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FLAVONOIDS OF *TINOSPORA MALABARICA*

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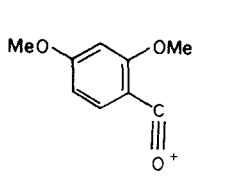
Key Word Index—*Tinospora malabarica*; Menispermaceae; 1,1-dibenzoylethane; allyloxyflavone.

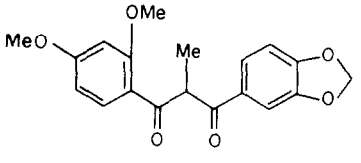
Abstract—A dibenzoylethane and an allyloxyflavone isolated from *Tinospora malabarica* have been assigned the structures 1-(2′,4′-dimethoxyphenyl)-3-(3″,4″-methylenedioxyphenyl)-2-methylpropan-1,3-dione and 5-allyloxy-6,7,4-trimethoxyflavone on the basis of chemical and spectroscopic evidence.

Tinospora cordifolia, under the name 'Giloe', is a well-known indigenous drug and *T. malabarica* is used as an antirheumatic in China [1]. Ethanol extracts from the latter, along with the bitter principle earlier isolated from *T. cordifolia* [2], gave a mixture of phenolics from which two have been characterized as tinosporinone (**1**) and 5-allyloxy-6,7,4′-trimethoxyflavone (**3**).

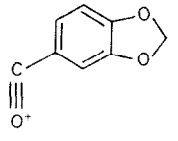
Tinosporinone (**1**) gives a positive Shinoda's test and has carbonyl bands at 1670 and 1660 cm^{-1} in its IR spectrum. The unusual dibenzoylethane structure follows from the presence of a doublet and a quartet at δ1.42 (3H) and 5.20 (1H) respectively in the ^1H NMR and ions at *m/z* 149, 163 and 311 in the mass spectrum in which the peak due to M^+ at 342 is missing. This situation favours the loss of a methoxyl, the resulting fragment **2** forming from the base peak. This behaviour is similar to that of 3, 5, 7, 2′, 4′-pentamethoxyflavone [3]. The resonances of methylenedioxy and one methoxyl group appear at expected values but that of the remaining methoxyl is shifted upfield to δ3.52, a regular feature of the



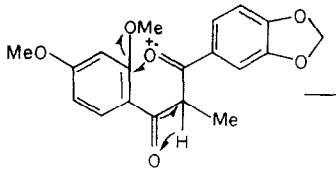
m/z 163 (86%)



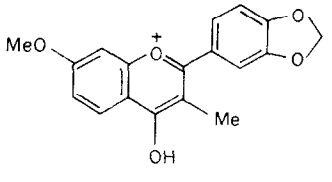
1



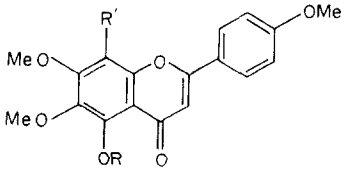
m/z 149 (40%)



$M^{+\cdot}$ *m/z* 342



2 *m/z* 311 (100%)



3 R = $-CH_2-CH=CH_2$, R′ = H

4 R = H, R′ = $-CH_2-CH=CH_2$

5 R = R′ = H

6 R = Ac, R′ = H

dibenzoylmethane NMR spectra [4]. The substitution pattern shown is in agreement with the coupling pattern of the aromatic protons.

The flavonoid nature of **3** is apparent from the singlet at δ6.55 in its NMR spectrum which, along with singlets of three methoxyls, shows protons of an *O*-allyl side-chain through a doublet at δ4.15 and multiplets at 6.20 and 5.30. The other singlet at δ6.75 can be assigned either to the hydrogen at positions 6 or 8 but the 4′-substitution in ring B is apparent from the AA′BB′ doublets of its aromatic protons.

The *O*-allyl side-chain is readily cleaved on treatment with dilute acids and the resulting compound gives a brown colour with ferric chloride. The mp of the hydrolysis product is identical with that of 5-hydroxy-6, 7, 4′-trimethoxyflavone [5], thus ruling out the possibility of its being 5-hydroxy-7, 8, 4′-trimethoxyflavone, mp 218° [6]. The NMR spectrum of **5** agrees with that reported earlier [7] but this is of little value since chemical shifts of 6 and 8 protons in such situations differ only slightly. In this context the complete absence of cyclization to a dihydrofuran during Claisen rearrangement [8], or on exposure of **4** to acids, and the magnitude of deshielding of the concerned proton in the NMR spectrum of the acetate **6**, 0.35 as against 0.27 for the proton *ortho* to the hydroxyl, is also important [9].

