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ANTIMICROBIAL CONSTITUENTS OF THE SPONGE *SIPHONODICTYON CORALLIPHAGUM*

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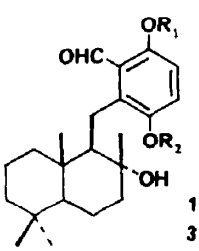
Abstract—The burrowing sponge *Siphonodictyon coralliphagum* contains two phenolic aldehydes, siphonodictyal-A (1) and siphonodictyal-B (2). The structure of siphonodictyal-A (1) was determined by interpretation of spectral data and the synthesis of a derivative. The structure of siphonodictyal-B (2) resulted from interpretation of spectral data and the synthesis of a degradation product. Both compounds exhibit antimicrobial activity.

Siphonodictyon coralliphagum (Rützler)[1] is one of a small group of sponges that burrow into limestone substrata. A study of the burrowing mechanism of *Cliona lampa*[2] revealed that 2–3% of the excavated substratum was dissolved while the remaining material was removed as small chips. The chemical mechanism for dissolution of calcium carbonate has not been determined. Unlike most *Cliona* species which tend to settle and excavate the dead regions of coral, *Siphonodictyon coralliphagum* is generally found in a living coral head. The major portion of the sponge is inside the coral head with only the oscular chimney protruding. In order to prevent overgrowth by the living coral polyps, the sponge maintains 5–10 mm zone of dead coral polyps around the base of the oscular chimney. Rützler[1] suggested that the dead zone was maintained by the production of mucus that flowed down to the base of the oscular chimney. In this paper, we will report the structure of secondary metabolites from *S. coralliphagum* that might play a role in either the burrowing process or the inhibition of coral growth.

The crude ethanolic extract of *S. coralliphagum* was shown to inhibit the growth of *Staphylococcus aureus*. Solvent partition gave dichloromethane, ethyl acetate, n-butanol and aqueous extracts, all of which showed antimicrobial activity. However, the ethyl acetate extract contained the majority of the material and was highly active. The ^{1}H NMR spectrum of the crude extract suggested the presence of several aldehydes. However, Florisil chromatography of the extract resulted in a very poor recovery of siphonodictyal-A (1) (0.12% dry weight) that showed antimicrobial activity. Much of the material remained firmly adsorbed to the Florisil. Chromatography of the extract of Sephadex LH-20 using methanol as eluant gave siphonodictyal-B (2) (0.9% dry weight) together with smaller quantities of siphonodictyal-A (1) and some products that appear to result from acid-catalyzed rearrangement of siphonodictyal-B (2).

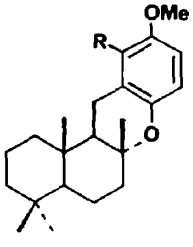


1 $R_1 = R_2 = H$
3 $R_1 = R_2 = Me$
4 $R_1 = H$ $R_2 = Ac$

Siphonodictyal-A (1), $[\alpha]_D$ +3.2°, was crystallized from methanol, m.p. 192–3°. High resolution mass measurement gave the molecular formula $C_{22}H_{32}O_4$. The IR (3250, 1645 cm^{-1}) and UV [390 nm (ϵ 5000), 280 nm (ϵ 12,000)] spectra were similar to those of 2,5-dihydroxybenzaldehyde. The ^{1}H NMR spectrum contained signals at δ 10.48 (s, 1 H), 7.07 (d, 1 H, J = 8 Hz) and 6.75 (d, 1 H, J = 8 Hz), indicating the presence of a 1,2,3,4 - tetra - substituted aromatic aldehyde. Methylation of siphonodictyal - A (1) with dimethyl sulfate and potassium carbonate in dry acetone gave a dimethyl ether 3 [δ 3.83 (s, 3 H) and 3.85 (s, 3 H)] but acetylation with acetic anhydride in pyridine produce a monoacetate 4 [δ 2.36 (s, 3 H)] in which a phenolic OH *ortho* to the aldehyde group had not been acetylated. From five possible 1,2,3,4 - substitution patterns for an alkyl group, a phenol and an *o* - hydroxyaldehyde, we selected the 2 - alkyl - 3,5 - didhydroxybenzaldehyde pattern by comparison of the chemical shifts of the ^{13}C NMR signals for the atomatic carbons with calculated values.[3]

