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Radical cyclisation approach for the synthesis of (+)dihydrocanadensolide, (+)dihydrosporothriolide and their C-3 epimers from D-xylose☆

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Abstract—Intramolecular radical cyclisation protocol on 5-hexenyl systems derived from D-xylose, was utilized for the synthesis of (+)dihydrocanadensolide, (+)-dihydrosporothriolide and their C-3 epimers, wherein a study on the impact of C-2′ stereocentre on radical cyclisation was conducted.

Synthetic application of free radical cyclistions[1] for C–C bond formation is a highly versatile protocol for the construction of a carbon framework, particularly c*is*-fused bicyclic systems. A suitably substituted 5-hexynyl radical usually undergoes a highly regioselective ring closure by a 5-*exo*-dig[2] mode preferentially. Such a protocol was earlier utilized by our group for the successful synthesis[3–7] of several natural products containing the bis-butyro lactone moiety such as avenaciolide, canadensolide, sporothriolide, 4-*epi*-ethisolide and discosiolide. Similarly, a properly positioned 5-hexenyl radical system results in the formation of the 5-*exo*-trig[8] product. The impact of stereocentres at the C-2, 3, 4 or 5 positions of such systems has been well studied both theoretically[9,10] and experimentally.[11] It is evident from the literature that the C-2 stereocentre in a 5-hexenyl system generates a 1,2- and 1,5-*cis* fused bicyclic system as the only or major product, however, a study on the impact of C-2′ stereocentre in addition to C-2 was not established. Earlier, such a study was conducted on the 5-hexenyl system derived from D-xylose by our group, resulting in the synthesis[12] of dihydrocanadensolide and its C-3 epimer. In continuation of our studies on radical routes, herein, we report a full account on the synthesis of (+)dihydrocanadensolide (**1**) and its C-3 epimer **2** and the first synthesis of the non-natural product dihydrosporothriolide (**1a**) and it's C-3 epimer **2a** (Fig. 1), using radical reactions on 5-hexenyl systems derived from 1,2-*O*-isopropylidene-D-xylose (**3**).

(+)Dihydrocanadensolide (**1**) was isolated as a mold metabolite from *Pencillium canadense*.[13,14] The synthesis of **1** and its C-3 epimer **2** was earlier reported.[12,15–17] Compounds **1a** and its C-3 epimer **2a** are non-natural products, while preparation of **2a** was earlier reported[18] by the hydrogenation of sporothriolide, a naturally occurring bis-butyro lactone.

Synthesis of **1**, **2**, **1a** and **2a** (Scheme 1) through an intramolecular radical cyclisation of appropriate radicals **A** and **B**, prepared from the respective xanthates was

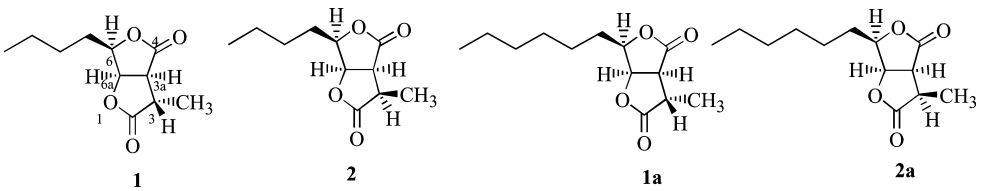

Figure 1.

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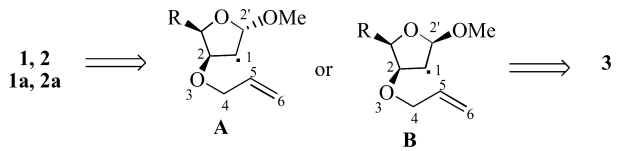


Scheme 1.

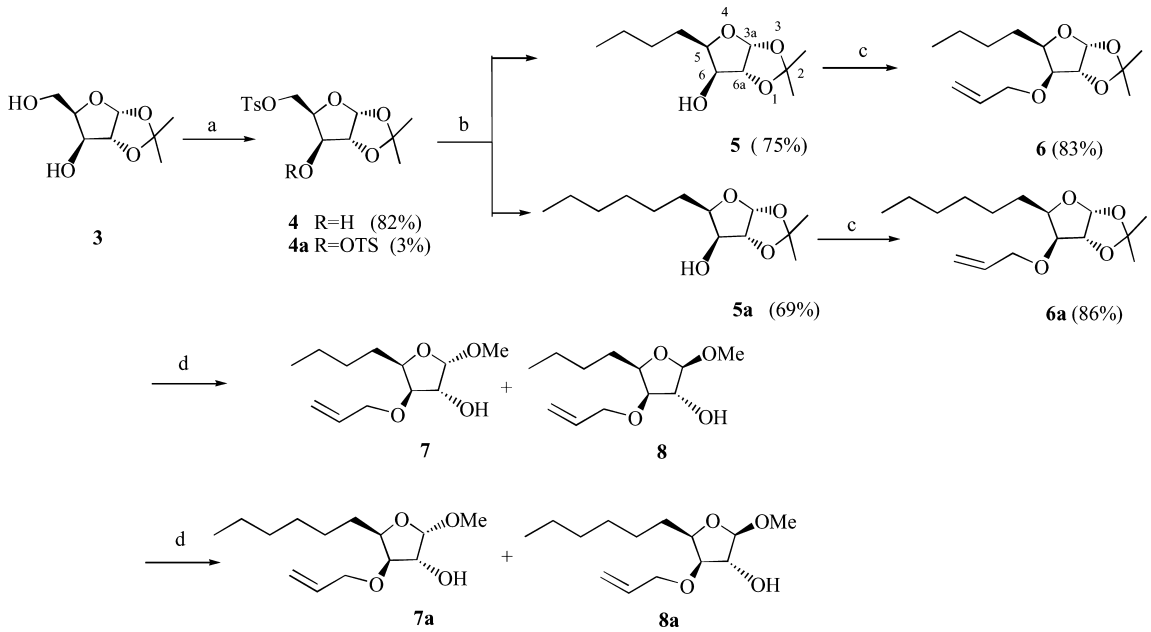
envisaged as the strategy for total synthesis. The advantages of the present protocol being (a) the stereochemistry at C-5 and C-6 of **3** is maintained the same throughout the synthesis; (b) the stereochemistry at C-3a in cyclised products (**11**, **11a**, **12**, **12a**, **17**, **17a**, **18** and **18a**) is defined by C-4 of **9**, **9a**, **10** and **10a** while forming the *cis*-fused bicyclic systems and (c) the anomeric stereocentre at C-2′ in **A** and **B**, in addition to the C-2 stereocentre, exerts influence on the stereochemical outcome of the methyl group at C-3 in the cyclised product during the intramolecular radical cyclisation (3a,3-*cis*/*trans*-3a*S*,3*R*/3a*S*,3*S*).

1. Synthesis of (+)dihydrocanadensolide 1 and its C-3 epimer 2

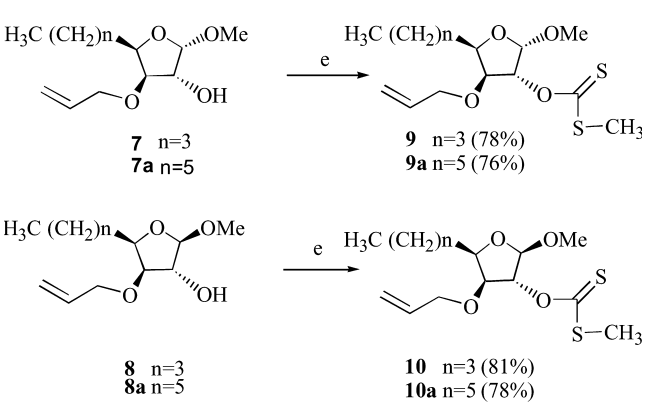
Accordingly, known[19] diol **3** (Scheme 2) was subjected to tosylation with TsCl and pyridine in CH_2Cl_2 to give predominently monotosylate **4** (ditosylate, **4a**, 3%). Compound **4** on reaction with *n*-propylmagnesium bromide afforded **5**, which on further reaction with allyl bromide (NaH, THF) gave **6**. Subsequently **6** was subjected to methanolysis (H^+, MeOH, reflux) to afford **7** and **8** in 1:1.5 ratio as a separable mixture.

The derived alcohols **7** and **8** (Scheme 3), independently on reaction with NaH, carbon disulfide and methyl iodide were converted into xanthate esters **9** and **10** respectively, thus providing the required radical precursors for cyclisation reactions.

