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TETRAHEDRON: *ASYMMETRY*

Radical cyclisation approach for the first synthesis and determination of absolute stereochemistry of discosiolide from diacetone glucose †

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Abstract

By the adoption of a regio- and stereoselective intramolecular radical cyclisation reaction onto a chiron derived from diacetone glucose, the crucial *cis*-fused bicyclo[3.3.0]octane system was made and utilized for the first synthesis of discosiolide **1**, thereby establishing the absolute stereochemistry of the natural product.

1. Introduction

Discosiolide **1**, 4-*epi*-ethisolide **2** and sporothriolide **4**, belonging to the furofurandione class of natural products such as avenaciolide **3**,[1] canadensolide **5**[2] etc., are biologically active fungal metabolites and were isolated[3] from *Discosia* sp. (Strain No. 1290), *Pezicula livida* (Strain No. 1156) and *Sporothrix* sp. (Strain No. 700), respectively. The structures of **1**, **2** and **4** have been determined from ^{1}H and ^{13}C NMR studies by comparing with the structures of **3** and **5**. All the metabolites **1**, **2** and **4** are shown to possess fungicidal, algicidal and antibacterial activity, while the later two have also shown herbicidal activity. Recently, avenaciolide **3** was found to inhibit glutamate transport in rat liver mitochondria.[4]

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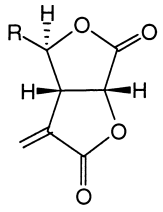
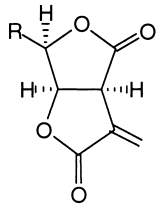


1 R = n-$C_{10}H_{21}$
2 R = C_2H_5
3 R = n-C_8H_{17}

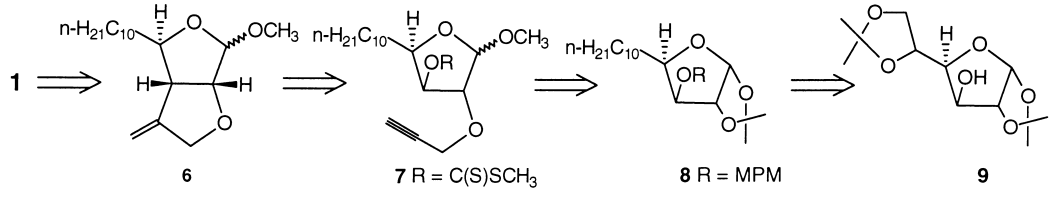


4 R = n-C_6H_{13}
5 R = n-C_4H_9

As part of our programme of using radical reactions[5–7] for the synthesis[8–10] of related natural products, we have earlier reported the first synthesis[11] and determination of absolute stereochemistry of **2** and **4**. Herein, we describe a protocol for the first synthesis of **1** in an enantiopure form through a regio- and stereoselective intramolecular radical cyclisation[5] of the appropriate xanthate derivative **7**, thereby arriving at the absolute stereochemistry of **1**. The advantages of this protocol are: (a) the stereochemistry[12] of the bicyclic system is derived from the carbon centre that is bearing the acetylenic appendage; and (b) an efficient way of introducing the *exo*-methylene group during the formation of *cis*-fused bicyclic system.

2. Results and discussion

From the antithetic analysis (Scheme 1), it was envisioned that the bicyclic system **6** would conveniently furnish the target **1**. Compound **6** could be derived by radical mediated cyclisation of xanthate ester **7**, which in turn could be visualised from 'diacetone glucose' (DAG, **9**), where the C-3 and C-2 carbon centres would define the new stereocentres in **1**.

