The Chemical Constituents of Australian *Flindersia* Species. XXII*

Some Extractives of *F. brassii*

Surachai Nimgirawath,A Ernest RitchieA,B and Walter C. TaylorA

A Department of Organic Chemistry, University of Sydney, N.S.W. 2006.

B Deceased 9 April 1976.

Abstract

From the bark of *Flindersia brassii* Hartley & Hyland, a new substance, flinderbrassin, C_{31}H_{40}O_{12}, m.p. 215°, [α]_{D}^{25} = -8.2°, was isolated; it was reserved for further study. The leaves gave a very small yield of brassilignan, shown to be the known (-)-trans-3,4-bis(3,4-dimethoxybenzyl)tetrahydrofuran.

Recently the new species *Flindersia brassii* Hartley & Hyland has been discovered and described. The tree, which occurs in dry rocky rain forest areas of the Cook district of northern Queensland, is medium to rather large, 13–30 m tall and 20–40 cm diameter at breast height. Through the kindness of its discoverers, who supplied the material, we have been able to examine the constituents of the bark and leaves.

The bark was extracted and the extracts worked up in the usual way but the only isolable constituent was a new substance, flinderbrassin, C_{31}H_{40}O_{12}, m.p. 215°. Since a preliminary examination indicated that its structure was quite complex, it was reserved for further study.

The leaves also gave only one isolable constituent in very low yield. This was a substance, brassilignan, C_{22}H_{28}O_{5}, m.p. 120°, [α]_{D}^{23} = -56°. Its infrared spectrum showed the absence of hydroxyl or carbonyl groups and a brief examination of its n.m.r. spectrum showed that the molecule contained four methoxyl groups but no C-methyl groups, and a high degree of symmetry to cause the exact doubling of peaks. In the mass spectrum, the only significant fragment ions were at m/e 152 (90%) and 151 (100%) corresponding to C_{9}H_{12}O_{2}+ and C_{9}H_{11}O_{2}+ respectively. It was therefore concluded that brassilignan was probably trans-3,4-bis(3,4-dimethoxybenzyl)tetrahydrofuran (1). Only one other lignan, sesamin, has been reported from a member of the genus, *F. pubescens* Bail., but lignans are not uncommon in other rutaceous genera (e.g.4).

No natural lignan of structure (1) has been previously described but the substance has been prepared synthetically and from other lignans on several occasions. The constants recorded are: m.p. 118–119°, [α]_{D}^{17} = 58·9°, m.p. 117–118°, [α]_{D}^{25} = 54·5°.


m.p. 118·8–119·8°, [α]D21 46°. For the (+)-isomer the values reported are:
m.p. 117°, [α]D10 +50°, m.p. 114–116°, [α]D30 +53°, for the (±)-form, m.p. 90–90·5°, and for the meso-isomer, m.p. 120–120·4°.

Although the agreement between the best values and the values for brassilignan was good, structure (1) was confirmed by a detailed examination of the n.m.r. spectral data. In the 1H n.m.r. spectrum a multiplet centred at about δ 6·6 could be assigned to H2, H5 and H6 of two identical 3,4-dimethoxybenzene residues; the pattern was matched by iterative computation (LAOCN3) yielding the following parameters: δ2 6·59, δ5 6·75, δ6 6·63, J2,5 1·97, J2,6 0·60, J5,6 7·95 Hz. The aliphatic region contained, in addition to singlets due to methoxyl at 3·84 and 3·83, five multiplets: four sets of doublets of doublets which could be assigned to the pairs of geminal protons Hα, Hβ and Hδ, Hε, and a broadened sextet attributable to Hε. A non-iterative computation, treating the system as one of five spins and using the following parameters: δα 3·89, δβ 3·52, δε 2·18, δδ 2·62, δε 2·53, Jαβ −8·5, JαC 6·8, JβC 6·6, JδC 6·5, JεC 6·5, and JεD −13·0 Hz, reproduced the spectrum to a good approximation, but not exactly since magnetic non-equivalence demands that the system be treated as one of ten spins; computational facilities to do this were not available. Although the value of Jεε could not therefore be obtained the substituents on the heterocyclic ring are trans-disposed by virtue of the optical activity of the molecule. The noise-decoupled and single frequency off-resonance decoupled 13C n.m.r. spectra of brassilignan were fully in accord with structure (1).

