Journal of Natural Products

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J. Nat. Prod., **1993**, 56 (1), 130-133• DOI:
10.1021/np50091a019 • Publication Date (Web): 01 July 2004

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Journal of Natural Products
Vol. 56, No. 1, pp. 130-133, January 1993

QUASSINOIDS FROM *QUASSIA MULTIFLORA*: STRUCTURAL ASSIGNMENTS BY 2D NMR SPECTROSCOPY

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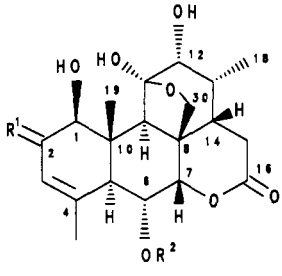
ABSTRACT.—Three quassinoids, 6α-tigloyloxychaparrinone [**1**], 6α-tigloyloxychaparrin [**2**], and 6α-hydroxychaparrinone [**3**], have been isolated for the first time from *Quassia multiflora*. Compounds **1** and **2** were previously isolated from other members of the Simaroubaceae, while this is the first reported natural occurrence of **3**. Structural assignments were made on the basis of 2D nmr spectroscopy. Base hydrolysis of **1** gave a mixture of **3** and a new compound, Δ^5-chaparrinone [**4**].

Quassia multiflora (A. Juss.) Nooteboom (=*Simaba multiflora*) is a member of the Simaroubaceae and is one of six species present in Guyana (1). Previous chemical investigations of this plant resulted in the isolation of chaparrinone-type quassinoids (2–6). One of the notable features of the quassinoids is the wide range of biological activities which they display (7). In the course of a continuing investigation of Guyanese medicinal plants, 6α-tigloyloxychaparrinone [**1**] (8), 6α-tigloyloxychaparrin [**2**] (8), and the new natural product 6α-hydroxychaparrinone [**3**] were isolated from the roots of *Q. multiflora*. We report here the characterization of **1–3** by 2D nmr spectroscopy.



1 R^1=O, R^2=tiglate
2 R^1=α-OH, β-H; R^2=tiglate
3 R^1=O, R^2=H

Compound **1**, mp 236–237°, had the molecular formula $C_{25}H_{32}O_9$, on the basis of hreims. The ^{1}H-nmr spectrum was identical to that reported for 6α-tigloyloxychaparrinone (8). The ^{13}C-nmr spectrum of **1** was not previously reported (8). In the COSY spectrum, the H-6 proton at δ 5.92 showed correlations with protons at δ 3.70 (H-5) and 4.89 (H-7), while a proton at δ 2.42 (H-13) correlated with H-12 (δ 3.95), H-14 (δ 2.09), and the C-18 methyl at δ 1.08 (J = 7.0 Hz). The H-14 proton (δ 2.09) also showed cross peaks with the C-15 methylene protons at δ 2.89 (dd, J = 18.9, 6.0 Hz) and δ 3.49 (dd, J = 18.9, 13.3 Hz). A ^{13}C-^{1}H shift correlated (HETCOR) experiment (9) revealed that the latter two protons were attached to a carbon at δ 30.6.

A FLOCK experiment (10) indicated that a quaternary carbon at δ 48.2 had long-range correlations with signals at δ 1.72 (H_3-19), 3.37 (H-9), 3.70 (H-30), and 4.51 (H-1), while another quaternary carbon at δ 47.1 had correlations with protons at δ 2.89 (H-15), 3.37 (H-9), 4.39 (H-30), and 4.89 (H-7). The stereochemistry of **1** was confirmed from the analysis of a 2D NOESY spectrum. From the NOESY spectrum, the H-15 proton at δ 2.89 had a cross peak with the H-14 proton (δ 2.09); this proton in

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turn had correlations with H-7 (δ 4.89) and H-13 (δ 2.42), indicating that they were all on the same face and that they had a β orientation. Similarly, H-1 (δ 4.51) had correlations with H-5 (δ 3.94) and H-9 (δ 3.37), thus showing that they were α-oriented.

Compound **2** (8), mp 278–279°, $C_{25}H_{34}O_9$, had ^{1}H- and ^{13}C-nmr spectra that were similar to those of **1** except for the differences expected due to the change on going from a ketone to a hydroxyl at C-2. Since only limited ^{1}H and ^{13}C data were available in the literature for **2**, complete assignments of its ^{1}H- and ^{13}C-nmr spectra were made (Table 1) by comparison with the assignments for compound **1** and by 2D nmr spectroscopy.