The crucial radical mediated intramolecular cyclisation of **9**



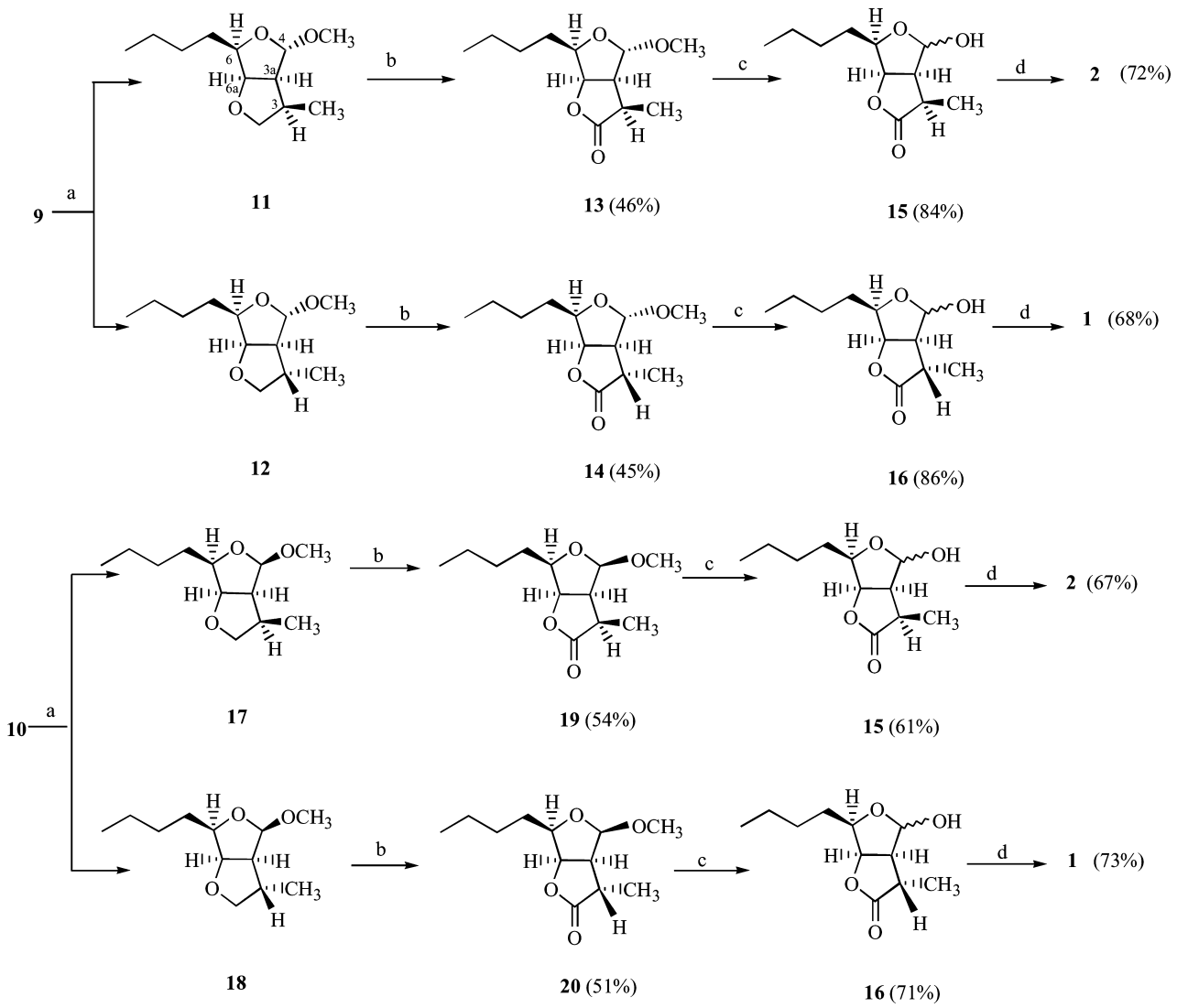
Scheme 2. *Reagents*: (a) TsCl, pyridine, CH_2Cl_2, room temperature (b) C_3H_7MgBr, dry THF, reflux (for 5) or $C_5H_{11}MgBr$, dry THF, reflux (for **5a**) (c) NaH, allyl bromide, dry THF, room temperature (d) MeOH, conc. HCl, reflux.



Scheme 3. *Reagents*: (e) NaH, CS_2, CH_3I, dry THF, 0°C to room temperature.

(Scheme 4) was effected with *n*-Bu_3SnH in the presence of AIBN in benzene at reflux to afford a separable mixture of isomers **11** and **12** in a 3:1 ratio, which on further oxidation[20] with $NaIO_4$–$RuCl_3{\cdot}H_2O$ gave the lactones **13** and **14**, respectively. The stereochemistry of the newly formed stereocentre at C-3 position was assigned as 3a,6a and 3a,3-*cis*(3a*S*,6a*R* and 3a*S*,3*R*) for **13** while 3a,6a-*cis* and 3a,3-*trans*(3a*S*,6a*R* and 3a*S*,3*S*) for **14** based on spectral analysis. Finally compounds **13** and **14** on hydrolysis with aq. AcOH–conc. HCl at 60°C gave lactols **15** and **16**, which on further oxidation with PDC in CH_2Cl_2, independently afforded **2** and **1** respectively, whose optical rotation values and spectroscopic data was comparable with the reported values.[16]

Similarly, **10** on cyclisation with *n*-Bu_3SnH (Scheme 4) gave **17** and **18** in a 1.5:1 ratio. Cyclisation of **9** with



Scheme 4. *Reagents*: (a) *n*-Bu_3SnH, dry benzene, AIBN, reflux; (b) CH_2Cl_2:CH_3CN:H_2O (2:2:3), $NaIO_4$, cat. $RuCl_3$, H_2O, room temperature; (c) 60% aq. CH_3COOH, conc. HCl (2 drops) 60°C; (d) PDC, dry CH_2Cl_2, reflux.

R=−OMe group (Fig. 2) at the C-2′ stereocentre gave **11** and **12** in a 3:1 ratio, wherein **10** with R′=−OMe group gave **17** and **18** in a 1.5:1 ratio. The enhancement in the ratio of *cis*/*trans*(6a*R*,3a*S*/3a*S*,3*S*) product **18** is attributable to the effect of β-OMe group at the C-2′ position. The steric interactions between R′(β-OMe) and the C-3 methyl group in **18** is less pronounced, hence it forms in an enhanced ratio through the boat like (**Ts-B**) transition state (Fig. 2).

Further, **17** and **18** were converted into lactones **19** and **20** respectively with $NaIO_4$–$RuCl_3{\cdot}H_2O$ and subsequent hydrolysis to the lactols **15** and **16**, which on further oxidation with PDC resulted in the formation of **2** and **1**, identical in all respects with the products synthesized from α-anomer **9**.

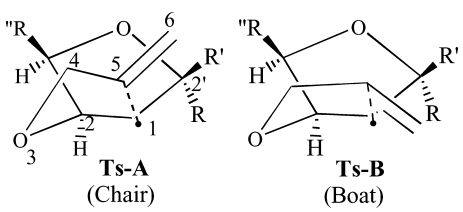
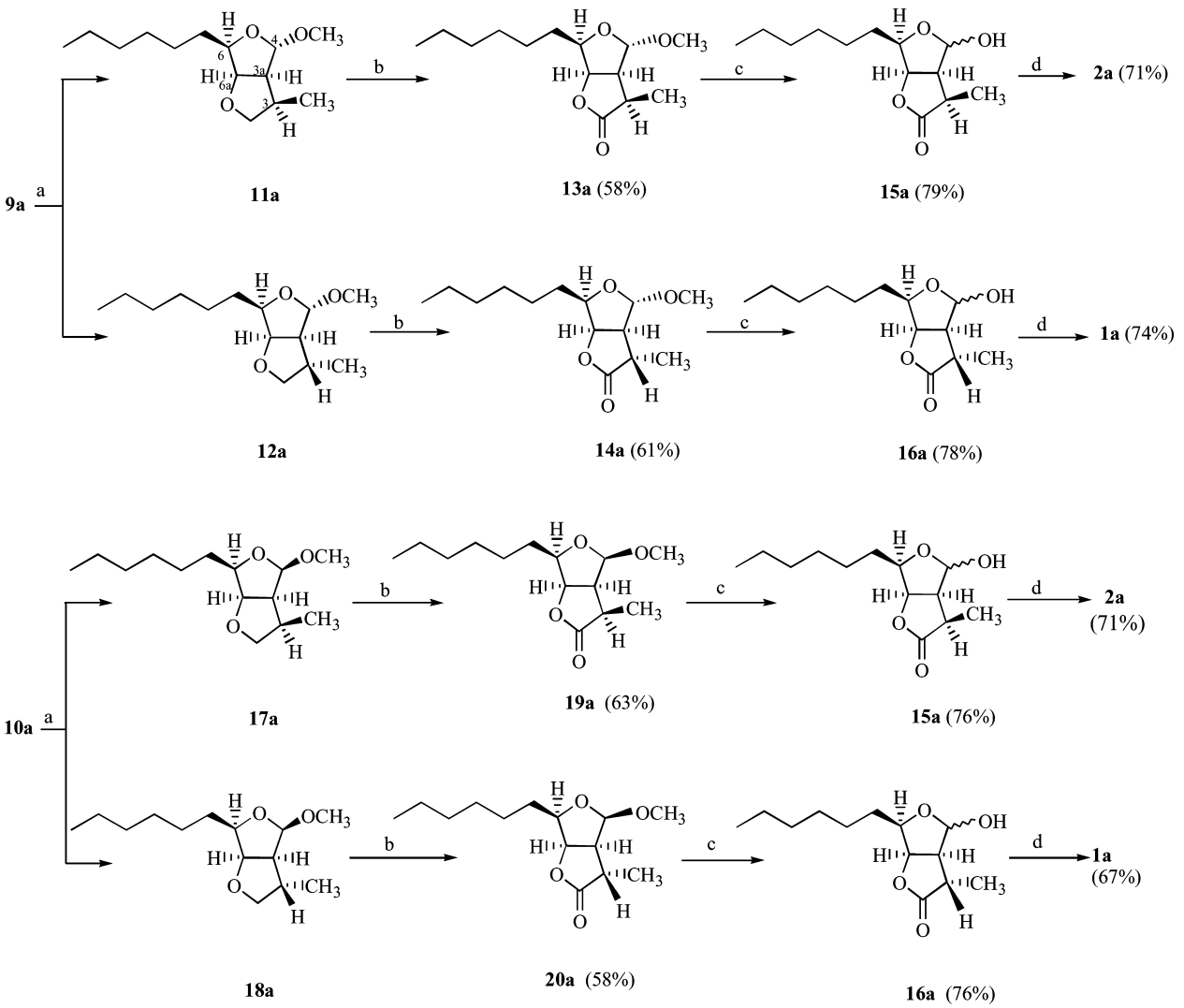


Figure 2.

2. Synthesis of dihydrosporothriolide 1a and C-3 epimer 2a

Having successfully synthesized **1** and **2** from D-xylose, wherein observation was made on the impact of 2′-stereocentre on the stereochemical outcome at the newly created methyl centre at C-3 in the cyclised product, our attention switched. To define the generality of the above study, it was extended to the synthesis of dihydrosporothriolide **1a** and its C-3 epimer **2a**, two non-natural products, adopting the similar strategy.

Accordingly, reaction of **4** (Scheme 2) with *n*-pentylmagnesium bromide gave **5a**, which on reaction with allyl



Scheme 5. *Reagents*: (a) *n*-Bu_3SnH, dry benzene, AIBN, reflux; (b) CH_2Cl_2:CH_3CN:H_2O (2:2:3), $NaIO_4$, cat. $RuCl_3$, H_2O, room temperature; (c) 60% aq. CH_3COOH, conc. HCL (2 drops), 60°C; (d) PDC, dry CH_2Cl_2, reflux.

bromide (NaH, THF) furnished **6a**. Further, methanolysis (H^+, MeOH, reflux) of **6a** afforded **7a** and **8a** in a 4.5:5.5 ratio as a separable mixture. The resultant alcohols **7a** and **8a** (Scheme 3) independently were converted into xanthate esters **9a** and **10a** respectively with NaH, CS_2 and MeI.

