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POLYANDROL, A C_{19} QUASSINOID FROM *CASTELA POLYANDRA*

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Key Word Index—*Castela polyandra*; Simaroubaceae; root bark; quassinoids; bitter principles; polyandrol; glaucarubolone; glaucarubol; peninsularinone.

Abstract—The structure of a new C_{19} bitter-tasting quassinoid, polyandrol, isolated from the root bark of *Castela polyandra*, was established.

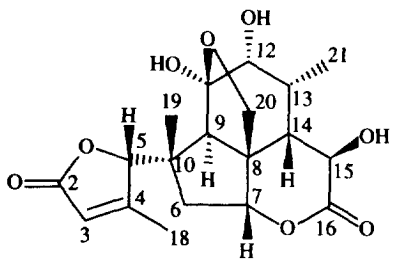
INTRODUCTION

Our continuing search for novel quassinoids from simaroubaceous plants, [1] led us to examine the root bark of *Castela polyandra*. We now report on the isolation and characterization of a new C_{19} quassinoid [(+)-polyandrol (**1**)] along with glaucarubolone (**2**), glaucarubol (**3**), and peninsularinone (**4**).

RESULTS AND DISCUSSION

The methanol extracts of the root bark of *Castela polyandra* afforded glaucarubolone (**2**), glaucarubol (**3**), peninsularinone (**4**), and a new C_{19} quassinoid (**1**) possessing the 1,2-seco-1-nor-6(5 → 10)-abeo-picrasan-2,5-olide skeleton. The structures of **2**–**4** were identified by comparison of their respective ^1H and ^{13}C NMR spectra with those obtained from either synthetic or natural material.

The structure of **1**, mp 190–192°, was established by a combination of IR, ^1H and ^{13}C NMR spectroscopy, and mass spectrometry. The mass spectrum as well as the elemental analysis of **1** indicated a molecular formula of $C_{19}H_{24}O_8$. A comparison of the ^1H NMR spectrum of **1** with that of glaucarubolone (Table 1) revealed that the spectra were strikingly similar with respect to the CDE rings of glaucarubolone. Thus the CDE tricyclic system



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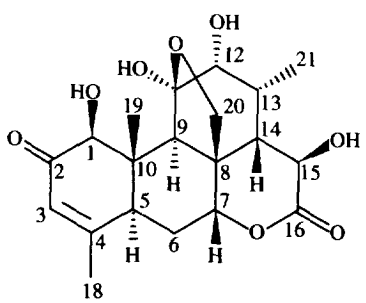

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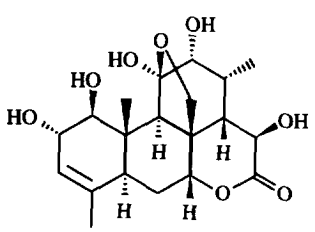

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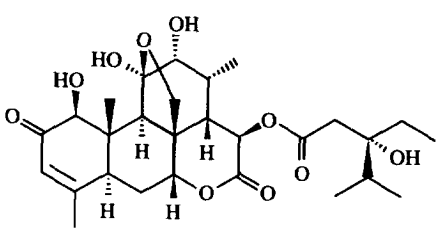

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common to **2** was proposed as a partial structure after extensive decoupling experiments were carried out.

The absence of protons in **1** corresponding to the ring A 1β-hydroxy-2-oxo-$\Delta^{3,4}$ olefin unit, which is common to numerous quassinoids, suggested the presence of a 1,2-seco-1-nor-6(5 → 10)-abeo-picrasan-2,5-olide skeleton which has been found on three previous occasions in C_{19} quassinoids isolated from simaroubaceous plants [2–5]. Consistent with this suggestion is the presence of an α,β-unsaturated γ-lactone (1730 cm^{-1}) in the IR spectrum and an olefinic proton (δ5.91, *br s*) and a methine hydrogen (δ5.01, *br s*) in the ^{1}H NMR spectrum. In addition, the ^{1}H NMR spectrum of **1** revealed that the C-6 protons at δ2.96 and 2.30 were only coupled to the C-7 proton at δ4.70.