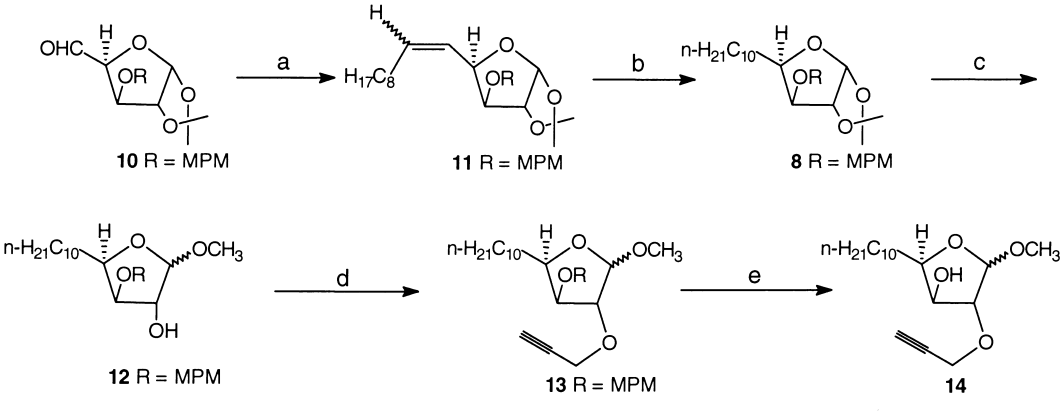


1 **6** **7** R = $C(S)SCH_3$ **8** R = MPM **9**

Scheme 1.

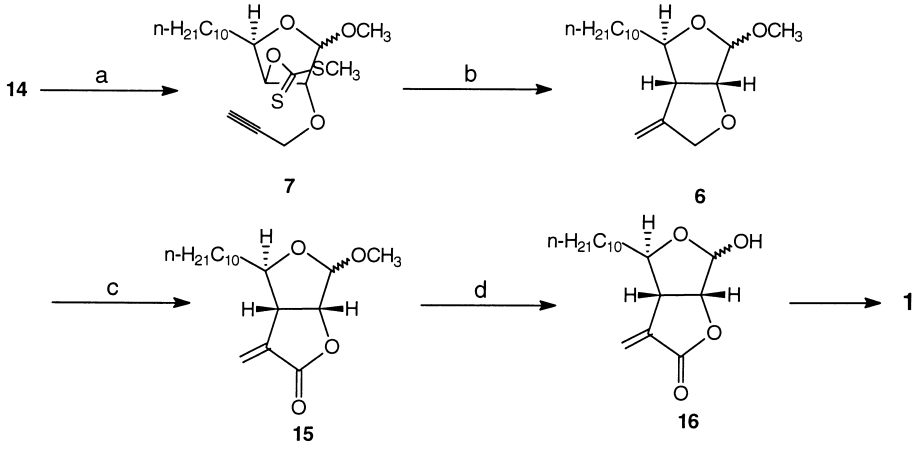
Accordingly, the known[13] aldehyde **10** (Scheme 2), that is made from DAG, by a Wittig olefination with *n*-nonyl triphenyl phosphorane (generated from *n*-nonyl triphenylphosphonium bromide, *n*-BuLi) in THF afforded the olefin **11**, which was subjected to catalytic hydrogenation with 5% Pd–C in ethanol to afford **8** in 93% yield. Compound **8**, on methanolysis with Amberlite IR 120 H^+ in methanol at reflux, provided methyl glycoside **12** as an α and β anomeric mixture. Chromatographic purification afforded pure α and β anomers of **12** with a free hydroxy group at C-2 position. Alcohol **12**, on subsequent reaction with propargyl bromide in the presence of NaH in THF, furnished **13**, which was subjected to oxidative deprotection of the MPM group with DDQ in wet dichloromethane to provide the free C-3 OH in compound **14**.