Radical cylcisation of xanthate **9a** with *n*-Bu_3SnH gave **11a** and **12a** in a 2.3:1 ratio as a separable mixture (Scheme 5). Oxidation of **11a** and **12a** with $NaIO_4$–$RuCl_3{\cdot}H_2O$ afforded the lactones **13a** and **14a** respectively. Further, hydrolysis of lactones **13a** and **14a** with aq. AcOH–conc. HCl and oxidation of the resultant lactols **15a** and **16a** with PDC in CH_2Cl_2 independently afforded **2a** and **1a** respectively, wherein compound **2a** displayed comparable spectral data with that reported.[18]

However, an interesting result was observed on a similar cyclisation of **10a** with *n*-Bu_3SnH, wherein it gave **17a** and **18a** in a 1:2.3 ratio, which is exactly reverse to that obtained from **9a**. This indicates that, in the case of β-OMe anomer (**10a**) formation of 3a,3-*trans*(3a*S*,3*S*) product is predominant during the radical cyclisation (Fig. 2). Further, oxidation of **17a** and **18a** with $NaIO_4$–$RuCl_3{\cdot}H_2O$ gave lactones **19a** and **20a**. Finally hydrolysis (aq. AcOH–conc. HCl) of lactones gave lactols **15a** and **16a**, which on further oxidation with PDC gave **2a** and **1a** respectively. The compounds **2a** and **1a** prepared from **9a** and **10a** displayed comparable spectral data.

Thus, in conclusion, the synthesis of natural products such as **1** and **2** along with the synthesis of non-natural products **1a** and **2a** was achieved very efficiently by utilizing radical cyclisation protocol on sugar derived chirons, wherein the study on the impact of 2′-(anomeric) stereocentre on the radical cyclisation was established for the first time.

3. Experimental

3.1. General

All moisture sensitive reactions were performed under nitrogen atmosphere using flame-dried glassware. Solvents

were dried over standard drying agents and freshly distilled prior to use. NMR spectra were recorded on Varian Gemini FT-200 MHz, Unity-400 MHz (21°C) and Inova-500 MHz (30°C) spectrometers, with 7–10 mM solutions in appropriate solvents using TMS as internal standard. ^{13}C NMR spectra were recorded with complete proton decoupling. Optical rotations were measured with a JASCO DIP-370 instrument, and $[\alpha]_D$-values are in units of 10^{-1} $^{\prime\prime\prime}$ $^{1deg\ cm2}$ g^{-1}. IR spectra were taken with a Perkin–Elmer 1310 spectrometer. Mass spectra were recorded on CEC-21-11013 or Finnigan Mat 1210 double focussing mass spectrometers operating at a direct inlet system and FABMS were measured using VG AUTOSPEC mass spectrometers at 5 or 7 K resolution using perfluorokerosene as an internal reference. Nomenclature mentioned in the Section 3 was adopted from ACD/Name Version 1.0β, Advanced Chemistry Development Inc., Toronto, Canada. Organic solutions were dried over anhydrous Na_2SO_4 and concentrated below 40°C in vacuo.

3.1.1. 6-Hydroxy-2,2-dimethyl-5-(4-methylphenylsulfonyloxymethyl)-(3a*R*,5*R*,6*S*,6a*R*)-perhydrofuro[2,3-*d*][1,3]dioxole (4). A solution of **3** (8.0 g, 42.1 mmol) in dry CH_2Cl_2 (40 mL) at 0°C was treated with pyridine (5.0 mL, 63.15 mmol) and *p*-toluenesulfonyl chloride (8.799 g, 46.31 mmol) at 0°C and stirred for 6 h at room temperature. The reaction mixture was quenched with 1N HCl (200 mL) and extracted with dichloromethane (2×100 mL). The organic layer was washed with water (2×100 mL), brine (100 mL), dried (Na_2SO_4), evaporated and purified the residue by column chromatography (silica gel, 60–120 mesh; ethylacetate–hexane, 1:4–4:6). First eluted was 2,2-dimethyl-6-(4-methylphenylsulfonyloxy)-5-(4-methylphenylsulfonyloxymethyl)-(3a*R*,5*R*,6*S*,6a*R*)-perhydrofuro[2,3-*d*]-[1,3]dioxole **4a** (0.630 g) in 3% yield as a light yellow syrup; [Found: C, 52.98; H, 5.20. $C_{22}H_{26}O_9S_2$ requires C, 53.01; H, 5.22%]; $[\alpha]_D$=−13.65 (*c* 0.7, $CHCl_3$); ν_{max} ($CHCl_3$) 2950, 1450 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.26 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 2.46 (s, 3H, Ar-CH_3), 2.50 (s, 3H, Ar-CH_3), 3.92 (dd, 2H, *J*=4.8, 2.0 Hz, H-5a, H-5b), 4.22–4.30 (m, 1H, H-5), 4.66–4.72 (m, 2H, H-6, H-6a), 5.82 (d, 1H, *J*=3.6 Hz, H-3a), 7.30, 7.38 (2d, 2H each, *J*=7.0 Hz, Ar-H), 7.70, 7.80 (2d, 2H each, *J*=7.6 Hz, Ar-H).

Second eluted was 6-hydroxy-2,2-dimethyl-5-(4-methylphenylsulfonyloxy-methyl)-(3a*R*,5*R*,6*S*,6a*R*)-perhydrofuro[2,3-*d*][1,3]dioxole **4** (11.87 g) in 82% yield as a white solid, mp 134°C; [Found: C, 51.98; H, 5.71. $C_{15}H_{20}O_7S$ requires C, 52.32; H, 5.85%]; $[\alpha]_D$=−0.79 (*c* 1.0, $CHCl_3$); ν_{max} ($CHCl_3$) 3250 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.30 (s, 3H, CH_3), 1.48 (s, 3H, CH_3), 2.10 (d, 1H, *J*=5.1 Hz, H-6), 2.48 (s, 3H, Ar-CH_3), 4.1 (m, 1H, H-5), 4.34 (dd, 2H, *J*=5.1, 2.5 Hz, H-5a, H-5b), 4.52 (d, 1H, *J*=3.8 Hz, H-6a), 5.86 (d, 1H, *J*=3.8 Hz, H-3a), 7.36, 7.80 (2d, 2H each, *J*=7.6 Hz, Ar-H); *m*/*z* (EIMS) 329 (M^+-15).

3.1.2. 5-Butyl-2,2-dimethyl-(3a*R*,5*R*,6*S*,6a*R*)-perhydrofuro[2,3-*d*][1,3]dioxole-6-ol (5). A solution of **4** (6.0 g, 17.44 mmol) in THF (15 mL) was treated with *n*-propylmagnesium bromide [prepared from Mg (1.255 g, 52.32 mmol) and *n*-propyl bromide (3.21 mL, 26.26 mmol)] and stirred at reflux for 10 h. The reaction mixture was quenched with aq. ammonium chloride solution (100 mL) and extracted with ethyl acetate (2×100 mL). The organic layer was washed with water (100 mL), brine (100 mL), dried (Na_2SO_4), evaporated and purified by column chromatography (silica gel, 60–120 mesh; ethyl acetate–hexane, 1.5:8.5) to afford 5-butyl-2,2-dimethyl-(3a*R*,5*R*, 6*S*,6a*R*)-perhydrofuro[2,3-*d*][1,3]dioxole-6-ol **5** (2.8 g) in 75% yield as a white solid, mp 72–73°C; [Found: C, 61.03; H, 9.29. $C_{11}H_{20}O_4$ requires C, 61.09; H, 9.32%]; $[\alpha]_D$=−13.6 (*c* 1.0, $CHCl_3$); ν_{max} ($CHCl_3$) 3270 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.92 (t, 3H, *J*=6.8 Hz, CH_3), 1.30–1.55 (m, 10H, $2CH_2$, $2CH_3$), 1.60–1.82 (m, 2H, H-5a, H-5b), 4.05 (d, 1H, *J*=3.6 Hz, H-6), 4.12 (ddd, 1H, *J*=9.5, 8.1, 3.6 Hz, H-5), 4.52 (d, 1H, *J*=4.6 Hz, H-6a), 5.88 (d, 1H, *J*=4.6 Hz, H-3a); *m*/*z* (EIMS) 201 (M^+-15).

3.1.3. 6-Allyloxy-5-butyl-2,2-dimethyl-(3a*R*,5*R*,6*S*,6a*R*)-perhydrofuro[2,3-*d*][1,3]dioxole (6). A stirred suspension of sodium hydride (0.622 g, 25.92 mmol) in dry THF (20 mL) under N_2 atm was treated with a solution of **5** (2.80 g, 12.96 mmol) in THF (10 mL) at 0°C for 30 min. Allyl bromide (1.9 mL, 15.55 mmol) was added to the reaction mixture at 0°C and stirred for 4 h at room temperature. It was quenched with aq. ammonium chloride solution (100 mL) and extracted with ethyl acetate (3×75 mL). The organic layer was washed with water (100 mL), brine (100 mL), dried (Na_2SO_4) and evaporated. Purification of residue by column chromatography (silica gel, 60–120 mesh; ethyl acetate–hexane, 0.5:9.5) afforded 6-allyloxy-5-butyl-2,2-dimethyl-(3a,5*R*,6*S*,6a*R*)-perhydrofuro[2,3-*d*][1,3]dioxole **6** (2.755 g) in 83% yield as a light yellow syrup; [Found: C, 65.56; H, 9.37. $C_{14}H_{24}O_4$ requires C, 65.60; H, 9.44%]; $[\alpha]_D$=−32.30 (*c* 0.5, $CHCl_3$); ν_{max} (Neat) 970, 1080, 1640 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.92 (t, 3H, *J*=6.9 Hz, CH_3), 1.32 (s, 3H, CH_3), 1.25–1.46 (m, 7H, $2CH_2$, CH_3), 1.62–1.76 (m, 2H, H-5a, H-5b), 3.74 (d, 1H, *J*=2.4 Hz, H-6), 3.96 (dd, 1H, *J*=12.0, 5.6 Hz, H-8), 4.06–4.22 (m, 2H, H-8a, H-5), 4.54 (d, 1H, *J*=4.6 Hz, H-6a), 5.21 (d, 1H, *J*=16.0 Hz, H-10), 5.28 (d, 1H, *J*=18.0 Hz, H-10a), 5.78–5.98 (m, 1H, H-9), 5.89 (d, 1H, *J*=4.6 Hz, H-3a); *m*/*z* (EIMS) 241 (M^+-15).

