A Novel Condensation with Acetic Anhydride

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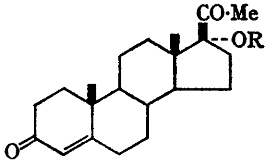
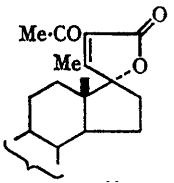
IN the course of studying the microbiological transformations of certain steroids, we had occasion to prepare 17α-acetoxyprogesterone (II) from (I) with boiling acetic anhydride and pyridine (1 : 1). In addition to (II), a second product $C_{25}H_{32}O_4$ (*m/e* 396), m.p. 218—219°, was isolated in 20% yield, to which we have assigned the novel structure (III) on the basis of the following evidence. The infrared spectrum (KBr) showed the C-3 carbonyl absorption at 1672 $cm.^{-1}$, an αβ-unsaturated γ-lactone band at 1757 $cm.^{-1}$, and a third band at 1692 $cm.^{-1}$ assigned to the second αβ-unsaturated keto-group. The n.m.r. spectrum showed the C-18 and C-19 methyl signals at τ 9·00 and 8·00 and, in addition two other three-proton singlets at τ 7·58 and 7·43, assigned to the vinyl methyl and methyl ketone respectively. Aside from the C-4 proton at τ 4·25 (one-proton singlet) no other olefinic-proton signals were observed. In support of the presence of the methyl ketone function, (III) gave a positive iodoform test.

The ultraviolet spectrum (methanol) of (III) showed a rather broad maximum at 242 mμ (ε 25,700) consistent with the superposition of the Δ^4-3-ketone chromophore on that of the 3-acetyl-2,5-dihydro-4,5,5-trialkylfuran-2-one system. In agreement with this, Lacy observed that 3-acetyl-2,4,5,6,7,8-hexahydrobenzofuran-2-one has an ultraviolet maximum at 237 mμ (ε 10,700).[1]

The formation of (III) can best be explained by the condensation of (I) with a four-carbon fragment, possibly represented by (IV), itself resulting from the self-condensation of two molecules of acetic anhydride. Supporting evidence for this postulate was obtained by the reaction of (I) with ethyl acetoacetate in boiling pyridine which also gave (III) albeit in poor yield . That (II) is not an intermediate on the way to (III) was shown by the fact that (II) was completely inert to the conditions under which (III) is formed.



(I) R=H
(II) R=Ac



(III)

$MeCO{\cdot}CH_2{\cdot}CO_2Ac$ (IV)

Although acetic anhydride is well known to provide the active methylene unit in the Perkin reaction in the presence of sodium acetate, we are unaware of any previously reported self-condensation of acetic anhydride in pyridine to form to a four-carbon moiety such as (IV) which appears to be involved in this reaction.[2]

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[1] R. N. Lacey, *J. Chem. Soc.*, 1954, 816.

[2] The acid-catalyzed self-condensation of acetic anhydride is well established; see P. F. G. Praill and A. L. Whitear, *Proc. Chem. Soc.*, 1961, 112.