Novel Products from a Mannich Reaction with Cyclododecanone: 13,16-Dimethyl-13,16-diazatricyclo[9,3,3,$1^{1,11}$]octadecan-18-one and 1-Dimethylaminomethyl-13-methyl-13-azabicyclo[9,3,1]pentadec-11-en-15-one

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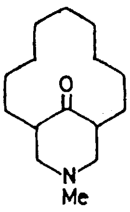
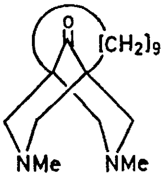
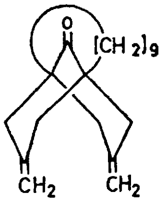
Summary Condensation of cyclododecanone with formaldehyde and methylamine gives the bridged bispidone (II) and the dihydropyridin-4-one (IV).



(I)



(II)



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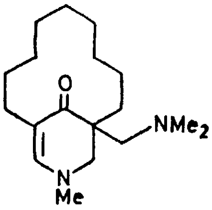

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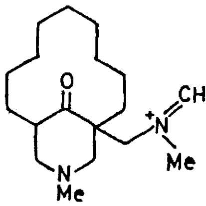
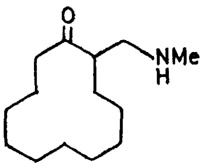
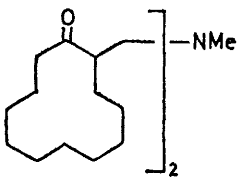


(V)



(VI)



(VII)

WHEN cyclododecanone was heated under reflux for 2 days with aqueous ethanolic formaldehyde (2·0 mol equiv.) and methylamine (1·0 mol. equiv.) a complex mixture resulted. Three compounds† were isolated from the basic fraction by column chromatography on silica and crystallization. In addition to the expected azabicyclopentadecanone (I), $C_{15}H_{27}NO$, m.p. 63°, there was found the bispidone, the diazatricyclo-octadecanone (II), $C_{18}H_{32}NO_2$, m.p. 94°. Molecular models indicate that cyclododecanone is the smallest cycloalkanone which can form a 1,5-polymethylene bridged [3,3,1]nonan-9-one. The model shows that the polymethylene bridge lies to one side of the carbonyl group and this observation is supported by the asymmetry seen in the n.m.r. spectrum where the methylene protons in the two six-membered rings are not identical. The only previous report of a [9,3,3,$1^{1,11}$]tricyclo-octadecane system is by Nozaki,[1] who prepared (III) by the reaction of cyclododecanone with αα′-dichloroisobutylene. Under similar conditions (NaH–toluene) no analogous product was formed with cycloundecanone.[2]

The major component isolated from the reaction mixture was the dihydropyridin-4-one (IV) (20%) $C_{18}H_{32}NO_2$, m.p. 116°. Mass spectroscopy confirmed the molecular formula [m/e 292·2511 (M^+), 247·1939, $(M-C_2H_7N)^+$, and 234·1854, $(M-CH_2NMe_2)^+$. The compound formed a methiodide, m.p. 226°. Only a few examples of dihydropyridin-4-ones have been reported[3] and a full analysis of the i.r. spectrum of the present example will be discussed later.[4] Since the bispidone (II) appears stable under the reaction conditions the dihydropyridin-4-one (IV) must arise in a competitive reaction by a transannular hydride abstraction in the sterically crowded Mannich intermediate (V).

Similar condensations carried out with shorter reaction times have allowed the isolation of the simpler bases (VI), $C_{14}H_{27}NO$, m.p. 102—104°, and (VII), $C_{27}H_{49}NO_2$, m.p. 95—96°.

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† All compounds reported gave satisfactory analytical and spectral data.

[1] T. Mori, K. Kimoto, M. Kawanisi, and H. Nozaki, *Tetrahedron Letters*, 1969, 3655.

[2] Ref. 1, footnote 7.

[3] D. L. Ostercamp, *J. Org. Chem.*, 1970, 35, 1632, and refs. therein; Y. Tamura, M. Kunitomo, T. Masui, and M. Terashima, *Chem. and Ind.*, 1972, 169.

[4] P. J. Taylor, forthcoming publication.