THE REACTION OF 3-HYDROXYCOUMARINS WITH CHALCONE

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Abstract - The reaction of 3-hydroxycoumarins with chalcone in presence of pyridine-piperidine afforded 2-hydroxy-2,4-diphenyl-10-oxo-3,4-dihydropyrano(2,3-c)(1) benzopyrans. The structures have been established spectroscopically.

3-Hydroxycoumarin (I) has an inhibiting effect on growth of avena roots[1] and 3-aminocoumarins which are intermediates for the synthesis of 3-hydroxycoumarins[2] are found to have antibacterial properties[3,4]. These are also known[5,6] to react with different reagents to give 4-substituted derivatives. It was observed that 3-hydroxycoumarin gives 4-isonitroso-, 4-iodo- and 4-aryl derivatives with nitrous acid, iodine-iodic acid and p-benzoquinone respectively. The formation of these derivatives can be explained due to ketonic character of 3-hydroxycoumarins, which has also been confirmed by the formation of quinoxalin derivatives with o-phenylene diamine[7]. In view of above interesting reactions, we were prompted to study the reactions of 3-hydroxycoumarin with α,β-unsaturated ketone.

A typical experiment involves the condensation of 3-hydroxycoumarin (Ia) (1.62 g) with chalcone (II) (2.08 g) by refluxing in pyridine - piperidine at 120° for 40 h to give a crystalline compound (2.30 g), $C_{24}H_{18}O_4$, m.p. 181-182°. In the IR (KBr) spectrum of the compound, a band at 1700 cm^{-1} confirmed the retention of the coumarin ring, while bands at 1220 cm^{-1} and 3300 cm^{-1} were indicative of an ether linkage and -OH group respectively. Its UV spectrum (MeOH) showed a maximum at 240 nm (ϵ 12000) and no shift was observed with NaOH and $AlCl_3$. NMR($CDCl_3$) showed two double doublets at δ 3.82 (J 6Hz, 17.5 Hz) and 4.60 (J 9 Hz, 17.5 Hz) each integrating for one proton assigned to two protons at C_3; one double doublet at δ 5.40 (J 6Hz, 9Hz) equivalent to one proton for C_4 in addition to two multiplets at δ 7.50 and 8.10 corresponding to 14 protons in all. The above spectral data led us to assign the structure 2-hydroxy-2,4-diphenyl-10-oxo-3,4-dihydropyrano(2,3-c) (1) benzopyran (IIIa) to the product. The alterna-

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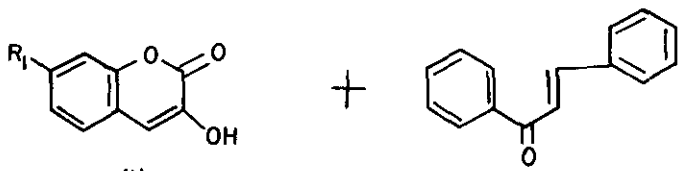
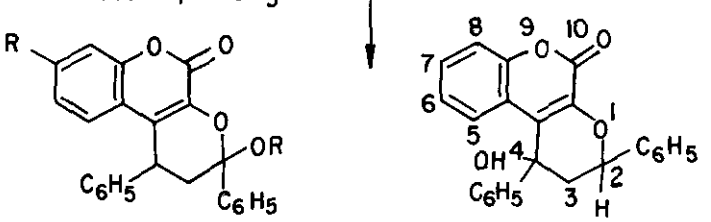
tive structure, viz. 4-hydroxy-2,4-diphenyl-10-oxo-3,4-dihydropyrano(2,3-c)(1) benzopyran (IV) was excluded on the basis of NMR spectrum, which is expected to show down field shift for C_2 proton (δ 5.9-6.2) due to deshielding effect of neighbouring oxygen atom. The presence of hydroxyl group in (IIIa) was further confirmed by its methylation to methyl ether, m.p. 119-120°, viz., 2-methoxy-2,4-diphenyl-10-oxo-3,4-dihydropyrano(2,3-c) (1) benzopyran (Va). Its IR spectrum showed the absence of hydroxy group and NMR($CDCl_3$) showed in addition to usual signals, a singlet at δ 3.64 equivalent to 3 protons assigned to methoxyl group. Acetylation of (IIIa) with acetic anhydride - pyridine (room temperature) gave its O-acetyl derivative, m.p. 167-168°, viz., 2-acetoxy-2,4-diphenyl-10-oxo-3,4-dihydropyrano(2,3-c) (1) benzopyran (VIa); its structure was also in agreement with the NMR spectral data.