3.1.4. Hydrolysis of 6. To a solution of **6** (2.70 g, 10.54 mmol) in dry methanol (30 mL) under N_2 atm was added 3 drops of conc. HCl and heated at reflux for 45 min. The reaction mixture was cooled to room temperature and neutralized with solid sodium hydrogencarbonate (0.5 g) at 0°C. It was filtered, solvent evaporated and the residue purified by column chromatography (silica gel, 60–120 mesh; ethyl acetate–hexane, 1.8:8.2). First eluted was 4-allyloxy-5-butyl-2-methoxy-(2*S*,3*R*,4*S*,5*R*)-tetrahydro-3-furanol **7** (0.880 g) in 40% yield as a light yellow syrup; [Found: C, 62.51; H, 9.56. $C_{12}H_{22}O_4$ requires C, 62.58; H, 9.63%]; $[\alpha]_D$=+49.27 (*c* 0.6, $CHCl_3$); ν_{max} (Neat) 3300, 1640, 1080, 980 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.92 (t, 3H, *J*=7.1 Hz, CH_3), 1.21–1.52 (m, 4H, $2CH_2$), 1.54–1.68 (m, 2H, H-5a, H-5b), 1.75 (br. s, 1H, OH), 3.48 (s, 3H, OCH_3), 3.68–3.72 (m, 1H, H-5), 3.90–4.26 (m, 4H, H-3, H-4, H-6, H-6a), 4.94 (d, 1H, *J*=7.0 Hz, H-2), 5.16 (d, 1H, *J*=18 Hz, H-8), 5.28 (d, 1H, *J*=15 Hz, H-8a), 5.86–5.90 (m, 1H, H-7); *m*/*z* (EIMS) 199 (M^+-OCH_3), 183 (M^+-47).

Second eluted was 4-allyloxy-5-butyl-2-methoxy-(2*R*,3*R*,4*S*,5*R*)-tetrahydro-3-furanol **8** (1.320 g) in 60%

yield as a light yellow syrup; [Found: C, 62.53; H, 9.56%]; $[\alpha]_D=-56.41$ (*c* 0.8, $CHCl_3$); ν_{max} (Neat) 3300, 1640, 1080, 980 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.92 (t, 3H, *J*=7.1 Hz, CH_3), 1.21–1.54 (m, 4H, $2CH_2$), 1.56–1.69 (m, 2H, H-5a, H-5b), 1.82 (s, br, 1H, OH), 3.36 (s, 3H, OCH_3), 3.76 (m, 1H, H-5), 3.92–4.21 (m, 4H, H-3, H-4, H-6, H-6a), 4.68 (d, 1H, *J*=2.3 Hz, H-2), 5.18 (d, 1H, *J*=18 Hz, H-8), 5.25 (d, 1H, *J*=15 Hz, H-8a), 5.82–5.90 (m, 1H, H-7); *m*/*z* (EIMS) 199 (M^+-OCH_3), 183 (M^+-47).

3.1.5. 4-Allyloxy-5-butyl-2-methoxy-3-methyldithiocarbonate-(2*S*,3*R*,4*S*,5*R*)-tetrahydro-furan (9). A stirred suspension of sodium hydride (0.177 g, 7.39 mmol) in dry THF (10 mL) under N_2 atm was treated with a solution of **7** (0.850 g, 3.69 mmol) in THF (5 mL) at 0°C and stirred at room temperature for 30 min. Carbon disulfide (0.42 mL, 5.53 mmol) was added at 0°C and stirred for 30 min at room temperature. Methyl iodide (0.78 mL, 5.53 mmol) was added at 0°C and stirred at room temperature for 4 h. The reaction mixture was quenched with aq. ammonium chloride (100 mL) solution and extracted with ethyl acetate (3×50 mL). Organic layer was washed with water (100 mL), brine (100 mL), dried (Na_2SO_4) and evaporated. Purification of the residue by column chromatography (silica gel, 60–120 mesh; ethyl acetate–hexane, 1:25) gave 4-allyloxy-5-butyl-2-methoxy-3-methyldithiocarbonate-(2*S*,3*R*,4*S*,5*R*)-tetrahydrofuran **9** (0.920 g) in 78% yield as a yellow syrup; $[\alpha]_D=+213.67$ (*c* 0.5, $CHCl_3$); ν_{max} (Neat) 1690, 1640, 1080, 980 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.92 (t, 3H, *J*=7.0 Hz, CH_3), 1.24–1.50 (m, 4H, $2CH_2$), 1.58–1.75 (m, 2H, H-5a, H-5b), 2.60 (s, 3H, S-CH_3), 3.36 (s, 3H, OCH_3), 3.88–4.28 (m, 4H, H-4, H-6, H-6a, H-5), 5.18–5.28 (m, 3H, H-3, H-8, H-8a), 5.65 (t, 1H, *J*=3.8 Hz, H-2), 5.82–5.86 (m, 1H, H-7).

3.1.6. 4-Allyloxy-5-butyl-2-methoxy-3-methyldithiocarbonate-(2*R*,3*R*,4*S*,5*R*)-tetrahydro-furan (10). Reaction of **8** (1.30 g, 5.65 mmol) in THF (10 mL) with sodium hydride (0.271 g, 11.30 mmol), carbon disulfide (0.65 mL, 8.47 mmol) and methyl iodide (1.20 mL, 8.47 mmol) as described for **9** afforded 4-allyloxy-5-butyl-2-methoxy-3-methyldithio-carbonate-(2*R*,3*R*,4*S*,5*R*)-tetrahydrofuran **10** (1.474 g) in 81% yield as a light yellow syrup; $[\alpha]_D=-111.00$ (*c* 0.5, $CHCl_3$); ν_{max} (Neat) 1690, 1640, 1080, 980 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.92 (t, 3H, *J*=6.8 Hz, CH_3), 1.26–1.52 (m, 4H, $2CH_2$), 1.62–1.80 (m, 2H, H-5a, H-5b), 2.60 (s, 3H, S-CH_3), 3.42 (s, 3H, OCH_3), 3.88 (d, 1H, *J*=4.5 Hz, H-4), 4.00–4.36 (m, 3H, H-6, H-6a, H-5), 4.94 (s, 1H, H-3), 5.18 (d, 1H, *J*=18 Hz, H-8), 5.28 (d, 1H, *J*=15 Hz, H-8a), 5.79 (s, 1H, H-2), 5.84–5.90 (m, 1H, H-7).

3.1.7. Cyclisation of 9. A solution of **9** (0.900 g, 2.81 mmol) in dry benzene (25 mL) under N_2 atmosphere was treated with tributyltin hydride (1.65 mL, 5.62 mmol) at room temperature and heated at reflux for 30 min. After 30 min., a catalytic amount of AIBN was added at reflux and continued the reflux for 12 h. The reaction mixture was cooled to room temperature, benzene evaporated under reduced pressure and residue purified by column chromatography (silica gel, 60–120 mesh; ethyl acetate–hexane, 1:50) to afford a mixture **11** and **12** (0.493 g) in 82% yield. First eluted was 6-butyl-3-methyl-(3*S*,3a*S*,4*S*,6*R*,6a*R*)-perhydrofuro[3,4-*b*]-furan-4-yl-methylether **12** (0.123 g) in 25% yield as a colorless syrup; [Found: C, 67.23; H, 10.30. $C_{12}H_{22}O_3$ requires C, 67.26; H, 10.35%]; $[\alpha]_D=+20.89$ (*c* 0.4, $CHCl_3$); ν_{max} (Neat) 2930, 1100, 1045 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.92 (t, 3H, *J*=7.2 Hz, CH_3), 1.12 (d, 3H, *J*=7.0 Hz, CH_3), 1.32–1.52 (m, 4H, $2CH_2$), 1.52–1.74 (m, 2H, H-7, H-7a), 2.12–2.16 (m, 1H, H-3), 2.32–2.36 (m, 1H, H-3a), 3.28 (s, 3H, OCH_3), 3.33 (dd, 1H, *J*=7.0, 5.0 Hz, H-6a), 3.80–3.84 (m, 2H, H-2, H-2a), 4.43–4.45 (m, 1H, H-6), 4.68 (s, 1H, H-4).

Second eluted was 6-butyl-3-methyl-(3*R*,3a*S*,4*S*,6*R*,6a*R*)-perhydrofuro[3,4-*b*]furan-4-yl-methylether **11** (0.370 g) in 75% yield as a colorless syrup; [Found: C, 67.20; H, 10.28%]; $[\alpha]_D=+32.05$ (*c* 0.6, $CHCl_3$); ν_{max} (Neat) 2930, 1100, 1045 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.92 (t, 3H, *J*=7.2 Hz, CH_3), 1.12 (d, 3H, *J*=5.5 Hz, CH_3), 1.32–1.50 (m, 4H, $2CH_2$), 1.59–1.74 (m, 2H, H-7, H-7a), 2.36–2.40 (m, 1H, H-3), 2.68–2.70 (m, 1H, H-3a), 3.19 (dd, 1H, *J*=10.0, 8.8 Hz, H-6a), 3.27 (s, 3H, OCH_3), 3.82–3.86 (m, 2H, H-2, H-2a), 4.42–4.46 (m, 1H, H-6), 4.87 (s, 1H, H-4).