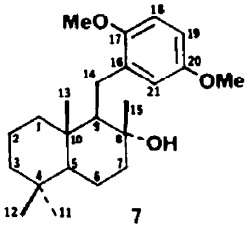
Having proposed the structure of the aromatic portion, we now had to assign a structure to the sesquiterpene portion of siphonodictyal - A (1). The ^{13}C NMR spectrum of siphonodictyal - A (1) indicated that the sesquiterpene portion of the molecule must be bicyclic and contain a tertiary alcohol. The ^{1}H NMR spectrum contained four methyl signals at δ 0.78 (s, 3 H), 0.83 (s, 3 H), 0.98 (s, 3 H) and 1.32 (s, 3 H) and benzylic methylene signals at 2.88 (d, 1 H, J = 16 Hz) and 3.23 (dd, 1 H, J = 16, 8 Hz). These data suggested a drimane ring skeleton and comparison of the ^{13}C NMR spectrum with those of model compounds[5] strongly supported this assignment. Confirmation of this assignment was accomplished using the following reaction sequence.

Dehydration of siphonodictyal-A (1) using *p*-toluenesulfonic acid in refluxing benzene gave a cyclic ether which was methylated using methyl iodide and potassium carbonate in dry acetone to obtain the methyl ether 5. Formylation of chromazonarol methyl ether 6[6] with



5 R = CHO
6 R = H

dichloromethyl methyl ether and titanium tetrachloride in dry dichloromethane at 0° for 15 min., followed by 1 hr at 20°, gave a mixture of the three possible mono-formyl derivatives, that were separated by LC and differentiated by ^{1}H NMR data. One of the aldehydes (22%) was identical in all respects to the methyl ether **5** prepared from aldehyde **1**. The remaining aldehydes had the formyl group *meta* (36%) or *para* (27%) to the alkyl group. The stereochemistry of the Me group at C-8 in siphonodictyal-A (**1**) was shown to be axial by comparison of its ^{13}C NMR chemical shift (δ 23.9) with the chemical shifts assigned to the C-8 axial (24.9) and equatorial (31.8) Me groups in the alcohols **7** and **8** respectively.[6]



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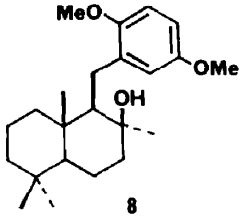

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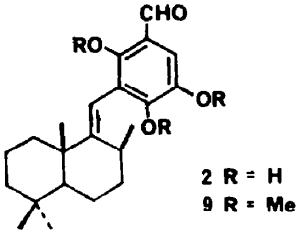
Siphonodictyal-B (**2**) was obtained as a crystalline solid, m.p. 145–147°. The IR spectrum suggested the presence of phenolic (3100–3500 cm^{-1}) and aldehyde (1685 cm^{-1}) functionalities. The aldehyde gave a green color with methanolic ferric chloride which, together with the UV spectrum [(MeOH) 280 nm (ϵ 6400), 380 nm (ϵ 1540); (MeOH + OH$^-$) 304 nm (ϵ 7300), 403 nm (ϵ 1800)], indicated the presence of a polyhydroxy benzaldehyde as part of the molecule. Since siphonodictyal-B (**2**) was insoluble in most organic solvents, the remaining spectral data were measured using the trimethoxy derivative **9**, obtained from the reaction of the alkehyde **2** with methyl iodide and potassium carbonate in acetone. The trimethoxy derivative **9** had the molecular formula $C_{25}H_{36}O_4$. The ^{1}H NMR spectrum contained three methoxy signals at δ 3.72, 3.85 and 3.91, an aldehyde proton signal at 10.40 (s, 1 H), an aromatic proton signal at 6.91 (s, 1 H), a signal assigned to the C-11 vinyl proton at 6.21 (s, 1 H), an allylic proton signal at 2.65 (m, 1 H) and four Me signals at 1.19 (s, 3 H), 0.91 (s, 3 H), 0.90 (d, 3 H, J = 7 Hz) and 0.89 (s, 3 H). These data could be assigned to a structure having the same carbon skeleton as siphonodictyal-A (**1**) with a benzylidene olefinic bond as found in spongiaquinone **10**.[7]