Compound **3**, mp 233–235°, $C_{20}H_{26}O_8$, had ir absorptions due to hydroxyl (3440 cm^{-1}), ester (1740 cm^{-1}), and α,β-unsaturated ketone (1680 cm^{-1}) functionalities. A uv absorption at 242 nm (ε 8000) supported the presence of an α,β-unsaturated ketone. The ^{1}H-nmr spectrum showed resonances characteristic of quassinoids of the chaparrinone type. In particular, an AB quartet at δ 3.85 and 4.32 (J = 8.9 Hz) was readily assigned to a C-11/C-30 hemiketal function, while a quartet at δ 6.21 (1H, J = 1.5 Hz) was consistent with the presence of an α proton (H-3) of

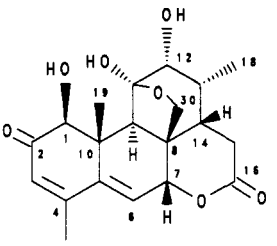
TABLE 1. ^{13}C- and ^{1}H-nmr Assignments for Compounds **1** and **2**.[a]

Position	Compound			
	1		**2**	
	δ_C	δ_H	δ_C	δ_H
1	84.6	4.51 (s)	83.9	4.13 (d, 8.0)
2	197.2	—	73.0	4.59 (d, 8.0)
3	128.7	6.17 (q, 1.3)	129.8	5.84 (bs)
4	162.0	—	134.6	—
5	45.6	3.70 (d, 11.9)	45.1	3.32 (d, 12.3)
6	68.3	5.92 (dd, 11.9, 2.6)	68.9	5.93 (dd, 12.3, 2.5)
7	79.3	4.89 (d, 2.6)	79.9	4.78 (d, 2.5)
8	47.1	—	47.2	—
9	43.4	3.37 (s)	43.1	3.17 (s)
10	48.2	—	49.7	—
11	110.8	—	111.0	—
12	79.8	3.95 (d, 4.0)	79.9	3.98 (d, 4.6)
13	31.6	2.42 (qdd, 7.0, 6.0, 4.0)	31.6	2.43 (qdd, 7.1, 6.3, 4.6)
14	42.7	2.09 (ddd, 13.3, 6.5, 6.0)	42.6	2.01 (ddd, 13.0, 6.3, 5.8)
15	30.6	H_α 3.49 (dd, 18.9, 13.3) H_β 2.89 (dd, 18.9, 6.0)	30.5	H_α 3.38 (dd, 19.0, 13.0) H_β 2.88 (dd, 19.0, 5.8)
16	169.9	—	169.9	—
18	13.2	1.08 (d, 7.0)	13.1	1.08 (d, 7.1)
19	11.8	1.72 (s)	11.7	1.84 (bs)
30	70.7	4.39 (8.6) 3.84 (8.6)	71.0	4.45 (8.6) 3.84 (8.6)
4-Me	25.3	1.99 (bs)	24.6	1.87 (s)
2′-Me	12.3	1.88 (dd, 1.4, 1.1)	12.2	1.87 (dd, 1.4, 1.0)
3′-Me	14.5	1.61 (dq, 7.0, 1.1)	14.3	1.58 (dq, 7.1, 1.0)
1′	167.0	—	167.2	—
2′	128.8	—	129.0	—
3′	139.8	7.12 (dq, 7.0, 1.4)	139.1	7.06 (dq, 7.1, 1.4)

[a]Data are for solutions in pyridine-d_5, δ_C at 100.6 MHz, δ_H at 400 MHz; coupling constants in parentheses are reported in Hz.

an α,β-unsaturated ketone, bearing a β-methyl substituent.

Resonances at δ 3.42 (1H, d, J = 11.7 Hz), δ 4.67 (1H, dd, J = 11.7, 2.6 Hz), and δ 4.84 (1H, d, J = 2.6 Hz) were assigned to H-5, H-6, and H-7 on the basis of a COSY spectrum. Moreover, the H-6 proton was 1.25 ppm upfield compared with the corresponding proton in **1**. This, along with the absence of resonances due to a tiglate ester side chain, indicated that C-6 in **3** had a free hydroxyl group. The ^{13}C-nmr spectrum of **3** showed resonances for all twenty carbon atoms; they were assigned by the use of HETCOR and FLOCK experiments (Table 2). Hydrolysis of **1** with 1% KOH in MeOH led to a mixture of **3** and the new compound **4**. Compound **3** had physical and spectroscopic data identical with the natural compound.



4

Compound **4**, $C_{20}H_{24}O_2$, was isolated as white crystals, mp 242–243°. The ^{1}H-nmr spectrum was similar to that of **3**. The most notable difference was that the resonances at δ 3.42 and 4.67 in **3** were replaced by a resonance at δ 6.39 in **4**, suggesting that the H-6 hy-

TABLE 2. ^{13}C- and ^{1}H-nmr Assignments for Compounds **3** and **4**.[a]

