Preparation of New Nitrogen-Bridged Heterocycles. 48.1) Syntheses and Reactions of Ethyl 3-[2-(Methylthio)indolizin-3-yl]acrylate Derivatives

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Title compounds were prepared in 20—72% yields from the S-alkylation of pyridinium 1-[3-ethoxycarbonyl-1-(methylthio)thiocarbonyl]alkylides with some alkyl halides, followed by the treatment of the resulting pyridinium salts with a base and then a dehydrogenating agent. In part of these reactions novel heterocycles, ethyl 1-cyano-3-(methylthio)indolizin-9-carboxylates, were also formed. The oxidation of the title compounds with m-chloroperbenzoic acid gave the corresponding sulfoxides in moderate to good yields, which smoothly underwent Pummerer reactions on treatment with acetic anhydride. The bromination of the 3-vinyl group in the title compounds, followed by treatment of the resulting dibromo adducts with a base afforded ethyl 2-bromo-3-[2-(methylthio)indolizin-3-yl]acrylates, 3-[1-cyano-2-(methylthio)indolizin-3-yl]propiolates, and ethyl thieno[2,3-b]indolizine-2-carboxylate depending upon the substrate used.

Key words 3-vinylindolizine; oxidation; bromination; pyridinium methylide; cyclization; Pummerer reaction

In recent papers from our laboratory we described the smooth syntheses of indolizines2) and pyrido[1,2-a][1,4]thiazepines3) starting from pyridinium methylides possessing a thioacarbonyl group at the anionic carbon. We also confirmed the usefulness of these products as precursors for some fused indolizines4,4) and hetero-cage compounds.5) The reactions of these pyridinium (1-thiocarbonyl)methylides were initiated by the attack of an electrophile on the sulfur atom of the thioacarbonyl group. On the other hand, other pyridinium methylides without a thiocarbonyl substituent on the ylidic carbon disulfide and dimethyl sulfate in the presence of a base underwent Pummerer reactions on treatment with acetic anhydride. The bromination of the 3-vinyl group in the title compounds, followed by treatment of the resulting dibromo adducts with a base afforded ethyl 2-bromo-3-[2-(methylthio)indolizin-3-yl]acrylates, 3-[1-cyano-2-(methylthio)indolizin-3-yl]propiolates, and ethyl thieno[2,3-b]indolizine-2-carboxylate depending upon the substrate used.

Results and Discussion

Preparations and Reactions of Pyridinium 1-[3-Ethoxycarbonyl-1-(methylthio)thiocarbonyl]alkylides These pyridinium 1-[3-ethoxycarbonyl-1-(methylthio)thiocarbonyl]-alkylides (2a—c) were formed in moderate yields from the reactions of the corresponding pyridinium salts 1a—c with carbon disulfide and dimethyl sulfate in the presence of a base. Interestingly, these ylides 2a—c are very stable compounds and did not show the tendency for the 1,5-dipolar cyclization at all as seen in pyridinium 1-allylides reported earlier.6) The S-alkylation of these pyridinium allylides (2a—c) with ethyl bromoacetate (3a), bromoacetonitrile (3b), and phenacyl bromide (3c), followed by the treatment of the resulting pyridinium salts with a base and then dehydrogenating agent afforded the expected ethyl 3-[1-ethoxycarbonyl-(4a—c), 3-[1-cyano-(4d—f), and 3-[1-benzyloxythio]-2-(methylthio)indolizin-3-yl]acrylates (4g—i) in 20—72% yields as yellow crystalline products. In the reactions of pyridinium allylides (2a, c) with 3b, quite different types of products, ethyl 1-cyano-3-(methylthio)thieno[3,4-b]indolizin-9-carboxylates 5d, f, were also formed in 10 and 20% yields, respectively, as strong fluorescent orange crystals. These results are shown in Chart 1.

