Chem. Pharm. Bull. **46**(6) 934—938 (1998) Vol. 46, No. 6

Preparation of New Nitrogen-Bridged Heterocycles. 44.[1)] Thermolysis of 12b*H*-1,4-Thiazepino[5,4-*a*]isoquinoline Derivatives

Akikazu KAKEHI,* Suketaka ITO, and Satoshi NISHIZAWA

Department of Chemistry and Material Engineering, Faculty of Engineering, Shinshu University, Wakasato, Nagano 380-8553, Japan. Received December 9,1997; accepted March 9, 1998

Thermolysis of trialkyl 4-alkylthio-12b*H*-1,4-thiazepino[5,4-*a*]isoquinoline-1,2,5-tricarboxylates in refluxing xylene did not afford the usually expected desulfurized products such as benzoquinolizine derivatives (5), but formed trialkyl 2-(1-isoquinolinyl)-4-alkylthio-2,3-dihydrothiophene-2,3,5-tricarboxylates (4) in low to moderate yields. A similar treatment of the title compounds in the presence of a base such as 1,8-diazabicyclo[5.4.0]undec-7-ene gave ring contraction and fragmentation products, trialkyl pyrrolo[2,1-*a*]isoquinoline-1,2,3-tricarboxylates in moderate yields. 1,5-Sigmatropic shift of 7-thianorcardiene intermediates is involved in the formation of 2-(1-quinolinyl)-2,3-dihydrothiophene derivatives.

Key words pyrido[1,2-*d*][1,4]thiazepine; thiophene; 7-thianorcaradiene; pyrrolo[2,1-*a*]isoquinoline; thermolysis; rearrangement

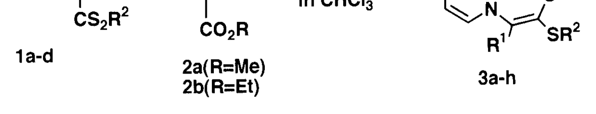
A number of syntheses and reactions of various seven-membered heterocycles have been investigated for the last three decades because of their theoretical and practical potential. Their full-conjugated compounds commonly show an equilibrium with their valence isomers, 7-heteronorcardienes, and many of their thermal reactivities are largely responsible for this phenomenon.[2)] For example, transformations of some 1*H*-azepines and oxepines to the corresponding anilines and phenols, respectively, were well documented,[3)] and smooth desulfurization of thiepines leading to benzene derivatives is also established.[4)]

Recently, we reported on syntheses and unique reactions of various 10a*H*-pyrido[1,2-*d*][1,4]thiazepine[5)] and 5a*H*-pyrido[1,2-*d*][1,3,4]thiadiazepine derivatives.[1,6)] The remarkable difference in reactivity between the intramolecular Diels–Alder reaction in the former compounds and the rearrangement in the latter prompted us to investigate further the thermal reaction using other substrates which cannot undergo such reactions. In this paper we wish to report on novel reactions of the title compounds in which, instead of expected desulfurized products, formation of unexpected 2-(1-quinolinyl)-2,3-dihydrothiophene and pyrrolo[2,1-*a*]isoquinoline derivatives was observed.

Results and Discussion

Preparation of 12b*H*-1,4-Thiazepino[5,4-*a*]isoquinoline Derivatives Trialkyl 4-alkylthio-12b*H*-1,4-thiazepino-[5,4-*a*]isoquinoline-1,2,5-tricarboxylates (**3a**—**h**) were prepared from reactions of 2-isoquinolinio[(alkylthio)-thiocarbonyl]methylides (**1a**—**d**) with dimethyl or diethyl acetylenedicarboxylate (**2a, b**) according to the procedure we previously reported (Chart 1).[5c)] Products **3a**—**h** were obtained as reddish crystalline compounds and their structures were determined by a comparison of their physical and spectral data with those of the known compounds **3a, b**.[5c)]

Thermolysis of 12b*H*-1,4-Thiazepino[5,4-*a*]isoquinoline Derivatives Trialkyl 4-alkylthio-12b*H*-1,4-thiazepino-[5,4-*a*]isoquinoline-1,2,5-tricarboxylates (**3a**—**h**) were very stable and did not decompose even on heating in refluxing benzene or toluene, because the intramolecular Diels–Alder reaction and the rearrangement as observed with 10a*H*-pyrido[1,2-*d*][1,4]thiazepines[5b,d)] and 5a*H*-pyrido[1,2-*d*][1,3,4]thiadiazepine derivatives,[1,6)] respectively, are unfavorable for the loss of the aromaticity of the additional benzene ring. However, when compounds **3a**—**h** were heated under reflux in xylene, they gradually underwent thermolysis to afford the colorless crystalline products **4a**—**h** in low to moderate yields (10—24%) (Chart 2). Products **4a**—**h** are usually expected to be the corresponding desulfurized products,[4)] trialkyl 3-alkylthio-11b*H*-benzoquinolizine-1,2,4-tricarboxylates (**5**), but their analytical data were not in accord with these products **5**. Their elemental analyses revealed that compounds **4a**—**h** have the same compositions as reactants **3a**—**h** have. IR spectra of **4a**—**h** showed some saturated (1730—1750 cm^{-1}) and an α,β-unsaturated ester carbonyl band (1690 cm^{-1}), and ^{1}H-NMR spectra disclosed the presence of a 1-isoquinolinyl group ($\delta = 7.0$—9.0 (m, 6H)) and a saturated methine proton (near $\delta = 6.3$), together with three alkoxycarbonyl groups. From these data we first assumed their structures to be trialkyl 5-alkylthio-3-(1-isoquinolinyl)-2,3-dihydrothiophene-2,3,4-tricarboxylates, which could be formed *via* a 1,3-sigmatropic shift of the bridgehead proton in **3a**—**h** to the 2-position, followed by another 1,3-sigmatropic shift of the C(5)–N(6)



