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THE STUDIES ON DIHYDROISOCOUMARIN (III). THE SYNTHESIS OF 3-(3'-HYDROXY-4'-METHOXYPHENYL)-3,4-DIHYDROIROCOUMARIN

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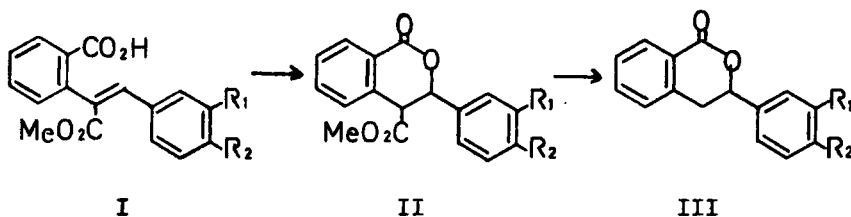
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THE STUDIES ON DIHYDROISOCOUMARIN (III). THE SYNTHESIS
OF 3-(3'-HYDROXY-4'-METHOXYPHENYL)-3,4-DIHYDROISOCOUMARIN.

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We have recently reported the preparation of stilbene dicarboxylic acids as useful precursors of phyllostulcin and hydrangenol¹, and now describe the preparation of 3-(3'-hydroxy-4'-methoxyphenyl)-3,4-dihydroisocoumarin (III, R₁ = OH, R₂ = OMe) from I (R₁ = OCH₂Ph, R₂ = OMe).



Application of the conditions of Pappo² and of Pinder³ for synthesis of II (R₁ = OH, R₂ = OMe) gave so many products. that II (R₁ = OH, R₂ = OMe) could not be obtained satisfactorily. The smooth cyclization of I (R₁ = OCH₂Ph, R₂ = OMe) was achieved by reaction at 40-50° in CHCl₃ while HBr gas was bubbled through the solution for 4 hrs. and yielded readily separated products; 3-(3'-hydroxy-4'-methoxyphenyl)-4-carbomethoxy-3,4-dihydroisocoumarin (II,

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$R_1 = OH, R_2 = OMe$) was isolated in 65 % yield and homophthalic acid and isovanillin were found as by-products. The decarboxylation of 3-(3'-hydroxy-4'-methoxyphenyl)-4-carbomethoxy-3,4-dihydroisocoumarin with water at 165° in an autoclave yielded 3-(3'-hydroxy-4'-methoxyphenyl)-3,4-dihydroisocoumarin in 21 % yield⁴; homophthalic acid and isovanillin were also obtained. The 3-aryl group of III is assigned to be in the axial position on the basis of the magnitude of the coupling constants between H_3 and the two hydrogens at C-4. The observed values $J_{AX} = 5$ Hz and $J_{BX} = 9-10$ Hz are consistent with a dihedral angle of 40° (H_3 and H_4) and 170° (H_3 and H_4) as shown by Dreiding model.

EXPERIMENTAL

3-(3'-Hydroxy-4'-methoxyphenyl)-4-carbomethoxy-3,4-dihydroisocoumarin (II). - Through a solution of 10 g. (0.024 mole) of 2-carboxy-3'-benzyloxy-4'-methoxy- α -carbomethoxy stilbene¹ in 30-40 ml. of $CHCl_3$ was bubbled hydrogen bromide gas at 40-50° for 4 hrs. The reaction mixture was evaporated in vacuo, then 50-100 ml. of ether was added to the residue. The white crystals which precipitated were recrystallized from methanol to yield 5.5 g. (70 %) of white plates, mp. 163-164°.

IR: 1745 cm^{-1} (ester C = O), 1720 cm^{-1} (lactone C = O).

NMR (DMSO- d_6): $\tau = 3.75$ (H_3 , d), 4.3 (H_4 , d), $J = 8$ Hz.

Mass Spectrum: m/e 328 (M^+).

Anal. Calcd. for $C_{18}H_{16}O_6$: C, 65.85; H, 4.91.

Found: C, 65.65; H, 5.14.

THE STUDIES ON DIHYDROISOCOUMARIN (III).

3-(3'-Hydroxy-4'-methoxyphenyl)-3,4-dihydroisocoumarin (III).

Twenty grams (0.061 mole) of 3-(3'-hydroxy-4'-methoxyphenyl)-4-carbomethoxy-3,4-dihydroisocoumarin was stirred with 200 ml. of water in 500 ml. autoclave at 165° for 10 hrs. After reaction, the presence of CO₂ gas was detected with saturated Ba(OH)₂ solution, and the autoclave was opened. The reaction mixture was evaporated in vacuo and the residue was chromatographed on alumina (solvent: benzene/methanol = 10/3). The first fraction was 3-(3'-hydroxy-4'-methoxyphenyl)-3,4-dihydroisocoumarin, which was recrystallized from benzene to yield 4.3 g. (21 %) of plates, mp. 142.5-143.5°.

IR: 3500 cm⁻¹ (OH), 1704 cm⁻¹ (lactone C = O).

NMR (DMSO-d₆): τ = 4.5 (H₃, q), τ = 6.7 (H₄, q), J_{AB} = 18 Hz,

J_{AX} = 5 Hz, J_{BX} = 10 Hz.

Mass Spectrum: m/e 270 (M⁺).

Anal. Calcd. for C₁₆H₁₄O₄: C, 71.10; H, 5.22.

Found: C, 71.33; H, 5.59.

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