The structures of pyridinium allylides 2a—c were determined by physical and spectral means and by spectral comparison with other pyridinium (thiocarbonyl)methylides.7,8) The vinyl protons in 1H-NMR spectra of 2a—c appeared as AB type signals coupled with 14.0 Hz at near δ 4.3 and 8.4. The upfield shift for one (near δ 4.3) of the vinyl protons showed the high electron density at the (1,5)-position, though the 1,5-dipolar cyclization was not observed. The IR spectra of 3-vinylindolizine derivatives 4a—i showed characteristic absorption bands due to the ester carbonyl and the 3-vinyl groups at 1685—1703 and 1610—1618 cm−1, respectively. The trans configuration of the 3-vinyl group was deduced from a large coupling constant (16.0 Hz) between two vinyl protons in their 1H-NMR spectra. The elemental analyses of 4a—i were also in good accord with the compositions of our proposed structures. Some physical and spectral data of compound 4d coincided with those reported earlier by Kobayashi and his colleagues.9) On the other hand, the structures for minor products 5d, f were initially suspected to be cyclo[3.2.2]azaine derivatives such as 6 owing to their strong fluorescence. However, this structure 6 was discarded by the presence of the signals {δ 6.84 (1H, br t, J = 7.0, 7.0 Hz, 6- H), 7.49 (1H, br q, J = 7.0, 9.0 H, 7-H), 8.44 (1H, br d, J = 9.0 Hz, 8-H), 9.05 (1H, d, J = 7.0 Hz, 5-H)} attributable to the 4 protons on the pyridine ring in 1H-NMR spectrum of 5d and by the involvement of two sulfur atoms in elemental analyses of 5d, f. Furthermore, the chemical shift (δ 8.44 ) for the 8-H of 5d was more suggestive of the structure: This is close to the value (δ 8.34 ) for the 8-H in ethyl 3-vinylindolizine-9-carboxylate (4a) but not to that (δ 7.70 ) in 3-vinylindolizine-9-carboxonitrile (4d). The structures, ethyl 1-cyano-3-(methylthio)thieno[3,4-b]indolizin-9-carboxylates for 5d, f were ultimately decided by examining these spectral data and their formation mechanisms in detail (see Meccha-

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In connection with the structural assignment for 5d, f, we also investigated thermal transformation of these 3-vinylindolizines (4a—f) to cyclo[3.2.2]azines (6) in the absence or presence of dehydrogenating agent such as Pd/C, but we were unable to obtain good results.

**Syntheses and Pummerer Reactions of 2-Methylsulfinyl-3-vinylindolizines**

We previously observed that the functionalization of 2-(alkylamino)indolizine derivatives having substituents at the 1- and 3-positions suffered severe steric interference. To investigate the reactivities of the 2-methylthio group in these 1,2,3-trisubstituted indolizines 4a—f and to accomplish the functionalization of this group we examined their reactions with an oxidizing agent. When 2-methylthio-3-vinylindolizines (4a—f) were treated with m-chloroperbenzoic acid (MCPBA) in ethanol–chloroform at room temperature, the corresponding 2-methylsulfinyl-3-vinylindolizines (7a—f) were smoothly formed in 45—75% yields. In these reactions no attack of MCPBA to the 3-vinyl group could be detected. The high reactivity of the 2-methylthio group in 4a—f in this oxidation may be owing to the reduction of the steric repulsion based upon its longer carbon-sulfur bond and/or to the small introducing atom (oxygen) derived from MCPBA.

Since the increase of the acidity of the methyl hydrogens in the 2-substituents through the transformation from sulfides 4a—f to sulfoxides 7a—f was expected, the alkaline treatment of 7a—f was examined with the expectation of the formation of 2-unsubstituted thieno[3,2-a]-(10) and thieno[2,3-b]indolizine-1-oxides (11). The transformations from 7a—f to 10 or 11 in the presence of a base such as 1,9-diazabicyclo[5.4.0]-7-undecene (DBU) or potassium tert-butoxide, however, could not be observed even under heating conditions. On the other hand, the reactions of 7a—f with acetic anhydride in the presence of sodium acetate at the refluxing temperature provided the expected Pummerer reaction products, 2-acetoxymethylthio-3-vinylindolizine derivatives.
(8a–f), in 46–80% yields. These results are shown in Chart 2.