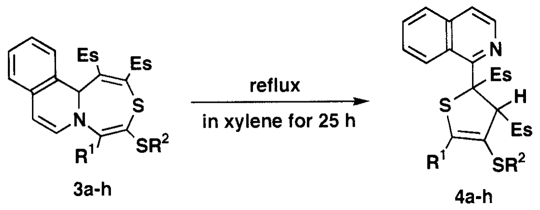
1	R^1	R^2
a	CO$_2$Me	Me
b	CO$_2$Me	Et
c	CO$_2$Et	Me
d	CO$_2$Et	Et

3	R^1	R^2	Es	Yield(%)
a	CO$_2$Me	Me	CO$_2$Me	59
b	CO$_2$Me	Et	CO$_2$Me	27
c	CO$_2$Et	Me	CO$_2$Me	70
d	CO$_2$Et	Et	CO$_2$Me	44
e	CO$_2$Me	Me	CO$_2$Et	48
f	CO$_2$Me	Et	CO$_2$Et	32
g	CO$_2$Et	Me	CO$_2$Et	64
h	CO$_2$Et	Et	CO$_2$Et	48

Chart 1

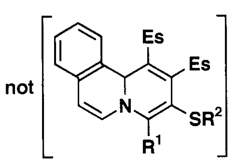
---

* To whom correspondence should be addressed.



3a-h

4a-h



5

4	R^1	R^2	Es	Yield(%)
a	CO_2Me	Me	CO_2Me	11
b	CO_2Me	Et	CO_2Me	20
c	CO_2Et	Me	CO_2Me	13
d	CO_2Et	Et	CO_2Me	17
e	CO_2Me	Me	CO_2Et	10
f	CO_2Me	Et	CO_2Et	24
g	CO_2Et	Me	CO_2Et	12
h	CO_2Et	Et	CO_2Et	17

Chart 2

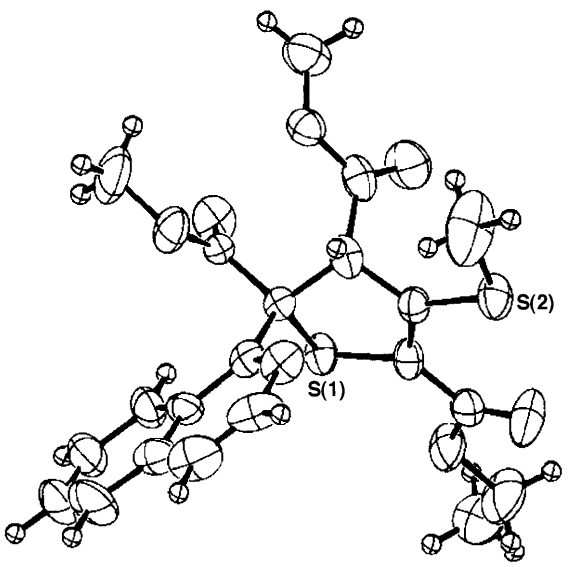
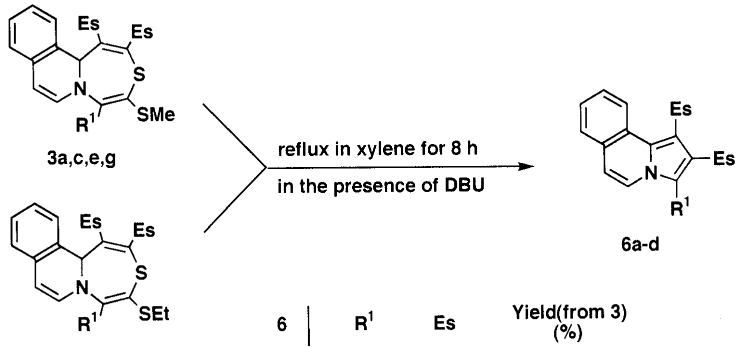


Fig. 1. ORTEP drawing of 5-Ethyl 2,3-Dimethyl 2-(1-isoquinolinyl)-4-methylthio-2,3-dihydrothiophene-2,3,5-tricarboxylate



3b,d,f,h

6	R^1	Es	Yield(from 3) (%)
a	CO_2Me	CO_2Me	20(3a) or 28(3b)
b	CO_2Et	CO_2Me	38(3c) or 28(3d)
c	CO_2Me	CO_2Et	25(3e) or 19(3f)
d	CO_2Et	CO_2Et	25(3g) or 16(3h)

Chart 3

bond in the resulting 2*H*-1,4-thiazepino[5,4-*a*]isoquinoline-1,2,5-tricarboxylates to the 1-position. However, an X-ray analysis on compound **4d** indicated that they are not **6** but trialkyl 3-alkylthio-2-(1-isoquinolinyl)-2,3-dihydrothiophene-2,3,5-tricarboxylates (**4a**—**h**). The ORTEP drawing7) of **4d** is shown in Fig. 1. Very interestingly, the positions of the ring sulfur atoms in **4a**—**h** were quite different from those in **3a**—**h**.

