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ON THE CONSTITUENTS OF CHIONANTHUS RETUSUS

by

Tetsuo Iwagawa, Miyuki Takarabe and Tsunao Hase

(Received Sep. 10, 1985)

Abstract

Three known compounds, phillyrin, ligustroside and (+)-piroresinol-D-glucoside have been isolated from the methanolic extract of the bark of Chionanthus retusus. (+)-Pinoresinol was also obtained from the ether extract of the wood of this plant.

Introduction

The deciduous tree Chionanthus retusus (Oleaceae) (Japanese name: Hitotsubatago) grows in the temperate zone of Asia and is the only member of the genus Chionanthus found in Japan. The family Oleaceae is known as a rich source of iridoid and secoiridoid glycosides and lignan glycosides. Since no previous investigations have been reported on the constituents of C. retusus, we have examined the constituents of the plant.

Results and Discussion

Compound (1) was crystallized as needles, mp 153–154° [α]D +37.5° with a molecular formula C27H34O11·1.5H2O. The IR spectrum showed absorption bands for a hydroxyl group at 3400 cm⁻¹ and a phenyl group at 1590 and 1515 cm⁻¹. The ¹H NMR spectrum indicated the presence of three methoxyl groups at δ 3.77–3.81 (3H × 3, s) and six phenyl protons at δ 6.84–7.51 (6H, m). On acetylation with acetic anhydride and pyridine, compound 1 gave an amorphous powder (5), whose ¹H NMR spectrum showed the presence of four alcoholic acetoxyl groups at δ 2.00 and 2.04 (3H × 4, s). The above data suggested that compound 1 was phillyrin, which had been isolated from C. virginica² and several plants of the family Oleaceae²–³. Its identity as phillyrin was established by comparing its spectroscopic data with those of an authentic sample.

Compound (2) was isolated as an amorphous powder, [α]D −125.2°. The presence of a conjugated iridoid skeleton was assumed from the absorption bands at 1750 and 1630 cm⁻¹ in the IR spectrum and the signals at δ 3.67 (3H, s, COOMe) and 7.42 (1H, s, H−3) in the ¹H NMR spectrum. The ¹H NMR spectrum also showed the presence of a CH₂CH=C−group [δ 1.64 (dd, J = 8 and 2 Hz) and 6.00 (br q, J = 8 Hz)]. One ABX system due to a −OCOC₂H₅CH−group appeared at δ 2.40, 2.69 and 3.93 (J = 14, 10 and 4 Hz). Two
triplets at $\delta$ 2.78 and 4.08 (2H each, $J=7$ Hz) and one A$_2$B$_2$ system at $\delta$ 6.88 and 6.70 ($J=8$ Hz) were arising from a $p$-hydroxyphenylester group. Moreover, the Mass spectrum of 2 showed a fragmentation of oleuropein-type glucosides at $m/z$ 167$^4)$. Compound 2 was acetylated with acetic anhydride and pyridine to afford an amorphous powder (6), C$_{35}$H$_{42}$O$_{17}$. The $^1$H NMR spectrum showed the presence of four alcoholic acetoxyl groups at $\delta$ 2.00 (3H x 4, s) and one phenolic acetoxyl group at $\delta$ 2.27 (3H, s). These results suggested that compound 2 was ligustroside$^5)$. The spectral data of 2 and 6 were identical those of authentic samples of ligustroside and its acetate.

Compound (3) was obtained as an amorphous powder, $[\alpha]_D^\circ +18.8^\circ$ with a molecular formula C$_{26}$H$_{32}$O$_{11}$.$\text{H}_2$O. The IR spectrum contained a hydroxyl group at 3300 cm$^{-1}$ and a phenyl group at 1600 and 1510 cm$^{-1}$. The $^1$H NMR spectrum showed characteristic signals for the skeleton of 2,6-diphenyl-3,7-dioxabicyclo[3.3.0]octane at $\delta$ 3.07 (2H, m, H-1 and H-5), 4.17 (2H, m, H$_6$-4 and H$_6$-8) and 6.79-7.18 (6H, s, Ar-H) together with signals of two methoxyl groups at $\delta$ 3.81 (3H x 2, s). Acetylation of 3 with acetic anhydride