While 3, 3-dimethylallyl side-chains are of very frequent occurrence in nature, allyl and especially *O*-allyl side-chains are seldom encountered, other examples being lacoumarin [10] and aurien [11].

EXPERIMENTAL

Isolation of tinosporinone (**1**). The defatted powdered heart-wood (5 kg) of the plant material (herbarium specimen kept at the National Botanical Research Institute, Lucknow) was exhaustively extracted with EtOH in a Soxhlet and the solvent removed under red. pres. The dark sticky residue (500 g) was extracted with EtOAc (3 × 500 ml), the extract evaporated to dryness and chromatographed on a column of Si gel. Elution with $CHCl_3$–petrol (2:1) afforded tinosporinone (**1**), purified further by repeated CC and crystallization from C_6H_6, mp 162°; $[M-OMe]^+$ *m/z* 311, $C_{18}H_{15}O_5$; $IR\nu_{max}^{Nujol}$ cm^{-1}: 1670, 1660, 1505, 815, 800; $UV\lambda_{max}^{CHCl_3}$ nm: 250, 275; ^1H NMR (100 MHz, $CDCl_3$, δ-values): –OMe (3H each *s*, 3.52, 3.80), $-O-CH_2-O-$(2H, *s*, 6.05); ArH (1H each *d*, 7.95, 6.85, *J* = 9 Hz); (1H each *dd*, 7.55, 6.85, *J* = 9, 2 Hz); (1H each *d*, 7.45, 6.35, *J* = 2 Hz); –Me (3H, *d*, 1.42, *J* = 7 Hz); –CH–Me (1H, *q*, 5.20, *J* = 7 Hz).

5-Allyloxy-6, 7, 4′-trimethoxyflavone (**3**). It was obtained on elution with $CHCl_3$, and crystallized from MeOH as colourless needles (300 mg), mp 162°; M^+ *m/z* 368, $C_{21}H_{20}O_6$; $IR\nu_{max}^{Nujol}$ cm^{-1}: 1660, 1600, 1510; $UV\lambda_{max}^{MeOH}$ nm: 270, 320; ^1H NMR (100 MHz, $CDCl_3$): –OMe (3H each *s*, 3.85, 3.90, 3.95); $-O-CH_2-CH$ (*d*, 4.15, *J* = 6 Hz); $-CH=CH2$ (*m*, 6.20); $-CH=CH_2$ (*m*, 5.30); H-3 (*s*, 6.55); ArH (2H, each *dd*, 6.95, 7.80, *J* = 9, 2 Hz); (1H, *s*, 6.75).

Claisen rearrangement of **3**. **3** (100 mg) in DMSO (5 ml) was refluxed under N_2 for 5 hr. Work-up and crystallization from $CHCl_3$-petrol gave **4** as pale-yellow needles (50 mg), mp 115°; ^1H NMR (60 MHz, $CDCl_3$): –OMe (3H each *s*, 3.90, 4.00, 4.15); $Ar-CH_2-$ (*d*, 3.65); $-CH=CH_2$ (*t*, 5.10); $-CH_2-CH=CH_2$ (*m*, 5.60); H-3 (*s*, 6.60); ArH (2H each *dd*, 7.05, 7.90, *J* = 9, 2 Hz).

Hydrolysis of **3**. **3** (100 mg) was refluxed with MeOH–HCl (10 ml, 5%) for 1 hr. Work-up of the reaction mixture gave **5** (75 mg), mp 190° (*lit.* mp 192–194°); ^1H NMR (100 MHz, $CDCl_3$) –OMe (3H each *s*, 3.80, 3.82, 3.85); H-3 (*s*, 6.40); ArH (2H each *dd*, 6.85, 7.75, *J* = 9, 2 Hz); (1H, *s*, 6.45).

Acetylation of **5**. **5** (50 mg) was heated with Ac_2O–pyridine (1 ml each) at 100° for 7 hr. Work-up and crystallization from MeOH gave **6** (50 mg), mp 137°; ^1H NMR (100 MHz, $CDCl_3$): –OAc (3H, *s*, 2.35); –OMe (3H each *s*, 3.75, 3.80, 3.90); H-3 (*s*, 6.30); ArH (2H each *dd*, 6.85, 7.70, *J* = 9, 2 Hz); (1H, *s*, 6.73).

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