The thermolysis of pyridothiazepines **3a**—**h** in refluxing xylene in the presence of a base, 1,8-diazabicyclo-[5.4.0]undec-7-ene (DBU), in contrast, afforded the corresponding trialkyl pyrrolo[2,1-*a*]isoquinoline-1,2,3-tricarboxylates (**6a**—**d**) in moderate yields (Chart 3). The structures of products **6a**—**d** were determined by physical and spectral comparisons with the authentic samples **6a**, **b**.8)

Reaction Mechanisms It is not clear why desulfurized products such as benzoquinolizine derivatives **5** could not be obtained in the thermolysis of the title compounds **3a**—**h**. However, considering the low yields of both products **4a**—**h** and **6a**—**d** which were actually isolated under quite drastic reaction conditions, the possibility of the decomposition of products like **5** during these reactions still remains. The mechanism of the formation from the title compounds **3a**—**h** to the corresponding 2-(1-isoquinolinyl)-2,3-dihydrothiophenes **4a**—**h** is not simple because of the involvement of the transfer of the ring sulfur atom, but we tentatively propose possible reaction mechanisms for this reaction (Chart 4). This reaction is believed to be initiated by the removal of the bridgehead hydrogen as a hydride. The disrotatory cyclization ($\pi 6s$) of the resulting 1,4-thiazepinium ions **8** to the tetracyclic thiirane derivatives **8**, followed by the 1,5-sigmatropic shift in the 3-aza-7-thiabicyclo[4.1.0]heptadienyl system, would afford the rearranged thiiranes **9**. The 1,3-sigmatropic shift of **9**, which is expected to proceed in a stepwise manner, provides the corresponding 2-aza-7-thiabicyclo[2.2.1]-hepta-2,5-dienes (**10**), and the subsequent fission of the C–N bond in **10** and the return of a hydride onto **11** should give the final products **4a**—**h**. An alternative path which is initiated by the removal of a hydrogen radical can also be considered, but is unlikely because the possible cyclization mode is conrotatory ($\pi 7a$), leading to a sterically impossible trans-fused ring system. The route from **3a**—**h**

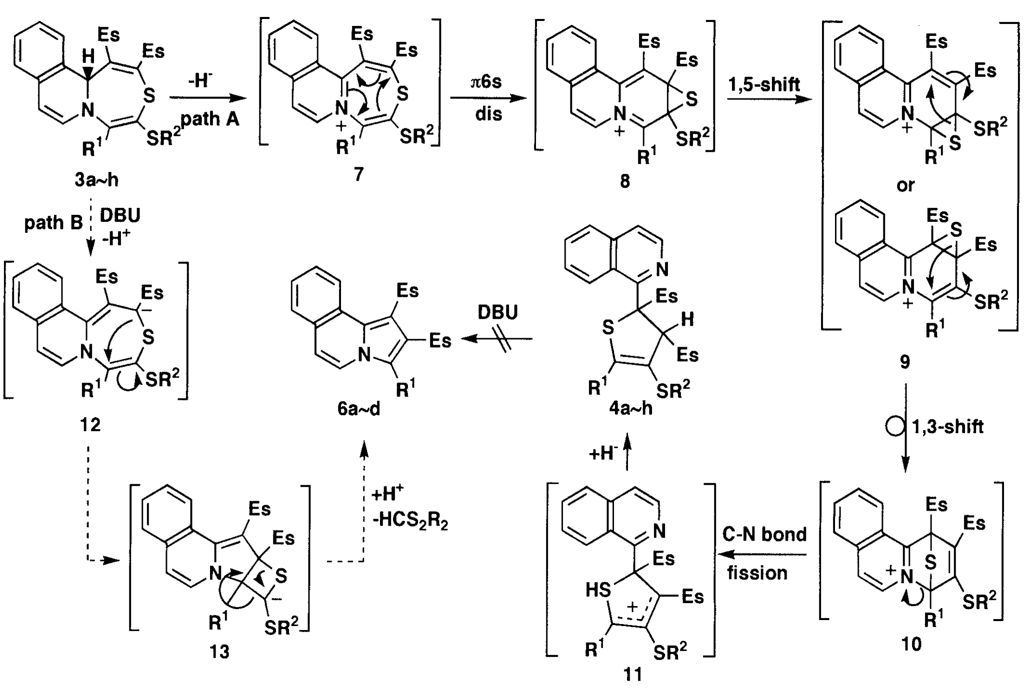


Chart 4

to **6a**—**d**, however, is thought to begin with the abstraction of the bridgehead proton under the characteristic action of a base (DBU). The disrotatory cyclization (π2s + ω2s + ω2a)[9] of the intermediate carbanions **12** to tetracyclic thietane derivatives **13**, followed by their aromatization with the elimination of alkyl dithioformate, can provide pyrrolo[2,1-*a*]isoquinoline derivatives **6a**—**d**. However, our isolation and detection of the fragmentation products, alkyl dithioformates, were unsuccessful. The alternative route to **6a**—**d** *via* dihydrothiophene derivatives **4a**—**h** is negligible because the thermolysis of **4a** in the presence of DBU did not afford any significant product.

