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Organic Chemistry

SYNTHESES OF NEW *Myroxilon peruiferum* ISOFLAVONOIDS

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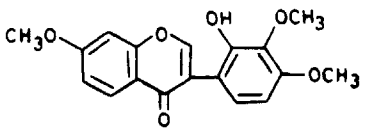
Two new isoflavonoids isolated from *Myroxylon peruiferum* were considered as 2′-hydroxy-7,3′,4′-trimethoxyisoflavone (I) and its corresponding isoflavanone (II). I and II have been now synthesised by the selective demethylation of 7,2′,3′,4′-tetramethoxyisoflavone (VII) obtained from 2′-hydroxy-2,3,4,4′-tetramethoxychalkone (III) by epoxide method. Catalytic hydrogenation of I yielded II.

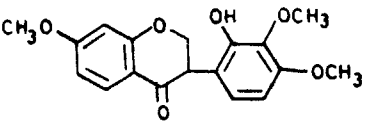
Keywords: *Myroxylon peruiferum*; **Isoflavonoids; Catalytic Hydrogenation**

INTRODUCTION

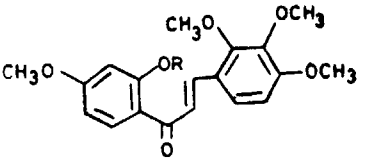
AMONG the compounds isolated from *Myroxylon peruiferum* (Maranduba *et al.*, 1979), two new compounds were considered as 2′-hydroxy-7,3′,4′-trimethoxyisoflavone (I) and 2′-hydroxy-7,3′,4′-trimethoxyisoflavanone (II) on the basis of their spectral data and colour reactions. The present paper reports the syntheses of I and II by a procedure based on biogenetic considerations (Grisebach & Patscheke, 1960; Grisebach, 1961; Pelter *et al.*, 1971; and Hahlbrock & Grisebach, 1975) which suggest chalkones as the precursor for the flavonoids. 2′-Hydroxy-2,3,4,4′-tetramethoxychalkone (III) used as the essential intermediate on benzylation yielded 2′-benzyloxy-2,3,4,4′-tetramethoxychalkone (IV). Treatment of IV with alkaline hydrogen peroxide yielded the corresponding 2′-benzyloxy-2,3,4,4′-tetramethoxychal-koneepoxide (V) which was converted into the corresponding α-formyldesoxybenzoin (VI) by treatment with boron trifluoride-etherate (Grover *et al.*, 1963; Bharara *et al.*, 1964, 1965; Jain *et al.*, 1965; and House, 1956). α-Formyl-2-benzyloxy-4,2′,3′,4′-tetramethoxydesoxybenzoin (VI) when treated with hydrochloric acid in acetic acid, underwent debenzylation as well as dehydro-cyclisation (Bhardwaj *et al.*, 1978*a*,*b*) to yield 7,2′,3′,4′-tetramethoxyisoflavone (VII). Selective demethylation of VII (Kalra *et al.*, 1966, 1967*a*, *b*, *c*; and Aghoramurthy *et al.*, 1961) using aluminium chloride in acetonitrile gave the required 2′-hydroxy-7,3′,4′-trimethoxyisoflavone (I). Further, catalytic hydrogenation of I (Gilbert *et al.*, 1957; King & Neill, 1952; Ramanujam & Seshadri, 1958; Balakrishna *et al.*, 1962; Campbell *et al.*, 1969; and Farkas *et al.*, 1969) using palladium-charcoal yielded its dihydro compound, 2′-hydroxy-7,3′,4′-trimethoxyisoflavanone (II). However, the direct comparison of the synthetic compounds (I & II) with the corresponding natural samples were not done as these could not be obtained.



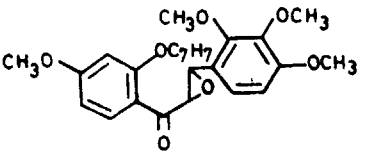
I



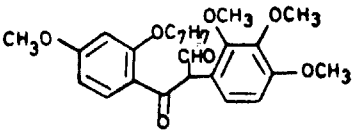
II



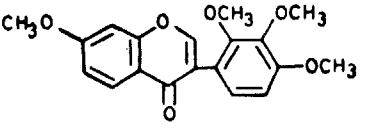
III, R = H
IV, R = C_7H_7



V



VI



VII

Experimental Procedure

Melting points are uncorrected. PMR spectra were recorded in $CDCl_3$ on a Perkin-Elmer R-32 spectrometer (90 MHz) using TMS as internal standard; chemical shifts are in δ-scale.

