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A SPATANE DITERPENE FROM THE BROWN ALGA *STOECHOSPERMUM MARGINATUM**

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Key Word Index—*Stoechospermum marginatum*; brown alga; diterpene; cytotoxic.

Abstract—A new spatane diterpene, 17,18-epoxy, 5(*R*),16-dihydroxyspat 13(14)-ene, has been isolated from a brown alga *Stoechospermum marginatum* and characterized by interpretation of spectral data and confirmed by synthesis.

INTRODUCTION

Spatanes are 5-4-5 membered tricyclic diterpenes which have not been reported from terrestrial sources. Spatol (**2**), the first member of this class of diterpenes, was first isolated from the brown alga *Spatoglossum schmittii* [1] and subsequently from *Stoechospermum marginatum* [2,3]. Some of this class of diterpenes show cytotoxic [1] and antibacterial [4] activities. In a continuation to our search for biologically active compounds from marine organisms [5, 6], we investigated *St. marginatum* collected from the Gulf of Mannar near Mandapam (9°16′ N, 79°12′E), during March 1994.

RESULTS AND DISCUSSION

The 1:1 dichloromethane–methanol extract of the alga afforded seven known spatane derivatives: 5(*R*)-hydroxy spata 13,17-diene (**3**, 40 mg); 5(*R*),18-dihydroxy spata 13,16-diene (**4**, 30 mg); 5(*R*),16-dihydroxy spata 13,17-diene (**5**, 400 mg); 5-oxo, 15,18,19-trihydroxy spata 13,16-diene (**6**, 36 mg); 5(*R*),15,18(*R*/*S*), 19-tetrahydroxy spata 13,16-diene (**7**, 130 mg); 19-acetoxy, 5(*R*), 15,16-trihydroxy spata 13,17-diene (**8**, 25 mg); an isomeric mixture of 5(*R*), 17(*S*/*R*)-dihydroxy spata 13,18-diene (**9**, 80 mg) and a new epoxy spatane (**1**). Compounds **3**–**9** were characterized by comparing their spectral data with those reported in the literature [2].

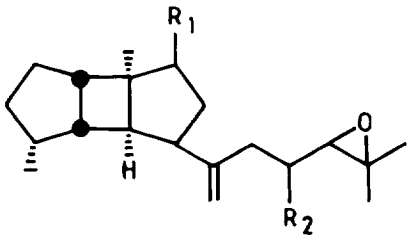
Compound **1** was analysed for $C_{20}H_{32}O_3$ and showed no UV absorption above 210 nm. Peaks in the IR spectrum at 3450 and 895 cm^{-1} indicated the presence of hydroxyl and methylene groups. Compound **1** formed a diacetate (**1a**) upon acetylation with Ac_2O/Py. Its ^1H NMR spectrum showed the presence of four methyl groups [δ0.93 (3H, *d*, J = 7 Hz), 1.0 (3H, *s*), 1.2 (3H, *s*), 1.35 (3H, *s*)], an end methylene group [δ4.85 (1H, *br s*), 4.95 (1H, *br s*)] and three oxygen-bearing methine groups [δ3.75 (1H, *d*, J = 4.5 Hz), 3.65 (1H, *q*, J = 7 Hz) and 2.65 (1H, *d*, J = 7 Hz)]. The signals at δ3.75 and 3.65 were shifted downfield to δ4.9 (2H, *m*) in the ^1H NMR spectrum of the diacetate (**1a**) and were thus attributable to two secondary hydroxyls. The signal at δ2.65 was attributed to the methine proton of the trisubstituted oxyrane ring. These findings were supported by the presence of ^{13}C NMR signals at δ80.3 *d*, 69.4 *d*, 67.8 *d* and 60.0 *s*. The foregoing spectral data indicated that compound **1** was a spatane derivative having a hydroxyl and oxyrane ring in the side chain [2]. In a decoupling experiment, irradiation of the signal at δ3.65 caused the collapse of the doublet at δ2.65 to a singlet, suggesting that the hydroxyl group was α to the oxyrane ring. Hence the structure of **1** was assigned as 17,18-epoxy, 5(*R*),16-dihydroxyspat 13(14)-ene. The structure was confirmed by converting the corresponding allylic alcohol (**5**) to **1** by selective epoxidation [7]. However, we could not establish the stereochemistry of the secondary alcohol and the epoxide.

EXPERIMENTAL

Collection, extraction and isolation. Freshly collected *St. marginatum* was washed with fresh water, shade dried, powdered (4 kg) and extracted with CH_2Cl_2–MeOH (1:1) (3 × 5 litres). The combined concentrated crude extract was subjected to silica gel chromatography, eluting with increasing polarities from hexane through hexane–EtOAc mixtures to EtOAc. Repeated silica gel column chromatography afforded compounds **1** and **3** to **9**.