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. ^{1}H-NMR spectra were determined with a Hitachi R-600 spectrometer (60 MHz) in deuteriochloroform with tetramethylsilane used as an internal standard and chemical shifts expressed in *d* values. IR spectra were taken with a JASCO FT/IR-5300 infrared spectrophotometer.

Preparation of Trialkyl 4-Alkylthio-12b*H*-1,4-thiazepino[5,4-*a*]isoquinoline-1,2,5-tricarboxylates. General Method A mixture of 2-isoquinolinio[(alkylthio)thiocarbonyl]methylide (**1**, 2 mmol) and dimethyl or diethyl acetylenedicarboxylate (**2**, 2.4 mmol) in chloroform (30 ml) was heated under reflux in a water bath until the starting methylide completely disappeared as confirmed by TLC monitoring (4—5 h). The reaction mixture was concentrated at reduced pressure and the residue was separated by column chromatography on silica gel using chloroform as an eluent. The red chloroform layers were combined and then concentrated at reduced pressure. A recrystallization of the crude product from chloroform–hexane provided the corresponding 12b*H*-1,4-thiazepino[5,4-*a*]isoquinoline derivative as red prisms. Compounds **3c**, **d** were completely in accord with the authentic samples in all respects.[5c] Some physical and spectral data of the new compounds **3a**, **b**, **e**—**h** are as follows:

Trimethyl 4-Methylthio-12b*H*-1,4-thiazepino[5,4-*a*]isoquinoline-1,2,5-tricarboxylate (**3a**): 59% (from **1a** and **2a**), mp 145—147 °C, IR (KBr) 1732 cm^{-1} (CO), ^{1}H-NMR (CDCl$_3$) 2.42 (3H, s, SMe), 3.33, 3.80, 3.84 (each 3H, s, CO$_2$Me), 5.71 (1H, d, J=8.0 Hz, 8-H), 6.22 (1H, d, J=8.0 Hz, 7-H), 6.63 (1H, s, 12b-H), 6.9—7.5 (4H, m, phenyl-H). *Anal.* Calcd for $C_{20}H_{19}NO_6S_2$: C, 55.41; H, 4.42; N, 3.23. Found: C, 55.34; H, 4.47; N, 3.16.

Trimethyl 4-Eethylthio-12b*H*-1,4-thiazepino[5,4-*a*]isoquinoline-1,2,5-tricarboxylate (**3b**): 27% (from **1b** and **2a**), mp 104—106 °C, IR (KBr) 1736 cm^{-1} (CO), ^{1}H-NMR (CDCl$_3$) 1.31 (3H, t, J=7.0 Hz, SCH$_2$C$\underline{H}_3$), 2.7—3.2 (2H, br q, J=7.0 Hz, SC$\underline{H}_2$CH$_3$), 3.38, 3.84, 3.87 (each 3H, s, CO$_2$Me), 5.73 (1H, d, J=8.0 Hz, 8-H), 6.27 (1H, d, J=8.0 Hz, 7-H), 6.70 (1H, s, 12b-H), 6.9—7.6 (4H, m, phenyl-H). *Anal.* Calcd for $C_{21}H_{21}NO_6S_2$: C, 56.36; H, 4.73; N, 3.13. Found: C, 56.39; H, 4.82; N, 3.04.

1,2-Diethyl 5-Methyl 4-Methylthio-12b*H*-1,4-thiazepino[5,4-*a*]isoquinoline-1,2,5-tricarboxylate (**3e**): 48% (from **1a** and **2b**), mp 85—87 °C, IR (KBr) 1728 cm^{-1} (CO), ^{1}H-NMR (CDCl$_3$) 0.93, 1.29 (each 3H, t, J=7.0 Hz, CO$_2$CH$_2$C$\underline{H}_3$), 2.43 (3H, s, SMe), 3.82 (2H, q, J=7.0 Hz, CO$_2$C$\underline{H}_2$CH$_3$), 3.89 (3H, s, CO$_2$Me), 4.33 (2H, q, J=7.0 Hz, CO$_2$C$\underline{H}_2$CH$_3$), 5.77 (1H, d, J=8.0 Hz, 8-H), 6.29 (1H, d, J=8.0 Hz, 7-H), 6.77 (1H, s, 12b-H), 6.9—7.6 (4H, m, phenyl-H). *Anal.* Calcd for $C_{22}H_{23}NO_6S_2$: C, 57.25; H, 5.02; N, 3.03. Found: C, 57.26; H, 5.11; N, 2.93.