Table 1. ^{1}H NMR spectral data for compounds **1** and **2** (in pyridine-d_5, 500 MHz)

H	1	2
1	—	4.31 *s*
3	5.91 *br s*	6.07 *br s*
5	5.01 *br s*	3.11 *br d* (11.6)
6α	2.96 *d* (16.0)	2.15 *ddd* (14.6, 3.2, 2.4)
6β	2.30 *dd* (16.0, 4.4)	2.00 *ddd* (14.6, 11.6, 1.2)
7	4.70 *d* (4.4)	4.68 *br s*
9	3.37 *s*	3.31 *s*
12	4.05 *d* (4.0)	4.10 *d* (4.5)
13	2.63 *m*	2.70 *m*
14	2.56 *dd* (10.1, 6.2)	2.34 *dd* (11.2, 6.2)
15	5.36 *d* (10.1)	5.46 *d* (11.2)
18	2.45 *br s*	1.71 *br s*
19	1.50 *s*	1.55 *s*
20	3.91 AB*q* (9.0)	3.98 AB*q* (8.6)
21	1.68 *d* (7.2)	1.72 *d* (7.8)

Table 2. ^{13}C NMR spectral data (125 MHz) for compound 1 (in pyridine-d_5)

C	1
2	172.6
3	119.0
4	170.0
5	92.1
6	46.2
7	83.5
8	58.2
9	45.7
10	46.5
11	111.4
12	81.1
13	34.6
14	46.3
15	68.5
16	174.2
18	16.1
19	18.4
20	72.3
21	15.6

The complete assignments of ^{1}H and ^{13}C NMR resonances were established by a combination of 2D techniques, ^{1}H–^{1}H COSY and ^{13}C–^{1}H COSY. The data in Tables 1 and 2 are in complete accord with the structure proposed for polyandrol. The stereochemistry at C-5 was determined by one-dimensional NOE experiments. Irradiation of the signal at δ3.37 (H-9) gave rise to NOE enhancements at H-5, H-15, and the C-4 methyl group (see Fig. 1). The observed NOE enhancement between H-9 and H-15 confirms the β-orientation of the hydroxyl group at C-15. Irradiation of the H-5 signal gave rise to NOE enhancements at H-6α, H-9, and the C-4 methyl group. On the basis of this analysis and biosynthesis considerations, the absolute stereochemistry at C-5 is assigned the *R* configuration.

EXPERIMENTAL

General. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM-500 MHz spectrometer. Chemical shifts are reported in ppm (δ) relative to tetramethylsilane (δ0.0). Elemental analyses were performed by Robertson Microlit Laboratories, Inc., Madison, N. J. Mp: uncorr. TLC was performed using E. Merck precoated silica gel 60 F-254 (0.25 mm thickness) plates. The plates were visualized by immersion in a *p*-anisaldehyde solution and warming on a hotplate. E. Merck silica gel 60 (230–400 mesh) was used for flash silica gel chromatography. All chromatography solvents are reagent grade unless otherwise stated. Fr. collecting commenced after the elution of one solvent front from the column.

Plant material. The root bark of *Castela polyandra* was procured from Baja California on April 15, 1993 by World Botanical Associates.

Extraction and isolation. Dried, ground root bark (426 g) was soaked in 1200 ml MeOH. After 3 days the plant material was drained and rinsed with MeOH (3 × 500 ml). The process was repeated on the same 426 g of plant material a total of nine times. The combined MeOH extracts and washings were concd *in vacuo* to a brown

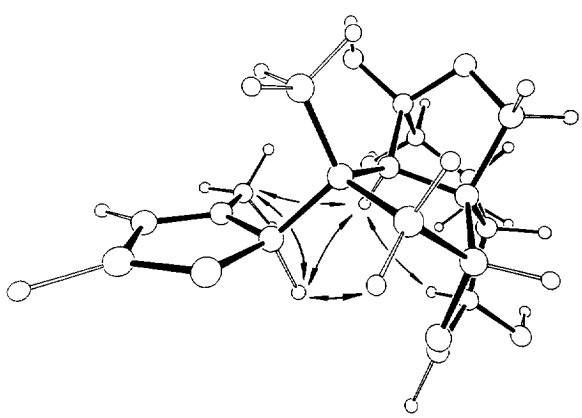

Fig. 1. Low energy conformer of **1** calculated by PC MODEL. Arrows show NOE relationship.

sludge which was diluted with 20% MeOH–$CHCl_3$ (950 ml), stirred for 16 hr, and filtered through a pad of flash silica gel (250 g), washing well with 20% MeOH–$CHCl_3$. The filtrate and washings were concd *in vacuo* to a brown foam (*ca* 26.7 g). The brown foam was purified by chromatography on 1180 g of flash silica gel (packed in 10% MeOH–$CHCl_3$). Elution (200 ml frs) with 10% MeOH–$CHCl_3$ followed by 15% MeOH–$CHCl_3$ after fr. 29 afforded four portions: frs 5–13 (portion I) provided 4.3 g of a brown sludge; frs 18–24 (portion II) provided 1.4 g of a yellow-white solid; frs 25–37 (portion III) provided 0.89 g of a yellow-white solid; and frs 39–48 (portion IV) provided 0.95 g of an off-white solid.