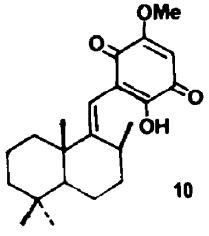
Ozonolysis of the trimethyl ether **9** in ethyl acetate at −78° followed by reductive work-up using dimethyl sulfide gave the ketone **11** and the dialdehyde **12**. The ^{1}H NMR spectral data for the ketone **11** was identical to that reported for the degradation product of spongiaquinone **10**.[7] The ^{1}H NMR spectrum of the dialdehyde **12** contained two aldehyde signals at δ 10.33 (s, 1 H) and 10.25 (s, 1 H), an aromatic proton signal at 7.48 (s, 1 H) and three OMe signals at 4.02 (s, 3 H), 3.97 (s, 3 H), 3.94 (s, 3 H), eliminating symmetrical molecules. Comparison of the chemical shifts of the aromatic proton with calculated values[8] for the aromatic protons of all possible unsymmetrical formyl - trimethoxy benzaldehydes suggested that the dealdehyde **12** was 3 - formyl - 2,4,5 - trimethoxybenzaldehyde. The structure of dialdehyde was confirmed by synthesis. Demethylation of 2,4,5 - trimethoxybenzaldehyde (**13**) with boron trichloride in dichloromethane gave 4,5 - dimethoxysalicaldehyde (**14**).[10] Treatment of 4,5 - dimethoxysalicaldehyde (**14**) with dichloromethyl methyl ether and titanium tetrachloride in dichloromethane[11] gave 4,5 - dimethoxy - 3 - formylsalicaldehyde (**15**) as the only dialdehyde together with recovered starting material. Treatment of 4,5 - dimethoxy - 3 - formylsalicaldehyde (**15**) with methyl iodide and potassium carbonate in dry acetone gave 3 - formyl - 2,4,5 - trimethoxybenzaldehyde (**12**), identical in all respects to the product from ozonolysis of the trimethoxy derivative **9**.

The ketone **11** and dialdehyde **12** can be formed from either the trimethoxy derivative **9** or the alternative structure **16**. In order to differentiate between these alternatives, we calculated[9] the expected chemical shifts for the aromatic proton in 3 - ethyl - 2,4,5 - trimethoxybenzaldehyde (δ 7.06) and 3 - ethyl - 2,5,6 - trimethoxybenzaldehyde (δ 6.78). Catalytic hydrogenation of the trimethoxy derivative **9** gave the alcohol **17** that was re-oxidized to the aldehyde **18** using manganese dioxide in acetone. The chemical shift of the aromatic proton in aldehyde **18** (δ 7.05) strongly suggested that the trimethoxy derivative had structure **9** rather than the alternative **16**.

The stereochemistry at C-8 in these compounds was determined by a ^{1}H NMR spin decoupling experiment on the trimethoxy derivative **9**. Irradiation of the doublet Me signal at δ 0.90 caused the multiplet at 2.65 to collapse to a signal with coupling constants of 6 and 2 Hz, indicating that the allylic proton at C-8 was equatorial. By way of contrast, a similar spin decoupling



2 R = H
9 R = Me



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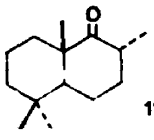
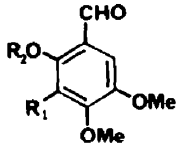
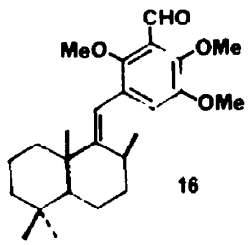


11



12 R_1 = CHO R_2 = Me
13 R_1 = H R_2 = Me
14 R_1 = H R_2 = H
15 R_1 = CHO R_2 = H



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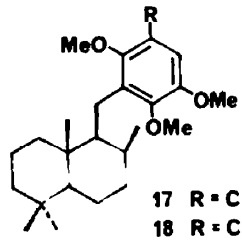
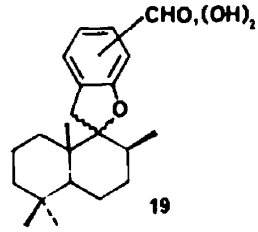


17 R = CH_2OH
18 R = CHO



19

experiment on the ketone **11**, in which the C-8 Me group had isomerized to the more stable equatorial configuration, gave a C-8 proton signal with coupling constants of 12 and 6 Hz. The geometry about the $\Delta^{9(11)}$ olefinic bond is presumed to be *E* since models suggest that there is unacceptable steric crowding in the corresponding *Z* isomer.

