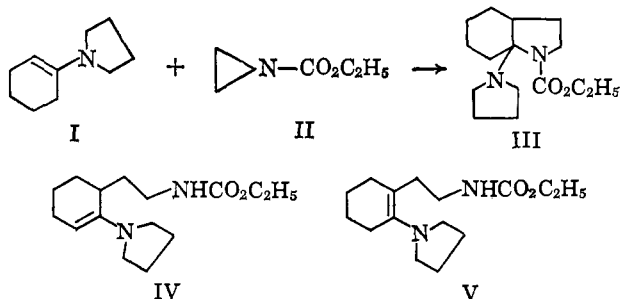


A New Heterocyclic Synthesis. Enamine Cycloaddition with N-Carboethoxyaziridine

Sir:

As part of a program concerning the reactivity and utility of small ring compounds in the synthesis of medium ring systems, we have examined the reaction of N-carboethoxyaziridine¹ with the pyrrolidine enamine of cyclohexanone.² This report is concerned with the first demonstration of the formal cycloaddition of an enamine with an N-acylaziridine.

Amines are known to participate in a facile nucleophilic ring opening of N-carboethoxyaziridine³ at room temperature, resulting in the formation of a product derived from alkylation of the amine nitrogen. However the reaction of an enamine, to proceed by carbon alkylation, is sluggish at best, even in refluxing ethanol or benzene solutions. At elevated temperatures a reaction does occur. Thus a xylene solution of equivalent amounts of 1-(1-pyrrolidinyl)cyclohexene (I) and N-carboethoxyaziridine (II) provides after refluxing for 14 hr. in an atmosphere of nitrogen a 42% yield of a 1:1 addition product, b.p. 105–113° (0.15 mm.), to which we assign an octahydroindole structure (III).



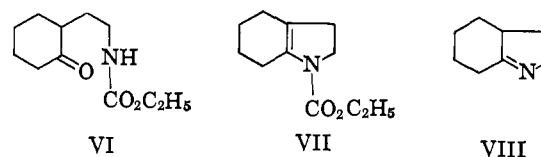
Alternative structures IV and V are not supported by the infrared spectrum, which possesses no absorptions characteristic of N—H or C=C groups. The p.m.r. spectrum is in accord with the proposed structure (III). A molecular weight determination gave a value of 265 (theoretical, 266).⁴ The combustion analysis of this unstable amine gave slightly low values for carbon. *Anal.* Calcd. for C₁₅H₂₆N₂O₂: C, 67.65; H, 9.85; N, 10.52. Found: C, 66.96; H, 9.68; N, 10.29. However, treatment of the octahydroindole compound (III) with aqueous-alcoholic 2,4-dinitrophenylhydrazine solution induced the formation and precipitation of a yellow derivative, m.p. 161–164° (*Anal.* Calcd. for C₁₇H₂N₅O₆: C, 51.90; H, 5.89; N, 17.80. Found: C, 51.89; H, 6.07; N, 17.71), of the keto urethan VI, the hydrolysis product of III.

The best conditions for performing the cycloaddition consisted of refluxing a solution of 0.05 mole of enamine and 0.10 mole of N-carboethoxyaziridine in 40 ml. of *p*-xylene for 4 hr. under nitrogen, the product being

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- (2) G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrell, *J. Am. Chem. Soc.*, **85**, 207 (1963).
- (3) G. E. Ham, *J. Org. Chem.*, **29**, 3052 (1964), and references therein.
- (4) Molecular weights were determined in benzene by a Mechrolab Model 301 vapor pressure osmometer.

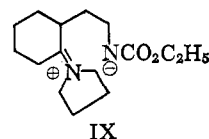
isolated in 65% yield upon removal of the solvent and distillation at reduced pressure.

A convenient elimination of the elements of pyrrolidine was achieved by distillation of the crude reaction product from a small amount of *p*-toluenesulfonic acid, this giving rise to the hexahydroindole compound VII



in 44% yield, b.p. 93–95° (0.15 mm.). *Anal.* Calcd. for C₁₁H₁₇NO₂: C, 67.66; H, 8.78; N, 7.17. Found: C, 67.57; H, 8.90; N, 6.99. This hexahydroindole (VII) was converted to the salt of the known hexahydroindole⁵ (VIII) with methanolic hydrogen chloride.

While this reaction represents a formal cycloaddition to an aziridine single bond, it seems reasonable that the zwitterionic material (IX) would be formed as an intermediate in the reaction course and cyclize spontaneously to the neutral indole derivative.



We intend to explore and extend this novel type of reaction further and clarify the stereochemistry of the ring fusion in bicyclic cases such as the one cited here.

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 Received August 2, 1965

Long-Range Interactions in Semidiones Derived from Bicyclo[2.2.1]heptanes and Bicyclo[2.2.2]octanes¹

Sir:

The e.s.r. spectra of acyclic or monocyclic semidiones (RC(O·)=C(O⁻)R) involve predominant hyperfine splitting by hydrogen atoms α to the dicarbonyl system.^{2–5} This splitting is a function of the dihedral angle ($\alpha^H \propto \cos^2 \theta$) between the carbon-hydrogen bond and the carbonyl carbon p_z orbital.² Hydrogen atoms β to the dicarbonyl system interact only weakly

(1) Application of E.s.r. Spectroscopy to Problems of Structure and Conformation. V. This work was supported by grants from the National Science Foundation and the Petroleum Research Fund.

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- (3) G. A. Russell and E. R. Talaty, *ibid.*, **86**, 5345 (1964).
- (4) G. A. Russell and E. R. Talaty, *Science*, **148**, 1217 (1965).
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