1,3-Dipolar Cycloaddition of Diphenylnitrone to Enamines*[1]

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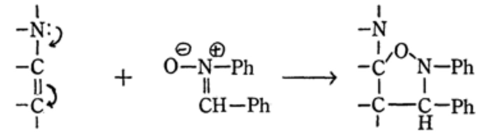
The 1,3-dipolar cycloaddition of nitrones to olefins to form isoxazolidines is well established,[1] and enamines are known to act as 1,3-dipolarophiles.[2,3]

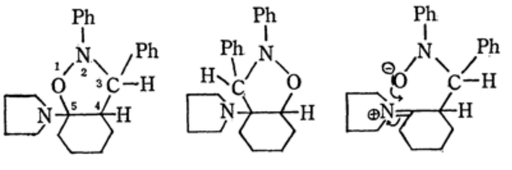
The present study shows the formation of isoxazolidines (III) by the reactions of enamines (I) with diphenylnitrone (II).



I II III

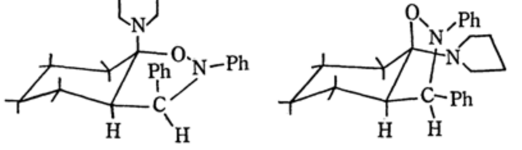
A solution of equivalent amounts of diphenylnitrone and 1-pyrrolidino-1-cyclohexene in dimethylformamide was stirred at room temperature for 24 hr. Evaporation of the solvent *in vacuo* and recrystallization from ethanol afforded 4,5-tetramethylene-2,3-diphenyl-5-pyrrolidino-isoxazolidine (IV), mp 147—148°C. Yield, 54.7%. Ultraviolet absorption $\lambda_{max}^{ethanol}$ 251 mμ (ε 11480).

Found: C, 79.32; H, 8.24: N, 7.89%. Calcd for $C_{23}H_{28}N_2O$: C, 79.27; H, 8.10; N, 8.04%.



IV IV′ V

The alternative structure IV′ can be excluded since the NMR spectrum displays a sharp doublet (J=10.5 cps) for the coupling between H-3 and H-4. This coupling constant corresponds to a dihedral angle $\mathrm{H{-}C_3{-}C_4{-}H}$ in IV of close to 0° or 180°.[4] Further study will be necessary to elucidate the configuration of IV. However, the thermodynamically more stable trans configuration A may be preferable, since addition to enamines proceeds in general by a two-step reaction path through a dipolar immonium anion intermediate (V). On the other hand, the cis configuration B would also be conceivable if a one-step cis addition took place.[5]



A B

In a similar manner, the cycloadduct 4,5-trimethylene-2,3-diphenyl-5-morpholino-isoxazolidine was obtained from II and 1-morpholino-1-cyclohexene in a 7.1% yield, mp 125—126°C.

Found: C, 74.83; H, 7.51; N, 8.00%. Calcd for $C_{22}H_{26}N_2O_2$: C, 75.40; H, 7.48; N, 7.99%.

In the expectation that the amine residue would be eliminated from the cycloadducts on acid treatment, we have treated IV with dilute hydrochloric acid. In this case, only intractable resins were obtained. However, on treatment with glacial acetic acid at room temperature for 2 days, IV (389 mg) gave yellow needles (55 mg), mp 117—118°C, ultraviolet absorption $\lambda_{max}^{ethanol}$ 233 mμ (ε 16670) and 330 mμ (ε 33060). From NMR, IR, UV and high-resolution mass spectra, the compound was identified as 2,6-dibenzylidene-1-cyclohexanone; this assignment was further confirmed by a mixed melting point with an authentic sample.[6]

Found: C, 87.62; H, 6.73%; mol wt, 274.137 (mass). Calcd for $C_{20}H_{18}O$: C, 87.56; H, 6.61%; mol wt, 274.135.

A study of the mechanism through which this compound arises is under progress in our laboratory.

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*[1] Presented at the 20th Annual Meeting of the Chemical Society of Japan, Tokyo, April, 1967, where the closely related work by Prof. O. Tsuge *et al.* was also read.

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