

ACETOPHENONE AND STILBENE DERIVATIVES FROM *GNETUM ULA*

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Key Word Index—*Gnetum ula*; Gnetaceae; acetophenones; stilbene; bergenin; isocoumarin.

Abstract—The isolation of bergenin, 2-hydroxy-4-benzoyloxyacetophenone and the related dimer and stilbene from *Gnetum ula* is reported.

The reported isolation of an alkaloid from *Gnetum indicum* [1] suggested that other members of this comparatively unexplored family might also contain physiologically active compounds. TLC and colour reactions of the acetone extract of *Gnetum ula* revealed the presence of several phenolic constituents but none was alkaloidal in nature. Chromatographic separation yielded, along with bergenin and 2-hydroxy-4-benzoyloxyacetophenone, the new compounds discussed below.

Compound 1, mp 143°, displays chelated —OH and >C=O bands in its IR spectrum and the UV curve is superimposable on that of resacetophenone. Except for the presence of a 4H singlet at 7.48 τ , the NMR spectrum is similar to that of resacetophenone. The symmetrically substituted structure 1 thus indicated for the compound is also in accord with the MS (M^{+} m/z 302) in which rupture of the bond linking the two acetophenone units gives rise to only one prominent peak at m/z 151. Such dimers of plant origin were not known until Majumdar *et al.* recently reported the isolation of one from *Berberis coriaria* [2].

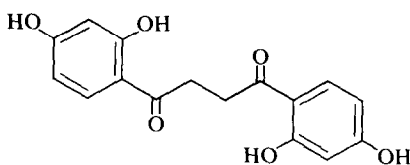
Compound 2, mp 168°, was obtained from the C_6H_6 -EtOAc eluate. Its IR spectrum is devoid of carbonyl absorption and λ_{max} 220, 330 nm as well as the absence of any signals except for one OMe group at higher field in the NMR spectrum in DMSO- d_6 suggested its stilbene nature. The singlet of the olefinic protons appears at 3.57 τ as in the spectrum of 3, 4, 5, 3', 4', 5'-pentahydroxystilbene [2]. The presence of three phenolic hydroxyls was further confirmed through acetylation and

methylation which led to products 2a and 2b respectively, showing methyl singlets at the expected value and integrating for the required number of protons.

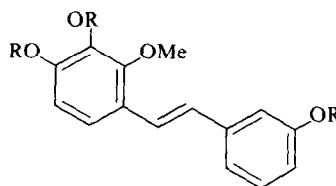
Since 2 is recovered unchanged after exposure to strongly acidic conditions, none of the three hydroxyls can be adjacent to the double bond. The clearly defined *ortho*-coupled doublets at 3.60 and 2.27 τ suggest that one ring must be tetrasubstituted. The lone hydroxyl in the other ring must be *meta* rather than *para* since otherwise the A_2B_2 coupling should have been clearly evident in the spectrum in DMSO- d_6 in which the signals of aromatic protons are well resolved, as noted for stilbene spectra in this solvent [3].

To obtain unambiguous evidence for the stilbene structure, 2 was hydrogenated and the dihydro derivative converted to the triacetate to allow measurement of its NMR spectrum in $CDCl_3$. The spectrum showed the expected 4H singlet of the benzylic methylenes at 7.32 and the molecular ion (M^{+} m/z 386), after three consecutive ketene losses, suffered benzylic cleavage to give strong peaks at 107 and 138 in the MS. These features establish the formation of dihydrostilbene on hydrogenation and support the assignment of substituents in 2.

Apart from the compounds discussed above, the acetone extract afforded two other phenolics in small amounts, the structures of which are under investigation. Extraction with alcohol yielded only one compound, mp 136°, which was identified as bergenin through comparison (NMR, mmp and co-TLC) with an authentic sample.



1



2 R = H
2a R = Ac
2b R = Me

EXPERIMENTAL

Extraction and isolation. Defatted plant material (5 kg) was extracted with Me_2CO , the solvent removed under red. pres. and the residue taken up in H_2O and extracted with EtOAc in a liquid-liquid extractor. Chromatography of the EtOAc-soluble material (25 g) over Si gel afforded 2-hydroxy-4-benzyloxyacetophenone (1 g), mp 90° , identified through comparison (mmp, IR) with a synthetic sample, **1** (700 mg) from the C_6H_6 and **2** (550 mg) from C_6H_6 -EtOAc eluate. Further extraction of the plant material with alcohol yielded bergenin, mp 136° , (400 mg) which was identified through direct comparison with an authentic sample.

1,4-Bis(2,4-dihydroxyphenyl)butanedione (1). Mp $142\text{--}143^\circ$ M^+ m/z 302, $\text{C}_{16}\text{H}_{14}\text{O}_6$; $\nu_{\text{max}}^{\text{null}} \text{cm}^{-1}$: 3300, 1630; $\tau \text{CDCl}_3/\text{DMSO}-d_6$: 2.45 (2 H, d , $J = 8 \text{ Hz}$, 6,6'-H); 3.65 (2 H, dd , $J = 8$, 2 Hz, 5,5'-H), 3.68 (2 H, d , $J = 2 \text{ Hz}$, 3,3'-H); 7.49 (4 H s , $-\text{CH}_2-\text{CH}_2-$).

2-Methoxy-3,4,3'-trihydroxystilbene (2). Mp 168° , M^+ m/z 258; $\text{C}_{15}\text{H}_{14}\text{O}_4$; $\lambda_{\text{max}} \text{nm}$: 220, 330; $\nu_{\text{max}}^{\text{null}} \text{cm}^{-1}$: 3300; $\tau \text{DMSO}-d_6$ 2.6, 3.22 (1 H, d each, $J = 8 \text{ Hz}$, 5,6-H), 2.8–3.1 (3 H m , 4',5',6'-H), 3.83 (1 H s , (br), 2'-H), 3.58 (2 H s , (br), $-\text{CH}=\text{CH}-$), 6.15 (3 H, s , $-\text{OMe}$).

Acetylation of 2. **2** (50 mg) was acetylated with Ac_2O -pyridine (1:1), crystallized with MeOH to yield **2a** (40 mg), mp 90° , M^+

m/z 384, $\text{C}_{21}\text{H}_{20}\text{O}_7$; τCDCl_3 : 3.0–4.0 (8 H, m , Ar-H and $-\text{CH}=\text{CH}-$), 6.15 (3 H, s , $-\text{OMe}$), 7.70 (9 H, s , $3 \times -\text{OAc}$).

Methylation of 2. **2** (300 mg) was refluxed with MeI (4 ml) and dry K_2CO_3 (300 mg) for 15 hr and the product purified by chromatography over Si gel to give **2b**, colourless oil (200 mg). M^+ m/z 300, $\text{C}_{18}\text{H}_{20}\text{O}_4$; τCDCl_3 3.0–4.0 (8 H, m , Ar-H and $-\text{CH}=\text{CH}-$), 6.15 (3 H, s , $-\text{OMe}$), 6.20 (9 H, s , $3 \times -\text{OMe}$).

Dihydro derivative acetate. **2** in MeOH was hydrogenated over Pd/C (10%) and acetylated with Ac_2O -pyridine to give a colourless oil which was purified by chromatography. M^+ m/z 386 (3), 344 (45), 302 (12), 260 (12), 138 (100), 107 (98); τCDCl_3 : 3.0–4.0 (6 H, m , Ar-H), 6.40 (3 H, s , $-\text{OMe}$), 3.2 (4 H, m , $-\text{CH}_2-\text{CH}_2-$), 7.8 (9 H, s , $3 \times -\text{OAc}$).

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