The derived alcohol **14**, on reaction (Scheme 3) with NaH and carbon disulphide followed by methyl iodide,[14] was converted to xanthate ester **7** (94%). Crucial radical cyclisation[5,15] was achieved by the treatment of **7** with tributyltin hydride in the presence of a catalytic amount of AIBN in dry benzene at 80°C where the simultaneous introduction of an *exo*-methylene group, the formation of a *cis*-fused bicyclic system and inversion at the C-3 centre to the required configuration, was accomplished in



Scheme 2.

accordance with literature precedence,[12,16] thus providing the single desired product **6** (67%). The specific rotation values for **6α** and **6β**, respectively, were recorded as $[\alpha]_D$ +48.37 (*c* 0.215, $CHCl_3$) and $[\alpha]_D$ +21.0 (*c* 0.5, $CHCl_3$). Furan **6** was subjected to oxidation with CrO_3–pyridine in dichloromethane at 40°C to afford **15** in 73% yield. Hydrolysis of lactone **15** with a catalytic amount of conc. HCl in 50% aq. acetic acid at 60°C gave lactol **16**, which on further oxidation with PDC in dichloromethane furnished **1** in 66% yield, whose spectral data were comparable with reported[3] values. The specific rotation of Compound **1** $[\alpha]_D$ −36.48 (*c* 0.466, $CHCl_3$) was comparable with the reported value of $[\alpha]_D$ −37.0 (*c* 0.43, $CHCl_3$).



Scheme 3.

3. Conclusion

In the present protocol for the first synthesis of **1** in an enantiopure form by the adoption of a regio- and stereoselective intramolecular radical cyclisation reaction on the ‘chiron’ derived from ‘diacetone

glucose', 'chiral economy' is well preserved where two of the three stereocentres have been retained, while C-2 and C-3 were used for effective incorporation of the new stereocentre during the C–C bond formation. This synthesis of **1** thus established the absolute stereochemistry of the natural product, which was assigned beyond doubt, by earlier comparative studies.

4. Experimental

NMR spectra were recorded for solutions in $CDCl_3$ (Internal Me_4Si) with a Varian 200-Gemini Spectrometer (^1H, 200 MHz). Optical rotations were measured with a Jasco DIP 360 or 370 polarimeter. Silica gel (60–120 and finer than 200 mesh, Acme) was used for column chromatography. TLC was performed on silica gel 60 F_{254} (E. Merck) with detection using a solution of 2% phosphomolybdic acid and 1% $Ce(SO_4)_2 \cdot 4H_2O$ in aq. H_2SO_4 at 130°C. All the reactions were carried out in dry solvents under anhydrous conditions unless otherwise stated.

*4.1. 5-Deoxy-1,2-*O*-isopropylidene-3-*O*-(*p*-methoxyphenyl)methyl-5-C-(*n*-nonyl)-α-*D*-xylofuranose **8***

A stirred suspension of *n*-nonyl triphenylphosphonium bromide (9.1 g, 19.4 mmol) in dry THF (50 mL) at 0°C was treated with *n*-BuLi (4.7 mL, 2 N in hexane, 14.6 mmol) and stirred at room temperature for 30 min under N_2 atmosphere. A solution of aldehyde **10** (3 g, 9.7 mmol) in dry THF (20 mL) was added and stirred for an additional hour. The reaction mixture was quenched with aq. ammonium chloride and extracted with ether. The organic layer was washed with water, dried (Na_2SO_4) and evaporated. Purification of residue by column chromatography (silica gel, 60–120 mesh; 25:1, pet. ether:ethyl acetate) afforded 5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-(*p*-methoxyphenyl)methyl-6-C-(*n*-octyl)-α-D-xylo-hex-5-eno-furanose (**11**, 2.97 g) in 73% yield, as an *E*:*Z* mixture. ^1H NMR ($CDCl_3$): δ 0.88 (t, 3H, J=7.8 Hz, CH_3), 1.2–1.8 (m, 18H), 2.0–2.15 (m, 2H), 3.73 (d, 1H, $J_{3,4}$=3.2 Hz, H-3), 3.79 (s, 3H, OCH_3), 4.39–4.6 (m, 4H, H-2,4 and $PhCH_2$), 5.5–5.9 (m, 3H, H-1), 6.9, 7.3 (2d, 2H each, J=9.6 Hz, Ar–H).

