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THE PREPARATION OF ETHYL α-(2-PYRIDYL) CARBOXYLATES.

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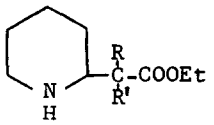
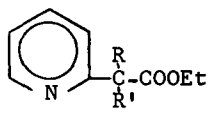
We recently required substituted piperidines of the type (I), the obvious precursors of which are the corresponding pyridines (II).



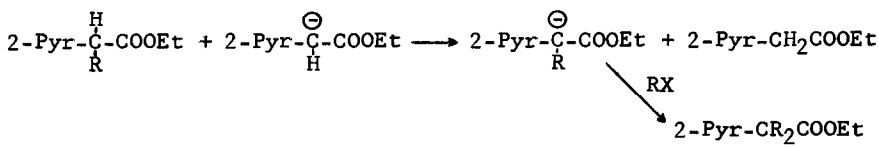
(I)



(II)

Although several of these pyridyl esters have been synthesised (1-5), yields were not good, and no satisfactory general method has been reported.

We found that, when ethyl 2-pyridylacetate is treated with one equivalent of sodium amide in liquid ammonia, followed by the addition of methyl iodide, ethyl 2-pyridylpropionate was produced in 85% yield. This reaction is similar to the alkylation in liquid ammonia of ethyl phenylacetate. A second alkyl group could be introduced by a similar reaction. When ethyl or benzyl halides were used, some unchanged starting material was recovered, together with a mixture of the products of mono- and dialkylation. This dialkylation, which does not occur appreciably with ethyl phenylacetate, presumably reflects the greater acidity of the side-chain protons in the case of the 2-pyridyl esters, such that the reactions:



occur to a significant extent. Dialkylation was minimised by adding the solution of ethyl 2-pyridylacetate anion in liquid ammonia to an ethereal solution of a tenfold excess of the alkyl halide. High yields of the monoalkylated products were then obtained.

TABLE

Ethyl α-(2-pyridyl)alkanoates (II) Prepared by Alkylations in Liquid Ammonia

R	R'	% Yield of distilled Product.	Reference to previous preparation.
H	CH_3	85	4,5
CH_3	CH_3	85	2
H	C_2H_5	87	3
CH_3	C_2H_5	74	2
C_2H_5	C_2H_5	71	a
H	$C_6H_5CH_2$	72	1

a: New compound. b.p. 120-121° /4 mm. Satisfactory analysis obtained.

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