\[ \begin{align*}
1 & \quad R=\beta-\text{Glc(OH)}_4 \\
2 & \quad R^1=R^2=H \\
3 & \quad R^1=\beta-\text{Glc(OH)}_4, \quad R^2=H \\
4 & \quad R^1=R^2=H \\
5 & \quad R=\beta-\text{Glc(OAc)}_4 \\
6 & \quad R^1=R^2=\text{Ac} \\
7 & \quad R^1=\beta-\text{Glc(OAc)}_4, \quad R^2=\text{Ac}
\end{align*} \]
and pyridine gave a penta-acetate (7), mp 111.5–112.5°. C₈₀H₆₀O₁₆ whose ¹H NMR spectrum showed signals of four alcoholic acetoxyl groups at δ 1.99 and 2.00 (3H x 2 each, s) and one phenolic acetoxyl group at δ 2.25 (3H, s). Enzymatic hydrolysis of 3 with β-glucosidase yielded D-glucose and an aglycone (4), [α]₀ +51.1°, C₂₀H₂₂O₆, which was also isolated from the wood of the plant. The ¹H NMR spectrum indicated a symmetrical structure for 4: δ 3.11 (2H, m, H-1 and H-5), 3.85 (3H x 2, s, OMe), 3.91–3.94 (2H, m, H₆₄ and H₆₅), 4.15–4.51 (2H, m, Hα–8), 4.73 (2H, d-like, J= 4 Hz, H-2 and H-6), 6.05 (2H, s, OH) and 6.84–6.91 (6H, m, Ar-H). The above data were identical with those of (+)-pinoresinol ⁶. Therefore, compound 3 should be (+)-pinoresional-β-D-glucoside, which was reported as a cAMP phosphodiesterase inhibitor⁷.

Acknowledgements We are indebted to Professor M. Kikuchi, Tohoku College of Pharmacy for kindly supplying the spectra of the compounds. We thank Dr. K. Matsuo, Kinki University, for the measurements of ¹H NMR spectra. We are grateful to Professor S. Higashi, Kagoshima University, for the identification of the plant material.

Experimental

Extraction and isolation. Plant material was collected in the campus of Kagoshima University. The bark of C. retusus (420 g) was extracted with MeOH (3.2 l x 2) at 55°. After concentration of the combined MeOH solns, H₂O was added. The aq. soln was extracted with Et₂O and then EtOAc. The EtOAc extract was evapdt to give a residue (26.5 g). Part of the residue (3 g) was subjected to CC on silica gel with CHCl₃-MeOH with increasing proportions of MeOH. The fractions eluted with CHCl₃-MeOH (93 : 7) gave phillyrin 1 (290 mg). Elution with CHCl₃-MeOH (9 : 1) gave ligustroside 2 (265 mg) and (+)-pinoresinol-β-D-glucoside 3 (137 mg), successively. (+)-Pinoresinol 4 (67 mg) was obtained from the Et₂O extract (2.5 g) of the wood of the plant (1.9 kg) by means of CC on silica gel with CHCl₃.

Phillyrin 1. Needles from MeOH, mp 153–154°, [α]₀ +37.5° (C₆H₅N, c 0.2); νₙᵤₐₐₒₜₙ cm⁻¹: 3400, 1590, 1515; ¹H NMR (100 MHz, C₆D₆): δ 3.77 (3H x 2, s, OMe), 3.81 (3H, s, OMe), 4.67 (1H, d-like, J= 4 Hz, H-5), 5.71 (1H, W 1/2 10 Hz, suger H-1), 6.93–7.69 (6H, m, Ar-H); MS m/z: 372 [M-glucose]⁺. (Found: C, 58.01: H, 6.42%. Calc. for C₂₇H₃₁O₁₁: C, 57.95; H, 6.30%.) Compound 1 (45 mg) was acetylated with Ac₂O and pyridine. CC of the crude product with CHCl₃-MeOH (98 : 2) gave 5 (45 mg), an amorphous powder; IR νₐ₅₅₆₅cm⁻¹: 1755, 1605, 1590, 1520, 1225; ¹H NMR (100 MHz, CDCl₃): δ 2.00 and 2.04 (3H x 2 each, s, OAc), 3.80, 3.87 and 3.88 (3H each, s, OMe), 6.72–7.11 (6H, m, Ar-H). The IR and ¹H NMR spectra of 5 were identical with those of an authentic sample of phillyrin tetra-acetate.

