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REACTIONS OF AZIRIDINES WITH DIMETHYLACETYLENE DICARBOXYLATE

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Two reports (1,2) have recently appeared dealing with the reactior of aziridines with dialkyacetylene dicarboxylates. We have also observed this reaction independently and have noted that the nature of the substituent on nitrogen of the three-membered ring influences the mode of reaction. The similarity of these reactions prompts us to publish a preliminary account of our results in this field.

Refluxing equimolar ratios of <u>cis</u>-2,3-diphenyl aziridine and dimethylacetylene dicarboxylate in benzene for 12 hours results in the formation of an adduct (I) in 85% yield. The structure of I is assigned as dimethyl-2-[1-(2,3-diphenylaziridyl)]-maleate on the basis of the following data. The pure adduct I was a solid, white needles from methanol, m.p. 94-95°C; Anal. Calcd. for $C_{20}H_{19}NO_4$: C, 71.20; H, 5.68; N, 4.15. Found: C, 71.11; H, 5.85; N, 4.32. The infrared spectrum shows strong carbonyl bands at 5.70 and 5.80 μ. The n.m.r. spectrum is in excellent agreement with the proposed structure. There is a multiplet at 2.85 τ and singlets at 4.45, 6.20, 6.29, and 6.33 τ. The peak areas are in the ratio of 10:1:3:2:3. The ultraviolet spectrum in 95% ethanol [λmax 262 mμ

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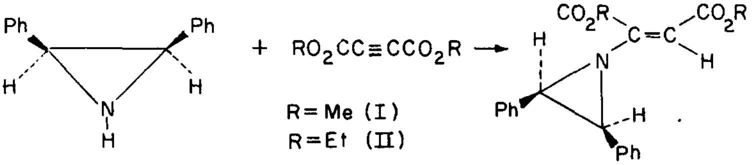
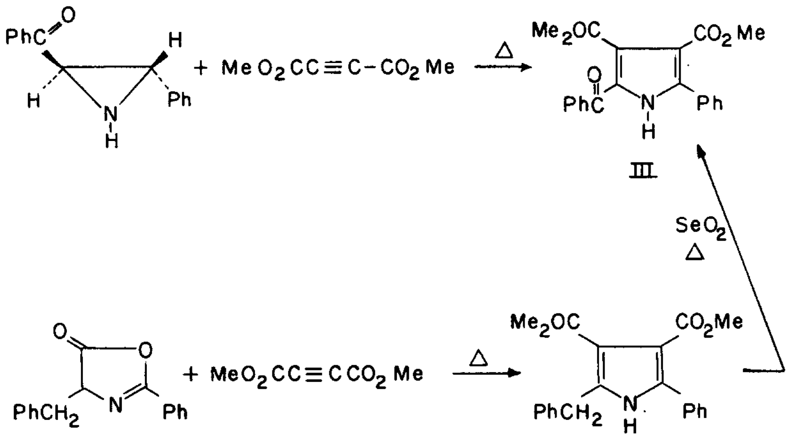
(ε 21,800)] is essentially identical to dimethyl-2-[1-aziridyl]-maleate (1). cis-2,3-Diphenyl aziridine also forms an analogous adduct (II) with diethylacetylene dicarboxylate.**



The stereochemistry of the reaction product obtained has been assigned as the cis-diester (I,II) by analogy with Dolfini's results (1). In the presence of a non-protic solvent, the initially formed zwitterion would be expected to undergo stereospecific collapse via intramolecular protonation, leading to the cis disposition of the ester functions.

The reaction course followed by refluxing trans-2-phenyl-3-benzoylaziridine with dimethylacetylene dicarboxylate in xylene for 18 hours proved to be dramatically different. The reaction product obtained in this case (80%) was identified as 2-benzoyl-3,4-dicarbomethoxy-5-benzoylpyrrole (III). Recrystallization from hexane-benzene gave material melting at 159½-160oC; Anal. Calcd for $C_{21}H_{17}NO_5$: C, 69.41; H, 4.72; N, 3.86. Found: C, 69.18; H, 4.82; N, 3.86. An authentic sample of 2-benzyl-3, 4-dicarbomethoxy-5-benzoyl-pyrrole, prepared by heating 2-phenyl-4-benzyl-5-oxazolone (IV) (3) with dimethylacetylene dicarboxylate followed by selenium dioxide oxidation, was identical to III with respect to the infrared spectrum and melting point. A mixed melting point of the two samples was not depressed.

