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THE REACTION OF CYCLOALKANONES WITH HEXAMETHYLPHOSPHORIC TRIAMIDE. AN UNUSUAL ROUTE TO 1,2,3,4,5,6,7,8-OCTAHYDROACRIDINES.

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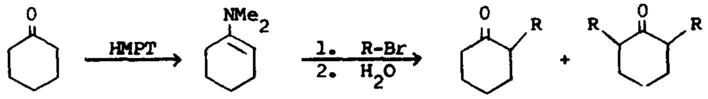
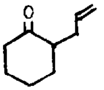
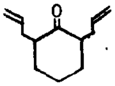
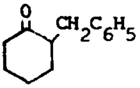
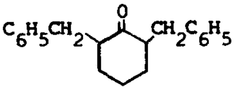
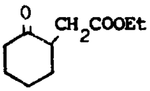
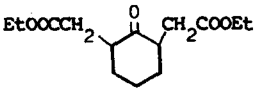
Continuing our studies on reactions initiated by hexamethylphosphoric triamide[1-5], we report here on the reactions of cycloalkanones in refluxing HMPT.

When cyclohexanone is refluxed in HMPT (215-220°) for forty minutes, there is a substantial conversion to 1-dimethylaminocyclohexene. If the reaction mixture is then cooled to room temperature, the enamine can be successfully alkylated in the same pot. The yields of several such alkylations are shown in Table I.

Table I. Alkylation of Cyclohexanone via HMPT-generated 1-Dimethylaminocyclohexene



Alkylating Agent	% Conversion[a]	Products (yield)[b]			
CH_2=CH-CH_2-Br	91		(49.2%)		(8.7%)
$C_6H_5CH_2$-Br	84		(52%)		(7.7%)[c]
Br-CH_2COOEt	30		(99%)		(trace)

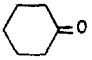
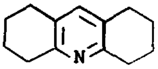
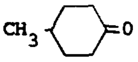
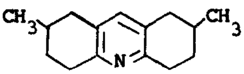
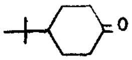
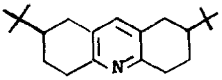
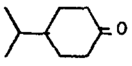
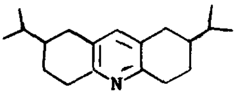
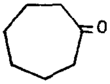
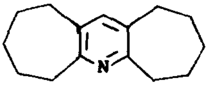
a. based on ketone b. by glpc analysis c. isolated yield, 5.6%

If the cyclohexanone-HMPT mixture is allowed to continue refluxing beyond forty minutes, the enamine is rapidly destroyed, and the major volatile product is cyclohexyldimethylamine. The yield of this amine was 45.2% after a four hour reflux.

In addition to cyclohexyldimethylamine, there was obtained upon distillation of the reaction mixture, a 15.2% yield of a mixture of oil and crystals, bp 91-100° (0.1 mm). Recrystallization from pentane afforded a 4.8% yield of 1,2,3,4,5,6,7,8-octahydroacridine, which was sublimed to obtain a satisfactory analytical sample, mp 74-75° (lit.[6] mp 73.4-74°). All physical and spectral properties of this product were consistent with reported[7] values.

In runs on other cycloalkanones, a modified isolation procedure was employed. The cooled reaction mixture was diluted with water, extracted with ether, the extract washed with brine and dried. Removal of the ether followed by recrystallization of the residue from pentane gave low yields of analogous products for each starting ketone. Table II shows the products of a series of such reactions.

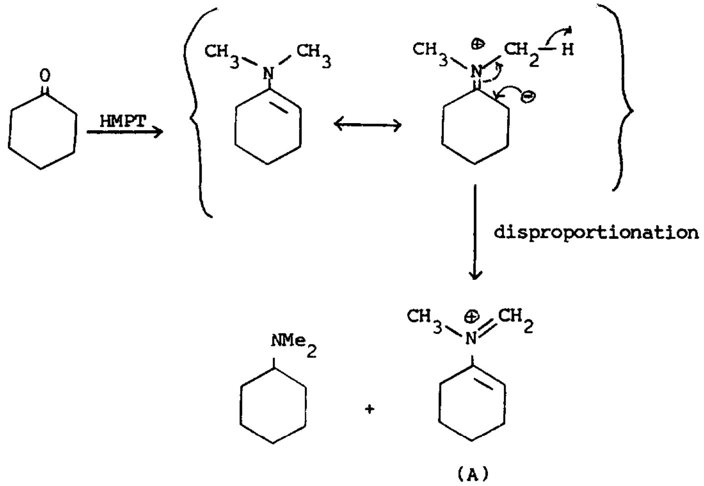
Table II. Octahydroacridines Obtained from Cycloalkanones by their Reaction in HMPT

Ketone	Product	Yield(%)	mp	lit.[8]mp
		4.8	74-75°	74°
		10.8	169-170°	167°
		2.7	123-125°	a
		4.9	100-103°	a
		6.0	113-114°	112°

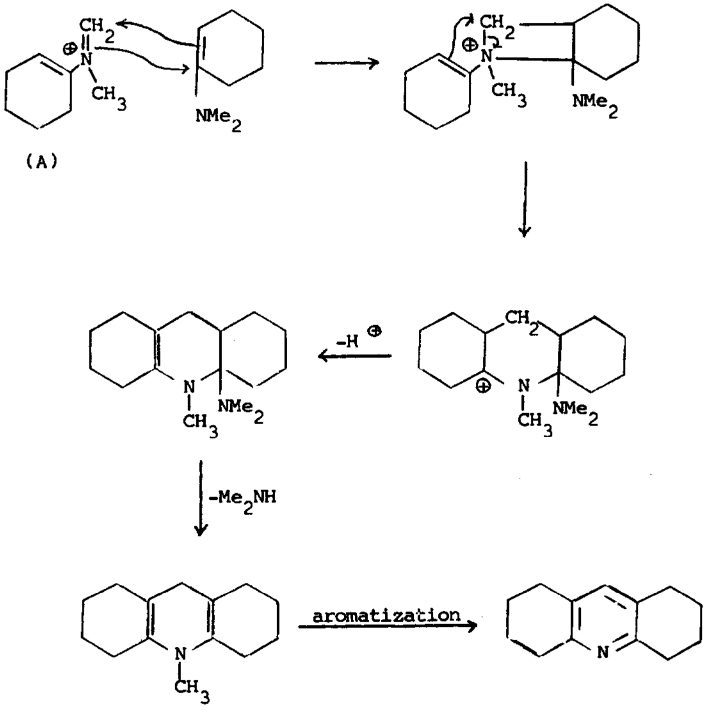
[a] satisfactory analysis obtained

We are at present attempting to illucidate the mechanism of this unusual reaction of dimethylamine enamines. Our preliminary proposal as to the reaction pathway follows:

1.



2.



The disproportionation of cyclohexanone enamines has been reported[9] to give saturated amines, but no oxidation products were identified. In the present case, disproportionation of 1-dimethylaminocyclohexene accounts for the formation of cyclohexyldimethylamine(equation 1) and suggests the formation of a reactive intermediate, A. The scheme of the reaction of A with additional enamine to give the observed product (equation 2) is essentially speculative, but the indicated pathway is certainly consistent with the formation of the octahydroacridines.

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