pounds, VI and VII, derived from IVb and Vb were readily obtained by use of 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) in refluxing benzene.[9]

Table I gives the physical constants of the series of 17-oxygenated-6,16α-dimethylprogesterones and their respective oral progestational activities.

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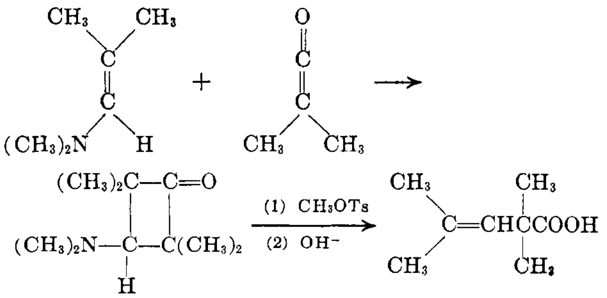
[9] D. Burn, D. N. Kirk, and V. Petrow, *Proc. Chem. Soc.*, 14 (1960).

Cycloaddition of Ketenes to Enamines

Sir:

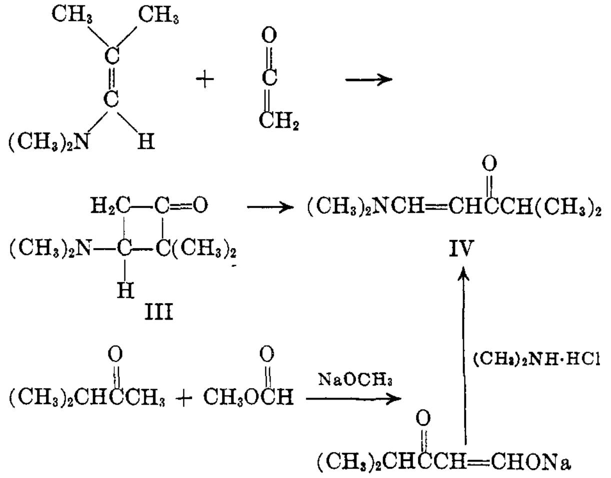
We wish to report some new reactions involving cycloaddition of ketenes to enamines derived from aldehydes. Ketene and dialkylketenes react with enamines having either one or no β-hydrogen to give 3-dialkylaminocyclobutanones. If the resulting cyclobutanones have one or more α-hydrogens (III, V, VII), they undergo an irreversible, ring-opening reaction; cyclobutanones that have no α-hydrogens (I) are quite stable.

Dimethylketene and *N,N*-dimethylisobutenylamine, when mixed in isopropyl acetate at room temperature, reacted to give a 64% yield of 3-dimethylamino-2,2,4,4-tetramethylcyclobutanone (I), b.p. 83–85° (24 mm.), n_D^{20} 1.4439, infrared maximum at 5.65 μ (cyclobutanone). The NMR spectrum of I was in complete agreement with the proposed structure. *Anal.* Calcd. for $C_{10}H_{19}NO$: C, 71.1; H, 11.2; N, 8.3. Found: C, 71.3; H, 11.2; N, 8.1. Quaternization of I with methyl tosylate followed by treatment with aqueous potassium hydroxide solution gave, after acidification, a 71% yield of 2,2,4-trimethyl-3-pentenoic acid (II), b.p. 86° (2 mm.), n_D^{20} 1.4472. *Anal.* Calcd. for $C_8H_{14}O_2$: C, 67.6; H, 9.9; neut. equiv., 142. Found: C, 67.6; H, 10.1; neut. equiv., 142.



