Tetrahedron Letters No.47, pp. 5847-5850, 1966. Pergamon Press Ltd.
Printed in Great Britain.

BICYCLIC ENAMINES. IV. HOMOENOLATE ION PARTICIPATION IN THE ADDITION OF MORPHOLINE TO NORBORNENONE (1-3)

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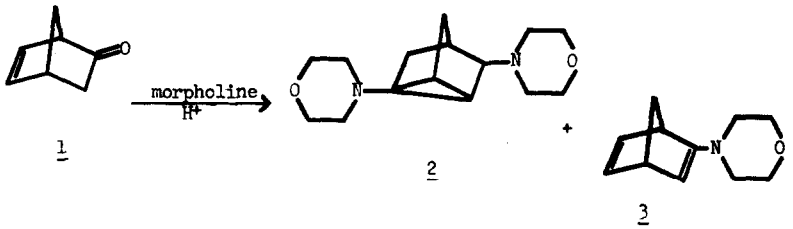
(Received 27 August 1966)

The reaction of secondary amines with ketones is a common synthetic method for the production of enamines. The acid-catalyzed addition of morpholine to norbornenone (1) to form the tricyclenamine, 2,5-bis-(N-morpholino)tricyclo[2.2.1.$0^{2,6}$]heptane (2), in a 28% yield has been previously reported (2). Subsequent investigation has shown that a small amount of an enamine, 2-N-hexamethyleniminobicyclo[2.2.1]hepta-2,5-diene



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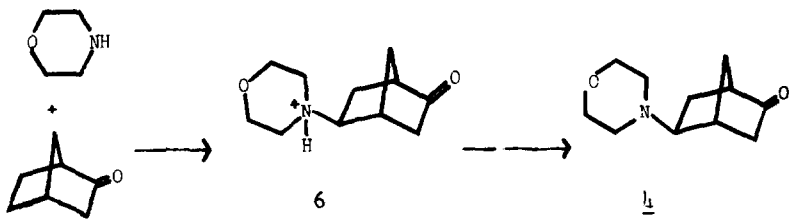
(3), is also produced during the reaction.

The reaction between morpholine and norbornenone in the absence of any acid catalyst produces tricyclenamine 2, enamine 3 and 5-N-morpholinobicyclo-[2.2.1]heptan-2-one (4) in 4%, 2% and 1% yields respectively (run for 50 hours in refluxing xylene with the water removed by a Dean-Stark trap). Tricyclenamine 2 was identified by comparison of its boiling point and infrared spectrum with that of an authentic sample (2). Enamine 3 was identified by its infrared spectrum (ν_{max}^{film} 1685 cm.$^{-1}$, $\geq C = C \leq_{N}$). Aminoketone 4 was identified by its boiling point, infrared spectrum

(ν_{max}^{film} 1750 cm^{-1}, >C = O) and gas-liquid chromatography (g.l.c.) retention time as compared with an authentic sample (2). The authentic sample was originally produced by acid-catalyzed addition of morpholine to tricyclo-[2.2.1.$0^{2,6}$]heptan-3-one (5). It has since been observed, however, that the reaction proceeds in approximately the same yield (55%) producing the same product in the absence of an acid catalyst. Since the presence of acid is not necessary for this reaction, it probably proceeds by a nucleophilic backside attack of morpholine on 5 to produce carbanion 6 followed by proton rearrangement to give product 4. This would mean that the com-



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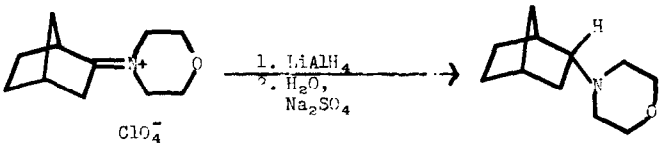
pound produced (4) is the exo isomer. Proof of its being the exo isomer was obtained by reducing aminoketone 4 by means of the Wolff-Kishner reduction to the corresponding amine (b.p. 80° (0.6 mm.), n_D^{27} 1.4972). The infrared spectrum of this amine was compared with that of an authentic sample of endo-2-morpholinobicyclo[2.2.1]heptane (8), synthesized by reduction of iminium salt 7 with lithium aluminum hydride. This type of reduction



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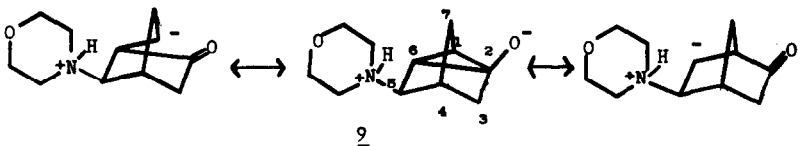
has been shown to produce the endo isomer (1). The infrared spectra have several distinct differences showing them to be non-identical. Therefore aminoketone 4 and its corresponding amine are indeed exo isomers.

The most plausible explanation for the formation of 4 from norbornenone (1) and morpholine is via a homoenolate ion intermediate (4,5) in a Michael type addition reaction. The ketone group must exert a homoconjugative effect on the carbon-carbon double bond since neither norbornene nor norbornadiene react with morpholine under these conditions (2). Michael addition reactions involving secondary amines and α,β-unsaturated carbonyl compounds have been reported before (2,6,7), but this is the first example of such a reaction involving the homoenolate ion.

The reaction mechanism may involve a direct intramolecular transfer of the proton from the nitrogen to the homoenolate ion. This type of protonation involving a homoenolate ion in basic medium has been shown by Nickon (4) to proceed by exo attack. This can be accommated by an exo-morpholinium group at carbon-5 since an endo-morpholinium group would have its proton in the wrong position for exo attack. The fact that the product has a morpholine group on the two-carbon bridge and is the only aminoketone product isolated (as shown by g.l.c.) can also be explained by this intramolecular mechanism. One might expect to find the one-carbon bridge substituted (10) as well as the two-carbon bridge substituted aminoketone present. However, the carbon-6 position would be favored over the carbon-1 position for such an attack because of the close proximity of C-6 to the attacking proton as compared to C-1. Nevertheless, a mechanism involving intermolecular protonation is also a possibility.



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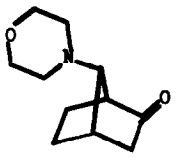

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The tricyclenamine 2 probably forms in both acidic and basic media by way of homoconjugate nucleophilic attack of morpholine on intermediate carbonium ion 11.

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1. Part III in press.

2. For Part II, see A. G. Cook, W. C. Meyer, K. E. Ungrodt and R. H. Mueller, J. Org. Chem., 31, 14 (1966).

3. Support of this work by a grant from the Petroleum Research Fund of the American Chemical Society and by a Valparaiso University Research Grant is gratefully acknowledged.

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