1,2-Diethyl 5-Methyl 4-Ethylthio-12b*H*-1,4-thiazepino[5,4-*a*]isoquinoline-1,2,5-tricarboxylate (**3f**): 32% (from **1b** and **2b**), mp 95—97 °C, IR (KBr) 1732 cm^{-1} (CO), ^{1}H-NMR (CDCl$_3$) 0.95, 1.31 (each 3H, t, J=7.0 Hz, CO$_2$CH$_2$C$\underline{H}_3$), 1.31 (3H, t, J=7.0 Hz, SCH$_2$C$\underline{H}_3$), 2.6—3.2 (2H, br q, J=7.0 Hz, SC$\underline{H}_2$CH$_3$), 3.67 (2H, q, J=7.0 Hz, CO$_2$C$\underline{H}_2$CH$_3$), 3.83 (3H, s, CO$_2$Me), 4.33 (2H, q, J=7.0 Hz, CO$_2$C$\underline{H}_2$CH$_3$), 5.65 (1H, d, J=8.0 Hz, 8-H), 6.19 (1H, d, J=8.0 Hz, 7-H), 6.68 (1H, s, 12b-H), 6.9—7.6 (4H, m, phenyl-H). *Anal.* Calcd for $C_{23}H_{25}NO_6S_2$: C, 58.09; H, 5.30; N, 2.95. Found: C, 58.06; H, 5.28; N, 2.83.

Triethyl 4-Methylthio-12b*H*-1,4-thiazepino[5,4-*a*]isoquinoline-1,2,5-tricarboxylate (**3g**): 64% (from **1c** and **2b**), mp 105—107 °C, IR (KBr) 1728 cm^{-1} (CO), ^{1}H-NMR (CDCl$_3$) 0.93, 1.38, 1.43 (each 3H, t, J=7.0 Hz, CO$_2$CH$_2$C$\underline{H}_3$, SCH$_2$C$\underline{H}_3$), 2.41 (3H, s, SMe), 3.79, 4.24, 4.32 (each 2H, q, J=7.0 Hz, CO$_2\underline{H}_2$CH$_3$), 5.65 (1H, d, J=8.0 Hz, 8-H), 6.21 (1H, d, J=8.0 Hz, 7-H), 6.72 (1H, s, 12b-H), 6.9—7.4 (4H, m, phenyl-H). *Anal.* Calcd for $C_{23}H_{25}NO_6S_2$: C, 58.09; H, 5.30; N, 2.95. Found: C, 58.13; H, 5.41; N, 2.88.

Triethyl 4-Methylthio-12b*H*-1,4-thiazepino[5,4-*a*]isoquinoline-1,2,5-tricarboxylate (**3h**): 48% (from **1d** and **2b**), mp 82—84 °C, IR (KBr) 1743, 1726 cm^{-1} (CO), ^{1}H-NMR (CDCl$_3$) 0.96, 1.29, 1.35, 1.46 (each 3H, t, J=7.0 Hz, CO$_2$CH$_2$C$\underline{H}_3$, SCH$_2$C$\underline{H}_3$), 2.6—3.2 (2H, br q, J=7.0 Hz, SC$\underline{H}_2$CH$_3$), 3.81, 4.27, 4.34 (each 2H, q, J=7.0 Hz, CO$_2$C$\underline{H}_2$CH$_3$), 5.70 (1H, d, J=8.0 Hz, 8-H), 6.28 (1H, d, J=8.0 Hz, 7-H), 6.79 (1H, s, 12b-H), 6.9—7.5 (4H, m, phenyl-H). *Anal.* Calcd for $C_{24}H_{27}NO_6S_2$: C, 58.88; H, 5.56; N, 2.86. Found: C, 58.77; H, 5.67; N, 2.78.

Thermolysis of 12b*H*-1,4-Thiazepino[5,4-*a*]isoquinoline Derivatives in

the Absence of Base. General Method A red solution of trialkyl 4-alkylthio-12b*H*-1,4-thiazepino[5,4-*a*]isoquinoline-1,2,5-tricarboxylate (**3**, 1 mmol) in xylene (20 ml) was heated at the reflux temperature for about 25 h until the characteristic color completely disappeared. The reaction mixture was then concentrated at reduced pressure. The residual oil was separated by column chromatography on alumina using chloroform as an eluent. The chloroform layers were concentrated and the crude crystals which had been collected from them were purified by recrystallization from chloroform–hexane. Compounds **4a**—**h** were obtained as colorless prisms.

Some data on these products **4a**—**h** are as follows:

Trimethyl 2-(1-Isoquinolinyl)-4-methylthio-2,3-dihydrothiophene-2,3,5-tricarboxylate (**4a**): 11% (from **3a**), mp 204—206 °C, IR (KBr) 1747, 1701 cm^{-1} (CO), ^{1}H-NMR (CDCl$_3$) 2.83 (3H, s, SMe), 3.66, 3.70, 3.87 (each 3H, s, CO$_2$Me), 6.12 (1H, s, 3-H), 7.5—8.7 (6H, m, aromatic protons of isoquinoline). *Anal.* Calcd for $C_{20}H_{19}NO_6S_2$: C, 55.41; H, 4.42; N, 3.23. Found: C, 55.54; H, 4.31; N, 3.21.

