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ISOCONCINNDIOL, A BROMINATED DITERPENOID FROM *LAURENCIA SNYDERAE* VAR. *GUADALUPENSIS*

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Key Word Index *Laurencia snyderae* var. *guadalupensis*; Rhodomelaceae; marine natural products; isoconcinndiol.

Abstract—A new brominated diterpenoid, isoconcinndiol, has been isolated from the marine red alga *Laurencia snyderae*.

INTRODUCTION

Previous investigations of the natural products chemistry of the marine alga *Laurencia snyderae* Dawson (Rhodomelaceae, Rhodophyta) have resulted in the isolation of the brominated diterpenoid concinndiol (**1**) [1]. Concinndiol was first isolated as a natural product from *Laurencia concinna* from Australia [2]. In our studies of the natural products chemistry of various unknown *Laurencia* species from the Galapagos Islands, we [3] have isolated the closely related brominated diterpenoid aplysin-20 (**2**) which was first described as a constituent of the Japanese sea hare, *Aplysia kurodai* [4]. More recently a tricyclic representative of this class, isoaplysin-20 (**3**), was also isolated from *Aplysia* [5]. We wish to report here the isolation and structure elucidation of a new diterpenoid of this class, isoconcinndiol (**4**).

RESULTS AND DISCUSSION

Open column silica gel chromatography of the chloroform–methanol extract of fresh *Laurencia snyderae* var. *guadalupensis* Dawson (Guadalupe Island, Mexico, 1978) gave, upon diethyl ether elution, isoconcinndiol (**4**), as a white crystalline solid, mp 173–174°. Mass spectral analysis of **4** established a molecular formula of $C_{20}H_{33}BrO$ for the $M^+ - H_2O$ fragment at *m/e* 368/370, and showed fragments at *m/e* 270/272 and 191 (Scheme 1) which are identical with the mass spectral behavior of both **1** and **2**. The infra-red spectrum showed hydroxyl (3500 cm^{-1}) and olefinic absorptions (3000, 999 and 920 cm^{-1}). The ^1H NMR spectrum of **4** revealed the presence of a terminal vinyl group [δ 5.91 (1H, *dd*, $J = 15, 10$ Hz), 5.17 (1H, *dd*, $J = 15, 2$ Hz) and 5.02 (1H, *dd*, $J = 10, 2$ Hz)], an alpha to bromine proton with bromine situated equatorial in a cyclohexane ring [δ 3.95 (1H, *dd*, $J = 12, 4$ Hz)], and five methyl singlets, which are similar features exhibited by compounds **1** and **2**.

Several attempts were made to interconvert **1**, **2** and **4**. Methods involving acid-catalysed allylic hydroxyl rearrangements gave only mixtures of inseparable brominated hydrocarbons. Treatment of **2** and **4** with pyridinium chlorochromate gave the same α,β-unsaturated aldehyde as determined by TLC. However, this aldehyde proved to be unstable and could not be isolated in pure form.

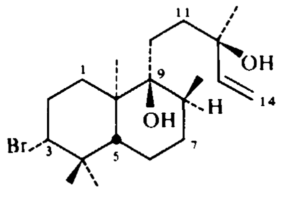
To place the structure proposal for isoconcinndiol on a more firm basis, a detailed comparison of the ^{13}C NMR spectra of compounds **1**, **2** and **4** was performed. Table 1 presents the ^{13}C NMR spectra of these brominated diterpenoids in which all methine and quaternary carbons are assigned. These assignments were greatly aided by off-resonance proton decoupling. The carbons which structurally differ between **1**, **2** and **4** are C-8, C-9, C-13, C-14 and C-15. However, isoconcinndiol (**4**) differs from concinndiol (**1**) only at C-8 and C-9 and aplysin-20 (**2**)

Table 1. ^{13}C NMR chemical shift assignments for concinndiol (**1**), aplysin-20 (**2**) and isoconcinndiol (**4**)*

