

**Studies on Indole Derivatives. XXII.¹⁾ Synthesis and Reactions of
Methyl 3-(2-Substituted 3-indolyl)thio-2-cyano-
3-methylthioacrylates**

In a continuation of our previous studies of the ketenethioacetals, the authors have been reported the synthesis of several heterocyclic compounds.²⁾ Recently, thiophene synthesis by various methods has been reported.³⁾

The reaction of 3-iodoindole with methyl 2-cyano-3-mercapto-3-(methylthio)acrylate (II) in the presence of potassium hydroxide in water gave yellow crystals of mp 154—156°, the physical data of which suggest a novel ketenethioacetal derivative (IIIa) (Yield 65%). Similarly the reaction of 2-substituted 3-iodoindole with II gave also ketenethioacetals (IIIb, IIIc) (IIIb; mp 196°, IIIc; mp 158°).

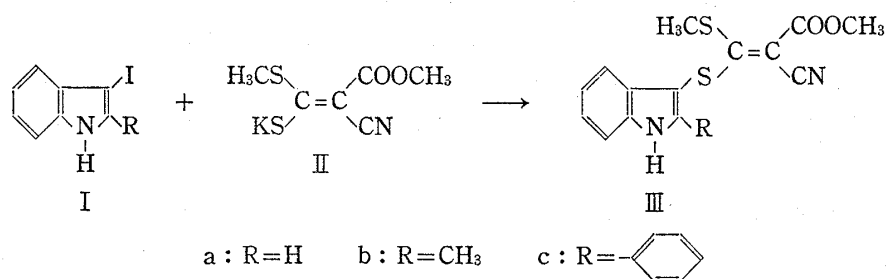


Chart 1

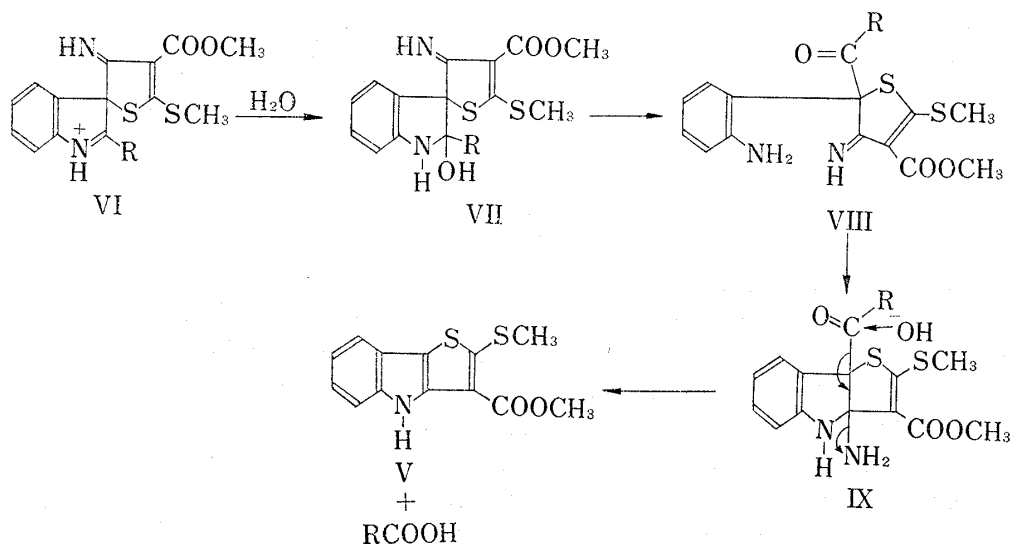
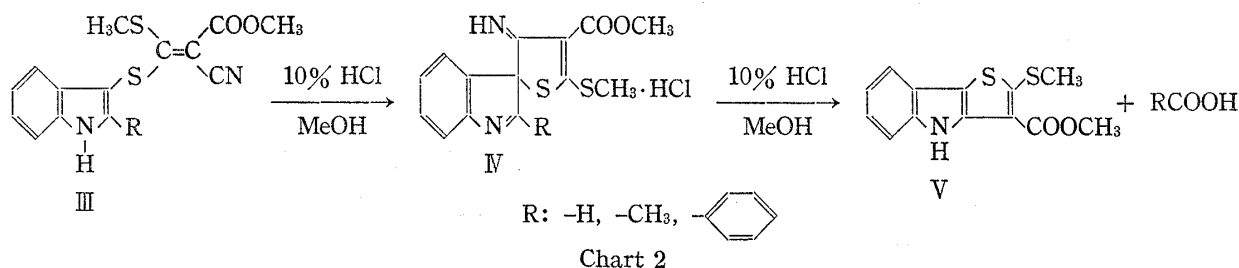
Treatment of IIIa with 10% hydrochloric acid in methanol under refluxing for 10 min gave red needles (IVa), C₁₄H₁₂O₂N₂S₂·HCl (mass spectrum *m/e*: 304 (M⁺)), mp 300°, in good yield. The infrared (IR) spectrum of IVa showed absorptions at 3200—3280 cm⁻¹ (shoulder) due to NH, at 1690 cm⁻¹ due to a carbonyl group, and 1660 and 1610 cm⁻¹ due to C=N. This IR spectrum did not show any absorption of a cyano group at 2200 cm⁻¹ present in IIIa. The ultraviolet (UV) spectrum revealed maxima at 234 (ε=4.66) and 280 (ε=4.39) and these absorption was not similar to that of the parent compound (IIIa) (287 (ε=4.12), 325 (ε=4.16)). From these spectroscopic data and elemental analysis, this compound, IVa, was found to be a cyclized product, 3-imino-4-methoxycarbonyl-5-(methylthio)thiophene-2-spiro-3-(3H-indole). In a similar manner as above, treatment of other compounds (IIIb, IIIc) with 10% hydrochloric acid gave spiro compounds (IVb, IVc) in good yield (IVb; mp 300°, *Anal. Calcd.* for C₁₅H₁₄O₂N₂S₂·HCl: C, 50.73; H, 4.23; N, 7.89. Found: C, 50.76; H, 4.17; N, 8.06. IR

