Rearrangements in Reactions of Diphenylcyclopropenone with Isoxazoles

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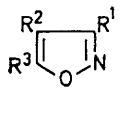
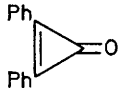
Summary Diphenylcyclopropenone and isoxazoles, on heating, give 4-pyridones by a reaction which involves loss of the isoxazole 5-substituent in 4,5-disubstituted isoxazoles and its retention, as a 3-acyl substituent of the pyridone, in the 4-unsubstituted isoxazole case.

TREATMENT of the isoxazole (**1**; $R^1 = R^2 = R^3 = Me$) with diphenylcyclopropenone (**2**) in boiling toluene gave a product corresponding to a 1:1 adduct minus the elements of keten ($CH_2=C=O$). Variation of the substituents of the isoxazole enabled the source of the keten fragment to be assigned to the C-5 methyl group. Thus, both (**1**; $R^1 = R^3 = Me$, $R^2 = Et$) and (**1**; $R^1 = H$, $R^2 = R^3 = Me$) gave 1:1 adducts with formal loss of keten. In contrast, the isoxazole (**1**; $R^1 = R^3 = Me$, $R^2 = H$) gave a 1:1 adduct



(1)



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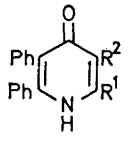

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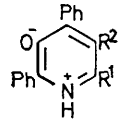

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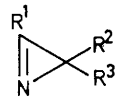
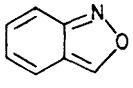


(5) a; $R^1 = Ph$, $R^2 = R^3 = Me$
b; $R^1 = Ph$, $R^2 = Me$, $R^3 = CO_2Me$



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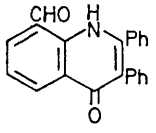

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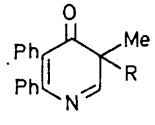
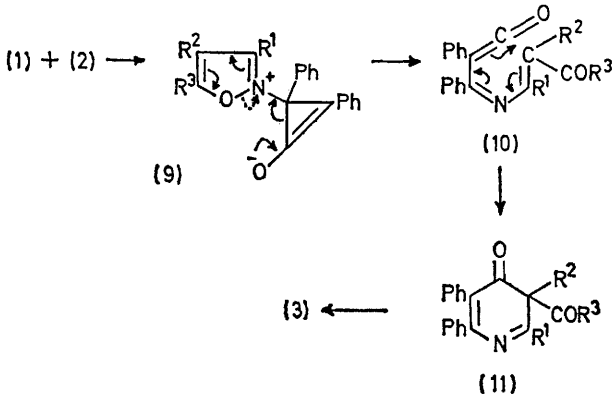


(8)

without loss but containing a methyl ketone group (n.m.r., i.r.). The adducts are all high melting point solids with low solubility in common organic solvents. N.m.r. studies demonstrated that the R^1 group in (**1**) was still adjacent to nitrogen in the product since the adducts from oxazoles with $R^1 = H$ exhibited doublet n.m.r. signals for this proton in trifluoroacetic acid but not deuteriotrifluoroacetic acid. Spectral data [*e.g.* the adduct from (**1**; $R^1 = R^2 = R^3 = Me$) and (**2**) had ν_{max} (KBr) 1505, 1613, 1628, and a broad band between 2750—3250 cm^{-1}; *m/e* 178, 8% abundance, $(PhC{\equiv}CPh)^+$] suggested a 4-pyridone structure (**3**) but did not provide a conclusive distinction between (**3**) and the related zwitterionic 3-hydroxypyridine (**4**). An *X*-ray structure determination on the adduct from (**1**; $R^1 = H$, $R^2 = R^3 = Me$) and (**2**) showed it to be the 4-pyridone (**3**; $R^1 = H$, $R^2 = Me$). Yields of 4-pyridones were 32—56% except for those derived from the trialkylisoxazoles which were *ca.* 10%. The major products in the case of (**1**; $R^1 = R^2 = R^3 = Me$ and $R^1 = R^3 = Me$, $R^2 = Et$) were 1:1 adducts with an i.r. band at 1766 and 1769 cm^{-1}, respectively. These products did not convert into 4-pyridones under the reaction conditions but did give 4-pyridones on more vigorous treatment.†



SCHEME

One of the problems with diphenylcyclopropenone chemistry is that the juxtaposition of two reactive groups makes mechanistic speculation hazardous.[1] In the present case an added problem was the possibility of the isoxazoles undergoing an initial thermal rearrangement to the corresponding 1-azirines (**5**). Such skeletal rearrangements have been reported[2] on heating 5-alkoxyisoxazoles to 200°, but we were unable to detect any azirines on heating several alkylisoxazoles in toluene for 24 h, and 3,4,5-trimethylisoxazole distils unchanged at *ca.* 180°. However, this does not exclude (**2**) acting as a catalyst for the conversion (**1**) →(**5**), but since anthranil (**6**) also undergoes reaction with (**2**) giving an aromatic aldehyde, formulated as (**7**) on the basis of spectroscopic data, it seems unlikely. Nevertheless, we find the 1-azirines (**5a** and **b**) do undergo cycloaddition reactions with (**2**) giving the corresponding pyridone derivatives (**8**). Others have also recently observed this type of reaction and discussed the mechanism.[3] Hydrolysis and decarboxylation of (**8**; $R = CO_2Me$) gave the correspondong 4-pyridone (**3**; $R^1 = Ph$, $R^2 = Me$).

Several mechanisms can be advanced for the formation of the pyridones (**3**) from isoxazoles. One of these is outlined in the Scheme.

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† These adducts will be discussed in detail in the full paper.

[1] M. A. Steinfels and A. S. Dreiding, *Helv. Chim. Acta*, 1972, **55**, 702; M. A. Steinfels, H. W. Krapf, P. Riedl, J. Sauer, and A. S. Dreiding, *ibid.*, p. 1759.
[2] T. Nishiwaki, T. Kitamura, and A. Nakano, *Tetrahedron*, 1970, **26**, 453.
[3] A. Hassner and A. Kascheres, *J. Org. Chem.*, 1972, **37**, 2328.