(I) (II)

(a) R_1 = H
(b) R_1 = OCH_3



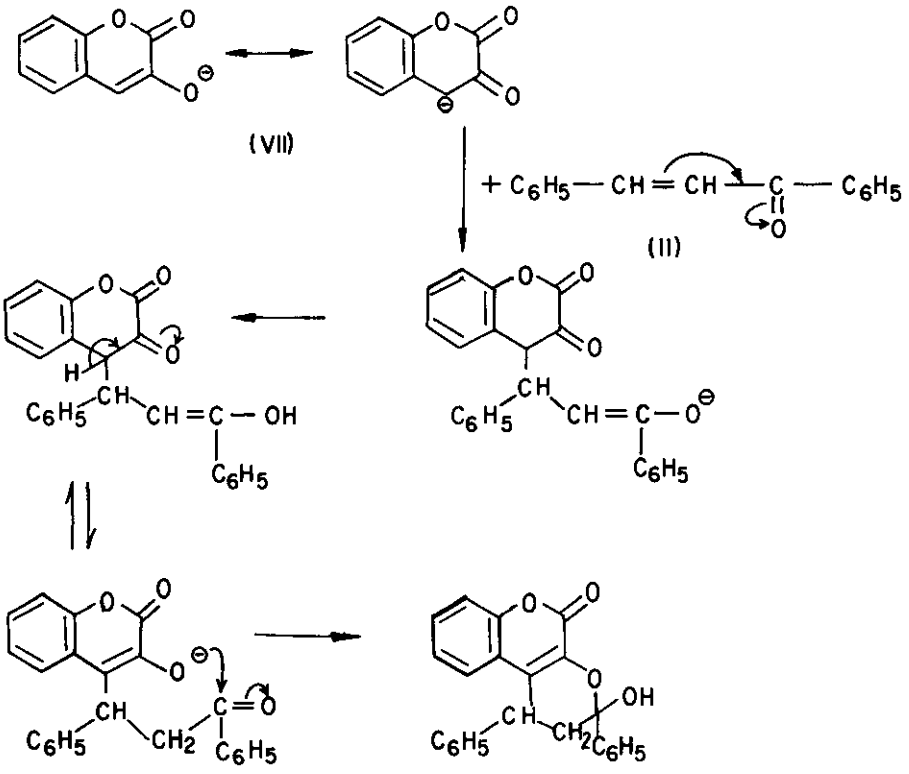
(III),(V),(VI). (IV)

(IIIa) R = H; R_1 = H
(IIIb) R = H; R_1 = OCH_3
(Va) R = CH_3; R_1 = H
(Vb) R = CH_3; R_1 = OCH_3
(VIa) R = $COCH_3$; R_1 = H
(VIb) R = $COCH_3$; R_1 = OCH_3

Similarly, condensation of chalcone (II) (2.08 g) with 3-hydroxy-7-methoxy-coumarin (Ib) (1.92 g) gave (IIIb) (2.20 g), m.p. 175-176°, which on methylation

with dimethyl sulphate yielded methyl ether (Vb), m.p. 180-181°. Acetylation of (IIIb) (acetic anhydride/pyridine) gave (VIb), m.p. 160-161°. The spectral data were in agreement with the proposed structures.

A plausible mechanism for the formation of (III) would involve the facile attack of the ambident 3-hydroxycoumarin anion (VII) at the β-position of the carbon-carbon double bond of chalcone (II) to yield a stable anion, which abstracts a proton from the solvent to produce enol form of the product. It is rapidly equilibrated to the more stable keto form, which gets cyclized. The various steps are shown below:



All compounds analysed well for C and H.

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