The structures of 2-methylsulfinyl-3-vinylindolizines (7a–f) and 2-(acetoxyethylthio)-3-vinylindolizines (8a–f) were principally determined by pursuing spectroscopically the structural change of the 2-substituent. For example, the IR spectra of 2-methylsulfinyl-3-vinylindolizines (7a–f) exhibited a sulfoxide absorption band at 1037–1053 cm⁻¹, and the chemical shifts and signal patterns in their ¹H-NMR spectra were similar to those of 2-methylthio-3-vinylindolizines (4a–f) except the 2-methylsulfinyl signal which appeared at considerably lower magnetic field (near δ 3.1). Similarly, the IR spectra of 2-(acetoxymethylthio)-3-vinylindolizines (8a–f) showed a new saturated carbonyl absorption band at 1734–1753 cm⁻¹ due to an acetoxyl group, and their ¹H-NMR spectra provided acetyl and methylene proton signals at δ 2.02–2.12 and δ 5.33–5.50, respectively, with the disappearance of methylthio proton signal. The elemental analyses for products 7a–f and 8a–f coincided with the expected structures.

Brominations of 2-Methylthio-3-vinylindolizines and Alkaline Treatment of Their Adducts

We next investigated the reactivity of the 3-vinyl group to a halogen. The reactions of 2-methylthio-3-vinylindolizines (4a–f) with bromine proceeded smoothly at room temperature, but the dibromo adducts (12a–f) were considerably unstable and their isolation and characterization were unsuccessful. This instability of dibromo adducts 12a–f seemed to be due to the change from the electron-withdrawing 2-(ethoxycarbonyl)vinyl group to the electron-releasing dihaloalkyl group as readily presumable by considering the resonance structures of indolizines. Therefore, dibromo adducts 12a–f, without the isolation, were immediately treated with DBU at 50–60 °C. Although no significant products were isolated by DBU at 50–60 °C. Although no significant products were isolated in the reaction of 12a with a base, the reactions of 12b, c with DBU gave 2-methylthio-3-(2-bromovinyl)indolizine (13b) and diethyl thieno[2,3-b]indolizine-2,9-dicarboxylate (14c) in 44 and 42% yields, respectively. Similar treatment of 12d–f afforded methylthio-3-(2-bromovinyl)indolizine (13d) and 2-methylthio-3-ethynylindolizines (15d–f) in moderate yields. These results are shown in Chart 3.

The structures of single (13b, d) and double dehydrobromination products (15d–f) were decided by their elemental analyses and IR and ¹H-NMR spectral comparisons with those of starting indolizines (4a–f). The (Z)-configuration of the 2-bromo-2-(ethoxy carbonyl)vinyl group in 13b, d was assigned by the lower chemical shifts (δ 8.67 or 8.47) of the remaining vinyl proton. Each characteristic absorption band for the carbon–carbon triple bond was indicated at 2185–2197 cm⁻¹ in the IR spectra of compounds 15d–f, though their intensities were very weak. The single crystal X-ray analysis of one compound 15f was also carried out and its structure was finally confirmed. The ORTEP drawing (10) for 15f is shown in Fig. 1. The bond length of the carbon–carbon triple bond was 1.178(6) Å and this value is much shorter than the bond length (1.203 or 1.205 Å) in acetylene (11) or cyanoacetylene (11). Furthermore, this triple bond is more deformed toward the ethoxycarbonyl group [its C(11)–C(12)–C(13) angle is 173.0(5)°] rather than to 3-indolizinyl moiety [its C(3)–C(11)–C(12) angle is 177.8(5)°]. The structure of

![Fig. 1. ORTEP Drawing of Ethyl 3-[1-Cyano-6,8-dimethyl-2-(methylthio)-indolizin-3-yl]propionate (15f)](image-url)
product 14c was decided by the disappearance of the 2-methylthio signal in the 1H-NMR spectrum and by the lack of involvement of any bromine in the molecule. The IR and 1H-NMR spectral data of 14c were closely similar to those of the thieno[2,3-b]indolizines prepared earlier by us.4–6

**Reaction Mechanisms** Possible formation mechanisms of 2-methylthio-3-vinylindolizines (4a–i) and ethyl 1-cyano-3-(methylthio)indolizine-9-carboxylates (5d, f) are shown in Chart 4. The route (path a) for the former is the same as that via pyrido[1,2-d][1,4]thiazine intermediates such as 18 we reported earlier.2) Path b for the latter compounds 5d, f is composed of the S-alkylation of pyridinium 1-(thiocarbonyl)allylides 2a, c with bromoacetonitrile (3b) providing E-16, followed by the intramolecular Michael addition of carbanions 19 generated under the basic conditions, the cyclization of 1,5-dipoles 21 after the dehydrogenation, and final aromatization. Although the reason why similar thieno[3,4-b]indolizines (5) could not be obtained when the other alkylation agents 3a, c were used was unclear, a higher stabilizing effect toward the carbanion intermediates 19 of the cyano group and/or its less steric interaction may promote this intramolecular Michael addition process.

