Aust. J. Chem., 1999, **52**, 157–158

A New Sideroxylonal from *Eucalyptus melliodora*

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Sideroxylonal C (3), (2*RS*,3*RS*,4*RS*)-2-(3,5-diformyl-2,4,6-trihydroxyphenyl)-5,7-dihydroxy-3-(1-methylethyl)-4-(2-methylpropyl)chroman-6,8-dicarbaldehyde, was isolated from *Eucalyptus melliodora* leaf, and its structure determined by spectroscopic methods.

Introduction

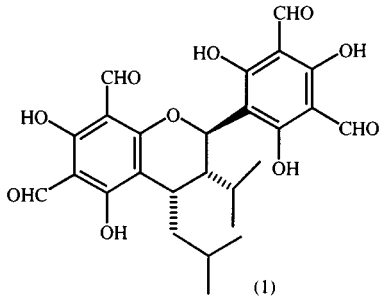
The sideroxylonals and related compounds act as potent mammalian antifeedants[1] and, as part of a project to isolate large quantities of sideroxylonal A (1) for feeding experiments with marsupials, a new diastereomer, sideroxylonal C (3), was isolated.

Results and Discussion

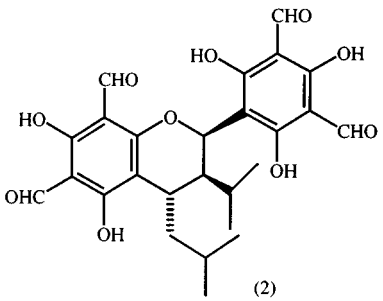
Sideroxylonal C (3) was isolated as a white powder from the 10% ethanol/hexane extract of the leaves of *Eucalyptus melliodora* in a 0·024% yield. The extraction solvent was removed and after chromatography and recrystallization a mixture of sideroxylonals B (2) and C (3) (*c.* 30 : 70) was obtained. Sideroxylonal B (2) was removed by washing the mixture with dichloromethane to give pure sideroxylonal C (3).

Spectroscopic data for sideroxylonal C (3) strongly indicated that it was an isomer of the previously described sideroxylonal A (1) and B (2).[2] In the mass spectrum, the compound exhibits a characteristic retro-Diels Alder fragmentation with a strong fragment at *m/z* 250 and a weak $M^{+\bullet}$ at *m/z* 500. The *m/z* 250 ion further fragments with loss of a C_4H_7 fragment to give another characteristic ion at *m/z* 195. The ^{1}H n.m.r. spectrum is also typical in that it shows four coincidental hydrogen-bonded phenolic protons and four aldehydic protons together with a single non-hydrogen-bonded phenolic centred at 13·4, 10·1 and 7·9 ppm, respectively. The aliphatic region closely corresponded to both sideroxylonal A (1) and B (2) except for the chemical shift of the proton in position 2 (5·2 ppm). This proton has a significant upfield chemical shift of *c.* 0·8 ppm, which suggested there is some strain in this part of the molecule. The i.r. spectrum has typically strong absorbances at 3296 (hydrogen-bonded phenolics), 2958 and 1640 cm^{-1} (aldehydes). The u.v. spectrum contains a distinct peak at 294 nm, which is different from that of sideroxylonals A (1) and B (2).[2] The lack of any optical activity indicates a racemic mixture confirming a previous report.[2]

The relative stereochemistry of sideroxylonal C (3) was determined on the basis of n.m.r. data. The ^{1}H n.m.r. spectrum evidence for this configuration came from the large *J* value (11 Hz) between H 2 and H 3 suggesting that they were near *trans* diaxial. The *J* value (2·7 Hz) between H 3 and H 4 is indicative of an axial equatorial arrangement. N.O.e. enhancements were observed between the methyl protons on the isopropyl side chain and H 2 and H 4 implying that they were all on the same side of the molecule. An n.O.e. enhancement found between H 3 and the methine proton on the isobutyl side chain indicates that they are also on the same side of the molecule; thus the stereochemistry is as shown. A single-crystal X-ray structure confirmed this stereochemistry. The X-ray structure will be discussed in detail along with two closely related structures in a forthcoming paper.



(1)



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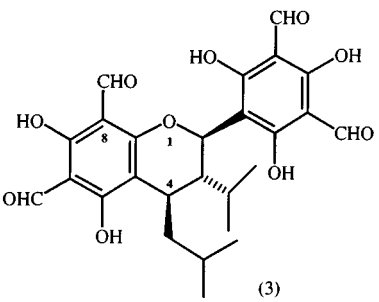

(3)

Manuscript received 18 December 1998 0004-9425/99/020157$05.00

Experimental

General Details

Melting points were determined on a Reichert hot-stage apparatus and are uncorrected. Low-resolution electron-impact mass spectra and high-resolution accurate mass measurements were recorded on a Fisons Instruments Autospec mass spectrometer. Infrared spectra were recorded on a Perkin Elmer 1800 (Fourier transform) spectrophotometer as KBr disks. The following abbreviations were adopted to indicate the intensity: vs (very strong), s (strong), m (medium), w (weak). ^{1}H, ^{13}C and two-dimensional n.m.r. spectra were recorded on a Varian VXR-300 spectrometer (300 and 75·5 MHz respectively). Ultraviolet–visible spectra were recorded on a Shimadzu UV-2101PC spectrophotometer. Leaf material was collected from a roadside woodland remnant of *Eucalyptus melliodora* at Kaleen in the Australian Capital Territory. A voucher specimen was deposited into the Gauba Herbarium, Australian National University.