Among the minor metabolites of *S. coralliphagum* was an inseparable 1:1 mixture of two cyclic ethers. The same mixture of cyclic ethers could be generated by acid-catalyzed cyclisation of siphonodictyal-B (**2**). Methylation of the mixture of cyclic ethers gave two dimethyl ethers that could be separated with difficulty. The ^{1}H NMR data[12] were compatible with structures of the type **19** but we had insufficient material to complete the structural elucidation.

Both siphonodictyal-A (**1**) and siphonodictyal-B (**2**) inhibit the growth of *Staphylococcus aureus* and *Bacillus subtilis* and both have been detected in the mucus from *S. coralliphagum*. However, we have not had the opportunity to determine whether the compounds alone can inhibit the growth of coral polyps. Both compounds, particularly siphonodictyal-B (**2**) are strongly adsorbed by Florisil and silica gel but we were unable to show that they are involved in calcium carbonate dissolution.

EXPERIMENTAL[13]

Collection and extraction of Siphonodictyon coralliphagum. The protruding portions (oscular chimney) of *S. coralliphagum* were collected by hand using SCUBA (−12 to −30 m) from coral heads on the leeward side of Lighthouse Reef and Glover Reef, Belize. The sponge, together with as much of the yellow mucus as possible, was frozen and maintained at −20° until required. The sponge (180 g dry weight) was homogenized in EtOH (1 l), filtered, steeped in fresh EtOH (1 l), filtered and the combined EtOH extracts evaporated to obtain an aqueous suspension. The aqueous phase was extracted with CH_2Cl_2 (2 × 250 ml), EtOAc (3 × 250 ml) and n-BuOH (500 ml). The CH_2Cl_2 extract was dried over Na_2SO_4 and evaporated to obtain a yellow oil (1.5 g, 0.8% dry weight). The EtOAc extract was dried over $NaSO_4$ and the solvent evaporated to obtain an orange oil (11.2 g, 6.2% dry weight). Evaporation of the n-BuOH extract gave an orange oil (6 g, 3.3% dry weight).

Isolation of siphonodictyal-A (**1**). The EtOAc extract (9 g) was preadsorbed onto Florisil (20 g) and applied to a column (60 × 5 cm diam) of Florisil. Fractions were obtained using eluants of increasing polarity from hexane through ether and EtOAc to 1:1 EtOAc/MeOH. The material eluted with 20% EtOAc in ether was purified on silica gel plates to obtain **1** (175 mg, 0.12% dry weight): m.p. 192–3°; $[\alpha]_D$ +3.2° (*c* 0.5, MeOH); UV (MeOH) 390 nm (ϵ 5000), 280 nm (ϵ 12,000); IR ($CHCl_3$) 3250, 1645, 1580 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.78 (s, 3 H), 0.83 (s, 3 H), 0.98 (s, 3 H), 1.32 (s, 3 H), 1.84 (d, 1 H, J = 8 Hz), 2.88 (d, 1 H, J = 16 Hz), 3.23 (dd, 1 H, J = 16.8 Hz), 6.75 (d, 1 H, J = 8 Hz), 7.07 (d, 1 H, J = 8 Hz), 10.48 (s, 1 H); ^{13}C NMR ($CDCl_3$/CD_3OD) δ 197.1 (s), 157.1 (s), 148.2 (s), 132.6 (s), 126.8 (d), 118.4 (s), 115.9 (d), 74.8 (s), 62.2 (d), 56.6 (d), 44.2 (t), 41.9 (t), 41.3 (t), 40.6 (s), 33.6 (q), 33.5 (s), 23.9 (t), 20.7 (q), 19.7 (q), 19.3 (q), 17.7 (t), 14.6 (q); high-resolution mass spectrum, obsd 360.233, $C_{22}H_{32}O_4$ requires: 360.230.