A suspension of 5% Pd–C (0.29 g), and the above crude olefin **11** (2.9 g) in ethanol (20 mL), was subjected to hydrogenation at room temperature for 12 h. The reaction mixture was filtered and the filtrate on evaporation furnished **8** (2.79 g) in 93% yield as a syrup. ^1H NMR ($CDCl_3$): δ 0.88 (t, 3H, J=8.0 Hz, CH_3), 1.2–1.8 (m, 24H), 3.67 (d, 1H, $J_{3,4}$=3.3 Hz, H-3), 3.78 (s, 3H, OCH_3), 4.03 (dt, 1H, $J_{3,4}$=3.3, $J_{4,5}$=7.1 Hz, H-4), 4.62, 4.88 (2d, 1H each, J=12.0 Hz, $PhCH_2$), 4.53 (d, 1H, $J_{1,2}$=4.2 Hz, H-2), 5.82 (d, 1H, $J_{1,2}$=4.2 Hz, H-1), 6.83, 7.22 (2d, 2H each, J=9.0 Hz, Ar–H); $[\alpha]_D$ −32.87 (*c* 0.87, $CHCl_3$). Analysis calcd for $C_{25}H_{40}O_5$: C, 71.39; H, 9.58; found: C, 71.22; H, 9.45%.

*4.2. Methyl 5-deoxy-3-*O*-(p-methoxyphenyl)methyl-5-C-(n-nonyl)-α,β-*D*-xylofuranoside **12***

A mixture of **8** (2.7 g, 6.4 mmol) and Amberlite IR 120 H^+ resin (0.9 g) in dry methanol (20 mL) was heated at 60°C for 6 h. The reaction mixture was cooled, filtered and washed with methanol. The filtrate was evaporated and residue purified by column chromatography (silica gel, 60–120 mesh, 7:1, pet. ether:ethyl acetate) to furnish **12** as an α,β mixture. First eluted was the α anomer (1 g) in 38% yield as syrup. ^1H NMR ($CDCl_3$): δ 0.89 (t, 3H, J=8.0 Hz, CH_3), 1.2–1.7 (m, 18H), 2.7 (d, 1H, $J_{2,OH}$=6.8 Hz, OH), 3.49 (s, 3H, OCH_3), 3.73 (dd, 1H, $J_{2,3}$=2.7, $J_{3,4}$=5.0 Hz, H-3), 3.8 (s, 3H, OCH_3), 4.05 (q, 1H, $J_{3,4}$=5.0, $J_{4,5}$=9.1 Hz, H-4), 4.12–4.2 (m, 1H, H-2), 4.43, 4.65 (2d, 1H each, J=10.0 Hz, $PhCH_2$), 4.94 (d, 1H, $J_{1,2}$=4.5 Hz, H-1), 6.83, 7.25 (2d, 2H each, J=9.4 Hz, Ar–H); IR (neat): 3590 cm^{-1}; $[\alpha]_D$ +46.28 (*c*

0.7, $CHCl_3$). Analysis calcd for $C_{23}H_{38}O_5$: C, 70.01; H, 9.7; found: C, 69.9; H, 9.61%. Eluted second was the β anomer (0.9g) in 34% yield as syrup. ^{1}H NMR ($CDCl_3$): δ 0.9 (t, 3H, J=6.8 Hz, CH_3), 1.2–1.65 (m, 18H), 1.75 (br.s, 1H, OH), 3.38 (s, 3H, OCH_3), 3.72–3.8 (m, 4H, H-3, OCH_3), 4.0–4.17 (m, 2H, H-2,4), 4.42, 4.6 (2d, 1H each, J=11.2 Hz, $PhCH_2$), 4.67 (s, 1H, H-1), 6.8, 7.28 (2d, 2H each, J=9.0 Hz, Ar–H); IR (neat): 3500–3600 cm^{-1}; $[\alpha]_D$ −27.77 (*c* 0.9, $CHCl_3$). Analysis calcd for $C_{23}H_{38}O_5$; found: C, 69.92; H, 9.63%.

