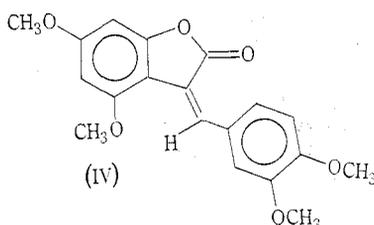
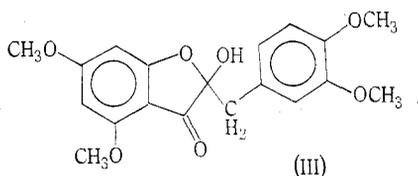
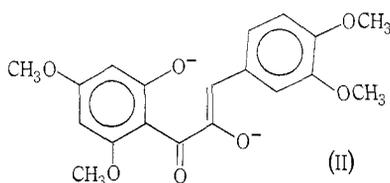
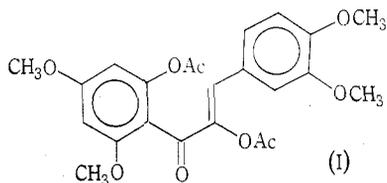


SYNTHESIS OF $\alpha,2'$ -DIACETOXY-3,4,4',6'-TETRAMETHOXYCHALCONE
AND 4,6,3',4'-TETRAMETHOXYISOAURONE*

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Acetylation of dihydroquercetin 5,7,3',4'-tetramethyl ether with acetic anhydride and sodium or potassium acetate was recently shown¹ to yield $\alpha,2'$ -diacetoxy-3,4,4',6'-tetramethoxychalcone (I) in the first recorded analogy in the dihydroflavonol series to the well-known flavanone-2'-hydroxychalcone equilibrium. The fact of the existence of the corresponding chalcone anions (II)² in alkaline solutions of 2-benzyl-2-hydroxycoumaran-3-ones (e.g. III) has now been applied to the synthesis of the diacetoxychalcone (I). The ultraviolet-light absorption of the anion (II) resembled



that of the diacetoxychalcone (I), and for preparation of the latter compound the sodium salt of the anion (II) was acetylated with acetic anhydride and sodium acetate, which gave the diacetoxychalcone (I) in 35% yield. Formation of the anion (II) was accompanied by benzylic acid rearrangement to the corresponding carboxylate anion, which led to isolation of 4,6,3',4'-tetramethoxyisoaurone (IV). The diacetoxychalcone (I) and isoaurone (IV) were separated by fractional crystallization, and the structure of the isoaurone was inferred from infrared, nuclear magnetic resonance, and mass spectrometric data. Variation in the proportion of sodium hydroxide used in preparation of the anion (II) did not appear to affect the extent of the benzylic rearrangement, although the best yield of the diacetoxychalcone was obtained when 2 equiv. of sodium hydroxide were used in preparing the anion (II) from the hydroxybenzylcoumaranone (III). Attempts to prepare the diacetoxychalcone by direct

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¹ Clark-Lewis, J. W., and Jemison, R. W., *Aust. J. Chem.*, 1967, **20**, 149.

² Dean, F. M., "Naturally Occurring Oxygen Ring Compounds." p. 342. (Butterworths: London 1963.)

acetylation of this hemiketal (III) with acetic anhydride and pyridine or sodium acetate were unsuccessful even under the conditions which convert dihydroquercetin tetramethyl ether into the diacetoxychalcone (I), so that the latter transformation appears not to proceed by intermediate formation of the coumaran-3-one (III).

The isoaurone (IV) belongs to the more stable series of geometrical isomers described as *trans*-isoaurones by Marathe, Byrne, and Vidwans.³ The vinylic proton is strongly deshielded by the aromatic rings and its nuclear magnetic resonance signal occurred as a singlet at lower field (2.08 τ) than recorded by the Indian authors for the *trans*-4'-methoxy-5-methyl analogue (2.65 τ), and considerably lower than the value 3.1 τ reported for *cis*-4'-methoxy-5-methyl-isoaurone.³ The assignment of configuration to the isoaurone (IV) is supported by the occurrence of the 2'-proton doublet at very low field (1.76 τ), indicating deshielding by the carbonyl group and the double bond.

