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A NEW CYCLO HEXADIONE FROM *MESUA FERREA*

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Key Word Index—*Mesua ferrea*; Guttiferae; stamens; cyclohexadione; mesuaferrol.

Abstract—Petrol extracts of the stamens of *Mesua ferrea* gave β-amyrin, β-sitosterol and a new cyclohexadione compound named mesuaferrol.

INTRODUCTION

Mesua ferrea is a well known medicinal plant, widely used in indigenous systems of medicine for the treatment of fever, dyspepsia and renal diseases. Its stamens are used for treating bleeding piles [1]. The plant elaborates biogenetically related flavonoids [2], xanthones [3–6], 4-phenyl coumarins [7–10], 4-alkyl coumarins [11] as well as a cyclohexadienone carboxylic acid, mesaunic acid [12]. The stamens have now been investigated. The isolation and the determination of the structure of β-amyrin, β-sitosterol and a new cyclohexadione derivative mesuaferrol (**1**) will be discussed in this paper. Some *Calophyllum* species, also belonging to the Guttiferae, elaborate 4-phenylcoumarins [13], 4-alkylcoumarins [11] and cyclohexadienone carboxylic acids such as calophyllic acid [14], calophynic acid [15], brasiliensic acid [16] and mesuanic acid [12]. Comparison of the spectral data of these cyclohexadienones with that of mesuaferrol was particularly helpful in the elucidation of its structure.

RESULTS AND DISCUSSION

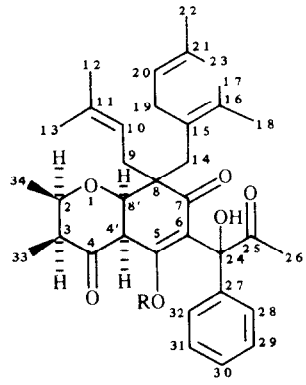
A cold petrol extract of stamens after usual work-up and chromatography on silica gel yielded β-amyrin, β-sitosterol and a light yellow glassy product. The latter on further purification gave a colourless compound designated as mesuaferrol (**1**), mp 75° $[\alpha]_D^{25}$ +27.5 (MeOH). The high resolution mass measurement ($[M]^+$ 562.3293) is in agreement with the molecular formula $C_{35}H_{46}O_6$.

Mesuaferrol gave a light reddish brown colour with alcoholic ferric chloride indicating a chelated hydroxyl. It is soluble in aqueous sodium carbonate and is regenerated but does not effervescence with aqueous sodium hydrogen carbonate. These results indicated the presence of only an acidic hydroxyl group and not carboxylic acid group. Mesuaferrol also decolourized an alkaline potassium permanganate solution indicating the presence of unsaturation in the molecule.

The IR spectrum of mesuaferrol showed the presence of a chelated hydroxyl (ν_{max} cm^{-1} 3400), three carbonyl groups (ν_{max} cm^{-1} 1748, 1720, 1680) and a monosubstituted phenyl group (ν_{max} cm^{-1} 760 and 690). However, the IR spectrum of mesuaferrol monoacetate $[M]^+$ *m/z* 604, $C_{37}H_{48}O_7$, showed the presence of hydroxy group (ν_{max} cm^{-1} 3400) indicating the presence of tertiary hydroxyl group in the compound.

