5. Anderson, J. A., *Math. Bio. Sci.*, 1970, **8**, 137.
6. Grossmen, A., *Text Book of Physiological Psychology*, John Wiley and Sons, Inc., New York, 1967.
7. Wichelgren, W. A., In D. Deutsch and J. A. Deutsch, (Eds.), *Short Term Memory*, Academic Press, New York, 1975, pp. 65–72.
8. Bajaj, M. M. and Khandelwal, O. P., *Bull. Am. Phys. Soc.*, 1979, **24**.
9. Desiraju, T., "Recent insights into understanding the problem of pattern generation and pattern recognition in the communication of coded information across nerve cells of brain" in Recent Developments in Pattern Recognition and Digital Techniques, Ed. D. Dutta Majumdar, I.S.I., Calcutta, 1977.
10. Bannister, R., *Brain's Clinical Neurology*, Oxford Univ. Press, V Ed., 1978, p. 481.

A CONVENIENT SYNTHESIS OF 6-METHOXY-7-HYDROXY-3',4'-METHYLENEDIOXYISOFLAVONE

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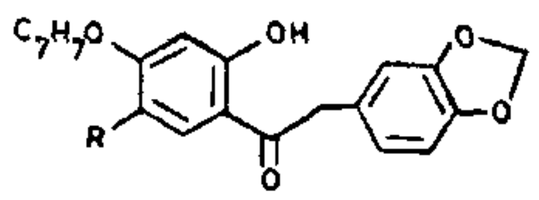
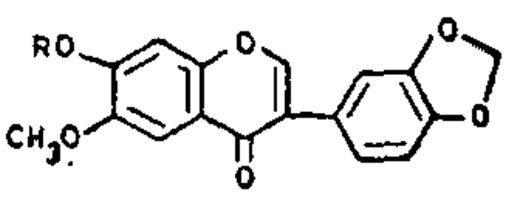
ABSTRACT

Nuclear hydroxylation of 2-hydroxy-4-benzyloxy-3', 4'-methylenedioxydesoxybenzoin(I) with alkaline potassium persulphate gave 2, 5-dihydroxy-4-benzyloxy-3', 4'-methylenedioxydesoxybenzoin (II) which was used to obtain 6-methoxy-7-hydroxy-3', 4'-methylenedioxyisoflavone(V).

NUCLEAR hydroxylation of 2-hydroxyacetophenones using alkaline potassium persulphate are commonly employed to prepare 2, 5-dihydroxyacetophenones needed to obtain 6-hydroxy (alkoxy) flavones. Similar synthesis of 6-hydroxy (alkoxy) isoflavones could not be effected as the nuclear hydroxylations of 2-hydroxydesoxybenzoins to obtain the corresponding 2, 5-dihydroxydesoxybenzoins did not give satisfactory results. The 6-oxygenated isoflavones were thus obtained by using either chalkones[1,2] or 2, 5-dihydroxydesoxybenzoins obtained directly from 1, 3, 4-trioxygenated phenols which are usually difficult to prepare[3,4]. This paper now reports the results of the nuclear hydroxylation of 2-hydroxydesoxybenzoins to obtain 2, 5-dihydroxydesoxybenzoins as well as provide a convenient synthesis of naturally occurring[5–8] 6-methoxy-7-hydroxy-3', 4'-methylenedioxyisoflavone (V). In this connection 2-hydroxy-4-benzyloxy-3', 4'-methylenedioxydesoxybenzoin[9] (I) when subjected to nuclear oxidation using alkaline potassium persulphate, gave 2, 5-dihydroxy-4-benzyloxy-3' 4'-methylenedioxydesoxybenzoin (II) obtained earlier by a cumbersome procedure[4]. Selective methylation of the desoxybenzoin(II) followed by cyclisation of the resulting methyl ether(III) using ethyl formate[10] and sodium instead of ethyl orthoformate[11] and pyridine-piperidine gave 6-methoxy-7-benzyloxy-3', 4'-methylenedioxyisoflavone(IV) in good yields. Debenzylation of IV using aluminium chloride in acetonitrile yielded 6-methoxy-7-hydroxy-3', 4'-methylenedioxyisoflavone(V) identical with the authentic sample. Aluminium chloride in acetonitrile is known to bring about debenzylation as well as demethylations of chelated C_5-methoxyls[12, 13]. In the present case, IV underwent debenzylation with this reagent giving better results, as debenzylation using catalytic hydrogenolysis, sometimes gave isoflavononones[14] instead of isoflavones whereas debenzylations using hydrochloric acid–acetic acid yielded resinous compounds also.