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- 3) a) R. Gompper, E. Kutter, and W. Töpfl, *Ann.*, **659**, 90 (1962); b) J.B. Hendrickson, R. Rees, and J.F. Templeton, *J. Am. Chem. Soc.*, **86**, 107 (1964); c) H. Wynberg and H.J. Kooreman, *J. Am. Chem. Soc.*, **87**, 1739 (1965); d) E.J. Smutny, *J. Am. Chem. Soc.*, **91**, 208 (1969); e) S. Rajappa and B.G. Advani, *Tetrahedron Letters*, **1969**, 5067; f) M. Takaku, Y. Hayashi, and H. Nozaki, *Bull. Chem. Soc. Japan*, **43**, 1917 (1970); g) I.T. Kay and N. Punja, *J. Chem. Soc. (C)*, **1970**, 2409; h) R. Laliberté and G. Médawa, *Can. J. Chem.*, **48**, 2709 (1970); i) K. Hirai and T. Ishiba, *Chem. Pharm. Bull.* (Tokyo), **19**, 2194 (1971).

(KBr) cm^{-1} : 3100—3200 (shoulder) (NH), 1680 (C=O), 1630 (C=N). UV $\lambda_{\text{max}}^{\text{EtOH}}$ nm ($\log \epsilon$): 232 (4.38), 280 (4.10), (IVc; mp 243°, *Anal.* Calcd. for $\text{C}_{20}\text{H}_{16}\text{O}_2\text{N}_2\text{S}_2 \cdot \text{HCl} \cdot 3/2\text{H}_2\text{O}$: C, 54.06; H, 4.51; N, 6.51. Found: C, 53.86; H, 4.35; N, 6.51. IR (KBr) cm^{-1} : 3200 (shoulder) (NH), 1669 (C=O), 1610 (C=N). UV $\lambda_{\text{max}}^{\text{EtOH}}$ nm ($\log \epsilon$): 231 (4.48), 265 (4.37), 300 (4.11)).

The compound (IVa) was added to a solution of 10% hydrochloric acid in methanol, and the mixture was refluxed for 5 hr on a steam bath. After cooling, the precipitate was collected by filtration and recrystallized from methanol to give white needles of V, $\text{C}_{13}\text{H}_{11}\text{O}_2\text{NS}_2$, mp 188°, in 60—80% yield. The mass spectrum of V showed a molecular ion peak at m/e : 277. Its nuclear magnetic resonance spectrum showed two three proton-singlets due to methylthio and methoxycarbonyl groups at 2.59 and 3.97 ppm. Its IR spectrum indicated absorption bands due to NH at 3440 cm^{-1} and due to a carbonyl band at 1670 cm^{-1} . Its UV spectrum revealed maxima at 236 ($\epsilon=4.57$), 280 ($\epsilon=4.09$), 326 ($\epsilon=4.03$), 356 ($\epsilon=4.04$). From these spectral data and elemental analysis, this compound, V, was found to be a rearranged product, 2-methylthio-3-(methoxycarbonyl)thieno[3,2-*b*]indole. This compound V was also obtained from IVb or IVc. In the case of 2-phenylindole derivatives, the reaction time was about 5 hr longer than those of other compound and benzoic acid was also obtained simultaneously in good yield.

A possible mechanism for the reaction is outlined in Chart 3.



Details of chemical properties, synthesis, and other reactions of these compounds will be reported later.

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