Reaction of an Enamine with 3-Acetyl-2-hydroxy-6-methylpyran-4-one, A New Synthetic Route to β-Triketone Derivatives

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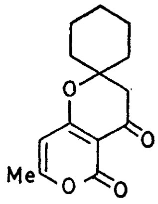
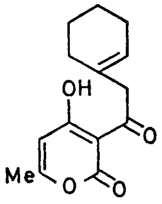
Summary The reaction of 1-morpholinocyclohex-1-ene with 3-acetyl-2-hydroxy-6-methylpyran-4-one (dehydroacetic acid) gave a condensation product (I), which was transformed subsequently into the 4-pyrone (V) and the β-triketone (VII).

Various syntheses and reactions of either protected or unprotected β-polyketones have been reported in connection with biogenetic syntheses of polyketide-derived natural products.[1] We have investigated the condensation of an enamine with dehydroacetic acid and subsequent transformation into a triketone, which provides a new method for the introduction of the β-triketone group. Although the reactions of dehydroacetic acid with primary amines,[2] secondary amines,[3] and bromine and related reagents[4] have been reported recently, the reaction with enamines has not been reported.

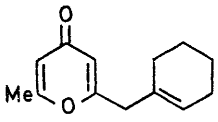
Reaction of 1-morpholinocyclohex-1-ene with dehydroacetic acid in toluene at 70° for 3 h gave a condensation product (I) (50%), m.p. 168—170°, which isomerized to (II), m.p. 108°, upon treatment with 1N-KOH–MeOH at room temperature for 2 days. Isomer (II) reverted to (I) when treated with conc. HCl or H_2SO_4. Structures (I) and (II) were supported by their physical data; i.r. and u.v.



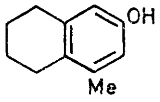
(I)



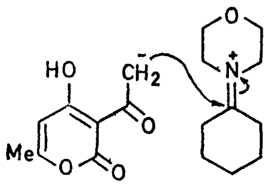
(II)



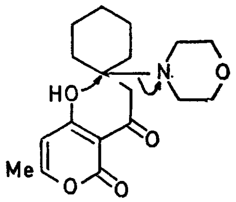
(V)

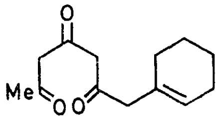


(VI)

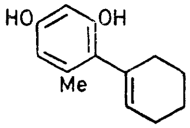


(III) (IV)





(VII)



(VIII)

spectra show the presence of the 2-pyrone nucleus in both (I) and (II), and the n.m.r. spectrum of (II) show the presence of an acidic proton at τ −6·80 and an olefinic proton at τ 4·35 which are absent in (I).

The reaction may take place *via* the anion (III) by Knoevenagel catalysis[5] which attacks the iminium structure of the enamine (IV), followed by elimination of morpholine by attack of the hydroxy-group to form (I).

Pyrone (I) was converted into the 4-pyrone (V) (60%), b.p. 118—125° at 0·2 mmHg and the phenol (VI) (20%), m.p. 104—105°, *m/e* 162 (M^+) when refluxed with conc. HCl. When treated with barium hydroxide, 4-pyrone (V) was transformed into the triketone (VII) (80%) (identified as the pyrrolidine dienamine, m.p. 104—106°). Further, triketone (VII) yielded an Aldol condensation product (VIII) (80%), m.p. 103—104·5° when treated with 20% aqueous KOH.

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