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CONVENIENT SYNTHETIC METHODS OF SOME FUNCTIONALIZED INDOLIZINES[1)]

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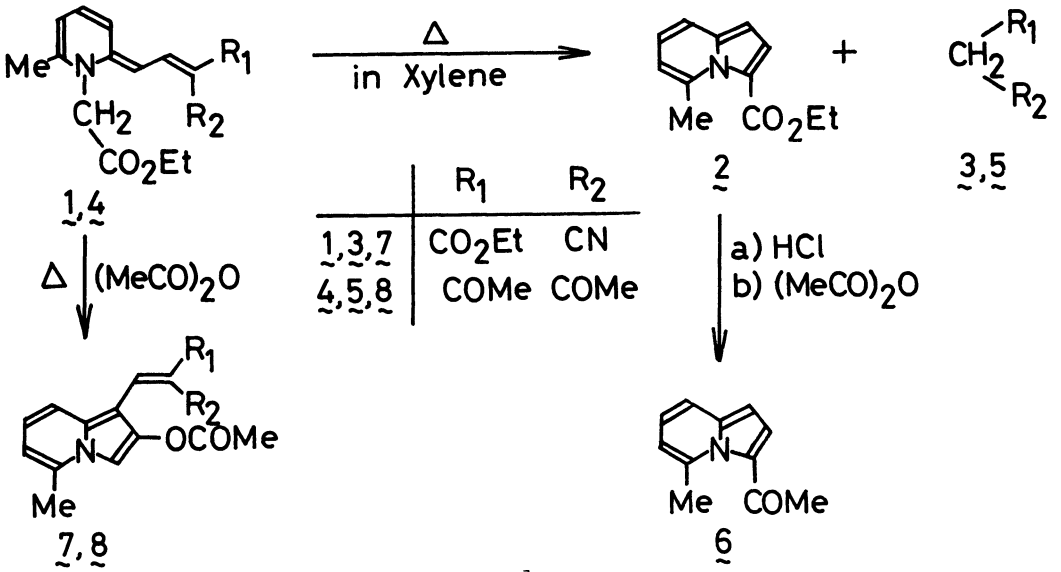
The thermolyses of 2-allylidene-1-ethoxycarbonylmethyl-1,2-dihydropyridines gave the corresponding 3-ethoxycarbonylindolizine with elimination of methylene compounds, and their reactions with acetic anhydride afforded 2-acetoxy-1-ethenylindolizines.

Although many synthetic routes of various heterocycles using 2-methylene-1,2-dihydropyridine have been well investigated,[2)] those using its vinylogue, 2-allylidene-1,2-dihydropyridine, have been scarcely reported. Recently, we reported that 2-allylidene-1,2-dihydropyridines possessing an electrophilic center in the 1-substituent are converted smoothly to the corresponding 3-ethenylpyrazolo[1,5-*a*]-pyridines.[3)] As a part of our study in this area, we now wish to report novel reactions of 2-allylidene-1,2-dihydropyridine derivatives to some indolizine derivatives.

When a solution of 1 (R_1=CO_2Et, R_2=CN)[4)] in xylene was refluxed for 3 days and then the reaction mixture was separated by the usual manner, compound 2, colorless oil, ν^{Neat} 1704 cm^{-1} (C=O), δ (CCl_4) 1.35 (3H, t, J=7.0 Hz, $OCH_2\underline{CH_3}$), 2.69 (3H, s, 5-CH_3), 4.33 (2H, q, J=7.0 Hz, $O\underline{CH_2}CH_3$), 6.48 (1H, d, J=4.0 Hz, 1-H), 6.57 (1H, d, J=7.0 Hz, 6-H), 6.95 (1H, q, J=7.0 and 8.5 Hz, 7-H), 7.41 (1H, d, J=8.5 Hz, 8-H), and 7.54 (1H, d, J=4.0 Hz, 2-H), was obtained in 93% yield together with ethyl cyanoacetate 3 (detected by means of glc). Thermolysis of 4 (R_1=R_2=COMe) gave also 2 in 38% yield with acetylacetone 5. The structure of 2 was determined to be 3-ethoxycarbonyl-5-methylindolizine by its IR and NMR spectral inspections and by the conversion of 2 to known 3-acetyl-5-methylindolizine 6.[5)] On the other hand, the reactions of 1 and 4 with acetic anhydride gave yellow crystalline compounds 7 and 8 in 83 and 50% yields, respectively.[6)] Compounds; 7, mp 123-125 °C,



ν^{KBr} 2240 (CN), 1762 (C=O), and 1705 cm^{-1} (C=O), δ ($CDCl_3$) 1.42 (3H, t, J=7.0 Hz, $OCH_2\underline{CH_3}$), 2.52 (3H, s, $COCH_3$), 2.60 (3H, s, 5-CH_3), 4.43 (2H, q, J=7.0 Hz, $O\underline{CH_2}CH_3$), 6.81 (1H, d, J=7.0 Hz, 6-H), 7.27 (1H, q, J=7.0 and 9.0 Hz, 7-H), 7.70 (1H, s, 3-H), 7.79 (1H, d, J=9.0 Hz, 8-H), and 8.42 (1H, s, 1[1']-H), and 8, mp 108-110 °C, ν^{KBr} 1769 (C=O) and 1705 cm^{-1} (C=O), δ ($CDCl_3$), *inter alia*, 2.55 (3H, s, 5-CH_3), 6.68 (1H, d, J=7.0 Hz, 6-H), 7.10 (1H, q, J=7.0 and 9.0 Hz, 7-H), 7.53 (1H, d, J=9.0 Hz, 8-H), 7.61 (1H, s, 3-H), and 8.02 (1H, s, 1[1']-H). The structures of 7 and 8 were concluded to be 2-acetoxy-1-(2,2-disubstituted ethenyl)-5-methylindolizine derivatives by their physical and spectral inspections and by comparison with the spectral data of 3-ethenylpyrazolopyridines prepared earlier by us.[3]

Mechanistically, the formation of 2 seems to proceed via stepwise shifts of a methylene proton in the 1-substituent onto the 2-allylidene group followed by the 1,5-dipolar cyclization of resulting 6-methyl-2-(3,3-disubstituted prop-1-enyl)pyridinium *N*-ethoxycarbonylmethylides,[7] while the formation mechanism of 7 and 8 are unclear but the intermediate of this reaction should be an electrophilic species[3] such as ketene or ketene acetal. Further investigations are in progress.

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