Ligustroside 2. An amorphous powder, [α]₀ +125.2° (MeOH, c 0.383); IR ν₈ₕₐ₄₅cm⁻¹: 3350, 1705, 1630, 1600, 1515; ¹H NMR (200 MHz, CD₃OD–(CD₃)₂CO): δ 1.64 (3H, dd, J= 8 and 2 Hz, H-7), 2.40, 2.69 and 3.93 (ABX, J=14, 10 and 4 Hz, H-6 x 2 and H-5), 3.67 (3H, s, COOME), 4.78 (1H, d, J=8 Hz, sugar H-1), 5.88 (1H, br s, H-1), 6.00 (1H, q, J= 8 Hz,
H-8), 6.66 and 7.70 (2H each, A2B2, J=8 Hz, Ar-H), 7.42 (1H, s, H-3). Compound 2 (46 mg) was acetylated as described to afford an amorphous powder 6 (44 mg); IR ν<sub>max</sub><sup>film</sup> cm<sup>-1</sup>: 1750, 1700, 1630, 1510, 1220; 1H NMR (100 MHz, CDCl<sub>3</sub>): δ 1.67 (3H, br d, J=8 Hz), 2.00 (3H x 4, s, OAc), 2.27 (3H, s, OAc), 2.89 (2H, t, J=6 Hz), 3.71 (3H, s), 5.69 (1H, br, q, J=8 Hz), 7.00 and 7.19 (2H each, A2B2, J=10 Hz), 7.45 (1H, s); MS m/z: 346, 167, 138, 120, 107. (Found: C, 56.05; H, 5.53%. Calc. for C<sub>26</sub>H<sub>24</sub>O<sub>4</sub>: C, 56.67; H, 5.68%.) The IR and 1H NMR spectra of 2 and 6 were identical with those of authentic samples.

(+)-Pinoresinol-β-D-glucoside 3. An amorphous powder, [α]<sub>D</sub> +18.8° (MeOH c 0.16); IR ν<sub>max</sub><sup>Nujol</sup> cm<sup>-1</sup>: 3300, 1600, 1510; 1H NMR (100 MHz, (CD<sub>3</sub>)<sub>2</sub>CO): δ 3.07 (2H, m, H-1 and H-5), 3.81 (3H x 2, s, OMe), 4.17 (2H, m, H<sup>α</sup>-4 and H<sup>α</sup>-8), 4.89 (1H, m W 1/2 10 Hz, sugar H-1), 6.79–7.18 (6H, m, Ar-H), MS m/z: 358 [M+glucose]<sup>+</sup>. (Found: C, 58.10; H, 6.35%. Calc. for C<sub>26</sub>H<sub>26</sub>O<sub>6</sub>O: C, 57.95; H, 6.36%.) Compound 3 (75 mg) was acetylated as described above to give fine needles 7 (36 mg) from EtOH, [α]<sub>D</sub> +10°(CHCl<sub>3</sub> c 0.15); IR ν<sub>max</sub><sup>Nujol</sup> cm<sup>-1</sup>: 1750, 1605, 1510; 1H NMR (100 MHz, CDCl<sub>3</sub>): δ 1.99 and 2.00 (3H x 2 each, s, OAc), 2.25 (3H, s, OAc), 3.07 (2H, m), 3.79 (3H x 2, s), 6.69–7.07 (6H, m). (Found: C, 59.59; H, 5.84%. Calc. for C<sub>28</sub>H<sub>30</sub>O<sub>6</sub>: C, 59.17; H, 5.79%.)

Enzymatic hydrolysis of 3. To a soln of β-glucosidase (14 mg) in acetate buffer soln (pH 4.9 0.1 mmol 2 ml), was added 3 (50 mg) and the mixture was stirred at 38°. After 3 days, the soln was extracted with EtOAc, washed with H<sub>2</sub>O and dried over Na<sub>2</sub>SO<sub>4</sub>. The solvent was removed to give a crude, which was subjected to CC on silica gel with CHCl<sub>3</sub>–MeOH (99 : 1) to afford an amorphous powder 4 [α]<sub>D</sub> +51.1° (MeOH c 0.597); IR ν<sub>max</sub><sup>film</sup> cm<sup>-1</sup>: 3450, 1605, 1515, 855, 820; 1HNMR (100 MHz, CDCl<sub>3</sub>): δ 3.11 (2H, m, H-1 and H-5), 3.85 (3H x2, s, OMe), 3.91–3.94 (2H, m, H<sup>α</sup>-4 and H<sup>α</sup>-8), 4.15–4.51 (2H, m, H<sup>α</sup>-4 and H<sup>α</sup>-8), 4.73 (2H, d-like, J=4 Hz, H-2 and H-6), 6.05 (2H, s, OH), 6.84–6.91 (6H, m, Ar-H); MS m/z: 358 [M]<sup>+</sup>. The 1H NMR spectrum of 4 was identical with that of (+)-pinoresinol.

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