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 6.85 (1H, br t, *J*=7.0 Hz, 6-H), 7.40 (1H, br q, *J*=7.0, 9.0 Hz, 7-H), 7.5—8.1(4H, m, phenyl-H), 8.34 (1H, br d, *J*=9.0 Hz, 8-H), 9.10 (1H, br d, *J*=7.0 Hz, 5-H). *Anal.* Calcd for $C_{21}H_{16}NO_3BrS_2$: C, 53.17; H, 3.40; N, 2.95. Found: C, 52.91; H, 3.26; N, 2.79.

**Ethyl 1-(*p*-bromobenzoyl)-7-methyl-3-(methylthio)thieno[3,4-*b*]indolizine-9-carboxylates (12n)**: yield 18% (from **9b** and **10c**), orange prisms, mp 169—171°C; IR (KBr) 1680, 1604 cm$^{-1}$; $^1$H-NMR ($CDCl_3$) 1.09 (3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 2.45 (3H, s, 7-$CH_3$), 2.71 (3H, s, $SCH_3$), 3.73 (2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 6.70 (1H, dd, *J*=7.0, 2.0 Hz, 6-H), 7.5—8.1 (4H, m, phenyl-H), 8.12 (1H, br s, 8-H), 8.98 (1H, d, *J*=7.0 Hz, 5-H). *Anal.* Calcd for $C_{22}H_{18}NO_3BrS_2$: C, 54.10; H, 3.71; N, 2.87. Found: C, 54.13; H, 3.74; N, 2.81.

**Ethyl 1-(*p*-bromobenzoyl)-6,8-dimethyl-3-(methylthio)thieno[3,4-*b*]indolizine-9-carboxylates (12o)**: yield 20% (from **9c** and **10c**), red prisms, mp 191—193°C; IR (KBr) 1716, 1608 cm$^{-1}$; $^1$H-NMR ($CDCl_3$) 1.23 (3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 2.31 (3H, s, 6-$CH_3$), 2.53 (3H, s, 8-$CH_3$), 2.70 (3H, s, $SCH_3$), 4.08 (2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 6.98 (1H, br s, 7-H), 7.5—8.1 (4H, m, phenyl-H), 8.70 (1H, br s, 5-H). *Anal.* Calcd for $C_{23}H_{20}NO_3BrS_2$: C, 54.98; H, 4.01; N, 2.79. Found: C, 54.97; H, 4.00; N, 2.81.

**Ethyl 1-(*p*-bromobenzoyl)-3-(ethylthio)thieno[3,4-*b*]indolizine-9-carboxylates (12p)**: yield 25% (from **9d** and **10c**), orange prisms, mp 136—138°C; IR (KBr) 1693, 1595 cm$^{-1}$; $^1$H-NMR ($CDCl_3$) 1.02 (3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 1.40 (3H, t, *J*=7.0 Hz, $SCH_2CH_3$), 3.08 (2H, q, *J*=7.0 Hz, $SCH_2CH_3$), 3.77 (2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 6.81 (1H, br t, *J*=7.0 Hz, 6-H), 7.37 (1H, br q, *J*=7.0, 9.0 Hz, 7-H), 7.5—8.1 (4H, m, 7-H, phenyl-H), 8.34 (1H, br d, *J*=9.0 Hz,

8-H), 9.10 (1H, br d, *J*=7.0 Hz, 5-H). *Anal.* Calcd for $C_{22}H_{18}NO_3BrS_2$: C, 54.10; H, 3.71; N, 2.87. Found: C, 54.27; H, 3.65; N, 2.76.

**Ethyl 1-(*p*-bromobenzoyl)-3-ethylthio-7-methylthieno[3,4-*b*]indolizine-9-carboxylates (12q)**: yield 17% (from **9e** and **10c**), orange prisms, mp 87—89°C; IR (KBr) 1672, 1583 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 1.02 (3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 1.41 (3H, t, *J*=7.0 Hz, $SCH_2CH_3$), 2.45 (3H, s, 7-$CH_3$), 3.09 (2H, q, *J*=7.0 Hz, $SCH_2CH_3$), 3.77 (2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 6.67 (1H, dd, *J*=7.0, 2.0 Hz, 6-H), 7.3—8.1 (4H, m, phenyl-H), 8.13 (1H, br s, 8-H), 9.15 (1H, d, *J*=7.0 Hz, 5-H). *Anal.* Calcd for $C_{23}H_{20}NO_3BrS_2$: C, 54.98; H, 4.01; N, 2.79. Found: C, 54.94; H, 3.89; N, 2.66.

**Ethyl 1-(*p*-bromobenzoyl)-3-ethylthio-6,8-dimethylthieno[3,4-*b*]indolizine-9-carboxylates (12r)**: yield 65% (from **9f** and **10c**), red prisms, mp 157—159°C; IR (KBr) 1687, 1593 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) 1.26 (3H, t, *J*=7.0 Hz, $OCH_2CH_3$), 1.40 (3H, t, *J*=7.0 Hz, $SCH_2CH_3$), 2.34 (3H, s, 6-$CH_3$), 2.58 (3H, s, 8-$CH_3$), 3.12 (2H, q, *J*=7.0 Hz, $SCH_2CH_3$), 4.17 (2H, q, *J*=7.0 Hz, $OCH_2CH_3$), 7.08 (1H, br s, 7-H), 7.3—8.1 (4H, m, phenyl-H), 9.01 (1H, br s, 5-H). *Anal.* Calcd for $C_{24}H_{22}NO_3BrS_2$: C, 55.81; H, 4.29; N, 2.71. Found: C, 55.56; H, 4.12; N, 2.60.

**Crystallography of ethyl 1-(*p*-chlorobenzoyl)-3-(methylthio)thieno[3,4-*b*]-indolizine-9-carboxylate (12g)**

A single crystal (0.04x0.18x0.88 mm) grown from ether–hexane was used for the unit-cell determination and data collection on a Rigaku AFC5S four-circle diffractometer, with graphite-monochromated Mo*K*$\alpha$ radiation ($\lambda$=0.71069 Å). Crystal data of **12g**: $C_{21}H_{16}NO_3ClS_2$; *M*=429.94; monoclinic, space group $P2_1/a$ (#14), *Z*=4 with *a*=7.765 (9) Å, *b*=18.141 (2) Å, *c*=14.127 (2) Å; $\beta$=103.78 (4)°; *V*=1933 (2) Å$^3$, and $D_{calc}$=1.477 g/cm$^3$. All calculations were performed using the TEXSAN program.[8] The structure was solved by a direct method (SIR).[9] The non-hydrogen atoms were refined anisotropically and the hydrogen atoms were refined isotopically. The final *R*- and $R_w$-factors after full-matrix least-squares refinements were 0.064 and 0.064, respectively, for 1904 ($I>2.00\sigma(I)$) observed reflections.

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