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NATURAL GLYCOSIDES OF CYCLOPENTENONE CYANOHYDRINS:[1]

REVISED STRUCTURE OF SO-CALLED EPITETRAPHYLLIN B

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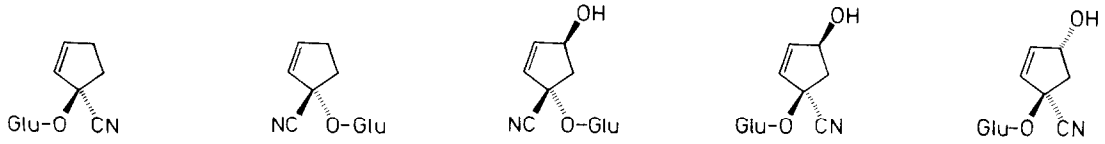
Summary: One of the major cyclopentenoid glucosides of Passifloraceae was shown to be (1R,4R)-1-(β-D-glucopyranosyloxy)-4-hydroxy-2-cyclopentenecarbonitrile, being thus a diastereoisomer and not an epimer of tetraphyllin B, another cyanohydrin glucoside characteristic of this plant family.

The pantropical plant family Passifloraceae and its close allies possess a unique ability to produce epimeric pairs of glucosides of 2-cyclopentenone cyanohydrin, (1) and (2).[2] Perhaps the most widely distributed cyclopentenoid glucoside is the hydroxylated derivative (3), tetraphyllin B,[3-14] and it is of interest to establish whether this intriguing biosynthetic duality also applies to (3).



1 2 3 4 5

Glu = β-D-Glucopyranosyl

Some years ago, a novel cyclopentenoid was isolated along with (3) from *Adenia volkensii* Harms (Passifloraceae),[4] an African desert shrub used to prepare arrow poisons.[15] It was not obtained as a pure compound, but was proposed from ^{1}H NMR data to be epimeric with (3) at C-1, and was hence named epitetraphyllin B (4).[4] The new glucoside was subsequently reported from many other sources,[8,9,11,13] usually co-occurring with (3). We wish to report that the second glucoside of *A. volkensii* has in fact the structure (5), *i.e.*, differs from tetraphyllin B at both asymmetric carbons of the aglucone.

Chromatography on silica gel of extracts of tubers of *A. volkensii*[16] (58 g), followed by preparative HPLC on octadecylsilyl silica, yielded 208 mg of a mixture of tetraphyllin B and the second glucoside in a ratio of 1:1 (^{1}H NMR). Separation of the mixture was carried out by

normal-phase preparative HPLC.[17] The pure glucosides thus obtained had physical and spectroscopic properties similar to those reported before,[18,19] the second glucoside moreover being dextrorotatory whereas tetraphyllin B is levorotatory. From the characteristic[20,21] changes of chemical shifts of the cyanohydrin carbons and of the anomeric protons, closely paralleling the differences observed in the pair (1) and (2),[2] it is evident that (3) and the second glucoside differ in configuration of C-1.[4]

Hydrolysis of (3) with mollusk β-glucosidase[22] afforded the levorotatory hydroxyenone (6),[3] $[\alpha]_D^{27}$ *ca.* -60° (*c* 0.1, methanol); the compound exhibited a positive Cotton effect around 320 nm and a negative around 220 nm (Fig. 1). These data prove the (4*S*) configuration[23] of (6), in agreement with structure (3).[14] Similar hydrolysis of the second glucoside yielded a hydroxyenone (7) with ^{1}H NMR spectrum identical to that of (6),[24] but exhibiting positive rotation at the sodium D line, $[\alpha]_D^{27}$ *ca.* +60° (*c* 0.1, methanol), and Cotton effects opposite to those of (6) (Fig. 1). Tetraphyllin B and the other glucoside therefore have opposite configurations at C-4.

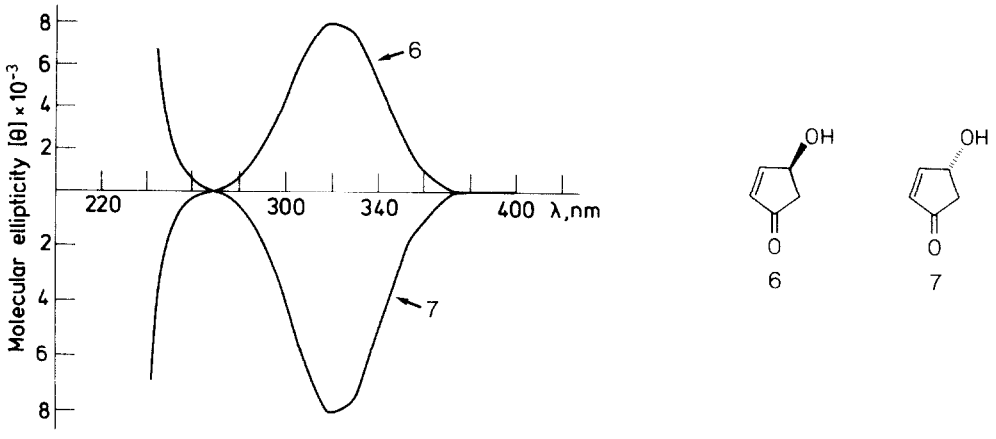


Fig. 1 CD spectra of hydroxyenones (6) and (7) (in methanol), obtained by enzymatic hydrolysis of tetraphyllin B and the second glucoside of *A. volkensii*, respectively.

Tetraphyllin B and the second cyclopentenoid of *A. volkensii* are thus glucosides of enantiomeric, not epimeric, cyanohydrins. We propose the trivial name volkenin[25] for the glucoside (5), since the name epitetraphyllin B is no longer appropriate. The biosynthetic duality, possibly universal[2] for plants producing (1) and (2), appears to continue with the hydroxylated derivatives, the hydroxy group being in each case introduced from the face *cis* to the cyano group of the cyclopentene ring.

