Proc. Indian natn. Sci. Acad., **46**, A, No. 6, 1980, pp. 576–578.

II. CHEMISTRY

Organic Chemistry

SYNTHESIS OF 3,6,7,3′,4′-PENTAHYDROXY-5-METHOXYFLAVONE

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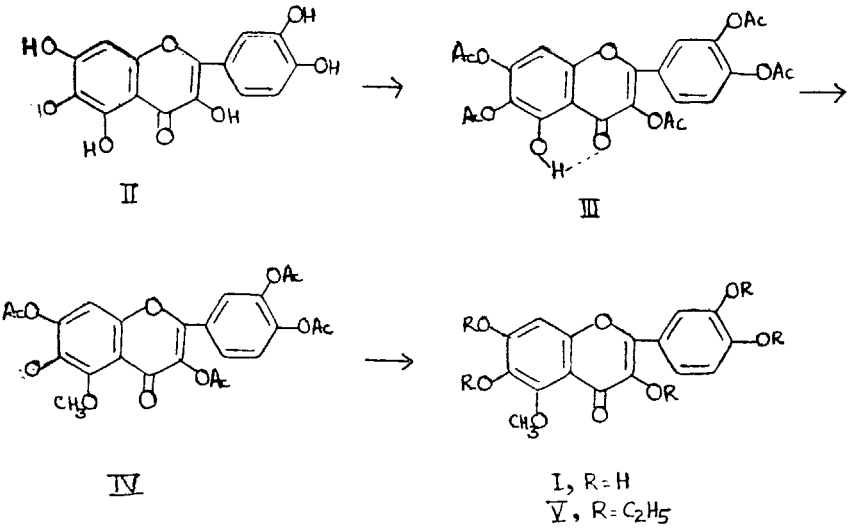
(*Received 6 May 1980*)

Constitution assigned to the flavonol isolated from *Tagetes patula* as 3,6,7, 3′4′-pentahydroxy-5-methoxyflavone (I) has now been confirmed by its synthesis. Methylation of 3,6,7,3′,4′-pentaacetoxy-5-hydroxyflavone (III) followed by the deacetylation of the resulting 5-methyl ether (IV) gave I which was ethylated to obtain its pentaethyl ether (V). I, IV and V were identical with the samples of natural allo-patuletin, its pentaacetate and pentaethyl ether respectively.

Keywords: Synthesis; 3,6,7,3′,4′-Pentahydroxy-5-Methoxyflavone; Allo-Patuletin; *Tagetes Patula.*

INTRODUCTION

ALLO-PATULETIN, a quercetagetin monomethyl ether isolated from the air-dried petals of *Tagetes patula* flowers had been considered (Bhardwaj *et al.*, 1980) to be 3,6,7, 3′,4′-pentahydroxy-5-methoxyflavone (I) which has now been confirmed by its synthesis using quercetagetin (II). The synthesis involved the selective methylation of C_5 hydroxyl of II which being chelated with the neighbouring carbonyl group, is least reactive and thus needs special conditions. This has been accomplished by a three step process that necessitated an initial protection of the other hydroxyl functions followed by the methylation of the C_5 hydroxyl and then the removal of the protecting groups to obtain the polyhydroxy 5-methyl ether. Similar selective methylation of the chelated hydroxyls in polyhydroxy compounds had been earlier carried out by protecting the other hydroxyls either by benzylation (Seshadri & Varadarajan, 1949; Robertson *et al.*, 1950; Narasimhachari *et al.*, 1951; and Ahluwalia *et al.*, 1953) or by acetylation (Kubota & Perkin, 1925; Lesser & Gad, 1926; Robertson & Waters, 1929; Chattaway, 1931; King *et al.*, 1953; Mahesh *et al.*, 1956; and Bhardwaj *et al.*, 1979*a*, 1979*b*). In the present case, the non-chelated hydroxyls in II were protected by acetylation (Mahesh *et al.*, 1956) using acetic anhydride and pyridine and the resulting 3,6,7,3′,4′-pentaacetoxy-5-hydroxyflavone (III) on methylation gave its 5-methyl ether (IV). The removal of the protecting acetoxyl functions using alcoholic hydrochloric acid yielded I which was ethylated to obtain its ethyl ether. Synthetic quercetagetin 5-methyl ether (I), its corresponding pentaacetate (IV) and pentaethyl ether (V) were identical with the samples of natural allo-patuletin, its acetate and ethyl ether respectively.



