

A New 1,2-Dihydroisoquinoline from the Sponge *Petrosia similis*[†]

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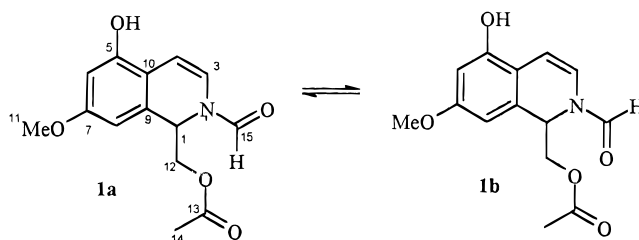
A new 1,2-dihydroisoquinoline (**1**) and a known isoquinolinequinone (**2**) have been isolated from the sponge *Petrosia similis* and characterized by the study of spectral data.

As a part of our research on the isolation and characterization of biologically active compounds from marine organisms, we investigated a bright-blue sponge *Petrosia similis* collected from the Mandapam coast (N 9°18', E 79°08'), near Sethukarai, Tamilnadu, of India during October 1997. A literature survey revealed that the genus *Petrosia* yields high molecular weight polyacetylenes,^{1,2} nitrogen-containing polyaromatic pigments^{3,4} and petrosin, a bisquinolizidine alkaloid.⁵

The 1:1 dichloromethane-methanol extract of the sponge *P. similis* was subjected to gel filtration chromatography followed by silica gel chromatography and afforded the known compounds mimosamycin,⁶ *O*-demethylrenierol acetate,⁷ *p*-hydroxybenzaldehyde, *N*-formyl-1,2-dihydrorenierone,⁸ and 4-aminomimosamycin,⁹ in addition to a new compound, *N*-formyl-1,2-dihydroisoquinoline derivative **1**, which exists as an inseparable mixture of conformers (**1a** and **1b**).

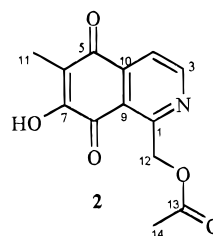
Compound **1** was obtained as an amorphous solid; $[\alpha]_D^{25} +208^\circ$ (*c* 0.725, CHCl₃), showed molecular ion at *m/z* 277, and analyzed for C₁₄H₁₅NO₅ by HREIMS. Ultraviolet measurements [(MeOH) λ_{\max} 224 (ϵ 6656), 228 (ϵ 6676), 231 (ϵ 6653), and 299 (ϵ 4786) nm; UV (MeOH + 10% NaOH) λ_{\max} 229 (ϵ 7013), 232 (ϵ 7002), 305 (ϵ 3385), and 327 (ϵ 3000) nm] indicated the phenolic nature of the compound. The IR spectrum showed bands for the presence of hydroxyl (3450 cm⁻¹), ester (1735 cm⁻¹), and amide (1630 cm⁻¹) groups. Both the ¹H and ¹³C NMR spectra (Table 1) of compound **1** showed the presence of a pair of signals as noticed for *N*-formyl-1,2-dihydrorenierone, an *N*-formyl-1,2-dihydroquinone derivative isolated from the sponge *Reniera* sp.⁸ From the study of ¹H and ¹³C NMR spectral data (Table 1), compound **1** was recognized as an *N*-formyl-1,2-dihydro-5-hydroxy-7-methoxyisoquinoline derivative. These spectra were readily interpreted by assuming that the partial double bond character of the *N*-formyl bond permits the observation of signals for two conformers on the NMR time scale.⁸ The structures of the minor (**1a**) and major (**1b**) conformers were assigned by the study of ¹H–¹H COSY, NOESY, and NOE difference experiments (Table 1).

The ¹H NMR data for the major conformer **1b** are recorded in Table 1. The signal at δ 8.35 (1H, s) was attributed to an *N*-formyl group. The signals at δ 6.71, 6.68, 6.49, 5.86, and 5.79 were attributed to a 1,2-dihydro-1,5,7-trisubstituted isoquinoline system. The ¹H–¹H COSY spectrum established a vicinal relationship between the C-1 methine proton at δ 5.79 and the C-12 methylene protons at δ 4.21 and 3.96. The disposition of the methoxyl group was established by a NOE difference experiment. Irradia-



tion of the methoxy signal at δ 3.90 caused enhancement (5%) of the signals at δ 6.71 (H-6) and 6.68 (H-8) which indicated that the methoxyl was at C-7. Irradiation of the *N*-formyl hydrogen of the major isomer (**1b**) at δ 8.35 caused enhancement (6%) of the signal at δ 6.49 (H-3), whereas irradiation the *N*-formyl hydrogen of the minor isomer (**1a**) at δ 8.10 caused enhancement (4%) of C-1 methine signal at δ 4.94 (H-1). Further, irradiation of the C-1 methine of minor isomer (**1a**) signal at δ 4.94 caused enhancement (6%) of signals at δ 6.68 (H-8) and formyl group at δ 8.10. The foregoing spectral data established the structure and geometry of the conformers **1a** and **1b**. Thus the structure of compound **1** was established as 2-formyl-5-hydroxy-7-methoxy-1,2-dihydro-1-isoquinolinyl-methyl acetate (**1**).

Compound **2** was identified as the known isoquinolinequinone, *O*-demethyl renierol acetate (**2**) by its characteristic ¹H NMR signals and mass spectral data.⁷ Compound



2 was earlier isolated by us from an unidentified sponge *Petrosia* sp.,⁷ and now its ¹³C NMR data¹⁰ are reported.

