Phytochemistry, 1980, Vol. 19, pp. 2493–2494. © Pergamon Press Ltd. Printed in England. 0031-9422/80/1101-2493 $02.00/0

SYNTHESIS AND STRUCTURE PROOF OF MORINDONE 6-*O*-GENTIOBIOSIDE FROM *MORINDA TINCTORIA*

BARBARA VERMES* and HILDEBERT WAGNER†

*Central Research Institute for Chemistry, Hungarian Academy of Sciences, Budapest, 114, p.0.B. 17, Hungary; †Institut für Pharmazeutische Arzneimittellehre der Universität München, D-8000 München 2, Karlstraße 29, West Germany

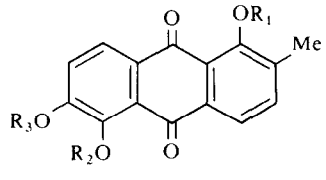
(*Received* 5 *March* 1980)

Key Word Index—*Morinda*; Rubiaceae; anthraquinone glycosides; morindone biosides; synthesis; structure proof.

Abstract—The naturally occurring 1,5-dihydroxy-2-methyl-6-*O*-β-gentiobiosylanthraquinone was synthesized and its structure confirmed.

In an earlier paper [1] we described the synthesis of two naturally occurring biosides of morindone (1,5,6-trihydroxy-2-methylanthraquinone) (**1**), those of the 6-*O*-β-primveroside and of the 6-*O*-β-rutinoside, respectively. From the root bark of *Morinda tinctoria* Roxb. Balakrishna and coworkers [2] isolated a diglucoside of morindone which was different from glycosides already reported in *Morinda* and *Coprosma* spp. [3–13] and from our synthetic products. The sugar moiety was assumed to be linked to the C-6 hydroxyl group because complete methylation and hydrolysis gave morindone 1,5-dimethyl-ether (**2**). The nature of the sugar linkage was established as ββ from the fact that the glycoside was unaffected by diastase and was hydrolysed by emulsin into morindone (**1**) and two molecules of glucose. It was therefore concluded that the new glycoside is a 6-*O*-disaccharide of morindone, most probably a gentiobioside.

For definite structure proof, we have synthesized morindone 6-*O*-β-gentiobioside (**4**). The aglycone morindone was synthesized according to a modified procedure of Jacobson and Adams [1, 14]. Of the three hydroxyl groups of morindone (**1**), the non-chelated one at C-6 is the most reactive in glycosidic coupling. Reaction of **1** with α-acetobromogentiobiose [15] in pyridine in the presence of Ag_2CO_3 was carried out and the product gave, after further acetylation and purification, morindone 6-*O*-gentiobioside-nonacetate (**3**), mp 259–261° and $[\alpha]_D$ − 106.5°. The structure of **3** was also confirmed by ^{1}H NMR spectra. **3** was deacetylated with NaOMe in MeOH to yield the morindone 6-*O*-gentiobioside (**4**) as orange-red needles, mp 252–255° (lit. [2] 256°). The natural sample was not available for direct comparison.



1 $R_1 = R_2 = R_3 = H$
2 $R_1 = R_2 = Me$; $R_3 = H$
3 $R_1 = R_2 = Ac$; R_3 = heptaacetyl-gentiobiosyl
4 $R_1 = R_2 = H$; R_3 = gentiobiose

EXPERIMENTAL

Mps were taken on a Kofler microhot stage and are uncorr. IR spectra were recorded on KBr pellets; NMR spectra at 100 MHz for ^{1}H with TMS as internal standard. Column chromatography was performed on silicic acid and TLC on ready-made plates (Merck). Solvent systems: A: toluene–EtOH (9:2); B: EtOAc–MeOH–H_2O (100:16.5:13.5).

