VISCOSOL, A C-3' PRENYLATED FLAVONOID FROM DODONAEA VISCOSA*

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(Revised received 28 November 1985)

Key Word Index—Dodonaea viscosa; Sapindaceae; viscosol; 3'-(y,y-dimethylallyl)-5,7-dihydroxy-3,6,4'trimethoxyflavone; penduletin.

Abstract—The structure of viscosol, a new prenylated flavonoid isolated from the aerial parts of *Dodonaea viscosa*, was established on the basis of spectral studies as well as by the conversion of the flavonol penduletin into permethyl viscosol.

INTRODUCTION

Earlier, we have reported the isolation of many flavonoids including two new prenylated flavonoids [1, 2] and a diterpenoid, dodonic acid, besides an inositol monomethyl ether and some known steroids [3]. In this communication we report the isolation and structure elucidation of one more hitherto unknown prenylated flavonoid designated as viscosol. Its structure has been confirmed by conversion of penduletin, previously isolated from *Dodonaea viscosa* [2], into the permethyl derivative of viscosol.

RESULT AND DISCUSSION

Viscosol (1), an amorphous solid $([M]^+ m/z 412)$, gave positive Shinoda and negative Quastel and Gossypetone tests which showed it to be a flavonoid without ortho and para dihydroxyl groupings, respectively. The presence of two hydroxyl groups was revealed by the formation of a dimethyl ether (2) $([M]^+ m/z 440)$ on methylation with dimethyl sulphate. Its solubility in 10% aq. sodium carbonate solution suggested the presence of one hydroxyl group at C-7.

The UV spectrum of 1 displayed maxima at 270, 300 sh and 337 nm characteristic of a flavone nucleus. With aluminium chloride and aluminium chloride-HCl band I showed a bathochronic shift of 27 and 23 nm, respectively, revealing the presence of a hydroxyl group at C-5 with an oxygen function at C-6 [4].

The ¹H NMR spectrum of the new compound revealed the presence of a y,y-dimethylallyl side chain displaying two 3H singlets at $\delta 1.67$ and 1.69 for two methyls situated on an olefinic carbon, a 2H doublet (J = 7 Hz) for a benzylic methylene at 3.28 and an olefinic triplet (J = 7 Hz) contred at 5.25. Three 3H singlets at $\delta 3.73$, 3.77 and 3.78 were attributed to three methoxyl groups present in the molecule. A singlet at $\delta 6.63$ was assigned to H-8 of ring A. A 1H singlet at $\delta 6.80$ and 7.80 were assigned to H-5', H-2' and H-6', respectively. This demonstrated the presence of substituents at C-3' and C-4' in ring B. Close chemical shifts of H-2' and H-6' suggested the lack of any oxygen function at C-3' which must, therefore, be occupied by the prenyl side chain. The remaining substituents, that is two methoxyl groups, were placed at the C-3 and C-4' positions.

In the mass spectrum peaks at m/z 412, 411, 397 and 394for $[M]^+$, $[M-H]^+$, $[M-Me]^+$ and $[M-H_2O]^+$ appeared with relative intensities of 100, 27, 37.5 and 15% respectively. In accordance with the generalization made by Goudard *et al.* [5], the relative intensities of these peaks suggested the location of two hydroxyl groups at C-5 and C-7 and the two methoxyl groups at C-3 and C-6, respectively. The appearance of a $[A_1 + H]^+$ peak at m/z183 also confirmed the presence of one methoxyl and two hydroxyl groups in ring A. Observation of a $[B_2]^+$ fragment at m/z 203 supported the placement of a methoxyl group and the prenyl chain in ring B.

Thus on the basis of above data, the structure of



^{*}CDRI Communication No. 3755.

viscosol was concluded to be $3'-(\gamma,\gamma-dimethylallyl)-5,7-dihydroxy-3,6,4'-trimethoxy flavone (1).$

With the view to confirm the structure assigned to viscosol, its permethyl ether was prepared by the introduction of a prenyl chain at C-3' in penduletin (3). As a first step in this transformation, 3 was treated with 3methylbut-2-enyl bromide where upon 4'-O-prenvlated product (4) was obtained as a major product instead of the required 3'-prenylated derivative. In another attempt, when penduletin was subjected to BF3-catalysed prenylation with 2-methylbut-3-en-2-ol, it furnished mainly 5. Finally, synthesis according to Scheme 1 successfully furnished product 2 albeit in very low yield. Penduletin (3) was treated with 2-chlora-2-methylbut-3-yne in the presence of potassium carbonate and sodium iodide. Spectral data (see Experimental) of the product revealed its structure to be 6. Several attempts to bring about the selective hydrogenation of the triple bond of 6 to a double bond did not yield satisfactory results. However, hydrogenation of 6 in presence of palladium-barium sulphate (10%) deactivated by quinoline afforded a mixture of 7 and 8.