Possible reaction mechanisms for products 13b, d, 14c, and 15d–f are indicated in Chart 5. The formations of 13b, d, and 15d–f are the results of single and double dehydrobrominations of the corresponding dibromo adducts 12b, d–f in the presence of a base (DBU), respectively. The reason why second dehydrobromination of ethyl 2-bromo-3-[2-(methylthio)indolizin-3-yl]acrylate (13b) did not occur may be due to the increased crowd of the pyrrole moiety. In contrast, thieno[2,3-b]indolizine (14c) must be formed via the intramolecular S-alkylation of dibromo adduct 12c, followed by the successive eliminations of methyl bromide and hydrogen bromide from the corresponding sulfonium salt 22. Since both processes, the dehydrobromination (the regeneration of the conjugated system) and the intramolecular S-alkylation (the generation of the strong electron-withdrawing group) of dibromo adducts 12, stabilize this indolizine ring system, it is not surprising to observe such reactions. However, the reason that no thieno[2,3-b]indolizines other than
14c were obtained is still unclear.

Experimental
Melting points were measured with a Yanagimoto micromelting point apparatus and are not corrected. Microanalyses were carried out on a Perkin-Elmer 2400 elemental analyzer. The 1H NMR spectra were determined with a Hitachi R-600 spectrometer (60 MHz) in deuteriochloroform with tetramethylsilane used as an internal standard; the chemical shifts are expressed in δ values. The IR were taken with a JASCO FT/IR-3300 IR spectrophotometer.

Preparation of Pyridinium 1-[3-Ethoxy carbonyl-1-[methylthio(thiocarbonyl)]allylides (1a–e) were prepared from the alkaline treatment of 1E-2-propenylpyridinium bromides (1a–e), carbon disulfide, and dimethyl sulfate in ethanol according to the procedure described earlier.2,7 Some data of compounds 2a–e are as follows:

Pyridinium 1-[3-Ethoxy carbonyl-1-[methylthio(thiocarbonyl)]allylides (1a-c)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Anhydrous</th>
<th>mp (°C)</th>
<th>IR (KBr) cm⁻¹</th>
<th>1H-NMR (CDCl₃)</th>
</tr>
</thead>
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| 1a       | 166.0–167.0 | 14.0, 16.0 | 1: 1693, 1670, 1610 | 1.38 (3H, t, J=7.0 Hz), 2.18 (3H, s), 2.70 (3H, s), 4.32 (2H, q, J=7.0 Hz), 6.80 (1H, d, J=6.0 Hz), 6.91 (1H, d, J=6.0 Hz), 7.89 (1H, d, J=6.0 Hz), 8.18 (1H, d, J=6.0 Hz), 8.81 (1H, br s), Anal. Calc. for C₁₇H₁₆N₂O₂S: C, 59.36; H, 4.66; N, 8.13. Found: C, 59.36; H, 4.66; N, 8.13.
| 1b       | 166.0–167.0 | 14.0, 16.0 | 1: 1693, 1670, 1610 | 1.38 (3H, t, J=7.0 Hz), 2.18 (3H, s), 2.70 (3H, s), 4.32 (2H, q, J=7.0 Hz), 6.80 (1H, d, J=6.0 Hz), 6.91 (1H, d, J=6.0 Hz), 7.89 (1H, d, J=6.0 Hz), 8.18 (1H, d, J=6.0 Hz), 8.81 (1H, br s), Anal. Calc. for C₁₇H₁₆N₂O₂S: C, 59.36; H, 4.66; N, 8.13. Found: C, 59.36; H, 4.66; N, 8.13.
| 1c       | 166.0–167.0 | 14.0, 16.0 | 1: 1693, 1670, 1610 | 1.38 (3H, t, J=7.0 Hz), 2.18 (3H, s), 2.70 (3H, s), 4.32 (2H, q, J=7.0 Hz), 6.80 (1H, d, J=6.0 Hz), 6.91 (1H, d, J=6.0 Hz), 7.89 (1H, d, J=6.0 Hz), 8.18 (1H, d, J=6.0 Hz), 8.81 (1H, br s), Anal. Calc. for C₁₇H₁₆N₂O₂S: C, 59.36; H, 4.66; N, 8.13. Found: C, 59.36; H, 4.66; N, 8.13.

