Preparation and Rearrangements of Some Bicyclic Isoxazolines

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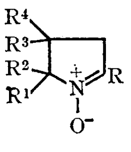
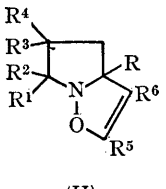
THE nitrone system functions as a 1,3-dipole in cycloaddition reactions[1] and the cycloaddition of unsymmetrical olefins to Δ^1-pyrroline *N*-oxides (I) has been studied.[2] It has now been found that dimethyl acetylenedicarboxylate, propiolic acid, and methyl phenylpropiolate react with Δ^1-pyrroline *N*-oxides to give bicyclic isoxazolines (II).

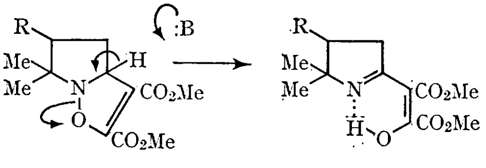


(I)



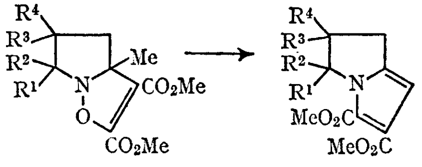
(II)

The cycloaddition reaction is violently exothermic in the absence of a solvent and is conveniently carried out in ether at room temperature. The adducts from aldonitrones and dimethyl acetylenedicarboxylate (III) are unstable and have not been obtained pure. They rearrange exothermically on keeping at room temperature to pyrroline derivatives (III → IV). This ring fission is similar to that of isoxazolium salts[3] but needs no external nucleophile.



(III; R=H or Me) (IV; R=H or Me)

The major products from the reaction of ketonitrones with dimethyl acetylenedicarboxylate are the 1 : 1 adducts (V) but small amounts of 1 : 4 adducts are also formed. The 1 : 1 adducts (V) are stable at room temperature but undergo an interesting rearrangement (V → VI) to pyrrole derivatives on heating to *ca.* 130°.

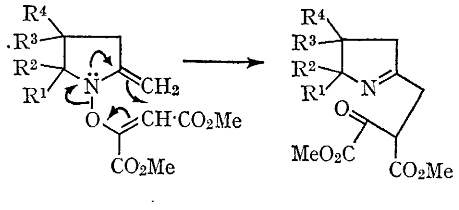


(V) (VI)

[a; $R^1=R^2=Me$, $R^3=R^4=H$
b; $R^1=R^2=H$, $R^3=R^4=Me$]

The rearrangement is visualised as a thermally induced fragmentation reaction promoted by the nitrogen atom and proceeding *via* the enamine

(VII) followed by rearrangement to (VIII) and finally cyclodehydration to give the pyrrole.

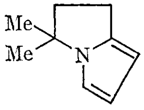


(VII) (VIII)

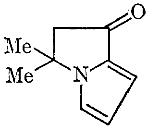
The structures of the rearrangement products have been conclusively established by degradation of (VIa) to the pyrrole (IX) and synthesis of (IX) by Michael addition of pyrrole to 3,3-dimethylacrylonitrile, followed by an internal Hoesch reaction to give (X).

The bicyclic ketone (X) was reduced to (IX) by the Wolff–Kishner method.

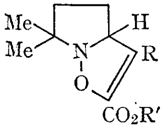
Two modes of cycloaddition are possible with unsymmetrical acetylenes, and propiolic acid was studied to determine which mode was favoured. The adducts from propiolic acid are unstable solids which decompose on keeping at room temperature. Several have been obtained pure by rapid crystallisation and infrared evidence demonstrates the presence of rotational isomers[4] of the carbonyl group indicating structures of type (XI; R = R′ = H). Adducts from methyl phenylpropiolate are stable at room temperature and infrared evidence again favours structures of the type (XI; R = Ph, R′ = Me).



(IX)



(X)



(XI)

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[3] R. B. Woodward and R. A. Olofson, *J. Amer. Chem. Soc.*, 1961, **83**, 1007.

[4] R. Grigg, J. A. Knight, and M. V. Sargent, *Tetrahedron Letters*, 1965, 1391; R. Grigg, *J. Chem. Soc.*, 1965, 5149.