2,3,4-Trimethoxybenzaldehyde

To a well-cooled mixture of pyrogallol trimethyl ether (7.5 g) and N:N-dimethyl-formamide (5 ml), phosphorus oxychloride (10 ml) was added in lots. The reaction mixture was heated at 100 °C for 5hrs, treated with aq. sodium acetate (15 g) and refluxed for 30 min. 2,3,4-Trimethoxybenzaldehyde thus obtained was extracted with ether and the ether layer was washed with cold water and then dried over anhydrous sodium sulphate. Removal of the ether gave a residue which was crystallised from petroleum ether as colourless needles (7.0 g) m.p. 37 °C.

2′-Hydroxy-2,3,4,4′-tetramethoxychalkone (III)

A solution of 2-hydroxy-4-methoxyacetophenone (Adams, 1919) (3 g) and 2,3,4-trimethoxybenzal-dehyde (4 g) in alcohol (150ml) was treated with aq. potassium hydroxide (3.5 g in 5ml) and left at room temperature for 48hrs. The reaction mixture was diluted with water and extracted with ether to remove the unreacted aldehyde and then acidified with hydrochloric acid to yield 2′-hydroxy-2,3,4,4′-tetramethoxychalkone

(III) which crystallised from benzene-petroleum ether as yellow needles (2.5 g), m.p. 146–47 °C (*Found*: C, 66.3; H, 6.2. $C_{19}H_{20}O_6$ requires C, 66.27; H, 5.85 per cent). It gave brown ferric reaction.

PMR: 3.81 (3H, s,—OCH_3), 3.87 (6H, s, 2X—OCH_3), 3.92 (3H, s, —OCH_3), 6.4 (2H, m, $C_{3'}$—H & $C_{5'}$—H), 6.65 (1H, d, J = 9 Hz, C_5—H), 7.3 (1H, d, J = 9 Hz, C_6—H), 7.53 (1H, d, J = 16 Hz, C_α—H), 7.75 (1H, d, J = 9 Hz, $C_{6'}$—H), 7.98 (1H, d, J = 16 Hz, C_β—H), 13.7 (1H, s, $C_{2'}$—OH).

2'-Benzyloxy-2,3,4,4'-tetramethoxychalkone (IV)

III (2g) in dry acetone (100 ml) was refluxed with benzyl chloride (2.8ml), potassium iodide (0.2g) and ignited potassium carbonate (7 g) for 35hrs. The reaction product was worked up as usual. 2'-Benzyloxy-2,3,4,4'-tetramethoxychalkone (IV) thus obtained, crystallised from ethyl acetate-petroleum ether as light yellow needles (2.1g), m.p. 134–35 °C (*Found*: C, 71.8; H, 6.4. $C_{26}H_{26}O_6$ requires C, 71.87; H, 6.03 per cent). It did not give any colouration with ethanolic ferric chloride.

PMR: 3.82 (12H, 4X—OCH_3), 5.08 (2H, s, —$OCH_2C_6H_5$) 6.52 (3H, m, $C_{3'}$—H, $C_{5'}$—H, & C_5—H), 6.94 1H, d, J = 9 Hz, $C_{6'}$—H), 7.21—7.53 (6H, m, —$OCH_2C_6H_5$ & C_α—H), 7.75 (1H, d, J = 9 Hz, C_6 —H), 7.82 (1H, d, J = 16 Hz, C_β—H).

2'-Benzyloxy-2,3,4,4'-tetramethoxychalkoneepoxide (V)

To a solution of IV (2 g) in alcohol-acetone mixture (4 : 1, 80 ml), hydrogen peroxide (2.2 ml, 30 per cent) and aq. sodium hydroxide (4.5 ml, 5 per cent) were added dropwise with stirring over a period of 20 min. at a 25–30 °C. The reaction mixture was left for another half-an-hour and then diluted with cold water. The epoxide (V) thus obtained was filtered, washed with water, dried and crystallised from ethanol as colourless needles (1.7 g), m.p 93–94 °C (*Found*: C, 69.5; H, 6.1. $C_{26}H_{26}O_7$ requires C, 69.32; H, 5.82 per cent).