Compounds **1** and **2** did not show any significant toxicity against brine shrimp. Compound **2** was found to be active against *Staphylococcus aureus* (14 mm), *Bacillus subtilis* (16 mm), *Escherichia coli* (12 mm), and *Klebsiella pneumoniae* (12 mm) at a concentration of 100 μ g per disk (6.5 mm diameter). Compound **1** did not show any bactericidal activity.

Experimental Section

General Experimental Procedures. The ¹H and ¹³C NMR spectra were recorded on Varian Unity 400 MHz or Varian Gemini 200 MHz spectrometers using TMS as internal standard. Chemical shifts are reported in parts

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Table 1. NMR Data for Compounds **1a** and **1b**

C no.	Compound 1a (minor)				Compound 1b (major)			
	¹³ C ^b	¹ H ^a mult., <i>J</i> (Hz)	COSY	NOESY	¹³ C ^b	¹ H ^a mult., <i>J</i> (Hz)	COSY	NOESY
1	51.14 d	4.94 dd, 3.75, 10.35	H-12a, H-12b	H-8, H-12a, H-12b, H-15	51.14 d	5.79 dd, 4.19, 8.60	H-12a, H-12b	H-8, H-12a, H-12b
2								
3	119.45 d	6.98 d, 7.72	H-4	H-4	122.71 d	6.49 d, 7.50	H-4	H-4, H-15
4	112.08 d	5.98 d, 7.72	H-3	H-3	111.56 d	5.86 d, 7.50	H-3	H-3
5	146.10 s				146.22 s			
6	111.40 d	6.72 s		H-11	110.25 d	6.71 s		H-11
7	146.10 s				145.78 s			
8	109.23 d	6.68 s		H-1, H-11	109.80 d	6.68 s		H-1, H-11
9	119.45*s				119.73 ⁺ s			
10	124.89*s				124.37 ⁺ s			
11	56.11 q	3.91 s		H-6, H-8	56.22 q	3.90 s		H-6, H-8
12a	63.71 t	3.98 dd, 3.75, 11.68	H-1, H-12b	H-1, H-12b	64.02 t	3.96 dd, 4.19, 11.45	H-1, H-12b	H-1, H-12b
12b		4.09 dd, 10.35, 11.68	H-1, H-12a	H-1, H-12a		4.21 dd, 8.60, 11.45	H-1, H-12a	H-1, H-12a
13	170.49 s				170.82 s			
14	20.69 q	2.11 s			20.82 q	2.02 s		
15	160.56 d	8.10 s		H-1	161.92 d	8.35 s		H-3

^a 400 MHz, CDCl₃. ^b 50 MHz, CDCl₃; for entries marked with "*" or "+", values may interchange.

per million, and coupling constants (*J*) are expressed in Hertz. UV spectra were recorded on a Shimadzu-240 spectrophotometer. IR spectra were recorded on a Perkin-Elmer 240-C spectrophotometer. The mass spectra were recorded on a VG Auto Spec-M instrument.

Animal Material. The sponge *P. similis* (Ridley & Dendy) was collected along the Mandapam coast in the Gulf of Mannar during October 1997, and a voucher specimen (IIC-273) is on deposit at National Institute of Oceanography, Goa, India.

Extraction and Isolation. The freshly collected specimen (0.5 kg dry weight after extraction) was extracted with CH₂Cl₂-MeOH (1:1, 3 × 1.5 L) at room temperature. The combined extract was filtered and the solvent was removed under reduced pressure to yield a brownish gum (30 g). The crude extract was partitioned between water and ethyl acetate. The organic layer was concentrated under vacuum and subjected to gel filtration chromatography [Sephadex LH-20, CH₂Cl₂-MeOH (1:1)] followed by silica gel chromatography eluting with hexane, hexane-EtOAc mixtures, and finally with EtOAc to afford mimosamycin (75 mg), *O*-demethylrenierol acetate (**2**) (30 mg), *p*-hydroxybenzaldehyde (5 mg), *N*-formyl-1,2-dihydrorenierone (50 mg), 4-aminomimosamycin (20 mg), and compound **1** (25 mg).

Compound 1: amorphous white solid; [α]_D²⁵ +208° (*c* 0.725, CHCl₃); UV (MeOH) λ_{\max} 224 (ϵ 6656), 228 (ϵ 6676), 231 (ϵ 6653), 299 (ϵ 4786) nm; UV (MeOH + 10% NaOH) λ_{\max} 229 (ϵ 7013), 232 (ϵ 7002), 305 (ϵ 3385), 327 (ϵ 3000) nm.; IR ν_{\max} (neat) 3450, 1735, 1630 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz), see Table 1; ¹³C NMR (CDCl₃, 50 MHz), see Table 1; EIMS *m/z* 277 [M]⁺ (3), 205 (10), 204 (100), 176 (80), 161 (45), 133 (25), 83 (30), 57 (50), 43 (60); HREIMS *m/z* 277.0957 [M]⁺, calcd for C₁₄H₁₅NO₅, 277.0950.

Compound 2: pale yellow oil; UV (MeOH) λ_{\max} 226 (ϵ 19, 400), 300 (ϵ 4094) nm; IR (neat) ν_{\max} 3500, 1735, 1680 cm⁻¹; ¹H NMR as reported in lit;⁷ ¹³C NMR (CDCl₃, 50 MHz) δ 8.50 (q, C-11), 20.73 (q, C-14), 65.34 (t, C-12), 119.08 (d, C-4), 120.34 (s, C-6), 120.49 (s, C-9), 139.87 (s, C-10), 153.62 (d, C-3), 155.19 (s, C-7), 156.62 (s, C-1), 170.32 (s, C-13), 181.17 (s, C-8), 183.41 (s, C-5); EIMS *m/z* 261 [M]⁺ (23), 233 (28), 219 (30), 191 (40), 147 (50), 117 (35), 43 (100).

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