Trimethyl 4-Ethylthio-2-(1-isoquinolinyl)-2,3-dihydrothiophene-2,3,5-tricarboxylate (**4b**): 20% (from **3b**), mp 201—203 °C, IR (KBr) 1747, 1711 cm^{-1} (CO), ^{1}H-NMR (CDCl$_3$) 1.51 (3H, t, $J=7.0$ Hz, SCH$_2$C$\underline{H}_3$), 3.32 (2H, q, $J=7.0$ Hz, SC$\underline{H}_2$CH$_3$), 3.66, 3.68, 3.86 (each 3H, s, CO$_2$Me), 6.12 (1H, s, 3-H), 7.5—8.6 (6H, m, aromatic protons of isoquinoline). *Anal.* Calcd for $C_{21}H_{21}NO_6S_2$: C, 56.36; H, 4.73; N, 3.13. Found: C, 56.42; H, 4.79; N, 3.01.

5-Ethyl 2,3-Dimethyl 2-(1-Isoquinolinyl)-4-methylthio-2,3-dihydrothiophene-2,3,5-tricarboxylate (**4c**): 13% (from **3c**), mp 179—181 °C, IR (KBr) 1745, 1693 cm^{-1} (CO), ^{1}H-NMR (CDCl$_3$) 1.18 (3H, t, $J=7.0$ Hz, CO$_2$CH$_2$C$\underline{H}_3$), 2.83 (3H, s, SCH$_3$), 3.71, 3.87 (each 3H, s, CO$_2$Me), 3.8—4.4 (2H, m, CO$_2$C$\underline{H}_2$CH$_3$), 6.15 (1H, s, 3-H), 7.5—8.6 (6H, m, aromatic protons of isoquinoline). *Anal.* Calcd for $C_{21}H_{21}NO_6S_2$: C, 56.36; H, 4.73; N, 3.13. Found: C, 56.36; H, 4.80; N, 3.04.

5-Ethyl 2,3-Dimethyl 4-Ethylthio-2-(1-isoquinolinyl)-2,3-dihydrothiophene-2,3,5-tricarboxylate (**4d**): 17% (from **3d**), mp 162—164 °C, IR (KBr) 1751, 1699 cm^{-1} (CO), ^{1}H-NMR (CDCl$_3$) 1.21 (3H, t, $J=7.0$ Hz, CO$_2$CH$_2$C$\underline{H}_3$), 1.51 (3H, t, $J=7.0$ Hz, SCH$_2$C$\underline{H}_3$), 3.32 (2H, q, $J=7.0$ Hz, SC$\underline{H}_2$CH$_3$), 3.71, 3.89 (each 3H, s, CO$_2$Me), 3.8—4.4 (2H, m, CO$_2$C$\underline{H}_2$CH$_3$), 6.17 (1H, s, 3-H), 7.5—8.6 (6H, m, aromatic protons of isoquinoline). *Anal.* Calcd for $C_{22}H_{23}NO_6S_2$: C, 57.25; H, 5.02; N, 3.03. Found: C, 57.29; H, 5.11; N, 2.91.

2,3-Diethyl 5-Methyl 2-(1-Isoquinolinyl)-4-methylthio-2,3-dihydrothiophene-2,3,5-tricarboxylate (**4e**): 10% (from **3e**), mp 156—158 °C, IR (KBr) 1741, 1711 cm^{-1} (CO), ^{1}H-NMR (CDCl$_3$) 1.09, 1.34 (each 3H, t, $J=7.0$ Hz, CO$_2$CH$_2$C$\underline{H}_3$), 2.85 (3H, s, SMe), 3.64 (3H, s, CO$_2$Me), 4.16, 4.21 (each 2H, q, $J=7.0$ Hz, CO$_2$C$\underline{H}_2$CH$_3$), 6.09 (1H, s, 3-H), 7.5—8.6 (6H, m, aromatic protons of isoquinoline). *Anal.* Calcd for $C_{22}H_{23}NO_6S_2$: C, 57.25; H, 5.02; N, 3.03. Found: C, 57.05; H, 5.07; N, 2.92.

2,3-Diethyl 5-Methyl 4-Ethylthio-2-(1-isoquinolinyl)-2,3-dihydrothiophene-2,3,5-tricarboxylate (**4f**): 24% (from **3f**), mp 189—191 °C, IR (KBr) 1739, 1714 cm^{-1} (CO), ^{1}H-NMR (CDCl$_3$) 1.08, 1.35 (each 3H, t, $J=7.0$ Hz, CO$_2$CH$_2$C$\underline{H}_3$), 1.52 (3H, t, $J=7.0$ Hz, SCH$_2$C$\underline{H}_3$), 3.36 (2H, q, $J=7.0$ Hz, SC$\underline{H}_2$CH$_3$), 3.66 (3H, s, CO$_2$Me), 4.17, 4.31 (each 2H, q, $J=7.0$ Hz, CO$_2$C$\underline{H}_2$CH$_3$), 6.10 (1H, s, 3-H), 7.5—8.6 (6H, m, aromatic protons of isoquinoline). *Anal.* Calcd for $C_{23}H_{25}NO_6S_2$: C, 58.09; H, 5.30; N, 2.95. Found: C, 58.09; H, 5.40; N, 2.88.