Preparations of 2-Methylthio-3-vinylindolizine Derivatives. General Method
A chloroform solution (20 mL) of pyridinium 1-[methylthio(thiocarbonyl)]allylides (2a–e) at room temperature for 1 d. Evaporation of the solvent from the reaction mixture, followed by the removal of the excess alkylation agent by washing three times with ether (20 mL) gave the corresponding pyridinium salt. The salt was again dissolved in chloroform (30 mL), and the resulting solution was treated with DBU and then chloranil or 2,3-dichloro-4,5-dicyano-p-benzoquinone (DDQ) under stirring at 0°C. The reaction mixture was allowed to react for a further 4 h under the same reaction conditions. The mixture was concentrated under reduced pressure and the residue was separated by column chromatography on alumina using ether and then chloroform. The yellow chloroform layers were combined and concentrated under reduced pressure. Recrystallization from chloroform-hexane of crude products gave the corresponding 3-vinylindolizines 4a–i as yellow needles. Other types of products 5d, f were also obtained as orange needles together with the expected 3-vinylindolizines 4d, f in the reactions of 2a, c with bromoacetonitrile (3b), respectively. Some data on compounds 4a–i and 5d, f are as follows:

Ethyl 3-[1-Ethoxy carbonyl-2-(methylthio)indolizin-3-yl]acrylate (4a): 35%, (from 2a and 3a), mp 112–114°C. IR (KBr) cm⁻¹: 1685, 1616. 1H-NMR (CDCl₃) δ: 1.36, 1.46 (each 3H, t, J=7.0 Hz), 2.49 (3H, s), 4.32, 4.45 (each 2H, q, J=7.0 Hz), 6.72 (1H, d, J=6.0 Hz), 6.93 (1H, br t, J=7.0, 7.0 Hz), 7.25 (1H, br q, J=7.0, 9.0 Hz), 8.10 (1H, d, J=6.0 Hz), 8.34 (1H, d, J=9.0 Hz), 8.37 (1H, d, J=7.0 Hz). Anal. Calc. for C₁₅H₁₅NO₂S: C, 67.76; H, 6.09; N, 4.83. Found: C, 67.76; H, 6.09; N, 4.83.

Preparations of 2-Methylthio-3-vinylindolizine Derivatives with MCPBA. General Method
A chloroform–ethanol solution (1:1, 10 mL) of 2-methylthio-3-vinylindolizine (4, 2 mmol) and MCPBA (2 mmol) was allowed to react under stirring at room temperature for 1 h. The separations of the reaction mixture by column chromatography on alumina using chloroform and re-crystallization of the product from chloroform-hexane afforded the corresponding 2-methylsulfonyl-3-vinylindolizine derivative (7a–j). Some data on compounds 7a–j are as follows:

Ethyl 3-[1-Ethoxy carbonyl-2-(methylthio)indolizin-3-yl]acrylate (7a): 60% (from 4a), yellow needles, mp 144–146°C. IR (KBr) cm⁻¹: 1707, 1687, 1612, 1039. 1H-NMR (CDCl₃) δ: 1.38, 1.46 (each 3H, t, J=7.0 Hz), 3.11 (3H, s), 4.35, 4.46 (each 2H, q, J=7.0 Hz), 6.53 (1H, d, J=6.0 Hz), 8.18 (1H, d, J=6.0 Hz), 8.40 (1H, d, J=9.0 Hz), 8.49 (1H, d, J=9.0 Hz). Anal. Calc. for C₁₅H₁₅NO₂S: C, 59.28; H, 4.68; N, 8.13. Found: C, 59.28; H, 4.68; N, 8.13.
Ethyl 3-[1-Ethoxybenzyl]-2-dimethylsulfanylindolizin-3-yl]acrylate (7c) 55% (from 4e), orange needles, mp 124—126°C. IR (KBr) cm⁻¹: 1714, 1691, 1616, 1053. 1H-NMR (CDCl₃) δ: 1.37 (3H, t, J=7.0 Hz), 2.34 (3H, s), 2.54 (3H, s), 3.09 (3H, s), 4.32, 4.44 (each 2H, q, J=7.0 Hz), 6.42 (1H, d, J=16.0 Hz), 6.85 (1H, br, s), 8.10 (1H, br, s), 8.41 (1H, d, J=16.0 Hz). Anal. Calc. for C₁₉H₂₁NO₅S: C, 59.59; H, 5.82; N, 3.85. Found: C, 59.24; H, 5.85; N, 3.65.