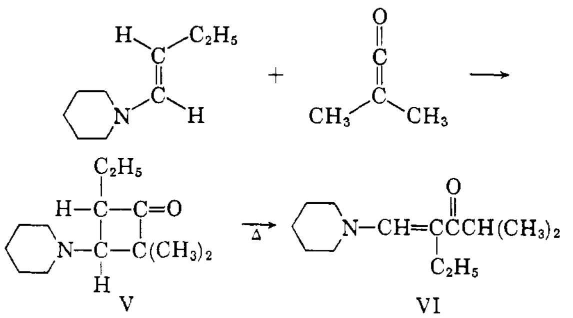
I II

Ketene reacted with *N,N*-dimethylisobutenylamine in hexane at 0° to give the intermediate 3-dimethylamino-2,2-dimethylcyclobutanone (III), identified by the characteristic infrared absorption of cyclobutanones at 5.65 μ. When this reaction product was warmed, its infrared spectrum changed radically; the band at 5.65 μ disappeared and three new bands at 6.05, 6.25, and 6.38 μ appeared. Distillation gave a 93% yield of 1-dimethylamino-4-methyl-1-pentene-3-one (IV), b.p. 105–107° (2 mm.), n_D^{20} 1.5301. *Anal.* Calcd. for $C_8H_{15}NO$: C, 68.0; H, 10.6; N, 9.9. Found: C, 68.0; H, 10.9; N, 9.7. The structure of IV was confirmed by independent synthesis from 3-methyl-2-butanone, methyl formate, and dimethylamine.[1]



Berchtold, Harvey, and Wilson have isolated a cycloaddition product similar to III (*N*-morpholino in place of the dimethylamino group) and noted its thermal rearrangement to the acyclic aminovinyl ketone.[2] It has also been brought to our attention that a keto base is found in the acylation of an enamine with acetyl chloride, apparently by abstraction of hydrogen chloride to form ketene, and subsequent cycloaddition to the enamine.[3]

Dimethylketene and *N*-(1-butenyl)piperidine[4] in hexane reacted at −20° to give 2-ethyl-4,4-dimethyl-3-piperidinocyclobutanone (V), which, on distillation, gave an 82% yield of 2-ethyl-4-methyl-1-piperidino-1-penten-3-one (VI), b.p. 119–121° (0.6 mm.), n_D^{20} 1.5424, infrared maxima at 6.05, 6.25, and 6.38 μ. *Anal.* Calcd. for $C_{13}H_{23}NO$: C, 74.6; H, 11.0; N, 6.7. Found: C, 74.6; H, 11.0; N, 6.8.



V VI

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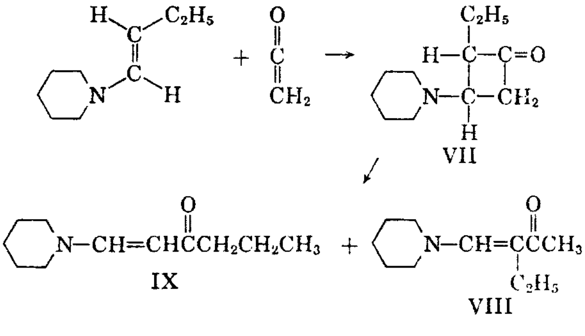
[1] E. Benary, *Ber.*, 63, 1573 (1930).

[2] G. A. Berchtold, G. R. Harvey, and G. E. Wilson, *J. Org. Chem.*, 26, 4776 (1961).

[3] G. Opitz, private communication.

[4] C. Mannich and H. Davidsen, *Ber.*, 69, 2106 (1936).

Ketene and *N*-(1-butenyl)piperidine in hexane reacted at −20° to give 2-ethyl-3-piperidinocyclobutanone (VII), as evidenced by the infrared maximum at 5.65 μ. Rearrangement of VII occurred during distillation to give a 70% yield of a mixture of 2-ethyl-1-piperidino-1-buten-3-one (VIII) and 1-piperidino-1-hexen-3-one (IX) that was not separated by fractional distillation. The mixture had a boiling point of 137° (0.3 mm.), n_D^{22} 1.5544, infrared maxima at 6.05, 6.25, and 6.38 μ. An estimate made from the NMR spectrum showed the mixture to be about two parts of IX to one part of VIII. *Anal.* Calcd. for $C_{11}H_{19}NO$: C, 72.9; H, 10.5; N, 7.8. Found: C, 72.7; H, 10.5; N, 7.7.