II III IV

I, R=H
V, R=C_2H_5

EXPERIMENTAL

3,6,7,3′,4′-Pentaacetoxy-5-hydroxyflavone (III)

To a well stirred suspension of quercetagetin (II) (1.0 g) in acetic anhydride (8 ml) at 35°, pyridine (4 drops) was added. The reaction mixture warmed up, became clear and the partial acetate (III) separated out (5 mts) which when worked up as usual and then crystallised from ethyl acetate, gave pale yellow needles (1.0 g), m.p. 204–5° (Found : C, 56.6; H, 3.5. $C_{25}H_{20}O_{13}$ requires C, 56.82; H, 3.79 per cent). It gave an olive-green colouration with alcoholic ferric chloride. NMR (δ, $CDCl_3$, TMS as internal standard) : 2.30 (12H, *s*, 4 X-$OCOCH_3$), 2.40 (3H, *s*, 1X-$OCOCH_3$), 6.95 (1H, *s*, C_8-H), 7.47 (1H, *d*, J=8 Hz, C_5'-H), 7.70 (2H, *m*, C_2'-H & C_6'-H), 12.27 (-OH).

3,6,7,3′,4′-Pentaacetoxy-5-methoxyflavone (IV)

A mixture of III (0.8 g), dimethyl sulphate (0.06 ml), potassium carbonate (2.5 g) in acetone (100 ml) was refluxed for 30hrs and the progress of the reaction was monitored by TLC using benzene-methanol (9 : 1) as the solvent system. The methylation product (IV) thus obtained, crystallised from ethyl acetate-petroleum ether as colourless needles (0.6 g), m.p. 215–16° (Found : C, 57.9; H, 4.2. ($C_{26}H_{22}O_{13}$ requires C, 57.56; H, 4.06 per cent). NMR (δ, $CDCl_3$, TMS as internal standard) : 2.35–2.47 (15H, 5 X -$OCOCH_3$), 3.97 (3H, 1 X -OCH_3), 6.84 (1H, C_8-H), 7.40 (1H, C_5'-H), 7.72 (2H, C_2'-H & C_6'-H). It did not give any colouration with alcoholic ferric chloride. It was identical with allo-patuletin acetate.

3,6,7,3′,4′-Pentahydroxy-5-methoxyflavone (I)

A solution of IV (0.5 g) in ethanolic-hydrochloric acid (50 ml; 5 per cent) was refluxed for 2hrs and the resulting deacetylation product (I) crystallised from ethanol as yellow needles (0.12 g), m.p. 234–36° (Found : C, 57.50; H, 3.70. $C_{16}H_{12}O_8$

requires C, 57.83; H, 3.64 per cent). UV (MeOH) : 260 and 350 nm; + $AlCl_3$: 270 and 400 nm; + $AlCl_3$ + HCl : 270 and 380 nm; + NaOAc : 255 and 395 nm; + NaOAc + H_3BO_3; 270 and 390 nm. It gave a green colouration with alcoholic ferric chloride and was identical with the natural sample of allo-patuletin.

3,6,7,3',4'-Pentaethoxy-5-methoxyflavone (V)

A mixture of I (0.1 g), diethyl sulphate (0.3 ml), potassium carbonate (2 g) in acetone (100 ml) was refluxed for 10hrs and the ethylation product (V) thus obtained crystallised from methanol as colourless needles, m.p. 125–26° (Found : C, 66.2; H, 6.9. $C_{26}H_{32}O_8$ requires C, 66.08; H, 6.83 per cent). It was identical with allo-patuletin ethyl ether. NMR (δ, $CDCl_3$, TMS as internal standard) : 1.22–1.56 (15H, 5 X $-OCH_2CH_3$), 3.97 (3H, 1 X $-OCH_3$), 4.11–4.21 (10H, 5 X $-OCH_2CH_3$), 6.71 (1H, C_8–H), 6.95 (1H, C_5'–H), 7.76 (2H, C_2'–H & C_6'–H).

ACKNOWLEDGEMENTS

The authors wish to thank the Council of Scientific and Industrial Research, New Delhi and the University Grants Commission, New Delhi for the financial grants.

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