

Biogenetic type Synthesis of Isoflavones

By

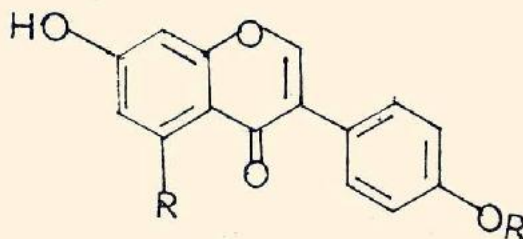
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ABSTRACT

The reaction of thallium nitrate with 2'-hydroxychalcone, 2'-hydroxy-4-methoxychalcone, 2'-hydroxy-3,4-dimethoxychalcone gave isoflavone, 4'-methoxyisoflavone, 3',4',-dimethoxyisoflavone respectively.

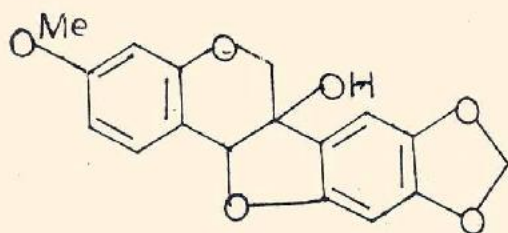
INTRODUCTION

Isoflavones are plant products with weak oestrogenic activity. Formononetin (1), biochanin A (11), genistein (111), equol, coumestrol and coumestans have been found to possess this activity³.

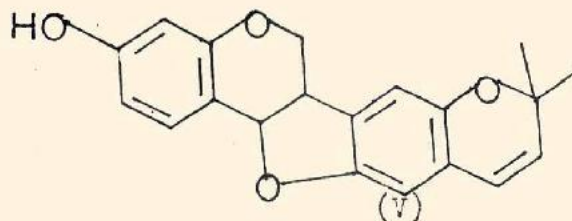


- (1) $R = Me, R_1 = H$
 (11) $R = Me, R_1 = OH$
 (111) $R = H, R_1 = OH$

Rotenoids have been found to be insecticidal⁴ whereas pterocapanoids e.g. pisatin (IV) and phaseollin (V) are antifungal⁵.

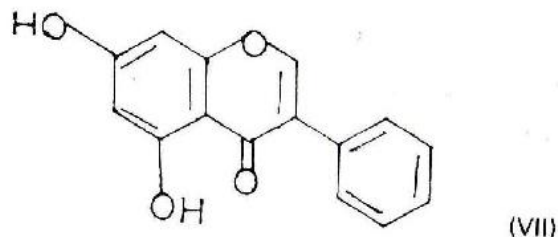
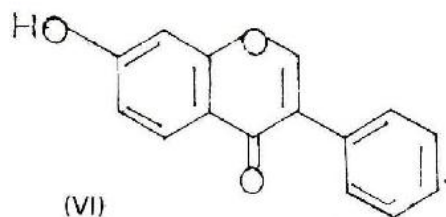


(IV)



(V)

Biogenetically, isoflavonoids are derived from both the shikimic and malonic acid pathways⁶. Chalcones have been implicated as key intermediates in this process involving aryl migration coupled with the cyclization of the chalcones⁷. In Nature two prototypes⁸ of the A ring in the isoflavones are known; the resorcinol derived type (VI) and the phloroglucinol derived type (VII).



Several methods⁹ have been used to synthesize isoflavones but none is universally applicable to both prototypes. The most recent method using thallium nitrate¹⁰ on chalcones seemed to alleviate this problem and also introduces the phenol prototype of ring A into isoflavone chemistry.

EXPERIMENTAL

Melting points (m.p) were determined using Electro-thermal melting point apparatus and are uncorrected, ultraviolet (u.v) spectra were run in ethanol using Pye Unicam Sp 8-100, the infrared (I.R) spectra were for nujol mull and run on Pye Unicam Sp 1100. The nuclear magnetic resonance (N.M.R.) spectra were for DMSO-d₆ and run on Perkin Elmer 60 MHz Spectrometer, b = broad s = singlet, d = doublet and m = multiplet.

Synthesis of Chalcones

2'-Hydroxychalcone, 2'-hydroxy-4-methoxychalcone and 2'-hydroxy-3, 4-dimethoxychalcone were prepared as described by Asahina,¹¹ Russell¹² and Manti¹³ respectively.

Synthesis of Isoflavones

GENERAL PROCEDURE¹⁰

To chalcone (0.01m) in methanol (100ml) was added thallium nitrate (0.011m) with stirring at 70° for 3 hrs. The methanol was removed in vacuo and the residue was dissolved in chloroform (150ml) followed by extraction with sodium hydroxide (10%, 50 × 5ml). The chloroform layer was washed with water, dried over sodium sulphate and the solvent distilled off. The residue was dissolved in methanol (100ml) and hydrolysed with hydrochloric acid (10%, 5ml) by boiling for 4 hrs. on cooling crystalline products were collected.

Hence, (a) 2'-hydroxychalcone (6.72g) gave isoflavone (5.55g) as light yellow needles, m.p. 143-145°

max: 270, 380m
max: 1650 (C=O), 1610, 760, 720 (C=C) cm⁻¹
: 8.8 (s, 1H); 8.3-8.45 (m, 1H); 7.6-7.95 (m, 4H); 7.25-7.3 (m, 4H).