The mixture of hydrogenated products (7 and 8) could not be separated due to the meagre amount but was used as such for Claisen rearrangement. It was refluxed with butyric anhydride for 8 hr under N₂ followed by hydrolysis with methanolic ammonia affording a mixture of products. This mixture was subjected to permethylation with dimethyl sulphate in the presence of potassium carbonate. The resulting product was chromatographed over a column of silica gel but the products could not be resolved. However, the mass spectrum of the mixture showed [M]⁺ peaks for 2, 9 and 10 at m/z 440, 428 and 426, respectively. Moreover, the ¹H NMR spectrum of the mixture exhibited, besides other signals all the signals of 2. On the basis of these data, one of the products, viz. 2 was found to be identical to the permethyl ether of viscosol.

EXPERIMENTAL

UV and IR spectra were recorded in MeOH and CHCl₃, respectively. Unless stated otherwise ¹H NMR spectra were recorded at 90 MHz in CDCl₃ with TMS as int. standard. C_6H_6 -MeOH (9.8:0.2) was used as the solvent system for TLC (silica gel). Visualization was carried out by spraying with 1% ceric sulphate in 2 N H₂SO₄.

Isolation. Aerial parts of D. viscosa L. were collected in Lucknow (voucher specimen deposited in C.D.R.I.). The chromatography of the CHCl₃ soluble fraction of the EtOH extractive has been reported earlier [3]. The C_6H_6 -EtOAc (7:3) eluate was chromatographed over silica gel using gradient elution with C_6H_6 -CHCl₃. The C_6H_6 -CHCl₃ (4:1) eluate was rechromatographed over silica gel. The *n*-bexane-Me₂CO (1.9:0.1) eluate was then subjected to prep. TLC which resulted in the isolation of viscosol (1) as a yellow coloured amorphous solid.

Viscosol (1). Amorphous solid. IR v_{max}^{HCI} cm⁻¹: 3450, 1650, 1600, 1370, 1175 and 820. UV $\lambda_{max}^{\text{MeX}\text{H}}$ nm: 272, 300 (sh), 367; + NaOMe 271, 298 (sh), 366; + AlCl₃ 278, 305 (sh), 364; + AlCl₃ - HCl 280, 298, 360; + NaOAc 273, 368; + NaOAc-H₃BO₃ 273, 300 (sh), 342. ¹H NMR: see text. MS *m/z* (rel. int.): 412 [M]⁺ (100), 411 [M - H]⁺ (27), 397 [M - Me]⁺ (37.5), 394 [M - H₂O]⁺ (15), 379 [M - Me - H₂O]⁺ (16), 369 [M - Ac]⁺ (16), 351 [M - Ac - H₂O]⁺ (9), 343 [M - 69]⁺ (10), 325 [M - 69 - H₂O]⁺ (7), 203 [B₂]⁺ (7), 183 [A₁ + H]⁺ (6), 175 [B₂ - CO]⁺ (3.5), 167 [A₁ - Me]⁺ (4), 139 [A₁ - Ac]⁺ (3.6), 133 [B₂ - H - 69]⁺ (2.3), 91 [B₂ - Ac - 69]⁺ (4).

Viscosol dimethyl ether (2). Viscosol (1, 10 mg) dissolved in Me_2CO (1 ml) was refluxed with Me_2SO_4 (0.25 ml) and K_2CO_3 (30 mg) for 4 hr. The mixture was filtered, concd, extracted with CHCl₃, washed with H_2O and dried (Na_2SO_4). A mixture of products was obtained which was chromatographed over silica gel. The *n*-hexane-Me₂CO (9:1) eluate on concn gave the permethylated product (2). ¹H NMR (CCl₄): $\delta 1.68$ (6H, s, =CMe₂), 3.22 (2H, d, J = 7 Hz, Ar-CH₂-), 3.72 (6H, s, 2 × OMe), 5.2 (1H, t, J = 7 Hz, Ar-CH₂-CH=C-), 6.46 (1H, s, H-8), 6.69 (1H, d, J = 9 Hz, H-5'), 7.61 (1H, br s, H-2'), 7.66 (1H, br d, J



Scheme 1. Synthetic methods used in the structural determination of viscosol.

