A Rearrangement of ββ-Disubstituted Mannich Bases

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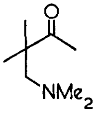
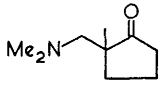
OUR interest in Mannich bases of ketones as enone-equivalents in the *thermal*-Michael reaction[1] has currently compelled us to investigate and verify their structures in certain cases where there has been disagreement.[2] For example, it can be shown by n.m.r. studies that the Mannich bases prepared from isopropyl methyl ketone and 2-methylcyclopentanone are formulated correctly as (I)[2,3] and (II)[2,4]. Nevertheless, we find that in the thermal-Michael reaction these bases behave as if they had the alternate structures (III) and (IV). Thus the condensation of (I) with cyclopentanone affords (V) in 45% yield, and the reaction of (II) with cyclopentanone affords (VII), the product also obtained by the thermal condensation of 2-methylcyclopentanone with (VIII). Under similar conditions (II) reacts with dihydroresorcinol to give a 60% yield of (IX), and

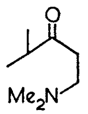
(X) reacts with cyclopentanone giving (XI). The structure of (XI) is corroborated by independent synthesis from (VIII) and 2-ethoxycarbonylcyclopentanone under thermal conditions, or (in 60% yield) by the *classical* Michael condensation of the latter with 2-methylenecyclopentanone. In each of these reactions, the structure of the product has been established by n.m.r. or u.v. spectroscopy and analysis.



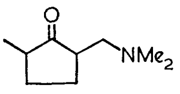
(I)



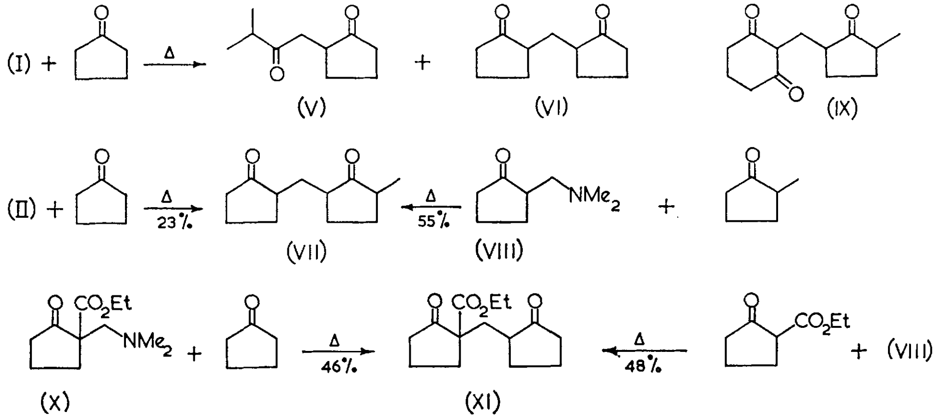
(II)



(III)

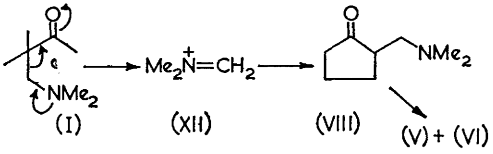


(IV)



In seeking to explain these findings, it is important to recognise that crude Mannich bases often contain small amounts of isomers,[2] *e.g.*, (III) and (IV), which could account for the above reaction products. However this explanation cannot account for the yields we have obtained, and it is therefore necessary to postulate a rearrangement. The intervention of a rearrangement is convincingly demonstrated by the formation of (XI) from (X) and by our observation that the thermal condensation of (I) with cyclopentanone yields not only the "expected" product (V) but in addition the symmetrical diketone (VI).[5]

The rearrangement is recognisable as a transaminomethylation similar to that previously observed by Hellmann and his co-workers[6] in certain esters, and is presumably general for $\beta\beta$-disubstituted Mannich bases. In mechanism, it must involve a thermal retro-Mannich process (*e.g.*, I → XII) followed by attack on the substrate, leading to (VIII), which will react as previously described,[1] yielding the products. Qualitative experiments suggest that the process is acid-catalysed. In view of the known[1] orientation rules in the thermal-Michael reaction, the formation of (VII) from (II) could be explained by *either* an inter- or an intra-molecular transaminomethylation: however the reactions which yield (XI) from (X), and (VI) from (I) can only be intermolecular migrations. This is in accord with our experimental practice of using a threefold excess of substrate.



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[2] G. L. Buchanan and A. C. W. Curran, unpublished work.
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