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FIRST SYNTHESIS OF PYRIDO[1',2':1,5]PYRAZOLO[3,4-*b*]PYRIDINE DERIVATIVE[1)]

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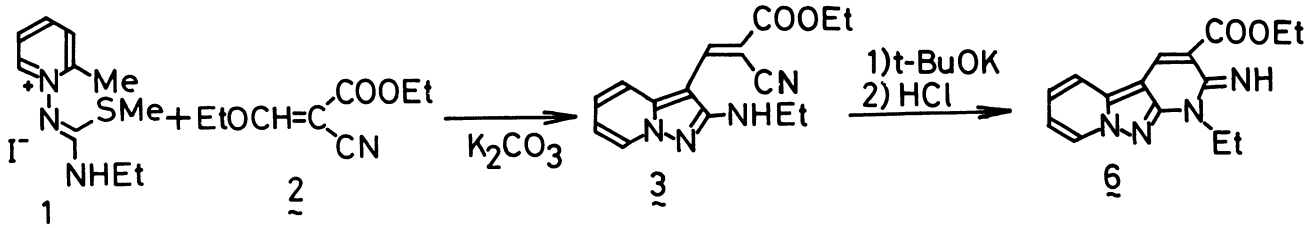
The treatment of 3-[2-cyano-2-(ethoxycarbonyl)ethenyl]-2-(ethylamino)pyrazolo[1,5-*a*]pyridine, obtainable from the reaction of the corresponding pyridinium salt with ethyl ethoxymethylenecyanoacetate in the presence of potassium carbonate, with strong base such as potassium *t*-butoxide gave a new condensed pyrazolopyridine derivative.

In a series of our studies on syntheses using allylidenedihydropyridines we have described that facile and effective transformation of 2-allylidene-1,2-dihydropyridines to the corresponding polyfunctionalized indolizine and pyrazolo[1,5-*a*]-pyridine derivatives.[2-5)] We now wish to report the first synthesis of 2-aminopyrazolo[1,5-*a*]pyridine derivative and its conversion to a further condensed heterocycle, pyrido[1',2':1,5]pyrazolo[3,4-*b*]pyridine derivative.

When an equimolar mixture of pyridinium salt 1, accessible from the reaction of the corresponding pyridinium *N*-ylide[6)] with methyl iodide, and ethyl ethoxymethylenecyanoacetate 2 was treated with excess potassium carbonate in chloroform at room temperature for 7 days and, then the reaction mixture was separated by the column chromatography (alumina) to give compound 3 in 74% yield as the only isolable product. 3,[7)] yellow needles, mp 145-147 °C, ν (KBr) 3335 (NH), 2225 (CN), and 1688 cm^{-1} (CO), δ ($CDCl_3$) 1.33 and 1.36 (each 3H, t, J=7.0 Hz, 2×$CH_2\underline{CH_3}$), 3.48 (2H, m, NH$\underline{CH_2}CH_3$), 4.35 (2H, q, J=7.0 Hz, O$\underline{CH_2}CH_3$), 5.60 (1H, br s, NH), 6.89 (1H, br t, J=7.0 and 7.0 Hz, 6-H), 7.40 (1H, br t, J=9.0 and 7.0 Hz, 5-H), 7.75 (1H, d, J=9.0 Hz, 4-H), 8.19 (1H, s, 3(1)-H), and 8.28 (1H, d, J=7.0 Hz, 7-H). The structure of the compound 3 was assigned to be 3-[2-cyano-2-(ethoxycarbonyl)ethenyl]-2-(ethyl-



amino)pyrazolo[1,5-*a*]pyridine by the inspection of its physical and spectral data and by the comparisons with those of various types of vinyl-substituted indolizines and pyrazolopyridines.[2-5] On the other hand, similar treatments of the salt 1 with ethyl ethoxymethyleneacetoacetate 4 and 3-ethoxymethylenepentane-2,4-dione 5 gave only complex mixtures and attempts to isolate any significant products were unsuccessful. The reason for the different reactivity of 4 and 5 is not clear, but it may be correlated to the some interactions between the acyl group in 4 or 5 and the amino group in the salt 1. Since the compound 3 has a favorable configuration for the intramolecular cyclization between the 2- and 3-substituents, an approach of 3 to a further condensed heterocycle was examined. An ethanolic solution of 3 was treated with excess potassium *t*-butoxide at room temperature for 10 min, and then, after the neutralization with diluted hydrochloric acid, the reaction mixture was concentrated to dryness. Purification of the crude product by recrystallizations from chloroform-ether gave compound 6, orange needles, mp 194-196 °C, ν (KBr) 3300 (NH) and 1678 cm^{-1} (CO), δ ($CDCl_3$) 1.38 and 1.39 (each 3H, t, J=7.0 Hz, 2×$CH_2\underline{CH_3}$), 4.30 (4H, q, J=7.0 Hz, $O\underline{CH_2}CH_3$ and $N\underline{CH_2}CH_3$), 6.90 (1H, dt, J=7.0, 7.0 and 2.0 Hz, 3-H), 7.37 (1H, br t, J=8.0 and 7.0 Hz, 2-H), 7.60 (1H, br d, J=8.0 Hz, 1-H), 8.32 (1H, s, 10-H), 8.41 (1H, d, J=7.0 Hz, 4-H), and 9.05 (1H, br s, NH), in 57% yield.[7] The structure of the compound 6 was concluded to be 9-(ethoxycarbonyl)-7-ethyl-8-imino-7,8-dihydropyrido[1',2':1,5]pyrazolo[3,4-*b*]-pyridine by the inspection of these spectral data and by comparisons with those of other pyrazolopyridines. Further scopes and limitation of this reaction will be given in near future.

REFERENCES AND NOTES

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(6) This ylide was prepared by the reaction of 2-picolinium *N*-imine with ethyl isothiocyanate in chloroform.
(7) The compounds 3 and 6 gave satisfactory elemental analyses.

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