**Satisfactory carbon, hydrogen, and nitrogen analyses were obtained for all the new compounds described herein.

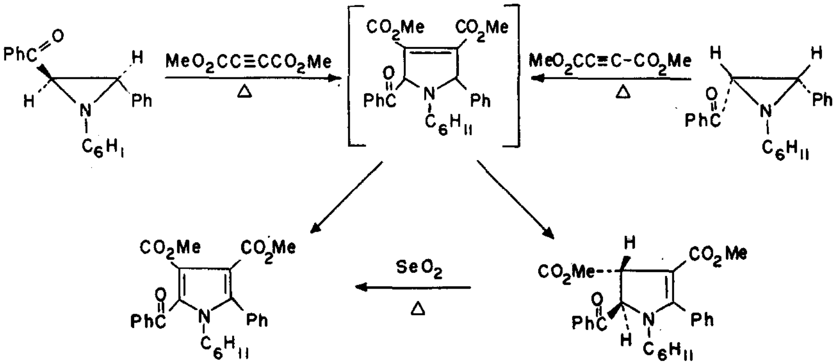


III

IV

In order to elucidate further the mechanistic nature of the transformation, we examined the reaction of dimethylacetylene dicarboxylate with cis and trans-1-cyclohexyl-2-phenyl-3-benzoylaziridine. In this case, dimethylacetylene dicarboxylate was observed to react with either cis or trans aziridine to form two products in high yield. These adducts are assigned structures V (m.p., 140-141°C) and VI (m.p., 155-156°C). The assignments are supported by elemental analysis, n.m.r. data, and analogy with other aziridine reactions, and they are consonant with the observed ultraviolet data.

Data supporting VI as 1-cyclohexyl-2-phenyl-3,4-dicarbomethoxy-5-benzoyl-2-pyrroline stems from consideration of the I.R., U.V., and n.m.r. spectra. The ultraviolet spectrum of VI in 95% ethanol has maxima at 255 mμ (ε 15,600) and 303 mμ (ε 16,350). The infrared spectrum has bands at 5.78, 5.96 and 6.37 μ. The n.m.r. spectrum (CCl_4) shows the aromatic hydrogens as a multiplet centered at 2.55 τ, the methyl protons as singlets at 6.18 and 6.63 τ, the methine protons as a pair of doublets at 5.15 and 6.42 τ ($J = 4$ cps.) and the cyclohexyl protons as a complex multiplet centered at 8.67 τ. The peak areas are in the ratio of 10:3:3:1:1:11.



Interestingly, adduct VI is markedly resistant to further oxidation. Heating VI with iodine in toluene or with palladium on charcoal in p-cymene resulted in recovered starting material. Only when VI was heated with selenium dioxide at 200° in a sealed tube was oxidation achieved. The stability of this adduct is the major reason for our current preference for the postulation of a trans relation of the hydrogens as opposed to a cis relationship. It is easier to account for the fact that the oxidation of a trans species is more formidable than that of the cis, as the geometry of the cis isomer would appear to be more conducive for elimination of molecular hydrogen. The data therefore suggests that V is not derived from VI but rather results from the initially-formed 3-pyrroline. Under the reaction conditions, the initial adduct may either rearrange to VI or lose hydrogen to give the substituted pyrrole.

We plan to report further on the reaction of substituted aziridines with other multiple bonds.

Acknowledgment

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REFERENCES

1. J. E. Dolfini, J. Org. Chem., 30, 1298 (1965).
2. H. W. Heine and R. Peavy, Tetrahedron Letters, No. 35, 3123 (1965).
3. H. E. Carter, ''Organic Reactions'', Vol. III, R. Adams, Ed., John Wiley and Sons, Inc., New York, N.Y., 1946, p. 205.