The ^1H NMR spectrum of mesuaferrol showed signals for two protons in the olefinic region [δ 5.18, 1H (*m*) and 4.8, 1H (*m*)], six methylene protons [δ 2.54, 2H, (*s*) and 1.4, 4H (*m*)] and 18 methyl protons [δ 1.7, 12H, (*m*) and 1.2, 6H (*s*)] which can be assigned to C_5 and C_{10} side chains, respectively. NMR also indicated one –CO–Me group [δ 2.04, 3H, (*s*)] and five aromatic protons [δ 7.48, 2H (*m*) and δ 7.12, 3H (*m*)] belonging to another side chain. Furthermore, it indicated the presence of a *cis* 2,3-dimethyltetrahydropyrone skeleton with signals at δ 4.26 (1H, *m*, C_2–H), 3.76 (1H, *d*, $J=7$ Hz, C-8, H), 3.12 (1H, *d*, $J=7$ Hz, C-4, H), 2.80 (1H, *m*, C-3, H), 1.08 (3H, *d*, $J=7$ Hz, C-2, CH_3), 0.94 (3H, *d*, $J=7$ Hz, C-3, Me). These values are in agreement with those of the *cis* 2,3-dimethyldihydropyrone system found in apetalic acid [17, 18] [(C-2, Me) δ 1.31 (3H, *d*, $J=7$ Hz), C-3, Me δ 1.09 (3H, *d*, $J=7$ Hz)] and mesuanic acid [12] [(C-2, Me) δ 1.35 (3H, *d*, $J=7$ Hz), C-3 Me δ 1.0 (3H, *d*, $J=7$ Hz)] but differ from that of the *trans*-2,3-dimethyldihydropyrone ring system found in chapelleric acid [18]. Hence, the *cis* configuration was assigned to the 2,3-dimethyltetrahydropyrone skeletone in the molecule. In addition, the coupling constant values for the two doublets at δ 3.76 for C-8′, H and 3.12 for C-4′, H indicated a *cis*-fusion between the pyranone and cyclohexadione systems.

The ^{13}C NMR spectrum of mesuaferrol indicated three carbonyls, a monosubstituted phenyl, two carbon atoms attached to hydroxyl groups, one of which is attached to a sp^3 carbon atom, the other to a sp^2 carbon atom, and also methines, methylene and methyl carbon atoms. In the ^{13}C NMR the singlet at δ 142.33 ppm and three doublets at δ 131.60, 127.54 and 126.35 ppm indicate the presence of a mono-substituted phenyl ring system in the compound. Furthermore, the two doublets at δ 124.39 and 119.74 ppm indicated two sp^2 hybridized carbon atoms each carrying an hydrogen atom while the four singlets at δ 134.09, 133.02, 132.76 and 132.36 ppm suggested four sp^2 hybridized carbon atoms with no hydrogen on them. ^{13}C NMR data also revealed six *gem* dimethyl carbon atoms (δ 29.32, 28.12, 23.69, 23.29, 18.09 and 17.66 ppm) connected to a double bond, comparable with the values reported for camboginol from *Garcinia cambogia* [19], and two methylene carbon atoms (δ 39.66, 38.66 ppm) [19]. Thus, the ^{13}C NMR suggested the



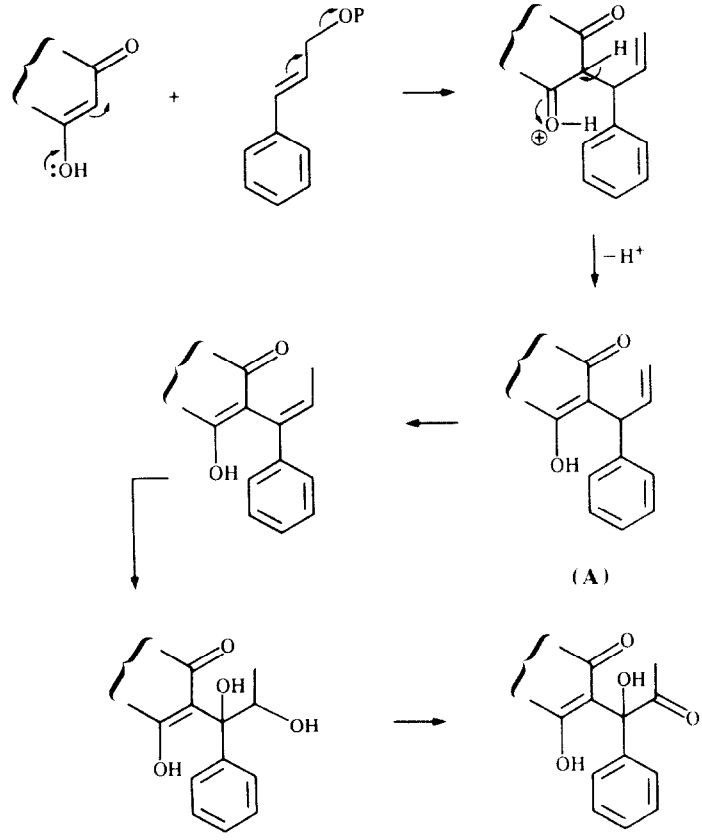
1 R = H
2 R = Ac
3 R = Me

presence of C_5 and C_{10} side chains attached to a quaternary carbon atom [19, 20]. The signal at δ 49.46 ppm revealed the presence of a quaternary carbon atom to which two alkyl chains (C_5 and C_{10}) are attached and it is comparable with the signal value of the quaternary carbon atom (δ 54.5 ppm) reported for wightianone from *Calophyllum wightianone* [20].