Bromination and Dehydrobromination of 2-Methylthio-3-vinylindolizines. General Method A chloroform-benzene solution (1:1, 10 ml) of 2-methylthio-3-vinylindolizine (4, 2 mmol) and bromine (2.4 mmol) was stirred at room temperature for 1 hr. The concentration of the bromine in the reaction mixture and column chromatographic separation (alumina) of the residue gave the corresponding ethyl 2-bromo-3-[2-(methylthio)indolizin-3-yl]acrylates (13b, diethyl 6,8-dimethylthieno[2,3-b]indolizin-2,9-dicarboxylate (14e), and 3-[1-cyano-2-(methylthio)indolizin-3-yl]propiolate (15f).

The isolation and purification of the dibromo adducts (12a—a) were successful, however, because the removal of the solvent caused their smooth decomposition, and the alkaline treatment of 12a gave a complex mixture and no significant product could be isolated.

Some data on compounds 13b, 14c, and 15f are as follows:

Ethyl 2-Bromo-3-[1-ethoxybenzyl]-2-(methylthio)indolizin-3-yl]acrylate (13b) 35% (from 4d), yellow needles (from CHCl₃-hexane), mp 135—137°C. IR (KBr) cm⁻¹: 2212, 1712, 1612. 1H-NMR (CDCl₃) δ: 1.42 (3H, t, J=7.0 Hz), 2.64 (3H, s), 4.44 (2H, q, J=7.0 Hz), 6.97 (1H, br t, J=7.0 Hz), 7.30 (1H, br q, J=9.0 Hz, 7.55, 7.19 (1H, br d, J=9.0 Hz), 7.89 (1H, s). Anal. Calc. for C₁₇H₁₇BrNO₅S: C, 50.70; H, 4.80; N, 3.23.

Diethyl 6,8-Dimethylthieno[2,3-b]indolizin-2,9-dicarboxylate (14e) 42% (from 4c), orange needles (from CHCl₃-hexane), mp 95—97°C. IR (KBr) cm⁻¹: 1753, 1724, 1709, 1616. 1H-NMR (CDCl₃) δ: 1.40, 1.43 (each 3H, t, J=7.0 Hz), 2.32 (3H, s), 2.69 (3H, s), 4.41, 4.43 (each 2H, q, J=7.0 Hz), 6.97 (1H, br s), 7.82 (1H, br s), 7.96 (1H, s). Anal. Calc. for C₁₉H₂₁NO₅S: C, 62.59; H, 5.54; N, 4.06. Found: C, 62.67; H, 5.79; N, 3.94.

Ethyl 3-[1-Cyano-2-(methylthio)indolizin-3-yl]propiolate (15f) 35%, (from 7d), colorless needles (from CHCl₃-hexane), mp 135—137°C. IR (KBr) cm⁻¹: 2197, 2197, 1693. 1H-NMR (CDCl₃) δ: 1.39 (3H, t, J=7.0 Hz), 2.78 (3H, s), 4.37 (2H, q, J=7.0 Hz), 6.84 (1H, d, J=16.0 Hz), 7.02 (1H, br t, J=7.0 Hz), 7.37 (1H, br q, J=7.0 Hz, 9.0 Hz), 7.69 (1H, d, J=9.0 Hz), 8.42 (1H, d, J=7.0 Hz). Anal. Calc. for C₁₇H₁₇NO₅S: C, 63.66; H, 4.25; N, 8.95. Found: C, 63.35; H, 4.40; N, 7.97.

Ethyl 3-[1-Cyano-7-methyl-2-(methylthio)indolizin-3-yl]propiolate (15e) 42% (from 4e), colorless needles (from CHCl₃-hexane), mp 139—141°C. IR (KBr) cm⁻¹: 2214, 2191, 1698. 1H-NMR (CDCl₃) δ: 1.39 (3H, t, J=7.0 Hz), 2.44 (3H, s), 2.75 (3H, s), 4.36 (2H, q, J=7.0 Hz), 6.83 (1H, dd, J=7.0, 2.0 Hz), 7.43 (1H, br, s), 8.26 (1H, d, J=7.0 Hz). Anal. Calc. for C₁₉H₁₇NO₅S: C, 64.41; H, 4.73; N, 9.39. Found: C, 64.33; H, 4.90; N, 9.31.