*4.3. Methyl 5-deoxy-3-*O*-(*p*-methoxyphenyl)methyl-5-C-(*n*-nonyl)-2-*O*-(3′-propynyl)-α,β-*D*-xylofuranoside **13***

A stirred suspension of sodium hydride (0.44 g, 9.6 mmol) in dry THF (5 mL) under nitrogen atmosphere was treated with a solution of **12** (1.9 g, 4.8 mmol) in THF (4 mL) at 0°C and stirred at room temperature for 2 h. After 30 min propargyl bromide was added at 0°C and stirred at room temperature for 2 h. The reaction mixture was quenched with aq. ammonium chloride solution and extracted with ether. The organic layer was washed with water, brine and dried (Na_2SO_4). Evaporation of solvent and purification of residue by column chromatography (silica gel, 60–120 mesh; 20:1, pet. ether:ethyl acetate) afforded **13** (1.85 g) in 89% yield as a syrup. First eluted was the α anomer, ^{1}H NMR ($CDCl_3$): δ 0.85 (t, 3H, J=6.7 Hz, CH_3), 1.2–1.7 (m, 18H), 2.4 (t, 1H, $J_{1',3'}$=2.1 Hz, H-1′), 3.38 (s, 3H, OCH_3), 3.77 (s, 3H, Ar–OCH_3), 3.95–4.25 (m, 5H, H-2,3,3′,4), 4.4, 4.6 (2d, 1H each, J=12.8 Hz, $PhCH_2$), 4.9 (d, 1H, $J_{1,2}$=4.1 Hz, H-1), 6.8, 7.2 (2d, 2H each, J=9.0 Hz, Ar–H); IR (neat): 3400 and 2100 cm^{-1}; $[\alpha]_D$ +33.66 (*c* 0.3, $CHCl_3$). Analysis calcd for $C_{26}H_{40}O_5$: C, 72.18; H, 9.31; found: C, 72.09; H, 9.22%. Eluted second was the β anomer, ^{1}H NMR ($CDCl_3$): δ 0.87 (t, 3H, J=6.3 Hz, CH_3), 1.22–1.7 (m, 18H), 2.38 (t, 1H, $J_{1',3'}$=1.9 Hz, H-1′), 3.38 (s, 3H, OCH_3), 3.45 (d, 1H, $J_{3,4}$=3.8 Hz, H-3), 3.8 (s, 3H, Ar–OCH_3), 4.0–4.32 (m, 4H, H-2,3′,4), 4.48, 4.67 (2d, 1H each, J=13.0 Hz, $PhCH_2$), 4.78 (s, 1H, H-1), 6.8, 7.22 (2d, 2H each, J=9.0 Hz, Ar–H); IR (neat): 3380 and 2100 cm^{-1}; $[\alpha]_D$ −45.76 (*c* 0.55, $CHCl_3$). Analysis calcd for $C_{26}H_{40}O_5$; found: C, 72.11; H, 9.25%.

*4.4. Methyl 5-deoxy-5-C-(*n*-nonyl)-2-*O*-(3′-propynyl)-α,β-*D*-xylofuranoside **14***