PMR: 3.78–3.82 (12H, 4X—OCH_3), 4.21 (1H, d, J = 2.5 Hz, C_α—H), 4.42 (1H, d, J = 2.5 Hz, C_β—H), 4.98 (2H, s, —$OCH_2C_6H_5$), 6.45–6.55 (3H, m, $C_{3'}$,—H, $C_{5'}$, —H & C_5 —H), 6.7 (1H, d, J = 8 Hz, C_6—H), 7.15 (5H, s, —$OCH_2C_6H_5$), 7.85 (1H, d, J = 8 Hz, $C_{6'}$, —H).

7,2',3',4'-Tetramethoxyisoflavone (VII)

A solution of V (1.5 g) in dry benzene (65 ml) was treated with BF_3-etherate (2 ml) and stirred for an hour. The reaction mixture was extracted with ether. Removal of solvent yielded the α-formyl-2-benzyloxy-4,2',3',4'-tetramethoxydesoxybenzoin (VI) which was directly treated with hydrochloric acid (6.5 ml) and acetic acid (20 ml) and then heated on a water-bath for 2hrs. Reaction mixture was cooled, diluted with water and then extracted with ether and then ethyl acetate. Removal of the solvent from ether and ethyl acetate extracts yielded VII which crystallised from ethyl acetate-petroleum ether as colourless needles (250 mg), m.p. 163–64° (*Found*: C, 66.8; H, 5.1. $C_{19}H_{18}O_6$ requires C, 66.66; H, 5.30 per cent). It did not give ferric reaction.

PMR : 3.8–3.95 (12H, 4X—OCH_3), 6.75 (1H, d, J = 9 Hz, $C_{5'}$—H), 6.9–6.95 (2H, m, C_6—H & C_8—H), 7.1 (1H, d, J = 9 Hz, $C_{6'}$—H), 7.95 (1H, s, C_2—H), 8.25 (1H, d, J = 9 Hz, $C_{5'}$—H).

2'-Hydroxy-7,3',4'-trimethoxyisoflavone (*I*)

VII (100 mg) in acetonitrile (10 ml) containing anhydrous aluminium chloride (100 mg) was refluxed for 3hrs. The solvent was removed and the product was treated with dil. hydrochloric acid and then heated on a boiling water-bath for half-an-hour. I thus obtained, crystallised from chloroform-pet. Ether as colourless needles (50 mg), m.p. 211–12 °C (*Found* : C, 65.5; H, 4.9. $C_{18}H_{16}O_6$ requires C, 65.85; H, 4.91 per cent). It gave brownish-green ferric reaction. UV (λ_{max}, nm) MeOH : 250, 270, 295 (sh), 308; + NaOAc; 250, 270, 295 (sh), 307; + $AlCl_3$: 252, 273, 310; + NaOH : 242, 270, 295.

PMR : 3.9 (9H, s, 3X—OCH_3), 6.53 (1H, d, J = 9 Hz, $C_{5'}$—H, 6.9–7.22 (3H, m, C_6—H, C_8—H & $C_{6'}$—H), 8.05 (1H, s, C_2—H), 8.23 (1H, d, J = 9 Hz, C_5—H).

2'-Hydroxy-7,3',4'-trimethoxyisoflavanone (*II*)

I (25mg) in acetic acid (20ml) and palladium-charcoal (20mg, 10 per cent) was stirred in an atmosphere of hydrogen till the absorption of hydrogen was completed. The catalyst was filtered off and washed with ethyl acetate. Removal of the solvent from the combined filtrate gave 2'-hydroxy-7,3',4'-trimethoxyisoflavanone (II) which crystallised from chloroform-petroleum ether as colourless needles, m.p. 157° (*Found*: C, 65.3; H, 5.3. $C_{18}H_{18}O_6$ requires C, 65.44; H, 5.49 per cent). UV (λ_{max}nm,) MeOH: 238, 310, 375; + NaOAc: 233, 309, 375; + $AlCl_3$: 240, 311, 376; + NaOH : 233, 304, 368.

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