A New General Synthesis of Polyhydroxyisoflavanones

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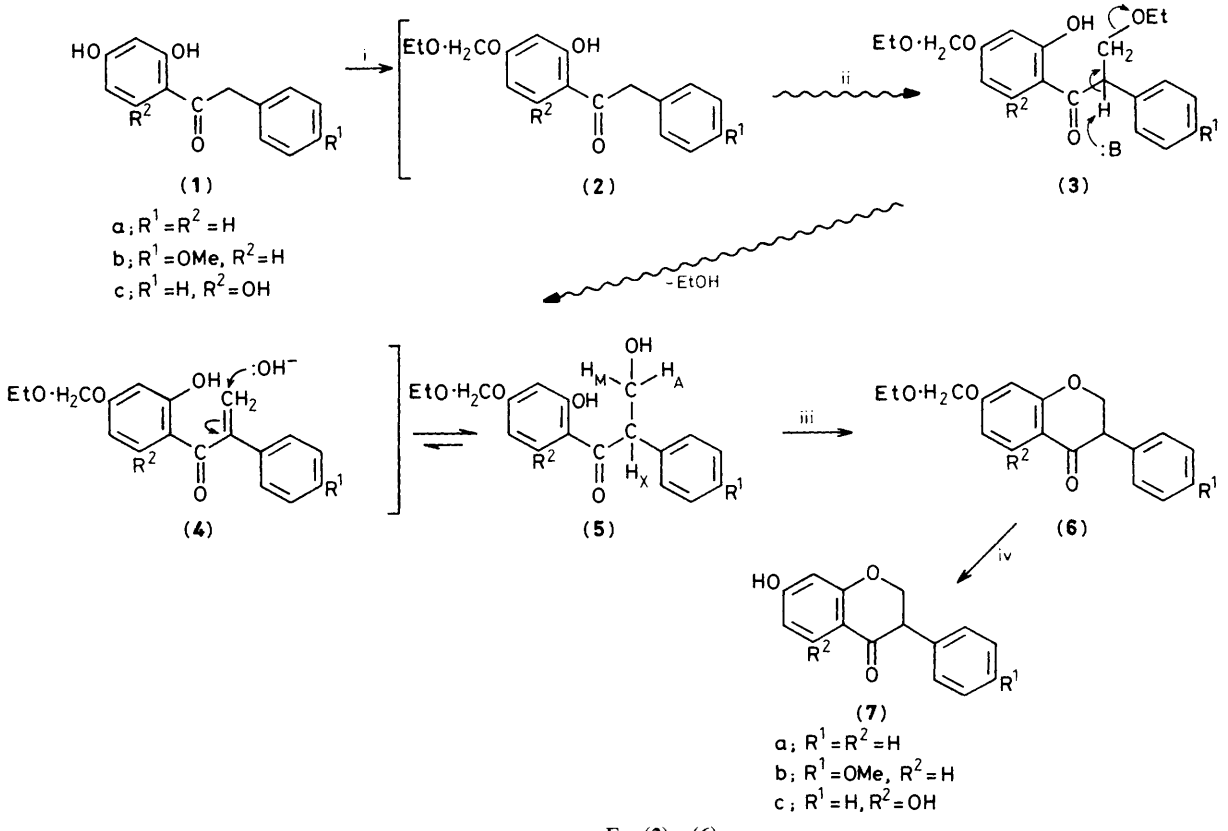
Hydroxyisoflavanones have been conveniently synthesised from hydroxydesoxybenzoins in 47—57% overall yields in four steps which could be carried out either continuously or by isolating the products at each stage.

Hydroxyisoflavanones, which occur in nature as such and also as further elaborated structures such as phytoalexinal pterocarpanoids and insecticidal rotenoids are considered difficult to synthesise in good yields.[1] Of the two methods available, one uses reduction, either catalytically or with complex metal hydrides, of isoflavones having hydroxy groups protected by methylation, acetylation, or tetrahydropyranylation.[2—5] In the other method, polyhydroxydesoxybenzoins [such as (**1a**) and (**1c**)] with all the hydroxy groups protected by methoxymethylation (except the hydrogen-bonded one) are condensed with di-iodomethane in the presence of dry potassium carbonate and boiling acetone (100—150 h) followed by removal of the protecting groups.[6] However in both methods the products are mixtures and the overall yield of desired product is very poor. We report here a new general synthesis of hydroxyisoflavanones from polyhydroxydesoxybenzoins



For (**2**)—(**6**)

	R¹	R²
a	H	H
b	OMe	H
c	H	OCH_2OEt

Scheme 1. *Reagents:* i, $ClCH_2OEt$, dry K_2CO_3, Me_2CO; ii, 1 mol $ClCH_2OEt$; iii, ethanolic 4% aq. Na_2CO_3, iv, methanolic 10% HCl.

giving 47—57% overall yield. It consists of four stages which can be carried out either continuously or by isolating the products at each stage.

The first stage involves protection of all the hydroxy groups (except the hydrogen-bonded one) of the desoxybenzoin (**1**) by stirring with an equivalent amount of chloromethyl ethyl ether† in the presence of dry K_2CO_3 and acetone at room temperature until completion of the reaction (15—45 min). The resulting mixture [containing (**2**)] is treated with another mole equivalent of chloromethyl ethyl ether at 60—70 °C (1—1.5 h). The products thus obtained in 85—91% yields were identified as α-hydroxymethyl derivatives (**5**) by their characteristic three double doublets of an AMX system between δ 3.6 and 5.1 in their ^{1}H n.m.r. spectra [*e.g.* (**5a**) showing these doublets at 3.67, 4.27, and 4.73 with J_{AM} 11.20, J_{AX} 4.8, J_{MX} 8.0 Hz] and explained on the basis of an elimination–addition mechanism analogous to reaction products of methoxydesoxybenzoins[7] *via* (**3**) and (**4**) as shown in Scheme 1. The third stage consists of cyclising (**5**) with 4% aqueous ethanolic sodium carbonate (2—3 h) to obtain the corresponding ethoxymethylated isoflavanones (**6**) in 59—68% yields (characteristic ABX ^{1}H n.m.r. pattern). The removal of the ethoxymethyl groups with 10% methanolic HCl (7—10 min) finally yielded the corresponding hydroxyisoflavanones (**7**) in 92—94% yields. Thus, 7-hydroxy-(**7a**), 7-hydroxy-4′-methoxy-(**7b**), and 5,7-dihydroxy-(**7c**) isoflavanones were obtained in 47.0, 56.0, and 57.0% overall yields respectively (error limit for the yields is ±0.5%).

† This reagent may be a carcinogen, analogous to chloromethyl methyl ether.

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References

1 P. M. Dewick in 'The Flavonoids: Advances in Research,' eds. J. B. Harborne and T. J. Mabry, Chapman and Hall, London, New York, 1982, 563.
2 R. B. Bradbury and D. E. White, *J. Chem. Soc.*, 1953, 871.
3 N. Inoue, *Sci. Repts. Tohoku Univ., Ser. 1*, 1961, **45**, 63; *Chem. Abs.*, 1963, **58**, 5619.
4 M. Miyano and M. Matsui, *Chem. Ber.*, 1958, **91**, 2044.
5 K. H. Budley and R. R. Corley, *J. Org. Chem.*, 1967, **32**, 2312.
6 J. K. Makrandi and S. K. Grover, *Curr. Sci.*, 1978, **47**, 85.
7 A. C. Jain and A. Sharma, *Indian J. Chem., Sect. B*, 1984, **23**, 451.