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COUMARIN AND RELATED COMPOUNDS II[+]

A NOVEL SYNTHESIS OF 5-HYDROXYDIHYDROCOUMARIN

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In a previous communication[1] we have revised the structure of 5-hydroxydihydrocoumarin m.p. 224-225° reported by Stephen et al[2] obtained along with dihydroumbelliferone during the condensation of resorcinol with acrylonitrile[3] in the presence of zinc chloride. We have reinvestigated the reaction and found that the reported 5-hydroxydihydrocoumarin by Stephen et al is 6:7-dihydro-8-oxo-pyrano (2.3-g)-3:4-dihydrocoumarin (V)[1] by n.m.r., i.r. and mass spectrometry. Catalytic reduction of 5-hydroxycoumarin by Pd-C (10%) in ethanol gave an authentic sample of 5-hydroxydihydrocoumarin m.p. 170-172° (III).

In the present communication we wish to report a novel synthesis of 5-hydroxydihydrocoumarin involving the condensation of methyl acrylate with methyl β-resorcylate in the presence of aluminium chloride at a high temperature. Dehydrogenation of the resulting 5-hydroxydihydrocoumarin over Pd-C (10%) in boiling diphenyl ether gave 5-hydroxycoumarin which may be considered as a simpler method of synthesis of the coumarin than those recorded earlier.[4,5]

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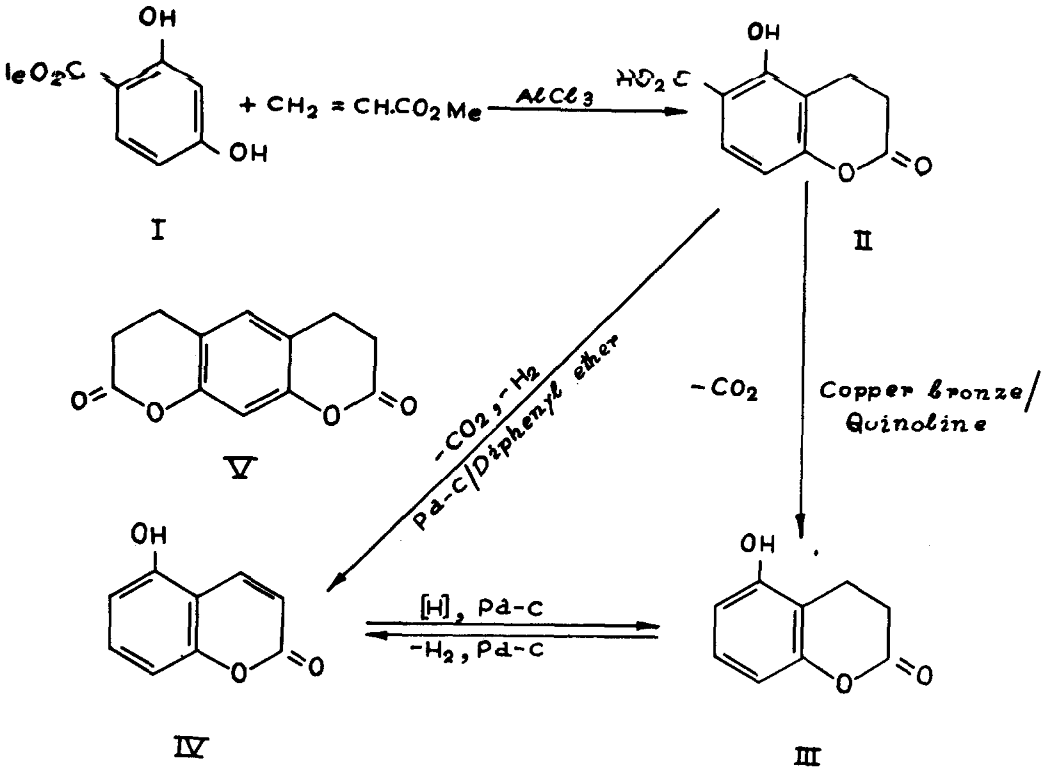
Dry hydrogen chloride was passed for an hour through an ethereal solution of methyl β-resorcylate (I) and methyl acrylate below 10° with portionwise addition of aluminium chloride. The reaction mixture, after the evaporation of ether was heated at 150-160° for 4 hours and then decomposed with dilute hydrochloric acid. Extraction with ether gave a semisolid mass which was heated to boiling with 2N methanolic potassium hydroxide for 2 hours. Acidification and reextraction with ether gave a mixture of 5-hydroxy-3:4-dihydrocoumarin m.p. 171-172° (III), R_f = 0.53 ν_{max} 3348 (hydroxyl), 1728 cm^{-1} (lactone) and 5-hydroxy-6-carboxy-dihydrocoumarin m.p. 228-229° (II), [ν_{max}~2700 (broad), 1770 (lactone), 1665, 880 (sh) cm^{-1} (carboxyl)] (total yield 85%). It is reasonable to consider the acid as 5-hydroxy-6-carboxy-dihydrocoumarin (II) in preference to 5-hydroxy-8-carboxy-dihydrocoumarin on the basis of the



infra-red spectrum which gives strong evidence of internal hydrogen bonding of the -OH to the -CO of the -COOH group, as a result of which the carbonyl frequencies are reduced. The spectrum has also strong similarity with that of salicylic acid and differs from that of p-hydroxy benzoic acid[6]. Decarboxylation of acid II on heating with quinoline and copper bronze gave 5-hydroxy-3:4-dihydrocoumarin m.p. 170-172° (toluene)as shiny white flakes (yield 50%). Dehydrogenation[7] of III over Pd-C (10%) in boiling diphenyl ether gave the desired 5-hydroxycoumarin (IV) m.p. 224-225° (ethanol-toluene; yield 60%) $R_f = 0.36$. ν_{max} 3175 (hydroxyl), 1695 ($\alpha\beta$-unsaturated lactone), 1613 cm^{-1} (olefinic stretch). The identity of the coumarin IV was confirmed by superimposable u.v. spectra (λmax 300 mμ; log $\epsilon = 4.2$) as well by mixed melting point with an authentic sample of 5-hydroxycoumarin m.p. 223-224° (prepared by the method of Shah *et al*[4]). It is interesting to note that acid II on heating with Pd-C (10%) in boiling diphenyl ether gave directly 5-hydroxycoumarin (IV) undergoing simultaneous dehydrogenation and decarboxylation (yield 55%) in one step.

Satisfactory elemental analyses have been secured for each new compound. Further studies are in progress and more details will be reported later.

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Melting points are uncorrected. All compounds are homogenous (t.l.c). IR spectra are determined as nujol mulls and uv spectra in ethanol solution. R_f values are recorded by ascending technique with Si-gel G (E. Merck) and eluted with benzene : dioxane : acetic acid (90:25:4).