

A NEW SYNTHESIS OF ISOFLAVONES USING 'ACTIVE FORMATE'

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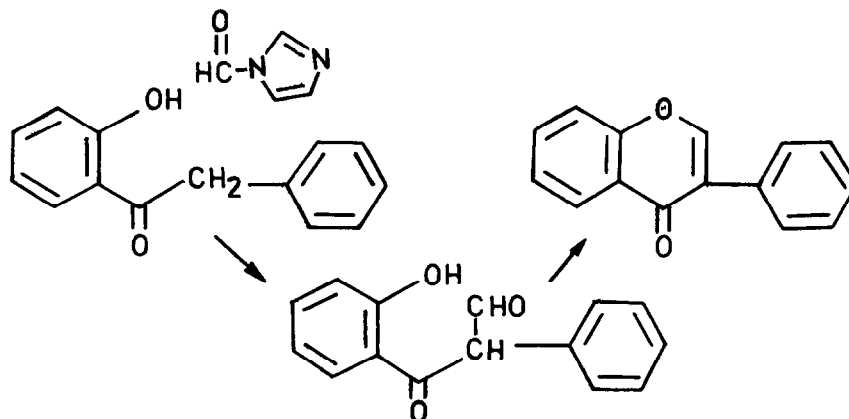
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The most widely used method of synthesis of isoflavones is to subject a suitably substituted 2-hydroxyphenyl benzyl ketone (O-hydroxydesoxybenzoin) to C-formylation on the methylene group followed by cyclization. A number of procedures have been developed¹ in the past based on this principle and for formylation ethyl formate, ethyl orthoformate, $Zn(CN)_2 \cdot HCl$, $POCl_3$ -DMF and ethoxalyl chloride are used. The procedures except the last three mentioned in general require protection of all hydroxyl groups in the desoxybenzoin other than the 2-hydroxyl group. More recently, the use of DMF dimethylacetal² and $DMF \cdot BF_3 \cdot MeSO_2$ ³ (Bass's method³) for isoflavone synthesis are described. Bass's method appears to be convenient and high yielding.

We now report a new and simple synthesis of isoflavones. This consists of the reaction between a O-hydroxydesoxybenzoin and N-formyl imidazole⁴ when C-formylation at the benzylic position and cyclization to the corresponding isoflavone takes place. The method appears to be general and does not necessitate the protection of hydroxyl groups. A typical procedure is as follows: Formic acid (98-100%, 5 eq) is gradually added to a solution of N,N'-carbonyl-di-imidazole (5 eq) in dry THF at 0-5°. A brisk evolution of CO_2 takes place. The resulting solution is stirred for 1h. The O-hydroxydesoxybenzoin (1 eq) is then added in one lot and stirring continued for 4 hours more. The solution is then heated on a steam bath for 15 min. and concentrated under reduced pressure. The residue is treated with ice and the solid thus obtained is readily purified by chromatography or crystallization. The following are a few isoflavones made by the new procedure: 5,7-Dihydroxy-2',5'-dimethoxyisoflavone, m.p. 202-4°, yield⁵ 76%; 5,7-Dihydroxy-2',4'-dimethoxyisoflavone⁶,

221^o, 65%; 5,7-Dihydroxyisoflavone, 200-1^o, 76% and 5,7-Dihydroxy-4'-methoxyisoflavone (biochanin A), 210-12^o, 60%. The identity of the isoflavones is confirmed by comparison with authentic samples (m.m.p., superimposable IR and NMR of acetate). In these examples we did not observe any products arising from ring formylation.

This synthesis utilizes formic acid in its activated form (N-formyl imidazole⁴), to provide one carbon unit in the isoflavone synthesis. In view of the easy availability of N,N'-carbonyl-di-imidazole, the method described now is convenient and useful for isoflavone synthesis. In this context, Bass's method has been evaluated and its usefulness confirmed.



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References and notes

1. H. Wagner and L. Farkas, in *The Flavonoids* (J.B. Harborne, T.J. Mabry and H. Mabry, eds.), Chapman and Hall, London, 184 (1974).
2. A. Pelter and S. Foot, *Synthesis*, **5**, 326 (1976).
3. R.J. Bass, *J. Chem. Soc. Chem. Comm.*, **2**, 78 (1976).
4. N-Acyl imidazoles (imidazolides) show enhanced carbonyl activity and function as efficient acyl transferring agents. H.A. Staab, *Angew. Chem., Int. Ed. Eng.* **1**, 351 (1962).
5. Percentage yield of the pure product based on the desoxybenzoin.
6. This isoflavone is reported to occur in *Virola caducifolia*. R. Brazfo, G. Pedreira, O.R. Gottlieb and J.G.S. Maia, *Phytochemistry*, **15**, 1029 (1976).