3.1.8. 6-Butyl-4-methoxy-3-methyl-(3*R*,3a*S*,4*S*,6*R*,6a*R*)-perhydrofuro[3,4-*b*]furan-2-one (13). A solution of **11** (0.350 g, 1.63 mmol) in CCl_4:CH_3CN:H_2O (2:2:3, 7 mL) was treated with sodium periodate (1.050 g, 4.90 mmol), a catalytic amount of $RuCl_3{\cdot}H_2O$ (0.01 g) and stirred at room temperature for 18 h. The reaction mixture was extracted with chloroform (3×50 mL) and combined organic layers were dried (Na_2SO_4) and evaporated. The resulting residue was diluted with ether (50 mL) and filtered through a celite pad. Solvent was evaporated and residue purified by column chromatography (silica gel, 60–120 mesh; ethyl acetate–hexane, 2:8) to afford 6-butyl-4-methoxy-3-methyl-(3*R*,3a*S*,4*S*,6*R*,6a*R*)-perhydrofuro[3,4-*b*]furan-2-one **13** (0.171 g) in 46% yield as a colorless syrup; [Found: C, 63.08; H, 8.81. $C_{12}H_{20}O_4$ requires C, 63.14; H, 8.83%]; $[\alpha]_D=+36.48$ (*c* 0.50, $CHCl_3$); ν_{max} (Neat) 1770 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.92 (t, 3H, *J*=7.3 Hz, CH_3), 1.20–1.50 (m, 7H, $2CH_2$, CH_3), 1.64–1.82 (m, 2H, H-7, H-7a), 2.86 (dq, 1H, *J*=9.8, 7.0 Hz, H-3), 3.0 (dd, 1H, *J*=9.8, 6.9 Hz, H-3a), 3.32 (s, 3H, OMe), 4.02 (ddd, 1H, *J*=7.9, 4.3, 3.6 Hz, H-6), 4.82 (dd, 1H, *J*=6.9, 3.6 Hz, H-6a), 4.96 (s, 1H, H-4); *m*/*z* (FABMS) 228 (M^+).

3.1.9. 6-Butyl-4-methoxy-3-methyl-(3*S*,3a*S*,4*S*,6*R*,6a*R*)-perhydrofuro[3,4-*b*]furan-2-one (14). Compound **12** (0.115 g, 0.537 mmol) in CCl_4:CH_3CN:H_2O (2:2:3, 7 mL) was treated with sodium periodate (0.344 g, 1.61 mmol), a catalytic amount of $RuCl_3{\cdot}H_2O$ (0.01 g) and worked up as described for **13** to afford 6-butyl-4-methoxy-3-methyl-(3*S*,3a*S*,4*S*,6*R*,6a*R*)-perhydrofuro[3,4-*b*]furan-2-one **14** (0.055 g) in 45% yield as a colorless syrup; [Found: C, 63.10; H, 8.79. $C_{12}H_{20}O_4$ requires C, 63.14; H, 8.83%]; $[\alpha]_D=+11.36$ (*c* 0.50, $CHCl_3$); ν_{max} (Neat) 1770 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.92 (t, 3H, *J*=7.35 Hz, CH_3), 1.16–1.50 (m, 7H, $2CH_2$, CH_3), 1.58–1.72 (m, 2H, H-7, H-7a), 2.50 (dq, 1H, *J*=9.1, 6.8 Hz, H-3), 2.64 (dd, 1H, *J*=9.1, 4.5 Hz, H-3a), 3.30 (s, 3H, OCH_3), 3.94 (ddd, 1H, *J*=6.9, 6.8, 4.5 Hz, H-6), 4.76 (s, 1H, H-4), 4.86 (dd, 1H, *J*=6.8, 4.5 Hz, H-6a); *m*/*z* (FABMS) 228 (M^+).

3.1.10. 6-Butyl-3-methyl-(3*R*,3a*S*,6*R*,6a*R*)-perhydrofuro[3,4-*b*]furan-2,4-dione (2). A solution of **13** (0.150 g, 0.65 mmol) in 60% aq. AcOH (6 mL) containing conc. HCl (catalytic) was heated at 60°C for 30 min. The reaction mixture was cooled to room temperature, treated with solid sodium hydrogencarbonate (6 g), water (50 mL) and ethyl acetate (50 mL). The aqueous layer was separated and extracted with ethyl acetate (3×25 mL). Combined organic layers were washed with aq. sodium hydrogencarbonate (50 mL), water (50 mL), brine (50 mL) and dried (Na_2SO_4). Evaporation of solvent and purification of the residue by column chromatography (silica gel, 60–120 mesh; ethyl acetate–hexane, 3:7) gave 6-butyl-4-hydroxy-3-methyl-(3*R*,3a*S*,6*R*,6a*R*)-perhydrofuro[3,4-*b*]furan-2-one **15** (0.118 g) in 84% yield as a colorless syrup; $[\alpha]_D$=+2.55 (*c* 0.90, $CHCl_3$); δ_H (200 MHz, $CDCl_3$) 0.92 (t, 3H, *J*=7.2 Hz, CH_3), 1.16–1.50 (m, 7H, $2CH_2$, CH_3), 1.70–1.74 (m, 2H, H-7, H-7a), 2.86–2.90 (m, 1H, H-3), 3.02–3.06 (m, 1H, H-3a), 4.22–4.26 (m, 1H, H-6a), 4.84–4.88 (m, 1H, H-6), 5.52 (s, 1H, H-4).

A solution of **15** (0.110 g, 0.514 mmol) and PDC [prepared from CrO_3 (1.54 g, 15.42 mmol) and pyridine (1.35 mL, 17.11 mmol)] in dry dichloromethane (20 mL) was heated at reflux for 2 h. The reaction mixture was cooled to room temperature and decanted. Residue was treated with aq. sodium hydrogencarbonate (50 mL) solution and extracted with chloroform (3×50 mL). The organic layer was washed with aq. sodium hydrogencarbonate (50 mL), water (50 mL), 2N HCl (50 mL), brine (50 mL), dried (Na_2SO_4) and evaporated. The residue was purified by column chromatography (silica gel, 60–120 mesh; ethyl acetate–hexane, 3:7) to afford 6-butyl-3-methyl-(3*R*,3a*S*,6*R*,-6a*R*)-perhydrofuro[3,4-*b*]furan-2,4-dione **2** (0.078 g) in 72% yield as a white solid, mp 53°C; [Found: C, 62.22; H, 7.58. $C_{11}H_{16}O_4$ requires C, 62.25; H, 7.60%]; $[\alpha]_D$=−18.02 (*c* 0.75, $CHCl_3$); lit.[14] $[\alpha]_D$=−20.2 (*c* 0.50, $CHCl_3$); ν_{max} (KBr) 1770 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.92 (t, 3H, *J*=7.2 Hz, CH_3), 1.30–1.54 (m, 7H, $2CH_2$, CH_3), 1.74–1.94 (m, 2H, H-7, H-7a), 3.08 (dq, 1H, *J*=10.0, 7.3 Hz, H-3), 3.45 (dd, 1H, *J*=10.0, 6.0 Hz, H-3a), 4.50 (ddd, 1H, *J*=7.2, 6.8, 4.5 Hz, H-6), 5.02 (dd, 1H, *J*=6.0, 4.5 Hz, H-6a); ^{13}C NMR (125 MHz, $CDCl_3$): δ_c 10.9, 13.8, 22.4, 27.4, 28.4, 36.6, 44.6, 77.9, 81.6, 172.0, 176.2; *m/z* (FABMS) 213 (M^++1).

3.1.11. 6-Butyl-3-methyl-(3*S*,3a*S*,6*R*,6a*R*)-perhydrofuro[3,4-*b*]furan-2,4-dione (1). Reaction of **14** (0.050 g, 0.219 mmol) with 60% aq. AcOH (3 mL) containing conc. HCl (catalytic) as described for **15** afforded 6-butyl-4-hydroxy-3-methyl-(3*S*,3a*S*,6*R*,6a*R*)-perhydrofuro[3,4-*b*]-furan-2-one **16** (0.040 g) in 86% yield as a colorless syrup; $[\alpha]_D$=+10.12 (*c* 0.45, $CHCl_3$); δ_H (200 MHz, $CDCl_3$) 0.92 (t, 3H, *J*=7.3 Hz, CH_3), 1.24–1.45 (m, 7H, $2CH_2$, CH_3), 1.62–1.68 (m, 2H, H-7, H-7a), 2.48–2.52 (m, 1H, H-3), 2.65–2.68 (m, 1H, H-3a), 2.78 (br s, 1H, OH), 4.20–4.23 (m, 1H, H-6a), 4.92–4.96 (m, 1H, H-6), 5.32 (s, 1H, H-4).

A solution of **16** (0.040 g, 0.18 mmol) in dry CH_2Cl_2 (15 mL) was treated with PDC [prepared from CrO_3 (0.560 g, 5.6 mmol) and pyridine (0.50 mL, 6.2 mmol)] as described for **2** to afford **1** (0.027 g) in 68% yield as a solid, mp 92°C; lit.[14] mp 94°C; [Found: C, 62.21; H, 7.57. $C_{11}H_{16}O_4$ requires C, 62.25; H, 7.60%]; $[\alpha]_D$=+30.9 (*c* 0.50, $CHCl_3$); lit.[14] $[\alpha]_D$=+29.8 (*c* 0.35, $CHCl_3$); ν_{max} (KBr) 1770 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 0.92 (t, 3H, *J*=7.6 Hz, CH_3), 1.38–1.55 (m, 7H, $2CH_2$, CH_3), 1.76–1.98 (m, 2H, H-7, H-7a), 3.02 (dq, 1H, *J*=8.0, 1.2 Hz, H-3), 3.08 (dd, 1H, *J*=6.4, 1.2 Hz, H-3a), 4.50 (ddd, 1H, *J*=7.2, 6.8, 4.4 Hz, H-6), 5.05 (dd, 1H, *J*=6.4, 4.4 Hz, H-6a); ^{13}C NMR (125 MHz, $CDCl_3$): δ_c 13.8, 17.1, 22.4, 27.5, 28.5, 38.3, 49.0, 78.3, 82.4, 174.6, 176.7; *m/z* (FABMS) 213 (M^++1).