Isolation of siphonodictyal-B (**2**). The EtOAc extract (3.2 g) was chromatographed on a column (100 × 5 cm diam) of Sephadex LH-20 using MeOH as eluant. Fractions were screened for antimicrobial activity against *Staphylococcus aureus*. A series of fractions that showed strong anitmicrobial activity were combined and the solvent evaporated to obtain **2** (495 mg, 0.9% dry weight) as yellow crystals from aqueous MeOH: m.p. 145–147°; UV (MeOH) 280 nm (ϵ 6400), 380 (ϵ 1540), (MeOH + NaOH) 304 nm (ϵ 7300), 403 nm (ϵ 1800); IR (KBr) 3100–3500, 1685 cm^{-1}; ^{1}H NMR (CD_3OD) δ 0.82 (d, 1 H, J = 7 Hz), 0.88 (s, 3 H), 0.92 (s, 3 H), 1.21 (s, 3 H), 6.40 (s, 1 H), 6.89 (s, 1 H), 10.27 (s, 1 H).

Methylation of siphonodictyal-A (**1**). A soln of **1** (7 mg, 0.02 mmol) and Me_2SO_4 (10 μl) in dry acetone (10 ml) containing anhyd K_2CO_3 (50 mg) was stirred at 80° for 15 hr. The mixture was filtered and the solvent evaporated under vacuum to give an oily residue that was chromatographed on a silica gel plate to obtain **3** (4 mg, 50% theoretical): IR ($CHCl_3$) 3600, 1685, 1600 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.78 (s, 3 H), 0.82 (s, 3 H), 0.98 (s, 3 H), 1.21 (s, 3H), 1.89 (dd, 1 H, J = 8, 4 Hz), 3.11 (dd, 1 H, J = 16, 4 Hz), 3.51 (dd, 1H, J = 16, 8 Hz), 3.83 (s, 3H), 3.85 (s. 3 H), 6.77 (d, 1 H, J = 9 Hz), 7.00 (d, 1 H, J = 9 Hz), 10.55 (s, 1 H); mass spectrum, *m/z* 388, 370, 355, 352.

Acetylation of siphonodictyal-A (**1**). A soln of **1** (10 mg, 0.03 mmol) in Ac_2O (0.5 ml) and pyride (1 ml) was stirred overnight at 25°. The solvents were evaporated under vacuum and the residue was chromatographed on a silica gel plate to obtain **4** (6 mg, 54% theoretical): IR ($CHCl_3$) 3450, 1755, 1640 cm^{-1}; UV (MeOH) 260 nm (ϵ 10,000), 345 (ϵ 4600); ^{1}H NMR ($CDCl_3$) δ 0.78 (s, 3 H), 0.83 (s, 3 H), 0.98 (s, 3 H), 1.27 (s, 3 H), 2.36 (s, 3 H), 2.88 (dd, 1 H, J = 16, 8 Hz), 3.23 (dd, 1 H, J = 16, 4 Hz), 6.80 (d, 1 H, J = 9 Hz), 7.10 (d, 1 H, J = 9 Hz), 10.67 (s, 1 H); mass spectrum, *m/z* 402, 384, 360, 342.

Dehydration and methylation of siphonodictyal-A (**1**). A soln of **1** (14 mg, 0.04 mmol) in benzene (10 ml) containing *p*-toluenesulfonic acid (1 crystal) was boiled under reflux for 2 hr. The cooled soln was washed with sat $NaHCO_3$ aq (5 ml), then water (5 ml), dried over $NaSO_4$ and the solvent evaporated to give a cyclic ether. The ether was methylated using the conditions

described above to obtain **5** (10 mg, 72% theoretical): IR ($CHCl_3$) 1690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.84 (s, 3 H), 0.89 (s, 3 H), 0.91 (s, 3 H), 1.14 (s, 3 H), 2.77 (dd, 1 H, J = 18, 12 Hz), 3.08 (dd, 1 H, J = 18, 4 Hz), 3.85 (s, 3 H), 6.79 (d, 1 H, J = 8 Hz), 6.97 (d, 1 H, J = 8 Hz).

