5-Acetoxyisoflavones and their Chloro-derivatives

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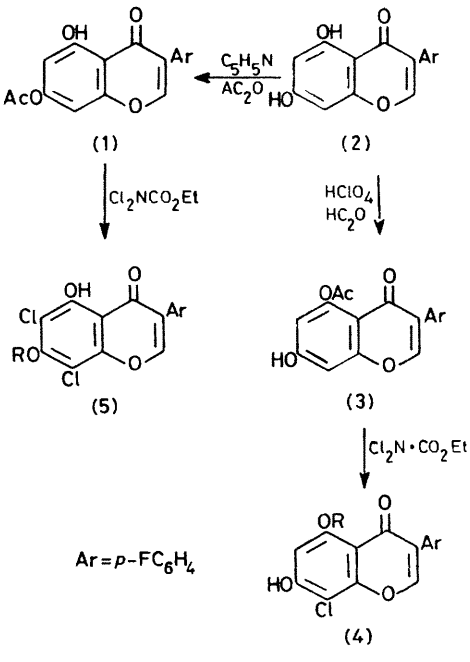
Summary The regiospecific *O*-acetylation of 5,7-dihydroxyisoflavones and their selective monochlorination with dichlorourethane is reported.

5,7-DIHYDROXY-SUBSTITUTED isoflavones are well known to form 7- and 5,7-di-acetoxy-derivatives, but 5-acetoxy-compounds have not been previously reported. Diacetoxyisoflavones are rapidly hydrolysed, first to the 7-acetoxy-compound and then to the parent dihydroxy-isoflavone. Hence it has been thought that the 5-acetoxy-derivatives would not be stable enough to allow isolation.

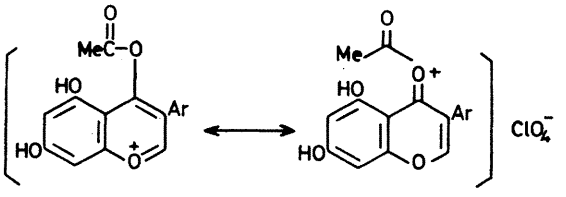
Treatment of 5,7-dihydroxy-isoflavones at room temperature with acetic anhydride under acid- or base-catalysed conditions affords the 7-acetoxy-derivative. More forcing conditions give the 5,7-diacetoxy-compounds. During an investigation of the acetylation of 5,7-dihydroxy-4'-fluoroisoflavone (**2**)[1] it was discovered that different monoacetoxy-isoflavones (**1**) and (**3**) were formed depending on whether pyridine or perchloric acid was used as catalyst. With pyridine as catalyst, a product with m.p. 194—197 °C, ν_{CO} 1780 cm^{-1}, τ(Me) 7·68, R_F (C_6H_6–MeOH–Me_2CO–AcOH, 80:20:5:5) 0·7, instantaneous colour reaction with $FeCl_3$, was obtained whereas use of perchloric acid led to a product with m.p. 195 °C, ν_{CO} 1750 cm^{-1}, τ(Me) 7·63, R_F 0·3, colour with $FeCl_3$ only on standing or heating. Accordingly, the former was assigned the 7-acetoxy-5-hydroxy-structure (**1**), and the latter the 5-acetoxy-7-hydroxy structure (**3**).

The lack of a bathochromic shift in the u.v. spectrum of the 5-acetoxy-7-hydroxy compound (**3**) on addition of aluminium chloride compared to the shift of 17 nm shown by the 7-acetoxy-5-hydroxy compound (**1**) also supported the assignment.[2] Increasing the amount of perchloric acid or allowing the reaction to continue for a longer time gave the 5,7-diacetoxy product. Optimum selectivity for acetylation at the intramolecularly bonded 5-OH group was found at −10 °C. Thus the initial intense red colour formed on addition of 3 or 4 drops of perchloric acid to a suspension (1·3 g) of the dihydroxyisoflavone (**2**) in acetic anhydride (10 ml), at −10 °C slowly faded and after 1·0 h the reaction product was poured into ice water. The initially oily product solidified overnight to give the 5-acetoxy-7-hydroxyisoflavone (**3**) (60%) as needles from ethyl acetate–petrol, m.p. 195 °C. It is suggested† that the regiospecific nature of the acetylation is due to participation of a resonance stabilised acetoxonium ion which then undergoes an intramolecular migration of the acetyl group to give the product.

The reaction was found to be a general one. Acetylation of 5,7-dihydroxy-4'-methoxyisoflavone under the same conditions gave the 5-acetoxy-7-hydroxy derivative as needles, m.p. 188—190 °C (from MeOH), ν_{CO} 1770 cm^{-1} (*cf.* 7-acetoxy-5-hydroxy, m.p. 153—155 °C).[3]



a, R = Ac
b, R = H



There was also a difference in the reactivity of the two acetoxy derivatives. Thus, on reaction with dichlorourethane[4] in acetic acid, (**3**) gave the 8-chloro-compound (**4a**) as micro-needles from ethyl acetate–petrol, m.p. 185—188 °C. However under the same conditions, (**1**) gave the dichlorosubstituted compound (**5a**), as needles from ethyl acetate–petrol, m.p. 173—175 °C. Hydrolysis of (**4a**) and (**5a**) with methanolic HCl gave (**4b**) as needles from acetonitrile, m.p. 224—225 °C and (**5b**) m.p. 224—226 °C, respectively. This modification of the reactivity of 5,7-dihydroxyisoflavones provides a useful route to monosubstituted products not readily available by other means. Satisfactory microanalytical data were obtained for all new compounds.

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[2] 'Naturally Occurring Oxygen Ring Compounds,' ed. F. M. Dean, Butterworths, London, 1963, p. 371.
[3] F. E. King, M. F. Grundon, and K. G. Neill, *J. Chem. Soc.*, 1952, 4580.
[4] R. J. Bass, *Tetrahedron*, 1971, **27**, 3263.