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SYNTHESIS AND REACTION OF 3-METHYLENE-2,3-DIHYDROINDOLIZIN-2-ONE[1)]

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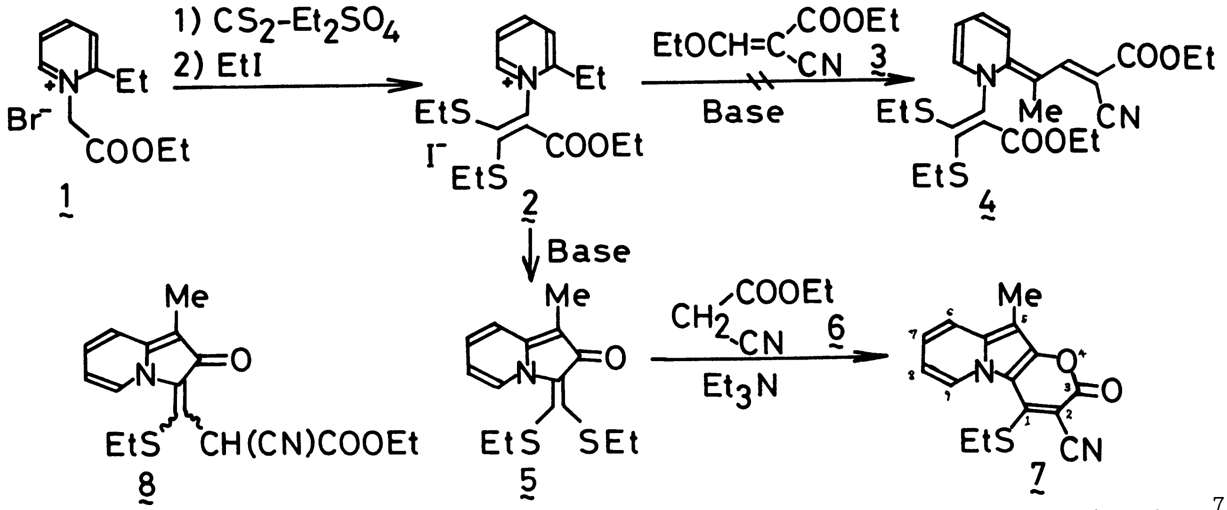
The alkaline treatment of 1-[1-ethoxycarbonyl-2,2-bis(ethylthio)-ethenyl]-2-ethylpyridinium iodide in chloroform gave the corresponding self-condensation product, 1-methyl-3-[1,1-bis(ethylthio)methylene]-indolizin-2-one, in good yield, and the reaction of the indolizinone with ethyl cyanoacetate in the presence of triethylamine afforded 2-cyano-1-ethylthio-5-methyl-3-oxo-3*H*-pyrano[2,3-*b*]indolizine in 34% yield.

Although a number of indolizines and pyrazolo[1,5-*a*]pyridines are synthesized by various methods, the conversions from these compounds to higher condensed heterocycles may be less fruitful except the cyclazine synthesis from indolizine.[2)] In the course of our recent study[3)] on polyfunctionalized indolizine and pyrazolo[1,5-*a*]-pyridine syntheses, we found a novel condensed-heterocycle formation from a pyridinium salt. In this letter, we wish to state the formation of 3-methylene-2,3-dihydro-indolizin-2-one derivative and its facile transformation to pyrano[2,3-*b*]indolizine.

When the reaction of 1-[1-ethoxycarbonyl-2,2-bis(ethylthio)ethenyl]-2-ethyl-pyridinium iodide **2**, readily available from 1-(ethoxycarbonylmethyl)-2-ethylpyridinium bromide **1** according to Tominaga's procedure,[4)] with ethyl ethoxymethylenecyanoacetate **3** in the presence of potassium carbonate in chloroform was examined in order to prepare the corresponding 2-allylidene-1,2-dihydropyridine derivative **4**, a dark green oily product **5**, ν (Neat) 1600 cm^{-1} (CO),[5)] δ ($CDCl_3$) 1.19 and 1.24 (each 3H, t, J=7.0 Hz, $2\times CH_2\underline{CH_3}$), 1.73 (3H, s, 1-Me), 2.82 and 3.11 (each 2H, q, J=7.0 Hz, $2\times S\underline{CH_2}CH_3$), 5.93 (1H, dt, J=7.0, 7.0, and 2.0 Hz, 6-H), 6.53 (1H, dd, J=9.0 and 2.0 Hz, 8-H), 6.76 (1H, q, J=9.0 and 7.0 Hz, 7-H), and 8.59 (1H, d, J=7.0 Hz, 5-H), was isolated.[6)] These spectral data reveal the product **5** not to be the expected allylidenedihydro-pyridine **4** but to be a self-condensation product of salt **2**; the treatment of **2** with base in the absence of **3** gave the same product **5** in 92% yield. The chemical shift (δ 1.73) due to methyl protons in the NMR spectrum suggests that the methyl



group should attach on an olefinic double bond rather than on an aromatic ring.7) Thus, the structure of compound **5** was concluded to be 1-methyl-3-[1,1-bis(ethylthio)-methylene]indolizin-2-one. In order to make sure this conclusion, the reaction between the ketene dithioacetal group in **5** and an active methylene compound was examined. When an ethanolic solution of **5** was treated with ethyl cyanoacetate **6** in the presence of triethylamine at the reflux temperature, compound **7**, brown needles, mp 259-261 $^{\circ}$C, ν (KBr) 2230 (CN) and 1695 cm^{-1} (CO), δ ($CDCl_3$) 1.42 (3H, t, J=7.0 Hz, $SCH_2\underline{CH_3}$), 2.27 (3H, s, 5-Me), 3.50 (2H, q, J=7.0 Hz, $S\underline{CH_2}CH_3$), 6.93 (1H, br t, J=7.0 and 7.0 Hz, 8-H), 7.33 (1H, br t, J=9.0 and 7.0 Hz, 7-H), 7.51 (1H, d, J=9.0 Hz, 6-H), and 9.47 (1H, d, J=7.0 Hz, 9-H), was obtained in 34% yield. From the inspection of these spectral data and its elementary analysis,6) compound **7** was determined to be 2-cyano-1-ethylthio-5-methyl-3-oxo-3*H*-pyrano[2,3-*b*]indolizine, which must be given by the further condensation of the initially formed displacement product **8**. Further investigation is in progress.

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(5) Such lowered absorption band due to the carbonyl group seems to exhibit the large contribution of polarized structure in **5**.
(6) Although the elementary analysis of **5** was unsuccessful because of its instability, that of **7** was in good accord with the proposed structure.
(7) The 1-methyl signal in 1-methylindolizine appeared at δ 2.27 in deuteriochloroform. Our unpublished data.

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