1,5-Di-O-acetyl-2-methyl-6-O-(hepta-O-acetyl-β-gentiobiosyl)-9,10-anthraquinone (**3**). To a soln of morindone (**1**) (200 mg) in pyridine (10 ml) was added first Drierite (500 mg) and Ag_2CO_3 (360 mg), and then a soln of acetobromogentiobiose (480 mg) in pyridine (5 ml). After stirring for 2.5 hr at room temp. with the exclusion of moisture and light, the mixture was diluted with $CHCl_3$ (50 ml), filtered and extracted with 5% HCl and washed with H_2O. After evapn the crude product was acetylated with Ac_2O in pyridine and worked up as usual. The product (200 mg, 21%) was purified by column chromatography (solvent A), R_f 0.7. Subsequent crystallization from EtOH–Me_2CO (99:5) gave yellow needles, mp 259–261° (lit. [2]: 252–253°). $[\alpha]_D^{25}$ − 106.5° (c = 1.08 in dioxane). (Found: C, 56.1; H, 5.27. $C_{45}H_{48}O_{24}$ requires: C, 55.5; H, 4.97%). UV (EtOH) nm: 258, 286, 359. IR cm^{-1}: 1670 (CO). ^{1}H NMR (in $CDCl_3$): δ 1.83, 1.90, 2.00, 2.01, 2.04, 2.06, 2.08 (21 H) (sugar-Ac), 2.32 (3 H, Me) 2.43, 2.50 (6 H, C_1–Ac, C_5–Ac), 3.6–5.4 (12 H, sugar) 7.40 (1 H, *d*, J = 9 Hz, C-7) 7.61 (1 H, *d*, J = 8 Hz, C-3) 8.06 (1 H, *d*, J = 8 Hz, C-4), 8.25 (1 H, *d*, J = 9 Hz, C-8).

1,5-Dihydroxy-2-methyl-6-O-β-gentiobiosyl-9,10-anthraquinone (**4**). **3** (100 mg) was deacetylated with 1 M NaOMe (0.5 ml) in MeOH (10 ml) at room temp. for 24 hr. After acidification to pH 6 with HOAc, the product was purified by column chromatography (solvent B), R_f 0.2. Orange-red needles (from 66% EtOH), mp 252–255° (lit. [2] 256°). (Found: C, 54.90; H, 5.15. $C_{27}H_{30}O_{15}$ requires: C, 54.54; H 5.08%). UV (EtOH) nm: 232, 259, 288, 440. IR cm^{-1}: 1660 (CO).

Acknowledgements—We are indebted to Dr. G. Toth for NMR spectra and to I. Balogh-Batta for the microanalyses.

REFERENCES

1. Vermes, B., Farkas, L. and Wagner, H. (1979) *Phytochemistry* **19,** 119.
2. Balakrishna, S., Seshadri, T. R. and Venkataraman, B. (1960) *J. Sci. Ind. Res. (India)* **19B,** 433.
3. Thorpe, T. E. and Greenall, T. H. (1887) *J. Chem. Soc.* **51,** 52.
4. Thorpe, T. E. and Smith, W. J. (1888) *J. Chem. Soc.* **53,** 171.
5. Oesterle, O. A. and Tisza, E. (1907) *Arch. Pharm. Berl.* **245,** 534; *idem* (1908) *ibid.* **246,** 150.
6. Simonsen, J. L. (1918) *J. Chem. Soc.* **113,** 766.
7. Perkin, A. G. and Hummel, J. J. (1894) *J. Chem. Soc.* **65,** 851.
8. Perkin, A. G. (1908) *Proc. Chem. Soc.* **24,** 149.
9. Briggs, L. H. and Dacre, J. C. (1948) *J. Chem. Soc.* 564.
10. Paris, R. and Ba Touc, Ng. (1964) *Ann. Pharm. Fr.* **12,** 794.
11. Briggs, H. L. and LeQuesne, P. W. (1963) *J. Chem. Soc.* 3471.
12. Rao, P. S. and Veera Reddy, G. C. (1977) *Indian J. Chem.* **15B,** 497.
13. Demagos, G. P. (1977) Ph.D. dissertation, Brussels.
14. Jacobson, R. A. and Adams, R. (1924) *J. Am. Chem. Soc.* **46,** 2788; *idem* (1925) *ibid.* **47,** 283.
15. Brauns, D. H. (1928) *J. Am. Chem. Soc.* **49,** 3170.