I, R = H
II, R = OH
III, R = OCH_3



IV, R = C_7H_7
V, R = H

EXPERIMENTAL

2, 5-Dihydroxy-4-benzyloxy-3', 4'-methylenedioxydesoxybenzoin(II)

To a solution of 2-hydroxy-4-benzyloxy-3', 4'-methylenedioxydesoxybenzoin(I) (12 g) in aqueous sodium hydroxide (10 g in 100 ml) cooled to 5°, was added in aqueous solution of potassium persulphate (15 g in 200 ml) dropwise with stirring during the course of 4 hr. The reaction mixture was allowed to stand for 24 hr at room temperature. The

solution was cooled in an ice-bath and acdified with hydrochloric acid to congo-red. It was extracted thrice with ether to remove the unchanged compound (I). To the remaining aqueous solution, concentrated hydrochloric acid (70 ml) and sodium sulphite (30 g) were added and the mixture was heated on a water-bath at 80° for 30 mts. The solution was cooled and 2, 5-dihydroxy-4-benzyloxy-3′, 4′-methylenedioxydesoxybenzoin(II) that separated, was filtered, washed and dried. It crystallised from benzene-acetone as colourless needles (3·2 g), m.p. 142°. It gave brownish-red colouration with alcoholic ferric chloride and also gave gossypetone test[15] characteristic for para-dihydroxy system. II (2·0 g) on methylation using dimethyl sulphate (0·62 ml) and potassium carbonate (8 g) in acetone (60 ml) gave 2-hydroxy-4-benzyloxy-5-methoxy-3′, 4′-methylenedioxydesoxybenzoin(III) which crystallised from benzene-petroleum ether as colourless silky needles (1·5 g), m.p. 156–57°, identical with the authentic sample[4].

6-Methoxy-7-benzyloxy-3′, 4′-methylenedioxyisoflavone (IV)

A solution of the above desoxybenzoin(III) (1·4 g) in ethyl formate (25 ml) was added in small portions to finely pulverized sodium (1·2 g) at 0° with stirring. It was stirred for 6 hr and then kept at 0° for 24 hr.. To the reaction product, water and hydrochloric acid were added and excess of ethyl formate was removed under reduced pressure. The product was dried, taken up in glacial acetic acid, refluxed for 20 mts., and then diluted wtth water. On crystallisation from benzene petroleum ether, the reaction product gave 6-methoxy-7-benzyloxy-3′,4′-methylenedioxyisolflavone (IV) as colourless needles (0·75 g), m.p. 167°. The present method was found to be more convenient and yield was also good.

6-Methoxy-7-hydroxy-3′, 4′-methylenedioxyisoflavone(V)

A mixture of the above isoflavone (IV) (0·6 g.) acetonitrile (25 ml) and anhydrous aluminium chloride (0·6 g) was refluxed on a water-bath for 3–4 hr. The solvent was removed under reduced pressure and the residue thus obtained, was treated with hydrochloric acid and then heated on a boiling water-bath for half an hour. It was cooled and the reaction product thus obtained was filtered, washed and dried. 6-Methoxy-7-hydroxy-3′, 4′-methylenedioxyisoflavone (V) crystallised from chloroform-methanol as colourless needles (0·4 g), m.p. 260–61° identical with the authentic sample[4].

1. Ollis, W. D., Ormand, K. L., Redman, B. T., Roberts, R. J. and Sutherland, I. O., *J. Chem. Soc. (C)*, 1970, p. 125.
2. Bhardwaj, D. K., Jain, R. K., Bisht, M. S. and Mehta, C. K., *Indian J. Chem.*, 1980, **19B**, 82.
3. Krishnamurti, M. and Seshagiri, S. N., *Ibid.*, 1976, **14B**, 951.
4. Bhardwaj, D. K., Jain, S. C. and Sharma, G. C., *Ibid.*, 1977, **15B**, 859.
5. Imamura, H., Hibino, Y. and Ohashi, H., *Mokuzai Gakkaishi*, 1972, **18**, 6; *Chem. Abst.*, 1972, **77**, 85677.
6. Brazfilho, R., Leite De Almeida, M. E. and Gottlieb, O. R., *Phytochemistry*, 1973, **12**, 1187.
7. Galina, E. and Gottlieb, O. R., *Ibid.*, 1974, **13**, 2593.
8. Parthasarthy, M. R., Seshadri, T. R. and Verma, R. S., *Ibid.*, 1976, **15**, 226.
9. Mahal, H. S., Rai, H. S. and Venkataraman, K., *J. Chem. Soc.*, 1934, p. 1769.
10. Joshi, P. C. and Venkataraman, K., *Ibid.*, 1934, p. 513.
11. Sathe, V. R. and Venkataraman, K., *Curr. Sci.*, 1949, **18**, 373.
12. Krishnamurti, M., Sharma, N. D. and Seshadri, T. R., *Indian J. Chem.*, 1973, **11**, 201.
13. Jain, R. K., *Ph.D. Thesis*, Delhi University, Delhi, 1978.
14. Kalra, V. K., Kukla, A. S. and Seshadri, T. R., *Tetrahedron*, 1967, **23**, 3221.
15. Perkin, A. G., *J. Chem. Soc.*, 1913, p. 650.