The thermally unstable cyclobutanones, III, V, and VII, were treated with lithium aluminum hydride to give the corresponding cyclobutanols, which showed no tendency to undergo a ring-opening reaction.

The cycloaddition of other ketenes and enamines has been observed; this work will be described in greater detail at a later date.

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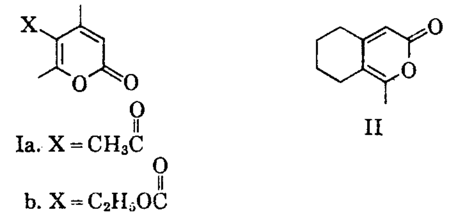
The Reaction of Enamines with Ketene

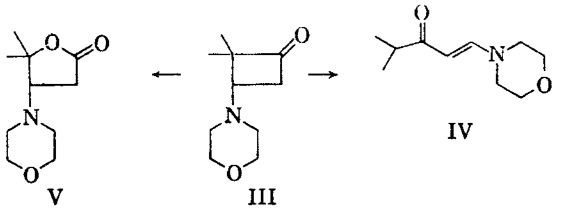
Sir:

We wish to report the results of our initial studies of the reaction of enamines with ketene. Treatment of 4-*N*-pyrrolidino-3-penten-2-one with three molar equivalents of ketene in ether at 0° and chromatography of the reaction mixture after evaporation of the solvent afforded 5-acetyl-4,6-dimethylcoumalin (Ia) (52%), m.p. 72.8–73.4° (C, 65.10; H, 5.69), $\lambda_{max}^{C_2H_5OH}$ 296 mμ (ε 6090).

Similarly, ethyl 3-*N*-pyrrolidinocrotonate reacted with ketene to produce ethyl isodehydroacetate (Ib) (35%), m.p. 18–20° (C, 61.42; H, 6.13), $\lambda_{max}^{C_2H_5OH}$ 247 mμ (ε 6530), 294 mμ (5240), which was identical to a sample prepared by the procedure of Wiley and Smith.[1] 1-*N*-Pyrrolidinocyclohexene reacted with excess ketene to produce II (16%), m.p. 82.0–84.5° (C, 72.93; H, 7.21), $\lambda_{max}^{C_2H_5OH}$ 312 mμ (ε 6800). The NMR spectra of the α-pyrones are in agreement with the proposed structures. These results are particularly interesting in view of the observations that diketene reacts with enamines to form γ-pyrones.[2,3]



The reaction of 1-*N*-morpholinoisobutene with ketene follows a different course. When either pentane or ether is the solvent, the product isolated is 2,2-dimethyl-3-*N*-morpholinocyclobutanone (III) (75%), m.p. 41.1–42.2° (C, 65.73; H, 9.38; N, 7.71). Compound III rearranges readily on warming to 4-methyl-1-*N*-morpholino-1-butene-3-one (IV), identical to a sample prepared from morpholine and ethynyl isopropyl ketone.[4] Treatment of III with aqueous hydrogen peroxide produced a lactone (48%), m.p. 103.4–104.3° (C, 60.41; H, 8.63; N, 7.10) which is assigned structure V. Hasek and Martin[5] have shown that ketene and dimethylketene react with enamines derived from aldehydes to yield the corresponding cyclobutanones. The rearrangement of these adducts has also been observed.



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(1) N. R. Smith and R. H. Wiley, *Org. Syn.*, **32**, 76 (1952).

(2) S. Hünig, E. Benzing, and K. Hübner, *Chem. Ber.*, **94**, 486 (1961).

(3) B. B. Millward, *J. Chem. Soc.*, 26 (1960).

(4) This sample was kindly supplied by Prof. N. J. Leonard of the University of Illinois.

(5) R. H. Hasek and J. C. Martin, *J. Org. Chem.*, **26**, 4775 (1961).