Preparation of 2-chloro-2-methylbut-3-yne. A mixture of 2-methyl-3-butyl-2-ol (21 g), $CaCl_2$ (28 g), hydroquinone (250 mg) and conc HCl (105 ml) was stirred at 20° for 45 min. The organic layer was separated and dried (K_2CO_3). Fractional distillation of this material gave the desired compound, 2-chloro-2-methylbut-3-yne, bp 74-77°.

Preparation of 6. A mixture of penduletin (3, 100 mg) and K₂CO₃ (250 mg) in Me₂CO-H₂O (9.7:0.3, 13 ml) was stirred at room temp. for 45 min. To this stirred soln, 2-chloro-2methylbut-3-yne (0.6 ml) and NaI (100 mg) were added and the mixture refluxed for 11 hr. It was then cooled and filtered. Concn of the filtrate under red. pres. furnished a residue which was extracted with EtOAc, washed with H_2O and dried (Na₂SO₄). CC of the crude product over silica gel using CHCl₃-Me₂CO gave the product (6) as an amorphous solid. IR v_{max} cm⁻¹: 3320, 1650, 1610, 1460, 1360, 1020. ¹H NMR: δ1.66 (6H, s, 2 × Me), 2.59 (1H, s, -C=C-H), 3.81, 3.84 and 3.87 (each 3H, s, OMe), 6.40 (1H, s, H-8), 7.26 (2H, br d, J = 10 Hz, H-3' and H-5'), 7.96 (2H, br d, J = 10 Hz, H-2' and H-6'). MS m/z (rel. int.); 410 [M]⁺ (100), $395 [M - Me]^+$ (55), $344 [M - 66]^+$ (75), $329 [M - Me - 66]^+$ (70), 301 $[M - Ac - 66]^+$ (10), 187 $[B_2]^+$ (5), 183 $[A_1 + H]^+$ (4), $167 [A_1 - Me]^+$ (11), 149 (25), 121 $[B_2 - 66]^+$ (15).

Hydrogenation of 6. Compound 6 (20 mg) was dissolved in quinoline-MeOH (9.99:0.01, 0.4 ml) and EtOAc (0.4 ml). After the addition of Pd-BaSO₄ (10%) (4 mg), it was stirred in an H₂ atm for 7 hr at room temp. After filtration and evapn of solvent, the residue (12 mg) was found to be a mixture of partially hydrogenated (7) and completely hydrogenated (8) products. Due to the close R_f values of these products, the mixture could not be resolved and it was subjected as such to further reaction. MS m/z: 414 and 412.

Claisen rearrangement of 7 in the mixture of 7 and 8 followed by

permethylation. Mixture of the hydrogenated products (7 and 8, 10 mg) dissolved in butyric anhydride (0.5 ml) was heated under N_2 at 180° for 8 hr. After decomposition of excess anhydride with ice cold H_2O , the mixture was extracted with EtOAc, washed with H_2O and then dried (Na_2SO_4). The concd residue was stirred for 30 min with 3 N methanolic NH₃ (1.5 ml). It was then concd under red. pres., extracted with EtOAc, washed, dried and concd. The residue (9 mg) in Me₂CO (2 ml) was refluxed for 3 hr with Me₂SO₄ (0.25 ml) and anhydrous K_2CO_3 (20 mg). After usual work up the crude methylated product showed a number of spots which were then subjected to CC on silica gel using *n*-hexane-Me₂CO (9:1) eluate on evapn left a residue (3 mg) which was found to be a mixture of three products (2, 9 and 10) of similar R_f values. MS m/z: 440, 428, 426.

Acknowledgements—The authors express their thanks to Dr. S. P. Popli for useful suggestions. They are also grateful to the staff of the Regional Sophisticated Instruments Centre, C.D.R.I., Lucknow, for providing spectral data. One of us (K.S.) thanks the CSIR, New Delhi for the award of a senior research fellowship.

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