Crystallography of Ethyl 3-[1-Cyano-6,8-dimethyl-2-(methylthio)indolizin-3-yl]propiolate (15f) 55%, (from 4f), colorless needles (from CHCl₃-hexane), mp 127—129°C. IR (KBr) cm⁻¹: 2206, 2185, 16891, 1624. 1H-NMR (CDCl₃) δ: 1.39 (3H, t, J=7.0 Hz), 2.35 (3H, s), 2.72 (6H, s), 4.38 (2H, q, J=7.0 Hz), 6.69 (1H, br, s), 8.02 (1H, br s). Anal. Calc. for C₁₇H₁₇NO₅S: C, 65.36; H, 5.16; N, 8.97. Found: C, 65.33; H, 5.25; N, 8.91.

Ethyl 3-[1-Cyano-6,8-dimethyl-2-(methylthio)indolizin-3-yl]propiolate (15f) 55% (from 4f), colorless needles (from CHCl₃-hexane), mp 127—129°C. IR (KBr) cm⁻¹: 2206, 2185, 16891, 1624. 1H-NMR (CDCl₃) δ: 1.39 (3H, t, J=7.0 Hz), 2.35 (3H, s), 2.72 (6H, s), 4.38 (2H, q, J=7.0 Hz), 6.69 (1H, br, s), 8.02 (1H, br s). Anal. Calc. for C₁₇H₁₇NO₅S: C, 65.36; H, 5.16; N, 8.97. Found: C, 65.33; H, 5.25; N, 8.91.

Crystallization of Ethyl 3-[1-Cyano-6,8-dimethyl-2-(methylthio)indolizin-3-yl]propiolate (15f) 55% (from 4f), colorless needles (from CHCl₃-hexane), mp 127—129°C. IR (KBr) cm⁻¹: 2206, 2185, 16891, 1624. 1H-NMR (CDCl₃) δ: 1.39 (3H, t, J=7.0 Hz), 2.35 (3H, s), 2.72 (6H, s), 4.38 (2H, q, J=7.0 Hz), 6.69 (1H, br, s), 8.02 (1H, br s). Anal. Calc. for C₁₇H₁₇NO₅S: C, 65.36; H, 5.16; N, 8.97. Found: C, 65.33; H, 5.25; N, 8.91.

Ethyl 3-[1-Cyano-6,8-dimethyl-2-(methylthio)indolizin-3-yl]propiolate (15f) 55% (from 4f), colorless needles (from CHCl₃-hexane), mp 127—129°C. IR (KBr) cm⁻¹: 2206, 2185, 16891, 1624. 1H-NMR (CDCl₃) δ: 1.39 (3H, t, J=7.0 Hz), 2.35 (3H, s), 2.72 (6H, s), 4.38 (2H, q, J=7.0 Hz), 6.69 (1H, br, s), 8.02 (1H, br s). Anal. Calc. for C₁₇H₁₇NO₅S: C, 65.36; H, 5.16; N, 8.97. Found: C, 65.33; H, 5.25; N, 8.91.
(3), $\gamma=65.06^{+}(2); V=807.9(5) \text{Å}^3$, and $D_{\text{calc}}=1.284 \text{g/cm}^3$. All calculations were performed using the TEXSAN program. The structure was solved by a direct method (SIR). The non-hydrogen atoms were refined anisotropically, and the hydrogen atoms were attached at the idealized position and not refined. The final $R$- and $R_p$-factors after full-matrix least-squares refinements were 0.082 and 0.097 for 2111 ($I>2\sigma(I)$), respectively, observed reflections.

References

1) For part 47 of this series, see Kakehi A., Ito S., Suga H., Takahashi H., Dobashi K., Heterocycles, in press.
6) There are numerous papers for the 1,3-dipolar cycloaddition. See following reviews: a) Stuckwisch C. G., Synthesis, 1973, 469—483; b) Uchida T., Matsumoto K., ibid, 1976, 209—236.