Triethyl 2-(1-Isoquinolinyl)-4-methylthio-2,3-dihydrothiophene-2,3,5-tricarboxylate (**4g**): 12% (from **3g**), mp 112—114 °C, IR (KBr) 1732, 1695 cm^{-1} (CO), ^{1}H-NMR (CDCl$_3$) 1.09, 1.21, 1.35 (each 3H, t, $J=7.0$ Hz, CO$_2$CH$_2$C$\underline{H}_3$), 2.85 (3H, s, SMe), 3.8—4.6 (6H, overlapped with others, 3 × CO$_2$C$\underline{H}_2$CH$_3$), 6.13 (1H, s, 3-H), 7.5—8.6 (6H, m, aromatic protons of isoquinoline). *Anal.* Calcd for $C_{23}H_{25}NO_6S_2$: C, 58.09; H, 5.30; N, 2.95. Found: C, 57.83; H, 5.35; N, 2.81.

Triethyl 4-Ethylthio-2-(1-isoquinolinyl)-2,3-dihydrothiophene-2,3,5-tricarboxylate (**4h**): 17% (from **3h**), mp 133—135 °C, IR (KBr) 1745, 1701 cm^{-1} (CO), ^{1}H-NMR (CDCl$_3$) 1.09, 1.22, 1.35 (each 3H, t, $J=7.0$ Hz, CO$_2$CH$_2$C$\underline{H}_3$), 1.53 (3H, t, $J=7.0$ Hz, SCH$_2$C$\underline{H}_3$), 3.37 (2H, q, $J=7.0$ Hz, SC$\underline{H}_2$CH$_3$), 3.9—4.6 (6H, overlapped with others, 3 × CO$_2$C$\underline{H}_2$CH$_3$), 6.20 (1H, s, 3-H), 7.5—8.6 (6H, m, aromatic protons of isoquinoline). *Anal.* Calcd for $C_{24}H_{27}NO_6S_2$: C, 58.88; H, 5.56; N, 2.86. Found: C, 58.89; H, 5.67; N, 2.77.

Thermolysis of 12b*H*-1,4-Thiazepino[5,4-*a*]isoquinoline Derivatives in the Presence of Base. General Method A solution of trialkyl 4-alkylthio-12b*H*-1,4-thiazepino[5,4-*a*]isoquinoline-1,2,5-tricarboxylate (**3**, 1 mmol) and DBU (0.2 g, 1.3 mmol) in xylene (20 ml) was heated at the reflux temperature for 8 h. The reaction mixture was concentrated at reduced pressure and the residual oil was then separated by column chromatography on alumina using ether and chloroform as eluents. The combined chloroform layers were concentrated at reduced pressure and the crude product was purified by recrystallization from ether–hexane. Compounds **6a**—**d** were obtained as pale yellow needles. Some data of **6a**—**d** are as follows:

Trimethyl Pyrrolo[2,1-*a*]isoquinoline-1,2,3-tricarboxylate (**6a**): 20% (from **3a**) and 28% (from **3b**), mp 153—155 °C (Lit. 154—155 °C$^{8a,b)}$ and 150—151 °C).$^{8c)}$

3-Ethyl 1,2-Dimethyl Pyrrolo[2,1-*a*]isoquinoline-1,2,3-tricarboxylate (**6b**): 38% (from **3c**) and 28% (from **3d**), mp 130—131 °C, IR (KBr) 1738, 1703 cm^{-1} (CO), ^{1}H-NMR (CDCl$_3$) 1.40 (3H, t, $J=7.0$ Hz, CO$_2$CH$_2$C$\underline{H}_3$), 3.99, 4.01 (each 3H, s, CO$_2$Me), 4.44 (2H, q, $J=7.0$ Hz, CO$_2$C$\underline{H}_2$CH$_3$), 7.30 (1H, d, $J=7.0$ Hz, 6-H), 7.5—8.0 (3H, m, 7, 8, 9-H), 9.48 (1H, d, $J=7.0$ Hz, 5-H), and 9.4—9.8 (1H, m, 10-H). *Anal.* Calcd for $C_{19}H_{17}NO_6$: C, 64.22; H, 4.82; N, 3.94. Found: C, 64.33; H, 4.86; N, 3.88.

1,2-Diethyl 3-Methyl Pyrrolo[2,1-*a*]isoquinoline-1,2,3-tricarboxylate (**6c**): 25% (from **3e**) and 19% (from **3f**), mp 120—121 °C (Lit. 120 °C).$^{8c)}$

Triethyl Pyrrolo[2,1-*a*]isoquinoline-1,2,3-tricarboxylate (**6d**): 25% (from **3g**) and 16% (from **3h**), mp 95—96 °C, IR (KBr) 1741, 1693 cm^{-1} (CO), ^{1}H-NMR (CDCl$_3$) 1.40 (6H, t, $J=7.0$ Hz, 2 × CO$_2$CH$_2$C$\underline{H}_3$), 1.43 (3H, t, $J=7.0$ Hz, CO$_2$CH$_2$C$\underline{H}_3$), 4.48 (6H, q, $J=7.0$ Hz, 3 × CO$_2$C$\underline{H}_2$CH$_3$), 7.30 (1H, d, $J=7.0$ Hz, 6-H), 7.5—8.0 (3H, m, 7, 8, 9-H), 9.50 (1H, d, $J=7.0$ Hz, 5-H), 9.4—9.8 (1H, m, 10-H). *Anal.* Calcd for $C_{21}H_{21}NO_6$: C, 65.79; H, 5.52; N, 3.65. Found: C, 65.99; H, 5.57; N, 3.63.