Extraction and Purification of Sideroxylonal C (3)

Coarsely ground, air-dried *E. melliodora* leaf material (*c.* 1 kg) was extracted with 10% ethanol/hexane (6·6 litres) for up to 48 h in the relevant Soxhlet apparatus. The solvent was removed to give a green residue (*c.* 100–130 g). The residue was dissolved in dichloromethane (300 ml), Celite (150 g) was added and the solvent removed. This material was placed on top of fresh Celite (150 g) in a vacuum column and washed successively with hexane (*c.* 1000 ml), diethyl ether (1000 ml), ethyl acetate (*c.* 1000 ml), 10% methanol in dichloromethane (*c.* 1000 ml) and methanol (*c.* 500 ml). The diethyl ether fractions were combined and the solvent was allowed to evaporate slowly to *c.* 25% of the original volume and filtered. The resultant green residue was placed on a sintered-glass filter and washed with 40–60 light petroleum (250 ml), diethyl ether (500 ml), dichloromethane (500 ml) and 10% methanol in dichloromethane (500 ml). The 40–60 light petroleum fraction gave a pale white solid which was made up of, by ^{1}H n.m.r., a mixture of sideroxylonals B (2) and C (3) (30 : 70). This material was washed with dichloromethane, which removed sideroxylonal B (2), to give pure *sideroxylonal C* (3) (242 mg, 0·024%) as a colourless amorphous solid, m.p. 198–201°C, $[\alpha]_D$ 0·0° (Found: C, 62·1; H, 5·6%; $M^{+\bullet}$, 500·1679. $C_{26}H_{28}O_{10}$ requires C, 62·4; H, 5·6%; $M^{+\bullet}$, 500·1683). ^{1}H n.m.r. (300 MHz, $CDCl_3$) δ 0·85, d, J 6·9 Hz, 3H, 3-CH(C**H**$_3$)$_2$; 0·90, d, J 6·0 Hz, 3H, 4-CH(C**H**$_3$)$_2$; 0·97, d, J 6·0 Hz, 3H, 4-CH(C**H**$_3$)$_2$; 1·00, d, J 6·9 Hz, 3H, 3-CH(C**H**$_3$)$_2$; 1·31–1·55, m, 3H, 4-C**H**$_2$C**H**(CH$_3$)$_2$; 1·71, dsep, J_d 2·4, J_{sep} 6·9 Hz, 1H, 3-C**H**(CH$_3$)$_2$; 2·29, ddd, J_1 2·7, J_2 2·7, J_3 11·1 Hz, 1H, C 3–H; 3·25, dt, J_d 2·7, J_t 6·9 Hz, 1H, C 4–H; 5·18, d, J 11·1 Hz, 1H, C 2–H; 7·93, br s, OH; 9·98, s, CHO; 10·21, br s, 2×CHO; 10·28, s, CHO; 13·12, s OH; 13·29, s, OH; 13·49, br s, OH; 13·53, br s, OH. ^{13}C n.m.r. (75·75 MHz, $CDCl_3$) δ 16·1, 3-CH(**C**H$_3$)$_2$; 20·7, 3-CH(**C**H$_3$)$_2$; 22·7, 4-CH(**C**H$_3$)$_2$; 23·1, 4-CH(**C**H$_3$)$_2$; 25·5, 4-CH$_2$**C**H(CH$_3$)$_2$; 26·1, C 4; 28·3, 3-**C**H(CH$_3$)$_2$; 50·2, 4-**C**H$_2$CH(CH$_3$)$_2$; 53·5, 3-**C**H(CH$_3$)$_2$; 79·2, C 2; 104·0, C; 104·7, C; 105·3, C; 105·9, C; 112·4, C; 164·9, C–O; 165·4, C–O; 167·1, C–O; 168·0, C–O; 168·3, C–O; 169·1, C–O; 191·2, CHO; 192·1, CHO; 192·3, CHO; 192·6, CHO. Mass spectrum m/z 500 ($M^{+\bullet}$, 22%), 443 (36), 305 (9), 250 (100), 235 (40), 223 (33), 207 (54), 195 (83). ν_{max} (KBr) 3296s (OH), 1640vs cm^{-1} (CHO). U.v. (MeOH) λ_{max} 294 nm ($\log \epsilon$ 4·50).

Acknowledgment

We thank Dr John MacLeod for advice in this study.

References

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[2] Satoh, H., Etoh, H., Watanabe, N., Kawagishi, H., Arai, K., and Ina, K., *Chem. Lett.*, 1992, 1917.