Novel Reaction Involving 2-Formylpyridine *N*-Oxides and Cyclohexyl Isocyanide

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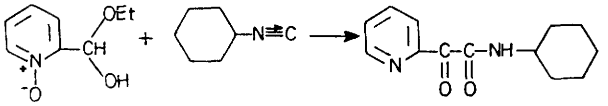
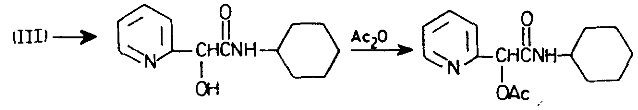
Summary Reaction of 2-formylpyridine (and quinoline) *N*-oxides (or hemiacetals) with cyclohexyl isocyanide (II) in the presence or absence of solvent gives *N*-cyclohexyl-α-oxocarboxamides (*e.g.*, III) of the corresponding heterocycles in excellent yields.

2-FORMYLPYRIDINE 1-OXIDE ETHANOL HEMIACETAL[1] (I; 3 mmol) reacted with cyclohexyl isocyanide[2] (II; 6 mmol) in MeOH (6 ml) at room temperature for 2 h to give a chromatographically homogeneous product (yield, 0·5 g, m.p. 75°) having the empirical formula $C_{13}H_{16}N_2O_2$ (M^+, 232 and elemental analysis). The structure of the product was deduced to be (III) on the basis of its spectral data (u.v., n.m.r., and i.r.) and the reactions below. Its u.v. spectrum, λ_{max} 254 (sh), 260, and 265 (sh) nm, was similar to that of 2-substituted pyridines rather than 2-substituted pyridine 1-oxides, and its i.r. spectrum showed CO absorptions at 1700 and 1650 cm^{-1} the former absorption disappearing on reduction with $NaBH_4$ to afford (IV). Acetylation of (IV) with Ac_2O–pyridine afforded a homogeneous monoacetylated product (V, 80%), δ 2·00 (3H, s, MeCO); *m/e* 277 $(M + 1)^+$, typical of 2-substituted pyridines. The n.m.r. spectrum of (III) is also consistent with the structure assigned.

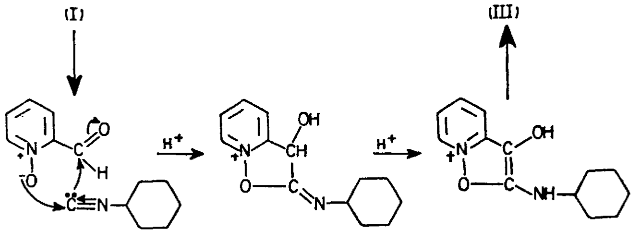


(I) (II) (III)



(IV) (V)

Parallel reactions with 2-formyl derivatives of 3- and 5-methyl-2-picoline 1-oxides and 2-formylquinoline 1-oxide (and its methanol hemiacetal) all afforded the corresponding *N*-cyclohexyl-α-oxocarboxamides in almost quantitative yield.† On the other hand, (II) did not react with the 1-oxides of 2-formylpyridine ethyleneacetal, 2-picoline, and 2-chloromethyl- and 2-cyanomethyl-pyridine.



Scheme

In order to explain the scope and limitations of this novel reaction we tentatively propose the mechanism in the Scheme, by analogy with the α-additions typical of isocyanide reactions.[3]

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† Characterized on the basis of spectral data (u.v., n.m.r., and mass).

[1] Prepared by treatment of hydrated 2-formylpyridine 1-oxide (D. Jerchel, J. Heider, and H. Wagner, *Annalen*, 1958, **613**, 153) with ethanol.

[2] I. Ugi and R. Meyer, *Chem. Ber.*, 1960, **93**, 239.

[3] I. Ugi, 'Newer Methods of Preparative Organic Chemistry,' Vol. IV, Interscience, New York, 1968, p. 1.