Crystallography of 5-Ethyl 2,3-Dimethyl 2-(1-Isoquinolinyl)-4-methylthio-2,3-dihydrothiophene-2,3,5-tricarboxylate (4d) A single crystal (0.08 × 0.38 × 0.86 mm) grown from CHCl$_3$–hexane was used for unit-cell determination and data collection by means of a Rigaku AFC5S four-circle diffractometer, with graphite-monochromated Mo*Kα* radiation ($\lambda=0.71069$ Å). Crystal data of **4d**: $C_{21}H_{21}NO_6S_2$; $M=447.52$; triclinic, space group $P\bar{1}$ (#2), $Z=2$ with $a=10.833$ (2) Å, $b=12.317$ (4) Å, $c=9.043$ (4) Å; $\alpha=110.88$ (3)°, $\beta=104.89$ (2)°, $\gamma=79.65$ (2)°; $V=1084.2$ (6) Å^3, and $D_{\text{calc}}=1.371$ g/cm^3. All calculations were performed using the TEXSAN program.$^{10)}$ The structure was solved by a direct method (MITHRIL).$^{11)}$ The non-hydrogen atoms were refined anisotropically and the hydrogen atoms were included in idealized positions in the structure factor calculation. The final R- and R_w-factors after full-matrix least-squares refinements were 0.081 and 0.116, respectively, for 2937 observed reflections.

References and Notes

1) For part 43 of this series, see Kakehi A., Ito S., Ishida F., Tominaga Y., *J. Org. Chem.*, **62**, 7788—7793 (1997).

2) For this type of equilibrium there are some reviews; see *a*) Vogel E., Günther H., *Angew. Chem.*, **79**, 429—446 (1967); *b*) Maier G., *ibid.*, **79**, 446—458 (1967); *c*) Paquette L. A., "Nonbenzenoid Aromatics," Vol. 1, ed. by Snyder J. P., Academic Press, New York, 1969, pp. 249—310.

3) *a*) Hafner K., Zinser D., Moritz K.-L., *Tetrahedron Lett.*, **1964**, 1733—1737; *b*) Vogel E., Böll W. A., Günther H., *ibid.*, **1965**, 609—615; *c*) Paquette L. A., Kuhla D. E., Barrett J. H., *J. Org. Chem.*, **34**, 2879—2884 (1969); *d*) Prinzbach H., Babsch H., Fritz H., Hug P., *Tetrahedron Lett.*, **1977**, 1355—1358; *e*) Padwa A., Xu S. L., *J. Am. Chem. Soc.*, **114**, 5881—5882 (1992).

4) *a*) Scott G. P., *J. Am. Chem. Soc.*, **75**, 6332—6333 (1953); *b*) Parham W. E., Koncos R., *ibid.*, **83**, 4034—4038 (1961); *c*) Parham W. E., Bhavsar M. D., *J. Org. Chem.*, **29**, 1575—1576 (1964); *d*) Hoffmann H., Westernacher H., *Angew. Chem.*, **79**, 238 (1967); *e*) Parham W. E., Weetman D. G., *J. Org. Chem.*, **34**, 56—61 (1969).

5) *a*) Kakehi A., Ito S., Hakui J., *Chem. Lett.*, **1992**, 777—780; *b*) Kakehi A., Ito S., *Heterocycles*, **36**, 1195—1198 (1993); *c*) Kakehi A., Ito S., Hakui J., *Bull. Chem. Soc. Jpn.*, **66**, 3475—3482 (1993); *d*) Kakehi A., Ito S., Mitani M., Kanaoka M., *ibid.*, **67**, 1646—1654 (1994)

6) Kakehi A., Ito S., Ishida F., Tominaga Y., *Hetrocycles*, **41**, 2657—2660 (1995).

7) Johnson C. K., "ORTEP II, Report ORNL-5138," Oak Ridge National Laboratory, Oak Ridge, Tennessee (1976).

8) *a*) Acheson R. M., Hole F., *J. Chem. Soc.*, **1962**, 748—752; *b*) Acheson R. M., Robinson D. A., *J. Chem. Soc.* (*C*), **1968**,

1633—1638; *c*) Kutsuma T., Fujiyama K.,Sekine Y., Kobayashi Y., *Chem. Pharm. Bull.*, **20**, 1558—1566 (1972).

9) Other reaction modes such as $\pi 2a+\omega 2s+\omega 2s$, $\pi 2a+\omega 2s+\omega 2s$, and $\pi 2a+\omega 2a+\omega 2a$ are also possible. For the rules on electrocyclic reactions, see Woodward R. B., Foffmann R., *Angew. Chem.*, **81**, 797—869 (1969).

10) "TEXSAN TEXRAY", Structure Analysis Package, Molecular Structure Corporation (1985).

11) Gilmore C. J., *J. Appl. Crystallogr.*, **17**, 42—46, (1984).