Portion I (4.3 g) was purified by chromatography on 250 g of flash silica gel (packed in 5% MeOH–$CHCl_3$). The column was successively eluted, collecting 15 ml frs: frs 18–61 were combined and concd *in vacuo* to provide 1.23 g of a brownish-yellow solid. The crude product (1.23 g) was repurified by chromatography on 237 g of flash silica gel (packed in 5% MeOH–$CHCl_3$). The column was successively eluted, collecting 15 ml frs: frs 17–26 were combined and concd *in vacuo* to provide 0.70 g of a yellow solid. The yellow solid (700 mg) was further purified by prep. TLC (6 plates, 2.0 mm thickness, 5% MeOH–$CHCl_3$, triple elution) to afford 334 mg of a yellow-white foam. The resultant yellow-white foam (334 mg) was purified by chromatography on 80 g of flash silica gel (packed in EtOAc). The column was successively eluted, collecting 8 ml frs: frs 21–60 were combined and concd *in vacuo* to provide (118.1 mg) a white solid. Additional purification of the white solid (118.1 mg) was accomplished by prep. TLC (8 plates, 0.5 mm thickness, EtOAc) and provided 78.6 mg of a white solid which crystallized from EtOAc giving rise to 33.1 mg of **4** as small needles: mp 219–221° (ref. [1] 220–222°). Peninsularinone (**4**) was identified by comparison of its spectroscopic data (IR, MS, ^1H, ^{13}C NMR) with those reported previously in the literature [1]. Purification of the mother liquor by prep. TLC (4 plates, 0.5 mm thickness, EtOAc) afforded another 24 mg of **4** as a solid.

Portion II was purified by chromatography on 243 g of flash silica gel (packed in 10% MeOH–$CHCl_3$). The column was successively eluted, collecting 15 ml frs: frs 18–62 were collected and concd *in vacuo* to afford 1.26 g of a yellow-white solid which was combined with 370 mg (IIIA) of crude **2** from portion III and crystallized from MeOH to give 0.582 g crystalline glaucarubolone (**2**), mp 254–257° (ref. [5] 255–258°), which was identified by comparison of its spectroscopic data (IR, MS, ^1H, ^{13}C NMR) with those reported previously in the literature [5]. Recrystallization provided a second crop of crystalline **2** (331 mg). The mother liquor (*ca* 600 mg) was purified by chromatography on 160 g of flash silica gel (packed with EtOAc). The column was successively eluted with 15 ml fractions: frs 29–68 were collected and concd *in vacuo* to provide 306 mg of a solid which crystallized from MeOH to give 140.7 mg of crystalline **2**. Purification of the mother liquor (1.10 g) by prep. TLC (6 plates, 0.6 mm thickness, EtOAc, triple elution) afforded another 40.3 mg of **2** as a solid.

Portion III (890 mg) was purified by chromatography on 140 g of flash silica gel (packed with 10% MeOH–$CHCl_3$). The column was successively eluted with 15 ml frs: frs 13–22 (IIIA) were combined and concd *in vacuo* to give *ca* 340 mg of crude **2** which was combined and purified with portion II: frs 23–53 (IIIB) were combined and concd *in vacuo* to give 365 mg of a yellow-white solid. The yellow solid was repurified by chromatography on 80 g of flash silica gel. Elution with 10% MeOH–$CHCl_3$ (7.5 ml frs) afforded (frs 21–36) 177 mg of a yellow-white solid. Further purification was provided by chromatography of the yellow-white solid (177 mg) on 75 g of flash silica gel (packed with EtOAc). The column was successively eluted, collecting 8 ml frs: frs 24–41 gave rise to 72.5 mg of **1** as a solid.

Portion (IV) (950 mg) was crystallized from MeOH to give 0.580 g of glaucarubol (**3**) as fine needles, mp 280–282° (ref. [6] 285°). Glaucarubol (**3**) was identified by comparison of its spectroscopic data (IR, MS, ^1H, ^{13}C NMR) with those reported previously in the literature [7]. Successive recrystallization from methanol provided an additional 300 mg of **3**.

(+)-*Polyandrol* (**1**). R_f 0.17 (EtOAc), 0.23 (5% MeOH–$CHCl_3$); FTIR ν^{KBr} cm^{-1}: 3435 (*br s*), 2936 (*m*), 1730 (*s*), 1634 (*m*), 1447 (*m*), 1383 (*m*), 1233 (*s*), 1190 (*s*), 1100 (*s*), 1015 (*s*), 985 (*s*), 868 (*m*). HRMS (CI) calcd for $C_{19}H_{25}O_8$ [M + 1] *m/z* 381.1549, found 381.1541. An analytical sample was prepared by recrystallization from EtOAc: mp 190–192°; $[\alpha]_D^{25}$ + 69.6° (MeOH; *c* 1.17). Anal. calcd. for $C_{19}H_{25}O_8$: C, 59.99; H, 6.36. Found: C, 59.84; H, 6.41.

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