(b) 2'-Hydroxy-4-methoxychalcone (5.08g) gave 4'-methoxyisoflavone (3.23g) as colourless needles m.p. 125-127°

max: 271, 306 nm
max: 1645 (C=O); 1615, 765, 720 (C=C) cm⁻¹
: 8.65 (s, 1H); 8.5 (s, 1H); 7.6-8.24 (m, 5H); 7.1 (s, 1H); 6.95 (s, 1H); 3.9 (s, 3H).

(c) 2'-Hydroxy-3, 4-dimethoxychalcone (7.52g) gave 3', 4'-dimethoxy isoflavone (6.37g) as colourless plates m.p. 141-143°

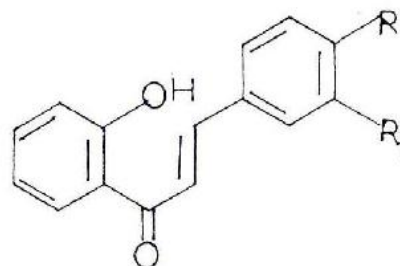
max: 271, 307 nm

max: 1640 (C=O); 1610, 760 (C=C) cm⁻¹

: 8.55 (s, H); 8.19-8.3 (d, 1H); 7.5-7.9 (m, 3H); 7.15-7.35 (m, 3H); 3.93 (s, 6H).

DISCUSSION

The chalcones, 2'-hydroxychalcone (VIII), 2'-hydroxy-4-methoxy-chalcone (IX) and 2'-hydroxy-3, 4-dimethoxy-chalcone (X) were synthesized by the cold condensation method¹⁴.



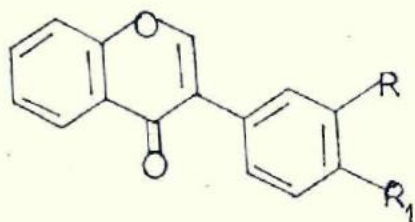
(VIII) $R=R_1=H$

(IX) $R=H, R_1=OMe$

(X) $R=R_1=OMe$

The u.v. spectra of these chalcones showed the characteristic absorption bands of chalcones—Band I between 316-375 nm which is intense¹⁵ and a minor Band II between 265-280 nm. The presence of hydrogenbonded hydroxyl group was shown in the i.r. spectra at 3780-3200cm⁻¹ and the α, β -unsaturated carbonyl function at about 1640 cm⁻¹. The absorption band at 990 cm⁻¹ is typical of *trans* double bonds.

The reaction of thallium nitrate with these chalcones gave isoflavone (XI), 4'-methoxyisoflavone (XII) and 3', 4'-methoxyisoflavone (XIII)



- (XI) $R=R_1=H$
 (XII) $R=H, R_1=OMe$
 (XIII) $R=R_1=OMe$

The u.v. spectra of these isoflavones showed the characteristic intense¹⁵ major Band II at 270nm and a minor Band I at 310nm.

The nmr spectra showed the typical H-2 proton¹⁵ as a singlet at about 8.5 in DMSO- d_6 . Isoflavone integrated for ten protons in the aromatic region, 4'-methoxyisoflavone, nine protons in the aromatic area and three protons in the methoxy area. 3'-4'-Dimethoxyisoflavone integrated for eight protons in the aromatic area and six protons in the methoxy area. The classical methods for the preparation of isoflavones by the formylation of deoxybenzoins⁹ with ethylformate in presence of sodium metal is not only explosive and tedious but also gave low yield (30–40%). It is not applicable to polyhydroxylated deoxybenzoins⁹. The reaction of thallium nitrate on easily prepared chalcones to give isoflavones is carried out under mild conditions and the yield is generally high (65–80%).

REFERENCES

1. T. A. Geismann, "The chemistry of flavonoid compounds", Pergamon Press, London and New York, 1962.
2. R. S. Badbury and D. E. White, *J. Chem. Soc.*, 3447, 1951.
3. E. M. Bickoff, R. R. Spencer *et al*, Tech. Bull. No. 1408, U.S.D.A; 1969
4. H. Fukami and M. Nakajima, "Naturally Occuring Insecticides", pp 71–97, 1971, Marcel Dekker Inc, New York.
5. D. R. Perrin and I. A. M. Cruickshank, *Phytochemistry*, 8, 971, 1969
6. J. B. Harbone, "Comparative Biochemistry of Flavonoids", 1967, Academic Press, London.
7. H. Grisebach and N. Doerr, *Ztsch. Naturf.*, 15, 284, 1960.
8. J. B. Harbone, "The Flavonoids" pp 743, 1975, Chapman and Hall, London.
Ref. 8 pp. 184.
9. L. Farkas, A. Gottsegen *et al*, *J. Chem. Soc. Perkin I*, 305, 1974
10. Tei-ichi Asahina, *Bull. Chem. Soc. Japan*, 9, 131, 1934
11. A. Russell and J. Todd, *J. Chem. Soc.*, 423, 1937.
12. Lydia Manti, *Chemical Abstracts*, 24, 4011, 1930
13. J. Wheeler, *J. Chem. Soc.*; 1320, 1938.
14. T. J. Mabry, *et al*, "The Systematic Identification of Flavonoids", pp 165, 227, 253 and 267, 1970, Springer-Verlag, Berlin and New York.

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