Experimental

N.m.r. spectra were recorded with a Varian A60A spectrometer and tetramethylsilane as internal standard. Ultraviolet and infrared spectra were recorded with Perkin-Elmer 137UV and 237 spectrometers, and the mass spectrum with a Perkin-Elmer-Hitachi RMU6D instrument. Thin-layer silica-gel plates were developed with ether and sprayed with 5% vanillin in sulphuric acid.

2-Hydroxy-4,6-dimethoxy-2-(3,4-dimethoxybenzyl)coumaran-3-one (III)

Cyclization¹ of 2'-hydroxy- α ,3,4,4',6'-pentamethoxychalcone gave the coumaran-3-one with broad hydroxyl absorption at 3520 and carbonyl absorption at 1705 cm^{-1} (CHCl_3); light absorption in 95% ethanol: λ_{max} 224 ($\log \epsilon$ 4.64) and 291 $\text{m}\mu$ ($\log \epsilon$ 4.53); λ_{max} 382 $\text{m}\mu$ ($\log \epsilon$ 3.32) in a 9:1 mixture of 95% ethanol and 10% aqueous sodium hydroxide. Its n.m.r. spectrum (CDCl_3) showed a two-proton peak at 6.8 (methylene group), twelve-proton methoxyl absorptions at 6.2, a two-proton phloroglucinol quartet (J_{AB} 1.8 c/s, ν_{A} 4.0 ν_{B} 4.2), and a three-proton multiplet at c. 3.1 τ (veratryl ring protons); the hydroxyl signal (removed by D_2O exchange) occurred at 5.7 τ .

α ,2'-Diacetoxy-3,4,4',6'-tetramethoxychalcone (I) and 4,6,3',4'-Tetramethoxyisoaurone (IV)

The coumaran-3-one (0.69 g, 1.92 mmole) in methanol (5 ml) was added to sodium hydroxide (0.154 g, 3.8 mmole) in methanol (5 ml). Evaporation under reduced pressure left an orange solid which was heated with fused sodium acetate (1 g) and acetic anhydride (10 ml) under reflux for 12 hr before dilution with water. Crystallization of the precipitated solid from ethanol gave a mixture of yellow prisms and needles which was separated by repeated crystallization into the diacetoxychalcone, yellow prisms (0.3 g, 35%), m.p. 135–136° not depressed by an authentic sample¹ of m.p. 139.5° (Found: C, 62.5; H, 5.5. Calc. for $\text{C}_{23}\text{H}_{24}\text{O}_9$: C, 62.2; H, 5.4%), and bright yellow needles of 4,6,3',4'-tetramethoxyisoaurone (0.15 g, 23%), m.p. 165–167° (lit.⁴ 173.5–174°) (Found: C, 66.9; H, 5.8. Calc. for $\text{C}_{19}\text{H}_{18}\text{O}_6$: C, 66.7; H, 5.3%). The infrared and n.m.r. spectra of the diacetoxychalcone were indistinguishable from those previously recorded.¹ The isoaurone showed absorption maxima at 1775, 1755, and 1630 cm^{-1} (CHCl_3) and at 261 ($\log \epsilon$ 3.16) and 403 $\text{m}\mu$ ($\log \epsilon$ 4.35) in 95% ethanol; its n.m.r. spectrum (CDCl_3) showed four three-proton peaks at 6.20, 6.08, 6.07, and 6.03 (methoxyls), the phloroglucinol quartet (J_{AB} 2.0 c/s, τ_{A} 3.71 τ_{B} 3.76), three one-proton multiplets (two doublets and a quartet) due to the veratryl ring protons (τ : 2'H, c. 1.76; 5'H, c. 3.13; 6'H, c. 2.56 τ ; $J_{2',6'}$ 2.0, $J_{5',6'}$ 8.5 c/s), and a sharp one-proton singlet at 2.08 τ (vinylic proton). Its mass spectrum showed a strong peak due to the parent ion at m/e 342. The diacetoxychalcone (R_F 0.31) and isoaurone (R_F 0.62) were well separated on t.l.c. plates.

³ Marathe, K. G., Byrne, M. J., and Vidwans, R. N., *Tetrahedron*, 1966, **22**, 1789.

⁴ Eneback, C., and Gripenberg, J., *J. org. Chem.*, 1957, **22**, 220.