The high resolution mass spectral data along with elemental composition indicated from the $[M-H_2O]^+$ ion (*m/z* 544.3190) a loss of C_5H_8 unit $[(M-H_2O-C_5H_8)^+$, *m/z* 476.2562) followed by the loss of a C_9H_{15} unit from the $C_{10}H_{17}$ side chain of the fragment ion *m/z* 476.2562 to give a methylene cation $[(M-H_2O-C_5H_8-C_9H_{15})^+$ *m/z* 353.1388]. This fragmentation pattern is characteristic of a cyclohexadienone such as calophynic acid [15] where side chains are attached to a sp^3 carbon atom. Further fragment ions *m/z* 413 $[M-C_9H_9O_2]^+$, *m/z* 407 $[M-H_2O-C_{10}H_{17}]^+$, *m/z* 149 ($C_9H_9O_2$) $[C_6H_5C(OH)-CO-Me]^+$, *m/z* 137 ($C_{10}H_{17}$) $[(Me)_2C=CH-CH_2C(CH_2)=C(Me)_2]^+$ and *m/z* 107 (C_7H_7O) $[C_6H_5CHOH]^+$ were observed supporting the presence of C_5H_9, $C_{10}H_{17}$ and $C_9H_9O_2$ units as side chains in the molecule. The mass fragmentation pattern and elemental composition of the ions is in agreement with the assigned structure of mesuaferrol (**1**).

The structure assigned to mesuaferrol is closely, related to the cyclohexadienone carboxylic acid, mesuanic acid, earlier isolated from the same source [12]. The stereochemistry of the OH group in the side phenyl propyl unit of mesuaferrol, however, could not be determined.

Biogenetically phenyl propyl units in the form of 2-phenyl allyl units are found to be associated with many Guttiferae constituents. The phenyl propyl side chain found in mesuaferrol may have been derived by a series of isomerisation and oxidative transformations indicated in Scheme 1 [21]. It is likely that as for the same unit in mesuanic acid, **A** may be the precursor.



Scheme 1.

EXPERIMENTAL

Mps: uncorr. Optical rotations were recorded at 25° using 0.5 dm cell. ^{1}H NMR were recorded at 90 MHz in $CDCl_3$ soln using TMS as int.std. ^{13}C NMR spectra at 23 MHz in $CDCl_3$. MS were run on a double focusing high resolution mass spectrometer (accelerating potential 6 kV, electron energy 70 eV). TLC was carried out on silica gel G.