Formylation of chromazonarol methyl ether **6**. A soln of $TiCl_4$ (20 mg, 0.1 mmol) in dry CH_2Cl_2 (5 ml) was added to a cooled soln of chromazonarol methyl ether (31 mg, 0.095 mmol) and dichloromethyl methyl ether (20 mg, 0.17 mmol) in dry CH_2Cl_2 (10 mL) and the resulting mixture was stirred at 0° for 15 min then at 22° for 1 hr. The mixture was washed with 3 N HCl (5 ml) and water (5 ml), dried over Na_2SO_4 and the solvent evaporated to obtain a yellow oil. The oil was chromatographed by LC on μ-porasil using 7% ether in hexane as eluant to obtain **5** (7.5 mg, 22% theoretical) together with the alternative mono-formyl derivatives with the formyl group *meta* (12 mg, 36% theoretical) or *para* (9 mg, 27% theoretical) to the alkyl group. Compd **5** had identical chromatographic properties and spectral data to the product from **1**.

Methylation of siphonodictyal-B (**2**). A soln of **2** (10 mg, 0.028 mmol) and Me_2SO_4 (0.2 ml) in dry acetone (10 ml) containing anhyd K_2CO_3 (50 mg) was stirred at 80° overnight (> 12 h). The cooled mixture was filtered and the solvent evaporated under vacuum to give an oil that was filtered through a plug of silica gel in ether soln to obtain **9** (10 mg, 90% theoretical): IR ($CHCl_3$) 1685, 1525 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (s, 3 H), 0.90 (d, 3 H, J = 7 Hz), 0.91 (s, 3 H), 1.19 (s, 3 H), 2.65 (m, 1 H), 3.72 (s, 3 H), 3.85 (s, 3 H), 3.91 (s, 3 H), 6.21 (s, 1 H), 6.91 (s, 1 H), 10.40 (s, 1 H); ^{13}C NMR (C_6D_6) δ 189.1 (s), 158.3 (s), 152.3 (s), 150.3 (s), 148.9 (s), 130.4 (s), 125.0 (s), 120.5 (d), 114.9 (d), 61.6 (q), 56.1 (q), 50.5 (q), 42.7, 42.4, 41.3, 40.0, 34.1, 33.4, 33.1, 32.7, 22.9, 22.4, 21.9, 20.5, 19.9; high-resolution mass spectrum, obsd 400.2576, $C_{25}H_{36}O_4$ requires: 400.2613.

Ozonolysis of trimethyl ether **9**. A stream of O_3 in O_2 was bubbled into EtOAc at −78° until a blue-colored soln was obtained. The soln was added dropwise to a stirred soln of **9** (10 mg, 0.025 mmol) in EtOAc (10 ml) at −78° until the starting material had completely reacted (as indicated by tlc). Me_2SO_4 (0.5 ml) was added and the mixture was stirred at 25° for 3 hr. The solvent was evaporated under vacuum and the resulting oil was chromatographed on a silica gel plate to obtain **11** (3 mg, 58% theoretical), having identical spectral data to those reported by Kazlauskas *et al.*,[7] and **12** (2.5 mg, 45% theoretical): UV (MeOH) 266 nm (ϵ 1920), 233 nm (ϵ 4600); IR ($CHCl_3$) 1690 cm^{-1}; ^1H NMR (CCl_4) δ 3.94 (s, 3 H), 3.97 (s, 3 H), 4.02 (s, 3 H), 7.48 (s, 1 H), 10.25 (s, 1 H), 10.33 (s, 1 H); mass spectrum, *m/z* 224, 223.