Carbon	**1**	**2**	**4**
3	71.2 *d*	70.9 *d*	70.6 *d*
4	40.2 *s*	40.4 *s*	40.0 *s*
5	47.5 *d*	57.0 *d*	57.1 *d*
8	38.3 *d*	72.2 *s*	70.6 *s*
9	76.8 *s*	59.1 *d*	62.3 *d*
10	44.2 *s*	39.8 *s*	41.7 *d*
13	73.2 *s*	138.1 *s*	73.7 *d*
14	147.0 *d*	125.7 *d*	147.2 *d*
15	111.4 *t*	59.5 *t*	111.2 *t*
	Unassigned Methyl and Methylene Carbons		
	37.1	44.0	45.9
	34.5	43.3	45.0
	32.7	41.3	32.7
	32.1	31.7	30.8
	†	31.6	30.6
	†	30.7	29.3
	†	30.7	24.4
	24.0	24.7	22.7
	18.7	20.7	20.0
	16.8	18.8	18.5
	16.7	15.7	15.8

* All spectra run in acetone-d_6 solution and reported in ppm relative to TMS(0).

† Signals obscured by acetone-d_6.



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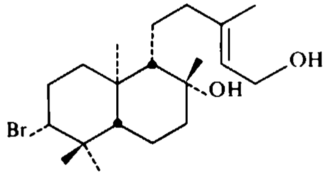

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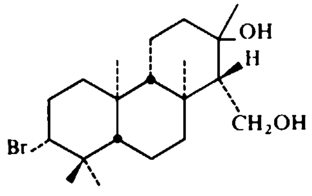

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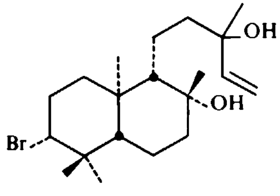

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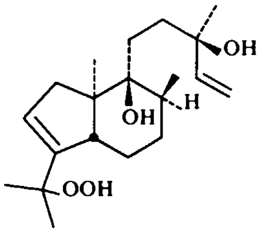

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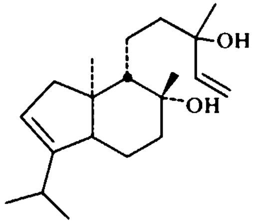

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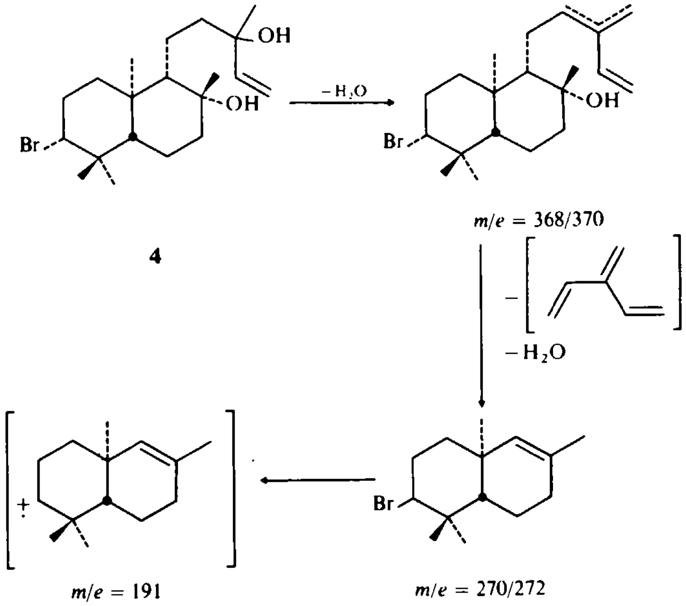

Scheme 1. Mass spectral fragmentation of isoconcinndiol.

differs from isoconcinndiol only at C-13, C-14 and C-15. These relationships are substantiated in their respective ^{13}C NMR spectra.

Evidence for the presence of a C-8 axial hydroxyl in isoconcinndiol as in **2** rather than a C-8 equatorial hydroxyl as in sclareol was provided by mass spectral analysis. Sclareol and similar diterpenes with a C-8 equatorial hydroxyl or an exocyclic double bond show a prominent fragmentation between C-6 and C-7 and C-9 and C-10 (an $M^+ - 170$ for sclareol) [6]. This fragmentation is absent in both **2** and **4** and suggests that the C-8 hydroxyl on **4** is axial.