Extraction and isolation of constituents. Shade-dried stamens of *Mesua ferrea* L. were supplied by Shri Prajapati Joshi (Officer in charge, Amalgamated Research Unit, Ranikhet, U. P., India). Cold extn of the stamens (1.5 kg) with petrol (60–80°) (3 × 5 l) for 7 days gave a reddish brown gummy semisolid (24 g) on concn *in vacuo*. This gummy mass was sepd into a MeOH sol (20 g) and MeOH insol portion (4 g). The former was dissolved in Et_2O and extd with cold 20% aq. Na_2CO_3 and 2% aq. NaOH. The Et_2O layer was concd to give a gummy mass (12 g). This gum (2.4 g) on chromatography on neutral alumina gave *β*-amyrin (0.4 g) and *β*-sitosterol (0.4 g). Acidification of the Na_2CO_3 washings on usual work-up gave a cherry red gummy mass (7 g) which on chromatography over silica gel (210 g) gave a yellow glassy mass (4 g) from C_6H_6 eluents (frs 38 and 39, 200 ml each). Further purification by extraction into 2% cold Na_2CO_3 soln followed by neutralization with ice-cold dil. HCl gave an amorphous powder (3 g) mp 75° $[\alpha]_D^{25}$ + 27.5 (MeOH), $[M]^+$ 562.3293 designated as mesuaferrol (**1**) $C_{35}H_{46}O_6$ mp 75°, $[\alpha]_D^{25}$ + 27.5 (MeOH), $[M]^+$ 562.3293. IR ν_{max}^{KBr} cm^{-1} 3400, 1748, 1720, 1680, 760, 690. ^{1}H NMR: *δ* 7.48 (2H, *m*), 7.12 (3H, *m*), 5.18 (1H, *m*), 4.80 (1H, *m*), 4.26 (1H, *m*), 3.76 (1H, *d*, *J* = 7 Hz), 3.12 (1H, *d*, *J* = 7 Hz), 2.80 (1H, *m*), 2.54 (2H, *m*), 2.04 (3H, *s*), 1.7 (12H, *m*), 1.4 (4H, *m*), 1.2 (6H, *m*), 1.08 (3H, *d*, *J* = 7 Hz), 0.94 (3H, *d*, *J* = 7 Hz). ^{13}C NMR: *δ* 17.66, 18.09, 23.29, 23.69, 26.00, 27.11, 28.12, 29.32, 30.17, 38.66, 39.66, 40.58, 43.18, 49.46, 60.06, 60.96, 70.80, 116.11 (*s*), 119.74 (*d*), 124.39 (*d*), 126.35 (*d*), 127.54 (*d*), 131.60 (*d*), 132.36 (*s*), 132.76 (*s*), 133.02 (*s*), 134.09 (*s*), 142.33 (*s*), 159.12 (*s*), 173.65 (*s*), 206.04 (*s*), 207.99 (*s*). MS: *m/z* [accurate measurement, (required value), molecular formula, relative intensity %)]562.3293 (562.3620) $[M]^+$ $C_{35}H_{46}O_6$ (16.32); 544.3190 (544.3470) $[M-H_2O]^+$ $C_{35}H_{44}O_5$ (4.43); 494.2670 (494.2980) $[M-C_5H_8]^+$ $C_{30}H_{38}O_6$ (33.09); 476.2562 (476.2830) $[M-C_5H_8-H_2O]^+$ $C_{30}H_{36}O_5$ (16.54); 461.2330 (461.2590) $[M-C_5H_8-H_2O-CH_3]^+$ $C_{29}H_{33}O_5$ (8.64); 413.2695 (413.2920) $[M-C_9H_9O_2]^+$ $C_{26}H_{37}O_4$ (31.09); 353.1388 (353.1630) $[M-C_5H_8-H_2O-C_9H_{15}]^+$ $C_{21}H_{21}O_5$ (49.34); 407 $[M-H_2O-C_{10}H_{17}]^+$ (12.78); 149 $[C_6H_5-C(OH)-CO-Me]^+$ (9.01); 137 $[(Me)_2C{=}CH-CH_2-C(CH_2){=}C(Me)_2]^+$ (7.53); 107 $[C_6H_5-CHOH]^+$ (35.67).

Acetylation of mesuaferrol. To mesuaferrol (10 mg) dissolved in Ac_2O (1 ml) few drops of pyridine were added and the mixt kept at room temp for 72 hr. After usual work-up a semisolid monoacetate **2** (homogeneous on TLC) was obtained, $[M]^+$, *m/z* 604. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3400, 1755, 1745, 1705, 1650, 760, 700.

Methylation of mesuaferrol. Mesuaferrol (10 mg) dissolved in Et_2O (10 ml) was treated with an excess of CH_2N_2 in Et_2O and left overnight. The residue obtained after evapn of solvent gave a semi-solid monomethyl ether **3** (homogeneous on TLC), $[M]^+$, *m/z* 576.

β-Amyrin. Colourless needles from EtOH, mp 197° (lit. 197°), identified by direct comparison with an authentic sample (Co-TLC, mmp and IR).

β-Sitosterol. Colourless needles from MeOH, mp 136° (lit. 136–137°), identified by direct comparison with an authentic sample (Co-TLC, mmp and IR).

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