Phytochemistry, 1980, Vol. 19, pp. 2494–2495. © Pergamon Press Ltd. Printed in England. 0031-9422/80/1101-2494 $02.00/0

COUMARINS FROM *FRAXINUS FLORIBUNDA* LEAVES

GOBICHETTIPALAYAM R. NAGARAJAN, USHA RANI and VIRINDER S. PARMAR

Department of Chemistry, University of Delhi, Delhi-110007, India

(*Received* 18 *February* 1980)

Key Word Index—*Fraxinus floribunda*; Oleaceae; coumarins; 8-acetyl-7-hydroxy-6-methoxycoumarin; 8-methoxycoumarin; fraxetin; aesculetin; 2,5-dihydroxy-6-methoxyacetophenone.

Fraxinus floribunda Wall, a large tree, grows in India in the eastern Himalayas and Khasi Hills. In an earlier communication [1], the chemistry of some of its bark constituents was discussed. We have now isolated 8-acetyl-7-hydroxy-6-methoxycoumarin (**1**), 8-methoxycoumarin (**2**), 2,5-dihydroxy-6-methoxyacetophenone (**3**), fraxetin and aesculetin from an alcoholic extract of the leaves.

Compound **1**

$C_{12}H_{10}O_5$, mp 178–179°, M^+ 234, gave a reddish brown ferric colour and had UV and IR spectra characteristic of a coumarin. Its NMR spectrum ($CDCl_3$) showed signals for an acetyl, a methoxyl and a chelated hydroxyl group, an aromatic proton and the two olefinic protons of the pyrone ring. Its UV maxima shifted bathochromically in the presence of $AlCl_3$, further supporting the chelation of a hydroxyl with an acetyl group. In the NMR spectrum, the benzene-induced upfield shift of the methoxyl signal was *ca* 0.3 ppm which excluded its presence at the C-5 and C-7 positions [2]. The presence of M − 15 peak in the MS supported this conclusion [3]. On the basis of the above spectral data and also its mp, **1** was considered to be 8-acetyl-7-hydroxy-6-methoxycoumarin, known synthetically [4]. Complete identity of **1** in all respects with a synthetic sample confirmed the above structure.

Compound **2**

$C_{10}H_8O_3$, mp 89–90°, M^+ 176, had IR absorption frequency at 1715 and 1610 cm^{-1} attributable to a coumarin system. Its NMR spectrum showed that the compound is a monomethoxycoumarin. The benzene-induced upfield shift of the methoxyl signal by 0.30 ppm, the presence of M − 15 peak in the MS [3] and the hypsochromic shift of the UV maxima of **2** with respect to the parent coumarin by 24 and 20 nm [5] suggested that **2** is 8-methoxycoumarin. Comparison with a synthetic sample confirmed the identity [6].

Compound **3**

$C_9H_{10}O_4$, mp 89–90°, gave a green ferric colour. Its NMR spectrum showed it to be a tetra-substituted benzene derivative having an acetyl, a methoxy and two hydroxyl groups, one of which is chelated. The two aromatic protons appeared as *ortho*-coupled doublets (J = 9 Hz) at δ 6.62 and 7.06. Absence of a shift with NaOAc–H_3BO_3 in the UV spectrum indicated that the two hydroxyl groups are not *ortho* to each other. From the above data, **3** has been identified as 2,5-dihydroxy-6-methoxyacetophenone. Its identity has been confirmed by comparison with a synthetic sample [7].

To our knowledge, this is the first reported isolation of