From the work of Row et al. on the (+)-form of (1), the absolute configuration of brassilignan is 3R,4R, as shown.

Experimental

General directions are as in Part XXI.13C n.m.r. spectra were determined at 20 MHz on a Varian Associates CFT-20 instrument. Resonances showed the expected multiplicity on single frequency off-resonance decoupling.

The plant material was collected at Iron Range, northern Queensland, by Mr B. P. M. Hyland (sample number: Hyland 2734 (CANB, QRS)).

Extraction of the Bark

The dried, ground bark (10·5 kg) was extracted by percolation at room temperature with ether and then methanol. Alkaloids were absent from each extract.

The ether extract was concentrated and the solution extracted rapidly with 4% aqueous sodium hydroxide. After recycling there were obtained an acidic fraction (12 g) and a neutral fraction (15 g).

Both acidic fractions were chromatographed on silica gel, but only material consisting essentially of fatty acids could be isolated. It was not further examined.

The neutral fractions were combined and chromatographed on alumina. Only the fraction eluted by ether–benzene (3:1) gave crystalline material (11·3 g). Recrystallization from methanol afforded flinderbrassin as colourless rectangular prisms, m.p. 215°, \([\alpha]_D^8 - 8·2^\circ, [\alpha]_{13}^m + 132^\circ\) (c, 0·7) (Found: C, 61·5; H, 6·6; O, 31·8; M⁺, 604·2543. C₃₁H₄₀O₁₂ requires C, 61·6; H, 6·7; O, 31·8%; M⁺, 604·2518). λmax 235sh, ε 7000; νmax 1755, 1730, 1611, 1504, 1315, 1245, 1225, 1166, 1142, 1060, 1042, 1028, 984, 950, 940, 900, 880, 818, 800, 750 cm⁻¹.

Extraction of the Leaves

The dried, milled leaves (4·5 kg) were extracted in turn with light petroleum, ether and methanol. Alkaloids were absent from each of the extracts, which were processed as above.

The acidic fractions (15 g, 30 g, and 3 g respectively) again appeared to consist of fatty acids and were not further examined.

The light petroleum neutral fraction (145 g) on chromatography on alumina gave fractions consisting only of paraffins and long chain alcohols. The same result was obtained from material which was saponified prior to chromatography.

The ether and methanol neutral fractions (97 g and 15 g respectively) were separately chromatographed on alumina but no crystalline fractions were obtained. The eluates from both chromatographs were combined and the material saponified with 10% aqueous ethanolic potassium hydroxide in the usual manner. The neutral portion (40 g) was chromatographed on alumina. Only the fraction eluted by ethyl acetate–benzene (1:1) contained crystalline material. This was rechromatographed. Elution by ethyl acetate–benzene (1:3) gave a colourless solid which on recrystallization afforded brassilignan, m.p. 120°, as colourless needles (Found: M⁺, 372·1933. Calc. for C₂₂H₂₅O₅: M⁺, 372·1936). The final yield was only 0·1 g, but much material was accidentally lost. νmax 1602, 1585, 1504, 1266, 1243, 1196, 1161, 1147, 1109, 1060, 1030, 950, 921, 875, 826, 813, 766, 742, 720 cm⁻¹. ¹³C n.m.r. spectrum: 148·8, 147·5, ArC 3, 4; 133·0, ArC 1; 120·6, ArC 6; 112·0, 111·2, ArC 2, 5; 73·3, OCH₃; 55·8, OCH₃; 46·6, CH; 39·1, ArCH₂. Mass spectrum, m/e 372 (70%), 152 (90), 151 (100), 137 (81), 212 (10), 107 (7), 106 (5).

Acknowledgment

This work was supported by a grant from the Australian Research Grants Committee.

Manuscript received 24 September 1976