Position	Compound			
	3		**4**	
	δ_C	δ_H	δ_C	δ_H
1	84.66	4.41 (s)	81.74	4.43 (s)
2	197.51	—	197.41	—
3	128.12	6.21 (1.5)	126.34	6.14 (1.2)
4	165.49	—	153.16	—
5	48.66	3.42 (11.7)	141.99	—
6	65.92	4.67 (11.7, 2.6)	126.05	6.39 (4.6)
7	83.22	4.84 (2.6)	74.68	4.99 (4.6)
8	47.18	—	45.34	—
9	43.52	3.36 (s)	42.36	3.39 (s)
10	48.18	—	44.34	—
11	110.90	—	111.00	—
12	79.85	4.01 (4.4, 4.3)	79.32	4.03 (4.6, 4.2)
13	31.58	2.47 (7.2, 6.8, 4.4)	31.51	2.52 (7.2, 6.8, 4.2)
14	42.89	2.06 (13.6, 6.8, 5.8)	41.62	2.16 (14.2, 6.8, 4.2)
15	30.76	H_α 3.53 (19.0, 13.6) H_β 2.90 (19.0, 5.8)	30.43	H_α 3.26 (18.8, 14.2) H_β 2.94 (18.8, 4.2)
16	170.33	—	170.65	—
18	13.24	1.13 (7.2)	13.63	1.15 (7.2)
19	11.69	1.74 (s)	18.52	1.84 (s)
30	70.96	4.32 (8.5) 3.85 (8.5)	72.62	4.00 (8.4) 3.97 (8.4)
4-Me	26.96	2.53 (bs)	20.70	1.98 (1.2)
12-OH	—	7.29 (4.3)	—	7.30 (4.6)

[a]Data are for solutions in pyridine-d_5, δ_C at 100.6 MHz, δ_H at 400 MHz; coupling constants in parenthesis are reported in Hz.

droxyl group was replaced by a double bond. The ^{13}C-nmr spectrum had signals for the new double bond at δ 126.05 and 141.99. Compound **4** was therefore determined to be Δ^5-chaparrinone. The complete assignment of the ^{1}H- and ^{13}C-nmr spectra (Table 2) was achieved by the use of HETCOR and FLOCK experiments.

Although not previously isolated as a natural product, 6α-hydroxychaparrinone [**3**] was obtained as a base hydrolysis product of 6α-senecioyloxychaparinone [**1**] (2).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Mp's were determined on a micro hot stage. Ir spectra were obtained on a Nicolet 3DX FTIR spectrometer. Uv spectra were obtained on a Cary 14UV spectrophotometer in MeOH. Nmr spectra were recorded on a Varian XL-400 spectrometer operating at 400 MHz for ^{1}H and at 100.6 MHz for ^{13}C, with TMS as the internal standard. A VG 70-250S mass spectrometer was used to obtain ms.

The plant material was collected at the Goethe Creek, Essequibo, in November, 1987. Voucher specimens (CAP 334) were deposited at the Jenman's Herbarium, University of Guyana and at the Institute for Systematic Botany, University of Utrecht.

The dried, ground roots (6.54 kg) were exhaustively extracted with 95% EtOH (93.5 liters). The extract was concentrated to a small volume (0.5 liters), defatted with hexane (5 × 200 ml), and subsequently extracted with CH_2Cl_2 to give a brown viscous syrup (167 g) on removal of the solvent. This material (5 g) was then chromatographed on Si gel using CH_2Cl_2 with increasing amounts of MeOH to give compounds **1** (56 mg), **2** (30 mg), and **3** (2 mg). Compounds **1** and **2** had spectroscopic and physical data in agreement with those reported in the literature (8).

Compound **3**.—Colorless needles (MeOH): mp 233–235°; ir (KBr) 3440, 1740, 1680 cm^{-1}; uv 242 nm (ε 8000); ^{1}H and ^{13}C nmr see Table 2; eims *m/z* [M]$^+$ 394 (72%), 376 (22), 347 (22), 329 (20), 245 (100), 231 (20), 227 (26), 199 (24); hreims 394.1644, calcd for $C_{20}H_{26}O_8$, 394.1628.

Compound **1** (300 mg) was hydrolyzed with 1% KOH/MeOH (10 ml) for 6 h under an N_2 atmosphere. The reaction mixture was acidified (10% HCl) and evaporated to dryness. Cc of the crude material gave compounds **3** (9.5 mg) and **4** (10.0 mg).

Compound **4**.—Mp 242–243°; [α]D −278.0° (*c* = 0.03, pyridine); ir ($CHCl_3$) 3450, 1735, 1680, 1602 cm^{-1}; uv (MeOH) 230 nm (ε 7,100) 280 nm (ε 14300); ^{1}H and ^{13}C nmr see Table 2; eims [M]$^+$ 376 (86%), 361 (52), 343 (100), 330 (27), 315 (16), 247 (25), 231 (18), 173 (13); hreims 376.1530, calcd for $C_{20}H_{24}O_7$, 376.1522.

ACKNOWLEDGMENTS

The Centre at the University of Guyana received support from the Canadian International Development Agency. Research at the University of Toronto was supported by grants from the Natural Sciences and Engineering Research Council of Canada.

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Received 20 April 1992