3.1.12. Cyclisation of 10. Reaction of **10** (1.550 g, 4.84 mmol) with tributyltin hydride (2.8 mL, 9.68 mmol) in dry benzene (30 mL) as described for **11** gave a mixture of **17** and **18** (0.860 g) in 83% yield. First eluted on chromatographic purification was 6-butyl-3-methyl-(3*S*,3a*S*,4*R*,6*R*,6a*R*)-perhydrofuro[3,4-*b*]furan-4-yl-methyl-ether **18** (0.344 g) in 40% yield as a colorless syrup; [Found: C, 67.21; H, 10.28. $C_{12}H_{22}O_3$ requires C, 67.26; H, 10.35%]; $[\alpha]_D$=+15.96 (*c* 0.50, $CHCl_3$); ν_{max} (Neat) 1045, 1100, 2930 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.92 (t, 3H, *J*=7.2 Hz, CH_3), 1.12 (d, 3H, *J*=6.3 Hz, CH_3), 1.22–1.45 (m, 4H, $2CH_2$), 1.58–1.73 (m, 2H, H-7, H-7a), 2.36–2.40 (m, 1H, H-3), 2.56–2.60 (m, 1H, H-3a), 3.34–3.36 (m, 1H, H-2), 3.44 (s, 3H, OCH_3), 3.52–3.56 (m, 1H, H-6a), 3.85 (t, 1H, *J*=7.6 Hz, H-2a), 4.30–4.38 (m, 1H, H-6), 4.72 (d, 1H, *J*=5.7 Hz, H-4).

Second eluted was 6-butyl-3-methyl-(3*R*,3a*S*,4*R*,6*R*,6a*R*)-perhydrofuro[3,4-*b*]furan-4-yl-methylether **17** (0.516 g) in 60% yield as a colorless syrup; [Found: C, 67.22; H, 10.33%]; $[\alpha]_D$=+27.13 (c 0.80, $CHCl_3$); ν_{max} (Neat) 1045, 1100, 2930 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.92 (t, 3H, *J*=7.2 Hz, CH_3), 1.02 (d, 3H, *J*=7.7 Hz, CH_3), 1.25–1.46 (m, 4H, $2CH_2$), 1.59–1.75 (m, 2H, H-7, H-7a), 2.38–2.40 (m, 1H, H-3), 2.58–2.62 (m, 1H, H-3a), 3.36 (dd, 1H, *J*=6.8, 3.4 Hz, H-6a), 3.46 (s, 3H, OCH_3), 3.58–3.60 (m, 1H, H-2), 3.87 (dd, 1H, *J*=7.7, 5.1 Hz, H-2a), 4.36–4.40 (m, 1H, H-6), 4.74 (d, 1H, *J*=6.8 Hz, H-4).

3.1.13. 6-Butyl-4-methoxy-3-methyl-(3*R*,3a*S*,4*R*,6-*R*,6a*R*)-perhydrofuro[3,4-*b*]furan-2-one (19). Compound **17** (0.500 g, 2.33 mmol) in CCl_4:CH_3CN:H_2O (2:2:3, 7 mL) on reaction with sodium periodate (1.495 g, 6.99 mmol) and catalytic amount of $RuCl_3 \cdot H_2O$ (0.01 g) as described for **13** afforded 6-butyl-4-methoxy-3-methyl-(3*R*,3a*S*,4*R*,6*R*,6a*R*)-perhydrofuro[3,4-*b*]furan-2-one **19** (0.287 g) in 54% yield as a colorless syrup; [Found: C, 63.10; H, 8.79. $C_{12}H_{20}O_4$ requires C, 63.14; H, 8.83%]; $[\alpha]_D$=+37.73 (*c* 0.50, $CHCl_3$); ν_{max} (Neat) 1770 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.92 (t, 3H, *J*=7.2 Hz, CH_3), 1.22–1.54 (m, 7H, $2CH_2$, CH_3), 1.64–1.80 (m, 2H, H-7, H-7a), 2.84 (dq, 1H, *J*=9.1, 6.8 Hz, H-3), 2.98 (dd, 1H, *J*=9.1, 6.9 Hz, H-3a), 3.32 (s, 3H, OMe), 3.98 (ddd, 1H, *J*=7.7, 7.4, 3.2 Hz, H-6), 4.80 (dd, 1H, *J*=6.9, 3.2 Hz, H-6a), 4.94 (s, 1H, H-4); *m/z* (FABMS) 228 (M^+).

3.1.14. 6-Butyl-4-methoxy-3-methyl-(3*S*,3a*S*,4*R*,6-*R*,6a*R*)-perhydrofuro[3,4-*b*]furan-2-one (20). Reaction of **18** (0.325 g, 1.51 mmol) CCl_4:CH_3CN:H_2O (2:2:3, 7 mL) with sodium periodate (0.969 g, 4.53 mmol) and catalytic amount of $RuCl_3 \cdot H_2O$ (0.01 g) as described for **13** gave 6-butyl-4-methoxy-3-methyl-(3*S*,3a*S*,4*R*,6*R*,6a*R*)-perhydrofuro-[3,4-*b*]furan-2-one **20** (0.175 g) in 51% yield

as a colorless syrup; [Found: C, 63.11; H, 8.82. $C_{12}H_{20}O_4$ requires C, 63.14; H, 8.83%]; $[\alpha]_D$=+13.96 (*c* 0.50, $CHCl_3$); ν_{max} (Neat) 1770 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.92 (t, 3H, *J*=7.4 Hz, CH_3), 1.18–1.50 (m, 7H, $2CH_2$, CH_3), 1.58–1.76 (m, 2H, H-7, H-7a), 2.50 (dq, 1H, *J*=8.2, 7.7 Hz, H-3), 2.65 (dd, 1H, *J*=8.2, 4.5 Hz, H-3a), 3.30 (s, 3H, OCH_3), 3.96 (ddd, 1H, *J*=6.9, 5.9, 4.1 Hz, H-6), 4.77 (s, 1H, H-4), 4.89 (dd, 1H, *J*=6.9, 4.5 Hz, H-6a); *m/z* (FABMS) 228 (M^+).

3.1.15. Conversion of 19 to 2. Reaction of **19** (0.15 g, 0.65 mmol) in 60% aq. AcOH (3 mL) containing conc. HCl (catalytic) as described for **15** afforded **15** (0.085 g) in 61% yield as a syrup. Reaction of **15** (0.07 g, 0.32 mmol) in dry dichloromethane (10 mL) with PDC [prepared from CrO_3 (0.981 g, 9.8 mmol) and pyridine (0.85 mL, 10.89 mmol)] as described for **2** furnished **2** (0.046 g) in 67% yield as a white solid, whose spectral data was comparable with **2** prepared from **13**.

3.1.16. Conversion of 20 to 1. Reaction of **20** (0.16 g, 0.70 mmol) in 60% aq. AcOH (3 mL) containing conc. HCl (catalytic) as described for **15** afforded **16** (0.106 g) in 71% yield as a syrup. Reaction of **16** (0.085 g, 0.397 mmol) in dry CH_2Cl_2 (10 mL) with PDC [prepared from CrO_3 (1.190 g, 11.91 mmol) and pyridine (1 mL, 13.22 mmol)] as described for **2** furnished **1** (0.061 g) in 73% yield as a white solid, which has identical spectral data with that of **1** prepared from **14**.

3.1.17. 5-Hexyl-2,2-dimethyl-(3a*R*,5*R*,6*S*,6a*R*)-perhydrofuro[2,3-*d*][1,3]dioxole-6-ol (5a). A solution of **4** (10 g, 29.0 mmol) in THF (15 mL) was treated with *n*-pentylmagnesium bromide [prepared from Mg (2.093 g, 87.2 mmol), *n*-pentyl bromide (5.50 mL, 43.5 mmol)] and workup as described for **5** afforded 5-hexyl-2,2-dimethyl-(3a*R*,5*R*,6*S*,6a*R*)-perhydrofuro[2,3-*d*][1,3] dioxole-6-ol **5a** (4.894 g) in 69% yield as a white solid, mp 76°C; [Found: C, 63.87; H, 9.86. $C_{13}H_{24}O_4$ requires C, 63.91; H, 9.90%]; $[\alpha]_D$=−16.47 (*c* 0.6, $CHCl_3$); ν_{max} (KBr) 3270 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.90 (t, 3H, *J*=6.8 Hz, CH_3), 1.24–1.52 (m, 14H, $4CH_2$, $2CH_3$), 1.52–1.72 (m, 2H, H-5a, H-5b), 3.80–4.12 (m, 2H, H-6, H-5), 4.44 (d, 1H, *J*=4.5 Hz, H-6a), 5.82 (d, 1H, *J*=4.5 Hz, H-3a); *m/z* (EIMS) 229 (M^+−15).

3.1.18. 6-Allyloxy-5-hexyl-2,2-dimethyl-(3a*R*,5*R*,6*S*,6a*R*)-perhydrofuro[2,3-*d*][1,3]dioxole (6a). Reaction of **5a** (6.0 g, 24.59 mmol) in THF (20 mL) with sodium hydride (1.180 g, 49.1 mmol) and allyl bromide (3.5 mL, 29.50 mmol) as described for **6** gave 6-allyloxy-5-hexyl-2,2-dimethyl-(3a*R*,5*R*,6*S*,6a*R*)-perhydrofuro[2,3-*d*][1,3]-dioxole **6a** (6.0 g) in 86% yield as a light yellow syrup; [Found: C, 67.51; H, 9.88. $C_{16}H_{28}O_4$ requires C, 67.57; H, 9.92%]; $[\alpha]_D$=−53.30 (*c* 0.5, $CHCl_3$); ν_{max} (Neat) 970, 1080, 1640 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.88 (t, 3H, *J*=6.5 Hz, CH_3), 1.22–1.48 (m, 14H, $4CH_2$, $2CH_3$), 1.56–1.76 (m, 2H, H-5a, H-5b), 3.68 (d, 1H, *J*=2.8 Hz, H-6), 3.94 (dd, 1H, *J*=9.4, 5.6 Hz, H-8), 4.04–4.08 (m, 1H, H-5), 4.13 (dd, 1H, *J*=9.4, 5.6 Hz, H-8a), 4.50 (d, 1H, *J*=4.7 Hz, H-6a), 5.24 (dd, 2H, *J*=18.8, 11.2 Hz, H-10, H-10a), 5.82 (d, 1H, *J*=4.7 Hz, H-3a), 5.80–5.90 (m, 1H, H-9); *m/z* (EIMS) 269 (M^+−15).