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16. We are indebted to Dr. H. Osore, The International Centre of Insect Physiology and Ecology, Nairobi, Kenya, for supplying the plant material. A voucher specimen is preserved at our laboratory.
17. Lichrosorb Si60, 7 μm, 1.6 x 25 cm column eluted with 5 ml/min of $CH_3COOC_2H_5/CH_3OH/H_2O$, 78:20:2.
18. Tetraphyllin B: m.p. 169.5-170°C, lit.[3] m.p. 169-170°C; $[\alpha]_D^{27}$ -75° (*c* 0.5, methanol), lit.[3] $[\alpha]_D^{25}$ -35.6° (*c* 1,0, water); ^{1}H NMR (D_2O, 500 MHz) δ 6.25 (A) and 6.44 (B) (olefinic, J_{AB} 5.5 Hz, J_{AX} 1.2 HZ, J_{BX} 2.0 Hz), 5.08 (H-4), 4.68 (anomeric, J_{AX} 7.9 Hz), 3.74 (A) and 3.92 (B) (H-6', J_{AB} -12.5 Hz, J_{AX} 5.5 Hz, J_{BX} 2.2 Hz), 3.51 and 3.41 (H-3' and H-4', $J_{2,3}\sim J_{3,4}\sim J_{4,5}\sim$9.3 Hz), 3.50 (H-5'), 3.28 (H-2', $J_{1,2}$ 7.9 Hz, $J_{2,3}$ 9.3 Hz), 2.38 (A) and 2.89 (B) (H-5, J_{AB} -15.0 Hz, J_{AX} 3.5 Hz, J_{BX} 6.5 Hz) (*cf.* ref. 3,5); ^{13}C NMR (CD_3OD, 125.7 MHz) δ 132.1 and 144.9 (olefinic), 121.0 (CN), 101.5 (anomeric), 82.6 (C-1), 76.0 (C-4), 62.9, 71.6, 75.0, 78.2 and 78.4 (remaining glucose carbons), 48.9 (C-5) (*cf.* ref. 7). Per-*O*-trimethylsilyl derivative: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.03 (A) and 6.20 (B) (olefinic, J_{AB} 5.5 Hz, J_{AX} 1,5 Hz, J_{BX} 2.0 Hz), 4.99 (H-4), 4.49 (anomeric, J_{AX} 7.4 Hz), 3.67 (A) and 3.80 (B) (H-6', J_{AB} -11.0 Hz, J_{AX} 5.5 Hz, J_{BX} 2.0 Hz), 3.2-3.5 (remaining glucose protons), 2.24 (A) and 2.93 (B) (H-5, J_{AB} -14.5 Hz, J_{AX} 4.5 Hz, J_{BX} 6.5 Hz) (*cf.* ref. 4,5,8).
19. Second glucoside of *A. volkensii* (colourless syrup): $[\alpha]_D^{27}$ +20° (*c* 0.5, methanol); ^{1}H NMR (D_2O, 500 MHz) δ 6.21 (A) and 6.38 (B) (olefinic, J_{AB} 5.5 Hz, J_{AX} 1.2 Hz, J_{BX} 2.0 Hz), 5.07 (H-4), 4.81 (anomeric, J_{AX} 7.9 Hz), 3.71 (A) and 3.90 (B) (H-6', J_{AB} -12.5 Hz, J_{AX} 5.5 Hz, J_{BX} 2.2 Hz), 3.53 and 3.39 (H-3' and H-4', $J_{2,3}\sim J_{3,4}\sim J_{4,5}\sim$ 9,3 Hz), 3.51 (H-5'), 3.28 (H-2', $J_{1,2}$ 7.9 Hz, $J_{2,3}$ 9.3 Hz), 2.46 (A) and 2.79 (B) (H-5, J_{AB} -15.0 Hz, J_{AX} 3.5 Hz, J_{BX} 6.5 Hz); ^{13}C NMR (CD_3OD, 125.7 MHz) δ 133.4 and 143.4 (olefinic), 120.4 (CN), 101.9

(anomeric), 83.4 (C-1), 75.7 (C-4), 62.7, 71.5, 75.0, 78.1 and 78.4 (remaining glucose carbons), 48.7 (C-5). Per-*O*-trimethylsilyl derivative: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.06 (A) and 6.18 (B) (olefinic, J_{AB} 5.5 Hz, J_{AX} 1.5 Hz, J_{BX} 2.0 Hz), 4.99 (H-4), 4.63 (anomeric, J_{AX} 7.4 Hz), 3.60 (A) and 3.78 (B) (H-6', J_{AB} -11.0 Hz, J_{AX} 5.5 Hz, J_{BX} 2.0 Hz), 3.2-3.5 (remaining glucose protons), 2.37 (A) and 2.70 (B) (H-5, J_{AB} -14.5 Hz, J_{AX} 4.5 Hz, J_{BX} 6.5 Hz) (*cf.* ref. 4,8).

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24. ^{1}H NMR ($CDCl_3$, 270 MHz) δ 6.25 (H-2), 7.57 (H-3) ($J_{2,3}$ 5.5 Hz), 5.07 (H-4) ($J_{2,4}$ -1.2 Hz, $J_{3,4}$ 2.5 Hz), 2.29 and 2.80 (H-5) (J_{AB} -18.7 Hz, J_{AX} 2.2 Hz, J_{BX} 6.0 Hz) (*cf.* ref. 23).
25. ^{1}H NMR and rotation data[19] do not support the recent proposal[26] that the glucoside is identical with barterin, a cyclopentenoid of Barteria fistulosa Mast. (Passifloraceae).[27]
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