It has been suggested that nonhalogenated terpenes in *Laurencia* may arise from halogenated precursors [7]. For instance, neoconcinndiol hydroperoxide (**5**) may be envisioned to be derived from concinndiol (**1**) via solvolysis of the C-3 equatorial bromine followed by concerted ring contraction, elimination and subsequent oxidation [3]. In an effort to examine the rearrangement potential of brominated labdanes, **4** was subjected to reaction with various silver salts. Treatment with $AgBF_4$ in anhydrous diethyl ether at -20° for 3 hr gave a smooth conversion to the ring-contracted product **6** (77 % yield). The facile nature of this reaction lends support to these previous contentions.

EXPERIMENTAL

Isolation of isoconcinndiol (**4**). Freshly collected *Laurencia snyderae* var. *guadalupensis* (10 kg) was homogenized with MeOH and the homogenate repeatedly extracted with $CHCl_3$ to yield 60 g of crude extract after solvent removal *in vacuo*. Fractionation over Si gel (Grace Chemical, grade 62) gave, upon Et_2O elution, fractions which yielded crystalline samples of **3**. Recrystallization from $CHCl_3$ gave analytically pure isoconcinndiol, mp 173-174° ^{1}H NMR (220 MHz, $CDCl_3$): δ 5.95 (1H, *dd*, J = 15, 10 Hz), 5.17 (1H, *dd*, J = 15, 2 Hz), 5.02 (1H, *dd*, J = 10, 2 Hz, 3.95 (1H, *dd*, J = 12, 4 Hz), 3.10 (1 H, *s*, OH), 2.42 (1 H, *s*, OH), 1.24 (3 H, *s*), 1.14 (3H, *s*), 1.06 (3H, *s*), 0.90 (3H, *s*), 0.81 (3H, *s*); IR $\nu_{\max}^{\mathrm{CHCl_3}}$: 3500, 3050, 2950, 1450, 1390, 1370, 1315, 1185, 1160, 999, 920; MS (70 eV) m/e: 368/370 ($M^+ - H_2O$), 270/272 ($M^+ - 2H_2O - C_6H_8$), 191 ($M^+ - 2H_2O - C_6H_8 - Br$).

Attempted oxidation of aplysin-20 (**2**) *and isoconcinndiol* (**4**) *with pyridinium chlorochromate*. In separate experiments 30 mg of compounds **2** and **3** were dissolved in CH_2Cl_2 (5 ml) and excess pyridium chlorochromate (100 mg) was added with stirring. After 1 hr TLC analyses (petrol–Et_2O, 80:20) of the reaction mixtures showed that identical UV active aldehydes had been produced. The reaction mixtures were passed over a Si gel column for work-up and the CH_2Cl_2 removed *in vacuo*. However, the aldehyde produced proved to be unstable to these work-up conditions and could not be isolated in pure form.

Silver tetrafluoroborate rearrangement of isoconncindiol. Isoconncindiol (**4**) (50 mg, 0.13 mmol) was dissolved in dry Et_2O (20 ml) and cooled to -20 with an ice Me_2CO bath. $AgBF_4$ (125 mg, 0.65 mmol; 5-fold excess) was added and the suspension was stirred at -20°. After 3 hr the reaction mixture was poured onto ice and extracted with Et_2O (3 × 50 ml). Prep. TLC of the reaction mixture (Si gel, Et_2O–hexane 1:1) gave pure samples of the rearrangement product, **6** (30 mg, 0.10 mmol, 77 % yield) as an oil. ^{1}H NMR (60 MHz, CCl_4): δ 5.83 (1H, *dd*, J = 17, 10 Hz), 5.13 (1H, *dd*, J = 17, 2 Hz), 4.90 (1H, *dd*, J = 10, 2 Hz), 1.28 (3H, *s*), 1.25 (3H, *s*), 0.98 (3H, *d*, J = 7 Hz), 0.92 (3H, *d*, J = 7 Hz), 0.85 (3H, *s*).

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