Synthesis of 3 - *formyl* - 2,4,5 - *trimethoxybenzaldehyde* (**12**). A soln of BCl_3 (~80 mg, excess) in CH_2Cl_2 (4 mL) was added to a cooled soln of **13** (50 mg, 0.26 mmol) in CH_2Cl_2 (10 ml) and the mixture was stirred at −78° for 2½ hr. The mixture was poured into a mixture of ice and 1 N HCl (5 ml) and the organic material was extracted with ether (3 × 20 ml). The combined extracts were washed with water (20 mL), dried over Na_2SO_4 and the solvent evaporated to obtain **14** (40 mg, 86% theoretical) as an oil: IR (CCl_4) 3300, 1665 cm^{-1}; UV (MeOH) 343 nm (ϵ 7800), 280 nm (ϵ 12,400), 239 nm (ϵ 18,500); ^1H NMR ($CDCl_3$) δ 3.89 (s, 3 H), 3.93 (s, 3 H), 6.46 (s, 1 H), 6.90 (s, 1 H), 9.68 (s, 1 H).

A soln of $TiCl_4$ (0.4 ml) in dry CH_2Cl_2 (3 ml) was added to a cooled soln of **14** (40 mg) in CH_2Cl_2 (5 ml) and the mixture was stirred at 0°. A soln of dichloromethyl methyl ether (0.2 ml) in dry CH_2Cl_2 (3 ml) was added to the cooled soln over 30 min and the mixture was then stirred at room temp for 2 hr. The mixture was poured into ice-cold 1 N HCl and extracted with ether (3 × 30 ml). The combined ether extracts were washed with water (10 ml), dried over Na_2SO_4 and the solvent evaporated to obtain an oil. The oil was chromatographed on a silica gel plate to obtain **14** (23 mg, 58% recovery) and **15** (3.5 mg, 8% theoretical): IR (CCl_4) 3300, 1670 cm^{-1}; UV (MeOH) 379, 267, 243 nm; ^1H NMR ($CDCl_3$) δ 3.88 (s, 3 H), 4.15 (s, 3 H), 7.67 (s, 1 H), 10.33 (s, 1 H), 10.39 (s, 1 H).

A soln of **15** (3.5 mg) and MeI (1 ml) in dry acetone (10 ml) containing anhyd K_2CO_3 (100 mg) was stirred at 80° under reflux for 4 hr. The cooled mixture was poured into water (10 ml) and extracted with EtOAc (2 × 20 ml). The EtOAc extract was washed with water, dried over $NaSO_4$ and evaporated under vacuum to obtain **12** (3.5 mg) identical in all respects to the material obtained from the natural product.

9,11 - *Dihydrosiphonodictyal* - *B trimethyl ether* (**18**). A soln of **9** (10 mg, 0.025 mmol) in ether (5 ml) containing 10% Pd–C catalyst (2 mg) was stirred under an atmosphere of H_2 until a tlc analysis revealed that the starting material had completely reacted. The catalyst was removed by filtration and the solvent evaporated to obtain **17** (10 mg, quantitative): IR (CCl_4) 3400 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.70 (d, 3 H, *J* = 7 Hz), 0.84 (s, 3 H), 0.87 (s, 3 H), 0.92 (s, 3 H), 2.34 (dd, 1 H, *J* = 16, 6 Hz), 2.67 (d, 1 H, *J* = 16 Hz), 3.73 (s, 3 H) 3.86 (s, 3 H), 3.87 (s, 3 H), 4.75 (bs, 2 H), 6.76 (s, 1 H); mass spectrum, *m/z* 404 (M^+).

A soln of **17** (10 mg) in dry acetone (10 ml) containing activated MnO_2[14] was stirred at 25° for 5 hr. The MnO_2 was removed by filtration and the solvent evaporated to obtain **18** (8 mg, 80% theoretical): IR (CCl_4) 1685 cm^{-1}; UV (MeOH) 334 nm (ϵ 1110), 264 (ϵ 3100); ^1H NMR ($CDCl_3$) δ 0.71 (d, 3 H, *J* = 7 Hz), 0.84 (s, 3 H), 0.87 (s, 3 H), 0.92 (s, 3 H), 2.44 (dd, 1 H, *J* = 16, 6 Hz), 2.67 (dd, 1 H, *J* = 16, 2 Hz), 3.75 (s, 3 H), 3.89 (s, 3 H), 3.91 (s, 3 H), 7.05 (s, 1 H), 10.41 (s, 1 H); mass spectrum, *m/z* 402 (M^+).

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