A solution of **13** (1.8 g, 4.1 mmol) in aq. dichloromethane (1:19, H_2O:CH_2Cl_2, 20 mL) was treated with DDQ (1.89 g, 8.3 mmol) at room temperature for 2 h. The reaction mixture was filtered and the filtrate was washed with aq. sodium bicarbonate solution and water. The organic layer was dried (Na_2SO_4) and evaporated and residue obtained was purified by column chromatography (silica gel, 60–120 mesh; 25:1, pet. ether:ethyl acetate) to give **14** (1.1 g) in 85% yield as a syrup. First eluted was the α anomer, ^{1}H NMR ($CDCl_3$): δ 0.89 (t, 3H, J=7.2 Hz, CH_3), 1.2–1.75 (m, 18H), 1.8 (br.d, 1H, $J_{3,OH}$=4.9 Hz, OH), 2.43 (t, 1H, $J_{1',3'}$=1.9 Hz, H-1′), 3.4 (s, 3H, O CH_3), 3.95–4.44 (m, 5H, H-2,3,3′,4), 4.9 (d, 1H, $J_{1,2}$=4.2 Hz, H^{-1}); IR (neat): 3450–3420 and 3130 cm^{-1}; $[\alpha]_D$ +98.66 (*c* 0.45, $CHCl_3$). Eluted second was the β anomer, ^{1}H NMR ($CDCl_3$): δ 0.9 (t, 3H, J=6.6 Hz, CH_3), 1.2–1.75 (m, 18H), 2.45 (t, 1H, $J_{1',3'}$ 1.9 Hz, H-1′), 3.36 (s, 3H, OCH_3), 3.92–4.25 (m, 5H, H-2,3,3′,4), 4.85 (s, 1H, H-1); $[\alpha]_D$ −42.0 (*c* 0.3, $CHCl_3$).

*4.5. Methyl 5-deoxy-3-*O*-[(*S*-methylthio)thiocarbonyl]-5-C-(*n*-nonyl)-2-*O*-(3′-propynyl)-α,β-*D*-xylofuranoside **7***

A suspension of sodium hydride (0.29 g, 6.4 mmol) in dry THF (5 mL) at 0°C under nitrogen atmosphere was treated with a solution of **14** (1 g, 3.2 mmol) in THF (5 mL) and stirred at room temperature for 30 min. Carbon disulphide (0.48 g, 6.4 mmol) was added at 0°C and stirred at room

temperature for 1 h. It was recooled to 0°C, treated with methyl iodide (0.86 g, 6.4 mmol) and stirred at room temperature for 1 h. The reaction mixture was quenched with aq. ammonium chloride solution and extracted with ether. The organic layer was washed with water, brine and dried (Na_2SO_4). Evaporation of solvent and purification of residue by column chromatography (silica gel, 60–120 mesh, 50:1, pet. ether:ethyl acetate) afforded **7** (1.18 g) in 92% yield as a syrup. First eluted was the α anomer, ^{1}H NMR ($CDCl_3$): δ 0.80 (t, 3H, J=7.9 Hz, CH_3), 1.15–1.5 (m, 18H), 2.36 (t, 1H, $J_{1',3'}$=2.1 Hz, H-1′), 2.55 (s, 3H, SCH_3), 3.39 (s, 3H, OCH_3), 4.2–4.35 (m, 4H, H-2,3′,4), 4.94 (d, 1H, $J_{1,2}$=4.1 Hz, H-1), 6.03 (d, 1H, $J_{3,4}$=5.0 Hz, H-3); IR (neat): 3120 and 2135 cm^{-1}; $[\alpha]_D$ +88.0 (*c* 0.7, $CHCl_3$). Eluted second was the β anomer, ^{1}H NMR ($CDCl_3$): δ 0.86 (t, 3H, J=8.1 Hz, CH_3), 1.2–1.7 (m, 18H), 2.38 (t, 1H, $J_{1',3'}$=2.0 Hz, H-1′), 2.52 (s, 3H, SCH_3), 3.36 (s, 3H, OCH_3), 4.1 (s, 1H, H-2), 4.25–4.35 (m, 3H, H-3′,4), 4.82 (s, 1H, H-1), 5.77 (d, 1H, $J_{3,4}$=4.4 Hz, H-3); $[\alpha]_D$ −38.85 (*c* 0.35, $CHCl_3$).