3.1.19. Hydrolysis of 6a. Reaction of **6a** (6.0 g, 21.1 mmol) in dry methanol (35 mL) containing few drops of conc. HCl as described for **7** furnished **7a** and **8a** as an α/β-anomeric mixture (4.900 g) in 90% yield. Chromatographic purification first gave 4-allyloxy-5-hexyl-2-methoxy-(2*S*,3*R*,4*S*,5*R*)-tetrahydro-3-furanol **7a** (2.150 g) in 44% yield as a colorless syrup; [Found: C, 64.92; H, 10.09. $C_{14}H_{26}O_4$ requires C, 65.09; H, 10.14%]; $[\alpha]_D$=+65.61 (*c* 0.8, $CHCl_3$); ν_{max} (Neat) 3270, 1640, 1080, 980 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.88 (t, 3H, *J*=6.7 Hz, CH_3), 1.18–1.48 (m, 8H, $4CH_2$), 1.50–1.66 (m, 2H, H-5a, H-5b), 2.70 (br s, 1H, OH), 3.44 (s, 3H, OCH_3), 3.68 (dd, 1H, *J*=5.5, 3.3 Hz, H-4), 3.88–4.24 (m, 4H, H-2, H-5, H-6, H-6a), 4.88 (d, 1H, *J*=4.4 Hz, H-2), 5.18 (dd, 2H, *J*=18.0, 11.2 Hz, H-8, H-8a), 5.74–5.96 (m, 1H, H-7); *m/z* (EIMS) 227 (M^+−31).

Second eluted was 4-allyloxy-5-hexyl-2-methoxy-(2*R*,3*R*,4*S*,5*R*)-tetrahydro-3-furanol **8a** (2.750 g) in 56% of the overall yield as a colorless syrup; [Found: C, 65.03; H, 10.11%]; $[\alpha]_D$=−44.43 (*c* 0.55, $CHCl_3$); ν_{max} (Neat) 3270, 1640, 1080, 980 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.88 (t, 3H, *J*=6.8 Hz, CH_3), 1.21–1.42 (m, 8H, $4CH_2$), 1.48–1.66 (m, 2H, H-5a, H-5b), 2.35 (br, s, 1H, OH), 3.38 (s, 3H, OCH_3), 3.75 (dd, 1H, *J*=5.5, 3.6 Hz, H-4), 3.98–4.18 (m, 4H, H-3, H-5, H-6, H-6a), 4.67 (d, 1H, *J*=2.2 Hz, H-2), 5.22 (dd, 2H, *J*=18.8, 11.2 Hz, H-8, H-8a), 5.77–5.97 (m, 1H, H-7); *m/z* (EIMS) 227 (M^+−31).

3.1.20. 4-Allyloxy-5-hexyl-2-methoxy-3-methyldithiocarbonate-(2*S*,3*R*,4*S*,5*R*)-tetrahydro-furan (9a). Reaction of **7a** (2.10 g, 8.1 mmol) in THF (10 mL) with sodium hydride (0.390 g, 16.2 mmol), carbon disulfide (0.920 mL, 12.2 mmol) and methyl iodide (1.73 0 mL, 12.2 mmol) as described for **9** furnished 4-allyloxy-5-hexyl-2-methoxy-3-methyldithio-carbonate-(2*S*,3*R*,4*S*,5*R*)-tetrahydrofuran **9a** (2.150 g) in 76% yield as a light yellow syrup; $[\alpha]_D$=+107.20 (*c* 0.6, $CHCl_3$); ν_{max} (Neat) 3290, 1640, 1080, 980 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.90 (t, 3H, *J*=6.7 Hz, CH_3), 1.23–1.45 (m, 8H, $4CH_2$), 1.54–1.70 (m, 2H, H-5a,5b), 2.58 (s, 3H, S-CH_3), 3.34 (s, 3H, OCH_3), 3.86–4.24 (m, 4H, H-4, H-5, H-6, H-6a), 5.12–5.32 (m, 3H, H-3, H-8, H-8a), 5.58 (t, 1H, *J*=3.6 Hz, H-2), 5.74–5.94 (m, 1H, H-7).

3.1.21. 4-Allyloxy-5-hexyl-2-methoxy-3-methyldithiocarbonate-(2*R*,3*R*,4*S*,5*R*)-tetrahydro-furan (10a). A solution of **8a** (2.500 g, 9.68 mmol) in THF (10 mL) on reaction with sodium hydride (0.465 g, 19.37 mmol), carbon disulfide (1.10 mL, 14.52 mmol) and methyl iodide (2.0 mL, 14.52 mmol) as described for **9** gave 4-allyloxy-5-hexyl-2-methoxy-3-methyldithiocarbonate-(2*R*,3*R*,4*S*,5*R*)-tetrahydrofuran **10a** (2.630 g) in 78% yield as a yellow syrup; $[\alpha]_D$=−96.02 (*c* 0.6, $CHCl_3$); ν_{max} (Neat) 3290, 1640, 1080, 980 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.88 (t, 3H, *J*=6.7 Hz, CH_3), 1.20–1.40 (m, 8H, $4CH_2$), 1.58–1.78 (m, 2H, H-5a, H-5b), 2.58 (s, 3H, S-CH_3), 3.38 (s, 3H, OCH_3), 3.88 (d, 1H, *J*=3.9 Hz, H-4), 3.97–4.30 (m, 3H, H-5, H-6, H-6a), 4.92 (s, 1H, H-3), 5.22 (dd, 2H, *J*=18.8, 11.2 Hz, H-8, H-8a), 5.77 (s, 1H, H-2), 5.78–5.96 (m, 1H, H-7).

3.1.22. Cyclisation of 9a. A solution of **9a** (2.150 g, 6.17 mmol) in dry benzene (30 mL) on reaction with tributyltin hydride (3.6 mL, 12.34 mmol) and catalytic

amount of AIBN as described for **11** gave a mixture of **11a** and **12a** (1.160 g) in 78% yield. Chromatographic purification (silica gel 60–120 mesh, ethylacetate–hexane 1:50) first gave 6-hexyl-3-methyl-(3*S*,3a*S*,4*S*,6*R*,6a*R*)-perhydrofuro[3,4-*b*]furan-4-yl-methylether **12a** (0.350 g) in 30% yield as a colorless syrup; [Found: C, 69.32; H, 10.78. $C_{14}H_{26}O_3$ requires C, 69.38; H, 10.81%]; $[\alpha]_D$=+57.45 (*c* 0.55, $CHCl_3$); ν_{max} (Neat) 1045, 1100, 2930 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.88 (t, 3H, *J*=6.7 Hz, CH_3), 1.08 (d, 1H, *J*=6.8 Hz, CH_3), 1.20–1.50 (m, 8H, $4CH_2$), 1.55–1.72 (m, 2H, H-7, H-7a), 2.06–2.20 (m, 1H, H-3), 2.26–2.38 (m, 1H, H-3a), 3.26 (s, 3H, OCH_3), 3.33 (dd, 1H, *J*=6.3, 4.5 Hz, H-6a), 3.78–3.82 (m, 1H, H-2), 4.16–4.20 (m, 1H, H-2a), 4.44 (dd, 1H, *J*=6.3, 3.6 Hz, H-6), 4.69 (s, 1H, H-4).

Second eluted was 6-hexyl-3-methyl-(3*R*,3a*S*,4*S*,6*R*,6a*R*)-perhydrofuro [3,4-*b*]furan-4-yl-methylether **11a** (0.810 g) in 70% yield as a colorless syrup; [Found: C, 69.35; H, 10.79%]; $[\alpha]_D$=+63.74 (*c* 0.70, $CHCl_3$); ν_{max} (Neat) 1045, 1100, 2930 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.88 (t, 3H, *J*=6.7 Hz, CH_3), 1.06 (d, 1H, *J*=5.2 Hz, CH_3), 1.26–1.46 (m, 8H, $4CH_2$), 1.52–1.75 (m, 2H, H-7, H-7a), 2.32–2.46 (m, 1H, H-3), 2.58–2.69 (m, 1H, H-3a), 3.21 (dd, 1H, *J*=8.8, 5.2 Hz, H-6a), 3.30 (s, 3H, OCH_3), 3.84–3.88 (m, 1H, H-2), 4.16–4.20 (m, 1H, H-2a), 4.44 (dd, 1H, *J*=8.8, 3.2 Hz, H-6), 4.92 (s, 1H, H-4).

3.1.23. 6-Hexyl-4-methoxy-3-methyl-(3*R*,3a*S*,4*S*,6-*R*,6a*R*)-perhydrofuro[3,4-*b*]furan-2-one (13a). Oxidation of **11a** (0.750 g, 3.09 mmol) in CCl_4:CH_3CN:H_2O (2:2:3, 7 mL) with sodium periodate (3.970 g, 18.59 mmol) and catalytic amount of $RuCl_3{\cdot}H_2O$ (0.01 g) as described for **13** afforded 6-hexyl-4-methoxy-3-methyl-(3*R*,3a*S*,4*S*,6*R*,6a*R*)-perhydrofuro[3,4-*b*]furan-2-one **13a** (0.460 g) in 58% yield as a colorless syrup; [Found: C, 65.57; H, 9.39. $C_{14}H_{24}O_4$ requires C, 65.60; H, 9.44%]; $[\alpha]_D$=+20.75 (*c* 0.50, $CHCl_3$); ν_{max} (Neat) 1770 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.88 (t, 3H, *J*=6.7 Hz, CH_3), 1.24–1.46 (m, 8H, $4CH_2$), 1.58–1.72 (m, 2H, H-7, H-7a), 2.84 (dq, 1H, *J*=9.2, 6.1 Hz, H-3), 2.96 (dd, 1H, *J*=9.2, 6.0 Hz, H-3a), 3.30 (s, 3H, OCH_3), 3.97 (ddd, 1H, *J*=9.2, 6.1, 3.8 Hz, H-6), 4.78 (dd, 1H, *J*=6.1, 3.0 Hz, H-6a), 4.92 (s, 1H, H-4). ^{13}C NMR ($CDCl_3$, 50 MHz): δ_c 115, 13.9, 22.3, 24.6, 26.0, 28.6, 29.1, 31.6, 35.4, 50.2, 79.8, 81.5, 103.2, 178.1; *m*/*z* (FABMS) 256 (M^+).

