A New Method for the Synthesis of Isoflavones

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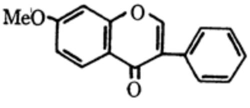
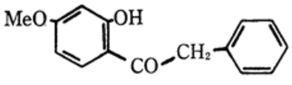
Of the several known methods[1] for synthesizing isoflavones, the formylation reaction, consisting of the condensation of benzyl 2-hydroxyphenyl ketones (*o*-hydroxydeoxybenzoins), is considered to be the most convenient. The Duff reaction,[2] in which formylation is effected by hexamine, has been used for the preparation of *o*-hydroxyaromatic aldehydes from phenols. The action of hexamine on the ketones has now been studied, since formylation at the reactive methylene group should lead to an isoflavone directly. Under the conditions used for the formylation of phenols, an isoflavone could be isolated in a highly pure state. This new method may be illustrated by the preparation of 7-methoxyisoflavone (I).[3] Benzyl 2-hydroxy-4-methoxyphenyl ketone (II)[4] was refluxed for several hours with an excess of hexamine in acetic acid. The resulting solution, when treated with hydrochloric acid and then poured into water, gave the isoflavone (I).



I



II

The general applicability of the method has been studied by the preparation of a number of other isoflavones, including dehydro-*O*-dimethylsophorol.[5] The results are summarized in Table I. This simple method proceeds satisfactorily when all the hydroxyl groups in the

TABLE I

	Isoflavone	Ketone from which prepared	Yield %	Form (solvent)	M. p. and mixed m. p., °C
1	7-Methoxy (I)	Benzyl 2-hydroxy-4-[4] methoxyphenyl (II)	10	Plates (EtOH)	155—156 [3,4]
2	7-Benzyloxy	Benzyl 4-benzyloxy-2-[a] hydroxyphenyl (II)	15	Plates (EtOH)	170—171 [a]
3	7-Methoxy-3′, 4′-methylenedioxy	2-Hydroxy-4-methoxyphenyl[b] 3, 4-methylenedioxybenzyl	10	Needles (EtOH)	179—180 [c]
4	7-Benzyloxy-3′, 4′-methylenedioxy	4-Benzyloxy-2-hydroxyphenyl[d] 3, 4-methylenedioxybenzyl	20	Needles (EtOH)	167—168 [c]
5	7, 2′, 4′, 5′-Tetramethoxy	2-Hydroxy-4-methoxyphenyl[e] 2, 4, 5-trimethoxybenzyl	5	Plates (EtOH)	190—191 [e]
6	7-Benzyloxy-2′, 4′, 5′-trimethoxy	4-Benzyloxy-2-hydroxyphenyl[e] 2,4,5-trimethoxybenzyl	15	Plates (EtOH)	143—144 [f]
7	7, 2′-Dimethoxy-4′, 5′-methylenedioxy (Dehydro-*O*-dimethyl[5]-sophorol)	2-Hydroxy-4-methoxyphenyl[g] 2-methoxy-4, 5-methylenedioxy-benzyl	20	Needles (MeOH)	209—210 [h]

a) H. S. Mahal, H. S. Rai and K. Venkataraman, *J. Chem. Soc.*, **1934**, 1120.
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c) K. Fukui, M. Nakayama and M. Hatanaka, *J. Chem. Soc. Japan, Pure Chem. Sec. (Nippon Kagaku Zasshi)*, **84**, 189 (1963).
d) H. S. Mahal, H. S. Rai and K. Venkataraman, *J. Chem. Soc.*, **1934**, 1769.
e) K. Fukui, M. Nakayama, M. Hatanaka, T. Okamoto and Y. Kawase, This Bulletin, **36**, 397 (1963).
f) New compound (Found: C, 71.99; H, 5.27. Calcd. for $C_{25}H_{22}O_6$: C, 71.76; H, 5.30%).
g) H. Suginome, *Tetrahedron Letters*, No. **19**, 16 (1960).
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[4] W. Baker, J. Chadderton, J. B. Harbone and W. D. Ollis, *J. Chem. Soc.*, **1934**, 1120.

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ketone except the one involved in cyclization are protected, but it fails with polyhydroxyketones.

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