*4.6. (3a*R,*4*R,*6a*R*)-4*-n-*Decyl-6-methoxy-3-methylidenehexahydro[3,4*-b*]furan or (1*R,*4*R,*5*R*)-4*-n-*decyl-2-methoxy-6-methylidene-3,8-dioxa-bicyclo[3.3.0]octane **6***

A solution of **7** (1 g, 2.48 mmol) in dry benzene (15 mL) containing AIBN under nitrogen atmosphere was heated at reflux and treated with tributyl tin hydride (1.43 g, 4.97 mmol). After 8 h, benzene was evaporated and the residue was purified by column chromatography (silica gel, 60–120 mesh, 20:1, pet. ether:ethyl acetate) to afford **6** (0.49 g) in 67% yield as a syrup. First eluted was the α anomer, ^{1}H NMR ($CDCl_3$): δ 0.89 (t, 3H, J=8.2 Hz, CH_3), 1.15–1.75 (m, 18H), 2.88 (br.t, 1H, $J_{3a,4}$=$J_{3a,6a}$=8.2 Hz, H-3a), 3.38 (s, 3H, OCH_3), 3.82 (q, 1H, $J_{3a,4}$ 8.2, J_{4,CH_2}=2.0 Hz, H-4), 4.3–4.78 (m, 3H, H-2,2′,6a), 4.82–4.95 (m, 3H, H-6, vinylic); $[\alpha]_D$ +48.37 (*c* 0.215, $CHCl_3$). Analysis calcd for $C_{18}H_{32}O_3$: C, 72.92; H, 10.88; found: C, 72.84; H, 10.79%. Eluted second was the β anomer, ^{1}H NMR ($CDCl_3$): δ 0.88 (t, 3H, J=8.1 Hz, CH_3), 1.15–1.65 (m, 18H), 2.9 (br.t, 1H, J=4.0 Hz, H-3a), 3.22 (s, 3H, OCH_3), 3.78–3.9 (m, 1H, H-4), 4.13–4.4 (m, 3H, H-2,2′,6a), 4.79 (s, 1H, H-6), 4.81, 4.82 (2d, 1H each, J_{gem}=2.6 Hz, vinylic); $[\alpha]_D$ −21.0 (*c* 0.5, $CHCl_3$). Analysis calcd for $C_{l8}H_{32}O_3$; found: C, 72.83; H, 10.73%.

*4.7. (3a*R,*4*R,*6a*R*)-4*-n-*Decyl-6-methoxy-3-methylidenetetrahydro[3,4*-b*]furan-2(3H)-one or methyl-3-C-(carboxymethylenemethyl)-3,5-dideoxy-5-C-(*n-*nonyl)-*D-*ribofuranoside 2,3-γ-lactone **15***

A solution of **6** (0.4 g, 1.3 mmol), chromium trioxide (1.3 g, 1.3 mmol) and pyridine (2.1 g, 27.0 mmol) in dichloromethane (10 mL) was heated at reflux for 4 h. It was cooled to room temperature and decanted. The residue was dissolved in an aq. sodium bicarbonate solution and extracted with dichloromethane. The combined organic layers were washed sequentially with an aq. sodium bicarbonate solution, water, 2 N aq. HCl and brine. It was filtered through a small pad of silica gel and evaporated. The residue was then purified by column chromatography (silica gel, 60–120 mesh; 10:1, pet. ether:ethyl acetate) to furnish **15** (0.3 g) in 73% yield as a syrup. First eluted was the α anomer, ^{1}H NMR ($CDCl_3$): δ 0.89 (t, 3H, J=7.6 Hz, CH_3), 1.2–1.8 (m, 18H), 3.0–3.15 (m, 1H, H-3a), 3.35 (s, 3H, OCH_3), 3.87 (q, 1H, $J_{3a,4}$=5.9Hz, H-4), 4.87 (dd, 1H, $J_{6,6a}$=4.5, $J_{3a,6a}$=9.4 Hz, H-6a), 4.98 (d, 1H, $J_{6,6a}$=4.8 Hz, H-6), 5.53, 6.23 (2d, 1H each, J_{gem}=2.7 Hz, vinylic); IR (neat): 1790 and 1650 cm^{-1}; $[\alpha]_D$ +93.5 (*c* 0.385, $CHCl_3$). Analysis calcd for $C_{18}H_{30}O_4$: C, 69.64; H, 9.74; found: C, 69.55; H, 9.63%. Eluted second was the β anomer, ^{1}H NMR ($CDCl_3$): δ 0.88 (t, 3H, J=7.7 Hz, CH_3), 1.2–1.8 (m, 18H), 3.25–3.4 (m, 4H, H-3a. OCH_3), 3.92–4.05 (m, 1H, H-4), 4.79 (d, H, $J_{3a,6a}$ 6.4Hz, H-6a), 5.01 (s, 1H, H-6), 5.6, 6.24 (2s, 1H each, vinylic); IR (neat): 1780 cm^{-1}; $[\alpha]_D$ −17.8 (*c* 0.28, $CHCl_3$). Analysis calcd for $C_{18}H_{30}O_4$; found: C, 69.51; H, 9.61%.