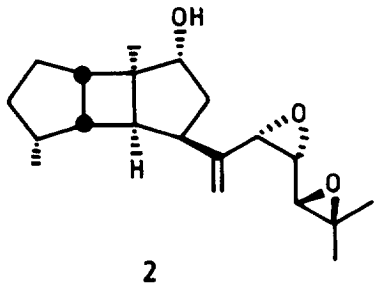
17,18-*Epoxy*, 5(*R*),16-*dihydroxyspat* 13(14)-*ene* (**1**). Oil (40 mg), $[\alpha]_D$ − 35.66 ($CHCl_3$, *c* 0.05). Elemental analysis C: 74.86, H: 10.32%, required for $C_{20}H_{32}O_3$, C: 74.95%, H: 10.06%; IR ν_{max} cm^{-1}: 3540, 2840, 1620, 1380, 895; ^1H NMR ($CDCl_3$, 200 MHz): δ 4.95 (1H, *br s*), 4.85 (1H, *br s*), 3.74 (1H, *d*, J = 4.5 Hz), 3.63 (1H, *q*, J = 7 Hz), 3.0 (1H, *m*), 2.65 (1H, *d*, J = 7 Hz), 2.1–2.4 (2H, *m*), 1.9–2.1

*Dedicated to Dr A. V. Rama Rao, on his 60th birthday. IICT communication No: 3500.



1 $R_1 = R_2 = OH$

1a $R_1 = R_2 = OAc$



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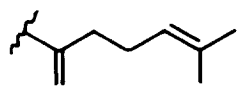

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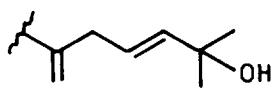

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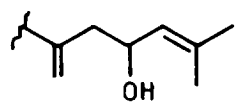

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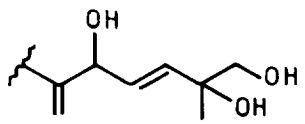
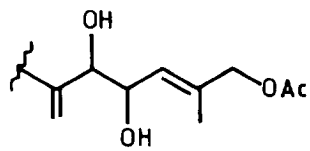
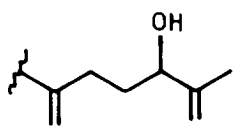


6 $R_1 = O$

7 $R_1 = OH$



8 $R_1 = OH$



9 $R_1 = OH$

(4H, *m*), 1.45–1.9 (6H, *m*), 1.35 (3H, *s*), 1.2 (3H, *s*), 1.0 (3H, *s*), 0.93 (3H, *d*, $J = 7$ Hz); ^{13}C NMR ($CDCl_3$, 50 MHz): δ144.7 *s*, 11.7 *s*, 80.3 *d*, 69.4 *d*, 67.8 *d*, 60.0 *s*, 46.8 *d*, 45.9 *s*, 43.2 *d*, 43.2 *t*, 41.4 *t*, 37.7 *d*, 36.6 *d*, 36.6 *d*, 35.14 *t*, 28.13 *t*, 24.9 *q*, 19.7 *q*, 14.6 *q*, 15.2 *q*; EIMS *m/z* (rel. int.); 287 $[M - 18\text{-}CH_3]^+$ (15), 187 (20), 120 (60), 105 (40), 91 (50).

Acetylation of **1**. A soln of **1** (10 mg) in Ac_2O/Py (0.5 ml) was allowed to stand at 0° for 6 hr. After usual workup, the crude product was chromatographed on silica gel to give the diacetate **1a** (8 mg). IR ν_{max} cm^{-1}: 2950, 1720, 1640, 140, 1370; ^1H NMR ($CDCl_3$ 200 MHz): δ4.9 (4H, *m*), 3.0 (1H, *m*), 2.75 (1H, *d*, $J = 7$ Hz), 2.1–2.5 (2H, *m*), 1.9–2.1 (4H, *m*), 1.4–1.9 (6H, *m*), 2.1 (3H, *s*), 2.03 (3H, *s*), 2.0 (3H, *s*), 1.3 (3H, *s*), 1.2 (3H, *s*), 1.0 (3H, *s*), 0.93 (3H, *d*, $J = 7$ Hz); EIMS *m/z* (rel. int.); 284 $[M - 2AcOH]^+$ (2), 269 (3), 202 (20), 187 (5), 159 (15), 54 (60).

Epoxidation of **1**. To a stirred and cooled ($-20°$) suspension of activated powdered 4A molecular sieves in CH_2Cl_2 under a N_2 atmosphere, ($-$) DIPT, $Ti(Oipr)_4$ catalytic amounts and TBHP (9 mg, 0.1 mmol) were added sequentially. The resulting mixture was treated after 20 min with compound **5** (20 mg, 0.06 mmol) in CH_2Cl_2 over a period of 20 min. and maintained at this temp for 4 h. The reaction mixture was allowed to warm to 0° and poured into a freshly prepared and cooled (0°) soln of ferrous sulphate and tartaric acid in distilled water. The two-phase mixture was stirred for 25–30 min, the aq phase separated and extracted with Et_2O. The combined organic phase was treated with a precooled (0°) soln of 30% (w/v) NaOH in saturated brine. The two-phase mixture was then stirred for 1 hr at room temp. and the aq. layer separated and extracted with Et_2O. The combined organic extract was dried (Na_2SO_4) and concentrated under reduced pressure to give compound **1**,

$[\alpha]_D$ − 7.2 ($CHCl_3$, *c* 0.05); IR, ^1H NMR and mass data identical with that of natural product 1.

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