*4.8. (3a*R,*4*R,*6a*R*)-4-*n-*Decyl-3a,6a-dihydro-3-methylidene-furo[3,4-*b*]furan-2,6-(3H,4H)-dione or 3-C-(carboxymethylenemethyl)-3,5-dideoxy-5-C-(*n*-nonyl)-*D*-ribofuranoside 1,4-lactone-2,3-γ-lactone (discosiolide)* ***1***

Compound **15** (0.3 g, 0.96 mmol) in 50% aq. acetic acid containing conc. HCl (catalytic) was heated at 60°C for 4 h. The reaction mixture was cooled to room temperature, treated with solid sodium bicarbonate, ether and water. The aqueous layer was separated and extracted with ether. The combined ether layers were washed with aq. sodium bicarbonate, water and dried (Na_2SO_4). The solvent was evaporated to afford lactol **16** (0.19 g) in 67% yield. ^{1}H NMR ($CDCl_3$): δ 0.9 (t, 3H, J=7.3 Hz, CH_3), 1.2–1.8 (m, 18H), 3.1–3.2 and 3.35–3.45 (2m, 1H, H-3a), 3.92–4.1 (m, 1H, H-4), 4.82–4.92 (m, 1H, H-6a), 5.5–5.6 (m, 1H, H-6), 5.65–6.3 (2m, 1H each, vinylic).

The above crude lactol **16** (0.15 g, 0.5 mmol) in dichloromethane (5 mL) was treated with PDC (0.282 g, 0.76 mmol) and sodium acetate (0.083 g, 1.02 mmol) at room temperature for 4 h. The reaction mixture was diluted with ether and filtered through a small pad of silica gel. Evaporation of solvent and purification of residue by column chromatography (silica gel, 60–120 mesh; 8:1, pet. ether:ethyl acetate) afforded **1** (0.098 g) in 66% yield as a syrup. ^{1}H NMR ($CDCl_3$): δ 0.88 (t, 3H, J=6.8 Hz, CH_3), 1.22–1.9 (m, 18H), 3.52–3.62 (m, 1H, H-3a), 4.38–4.5 (dt, 1H, $J_{3a,4}$=3.9, J_{4,CH_2}=6.5 Hz, H-4), 5.05 (d, 1H, $J_{3a,6a}$=8.5 Hz, H-6a), 5.87 (d, 1H, J_{gem}=1.9 Hz, vinylic), 6.47 (d, 1H, J_{gem}=2.4 Hz, vinylic). ^{13}C NMR ($CDCl_3$): δ 14.01 (q), 22.57 (t), 24.75 (t), 29.62 (t), 29.18 (t), 29.27 (t), 29.37 (t), 29.43 (t), 31.78 (t), 35.93 (t), 44.03 (d), 74.28 (d), 85.20 (d), 126.19 (t), 134.56 (s), 168.0 (s), 169.82 (s); $[\alpha]_D$ −36.48 (*c* 0.466, $CHCl_3$), lit. $[\alpha]_D$ −37.0 (*c* 0.43, $CHCl_3$). Analysis calcd for $C_{17}H_{26}O_4$: C, 69.35; H, 8.9; found: C, 69.27; H, 8.81%.

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