3.1.24. 6-Hexyl-4-methoxy-3-methyl-(2*S*,3a*S*,4*S*,6-*R*,6a*R*)-perhydrofuro[3,4-*b*]furan-2-one (14a). A suspension of **12a** (0.350 g, 1.44 mmol) in CCl_4:CH_3CN:H_2O (2:2:3, 7 mL) on reaction with sodium periodate (1.856 g, 8.67 mmol) and catalytic amount of $RuCl_3{\cdot}H_2O$ (0.01 g) as described for **13** gave 6-hexyl-4-methoxy-3-methyl-(2*S*,3a*S*,4*S*,-6*R*,6a*R*)-perhydrofuro[3,4-*b*]furan-2-one **14a** (0.225 g) in 61% yield as a colorless syrup; [Found: C, 65.59; H, 9.42. $C_{14}H_{24}O_4$ requires C, 65.60; H, 9.44%]; $[\alpha]_D$=+13.46 (*c* 0.50, $CHCl_3$); ν_{max} (Neat) 1770 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.88 (t, 3H, *J*=6.7 Hz, CH_3), 1.22–1.47 (m, 8H, $4CH_3$), 1.62–1.69 (m, 2H, H-7, H-7a), 2.50 (dq, 1H, *J*=8.6, 6.9 Hz, H-3), 2.65 (dd, 1H, *J*=9.2, 6.9 Hz, H-3a), 3.30 (s, 3H, OCH_3), 3.96 (ddd, 1H, *J*=8.5, 5.2, 3.4 Hz, H-6), 4.78 (s, 1H, H-4), 4.88 (dd, 1H, *J*=6.9, 5.2 Hz, H-6a). ^{13}C NMR (50 MHz, $CDCl_3$,): δ_c 13.9, 17.2, 22.5, 26.0, 28.5, 28.7, 31.6, 38.4, 53.9, 54.4, 79.4, 81.4, 108.0, 179.1; *m*/*z* (FABMS) 256 (M^+).

3.1.25. 6-Hexyl-3-methyl-(3*R*,3a*S*,6*R*,6a*R*)-perhydrofuro[3,4-*b*]furan-2,4-dione (2a). Reaction of **13a** (0.250 g, 0.976 mmol) in 60% aq. AcOH (5 mL) containing conc. HCl (catalytic) as described for **15** furnished 6-hexyl-4-hydroxy-3-methyl-(3*R*,3a*S*,6*R*,6a*R*)-perhydrofuro[3,4-*b*]-furan-2-one **15a** (0.188 g) in 79% yield as a colorless syrup. $[\alpha]_D$=−14.25 (*c* 0.80, $CHCl_3$); δ_H (200 MHz, $CDCl_3$) 0.88 (t, 3H, *J*=6.7 Hz, CH_3), 1.22–1.52 (m, 11H, $4CH_2$, CH_3), 1.64–1.78 (m, 2H, H-7, H-7a), 2.90 (dq, 1H, *J*=9.5, 6.6 Hz, H-3), 3.03 (dd, 1H, *J*=8.2, 6.6 Hz, H-3a), 4.24 (ddd, 1H, *J*=7.7, 6.1, 4.0 Hz, H-6), 4.84 (dd, 1H, *J*=5.7, 2.3 Hz, H-6a), 5.50 (s, 1H, H-4).

Reaction of **15a** (0.150 g, 0.61 mmol) in dichloromethane (15 mL) with PDC [prepared from CrO_3 (1.860 g, 18.59 mmol) and pyridine 1.6 mL, 20.3 mmol)] as described for **2** gave 6-hexyl-3-methyl-(3*R*,3a*S*,6*R*,6a*R*)-perhydrofuro[3,4-*b*]furan-2,4-dione **2a** (0.105 g) in 71% yield as a white solid, mp 56–57 °C; lit.[18] mp 57 °C; [Found: C, 64.92; H, 8.35. $C_{13}H_{20}O_4$ requires C, 64.98; H, 8.39%]; $[\alpha]_D$=−22.06 (*c* 0.5, $CHCl_3$); ν_{max} (KBr) 1770 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.88 (t, 3H, *J*=6.7 Hz, CH_3), 1.22–1.52 (m, 11H, $4CH_2$, CH_3), 1.70–1.92 (m, 2H, H-7, H-7a), 3.01 (dq, 1H, *J*=10.2, 7.4 Hz, H-3), 3.39 (dd, 1H, *J*=10.2, 6.2 Hz, H-3a), 4.48 (ddd, 1H, *J*=7.2, 6.6, 4.0 Hz, H-6), 4.98 (dd, 1H, *J*=6.2, 4.0 Hz, H-6a); ^{13}C NMR (100 MHz, $CDCl_3$): δ 10.8, 13.9, 22.4, 25.3, 28.7, 31.5, 36.6, 44.6, 77.9, 81.6, 172.1, 176.2; *m*/*z* (FABMS) 241 (M^++1).

3.1.26. 6-Hexyl-3-methyl-(3*S*,3a*S*,6*R*,6a*R*)-perhydrofuro[3,4-*b*]furan-2,4-dione (1a). A suspension of **14a** (0.200 g, 0.78 mmol) in 60% aq. AcOH (5 mL) containing conc. HCl (catalytic) on hydrolysis as described for **15** gave 6-hexyl-4-hydroxy-3-methyl-(3*S*,3a*S*,6*R*,6a*R*)-perhydrofuro[3,4-*b*]-furan-2-one **16a** (0.148 g) in 78% yield as a colorless syrup; $[\alpha]_D$=+20.54 (*c* 1.10, $CHCl_3$); δ_H (200 MHz, $CDCl_3$) 0.88 (t, 3H, *J*=6.2 Hz, CH_3), 1.24–1.46 (m, 8H, $4CH_2$), 1.60–1.75 (m, 2H, H-7, H-7a), 2.54 (dq, 1H, *J*=6.0, 1.8 Hz, H-3), 2.67 (dd, 1H, *J*=6.0, 3.4 Hz, H-3a), 3.20 (br. s, 1H, OH), 4.20 (ddd, 1H, *J*=7.8, 6.8, 4.3 Hz, H-6), 4.94 (dd, 1H, *J*=6.6, 4.3 Hz, H-6a), 5.30 (s, 1H, H-4).

A solution of **16a** (0.085 g, 0.35 mmol) in dichloromethane (15 mL) on reaction with PDC [prepared from CrO_3 (1.045 g, 10.45 mmol) and pyridine (0.9 mL, 11.32 mmol)] as described for **2** afforded 6-hexyl-3-methyl-(3*S*,3a*S*,6*R*,6a*R*)-perhydrofuro [3,4-*b*]furan-2,4-dione **1a** (0.062 g) in 74% yield as a white solid, mp 88–89°C; [Found: C, 64.95; H, 8.37. $C_{13}H_{20}O_4$ requires C, 64.98; H, 8.39%]; $[\alpha]_D$=+36.12 (*c* 0.90, $CHCl_3$); ν_{max} ($CHCl_3$) 1770 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.90 (t, 3H, *J*=6.7 Hz, CH_3), 1.20–1.56 (m, 11H, $4CH_2$, CH_3), 1.70–1.96 (m, 2H, H-7, H-7a), 2.92–3.10 (m, 2H, H-3a, H-3), 4.48 (ddd, 1H, *J*=7.0, 6.8, 4.0 Hz, H-6), 5.04 (dd, 1H, *J*=6.0, 4.0 Hz, H-6a); ^{13}C NMR (100 MHz, $CDCl_3$): δ_c 14.0, 17.40, 22.51, 24.61, 28.76, 31.52, 33.04, 38.18, 47.2, 80.48, 84.24, 174.70, 176.56; *m*/*z* (FABMS) 241 (M^++1).

3.1.27. Cyclisation of 10a. Reaction of **10a** (2.5 g, 7.18 mmol) in dry benzene (30 mL) with tributyltin hydride

(4.15 mL, 14.37 mmol) as described for **11** gave a mixture of **17a** and **18a** (1.390 g) in 80% yield, which on chromatographic purification (silica gel 60–120 mesh, ethyl acetate–hexane 1:50) first gave 6-hexyl-3-methyl (3*S*,3a*S*,.4*R*,6*R*,6a*R*)-perhydrofuro[3,4-*b*]furan-4-yl-methyl ether **18a** (0.975 g) in 70% yield as a colorless syrup; [Found: C, 69.33; H, 10.77. $C_{14}H_{26}O_3$ requires C, 69.38; H, 10.81%]; $[\alpha]_D$=+13.96 (*c* 0.45, $CHCl_3$); ν_{max} (Neat) 1045, 1100, 2930 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.90 (t, 3H, *J*=6.7 Hz, CH_3), 1.02 (d, 3H, *J*=6.5 Hz, CH_3), 1.24–1.46 (m, 8H, $4CH_2$), 1.62–1.70 (m, 2H, H-7, H-7a), 2.40 (dq, 1H, *J*=5.2, 2.9 Hz, H-3), 2.54–2.64 (m, 1H, H-3a), 3.36 (dd, 1H, *J*=7.8, 4.0 Hz, H-2), 3.44 (s, 3H, OCH_3), 3.58 (dd, 1H, *J*=5.8, 3.5 Hz, H-6a), 3.88 (dd, 1H, *J*=7.8, 5.8 Hz, H-2a), 4.38 (dd, 1H, *J*=5.8, 4.0 Hz, H-6), 4.74 (d, 1H, *J*=5.8 Hz, H-4).

Second eluted was the 6-hexyl-3-methyl-(3*R*,3a*S*,4*R*,6-*R*,6a*R*)-perhydrofuro[3,4-*b*]furan-4-yl-methylether **17a** (0.415 g) in 30% yield as a colorless syrup; [Found: C, 69.36; H, 10.78%]; $[\alpha]_D$=+37.73 (*c* 0.50, $CHCl_3$); ν_{max} (Neat) 1045, 1100, 2930 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.88 (t, 1H, *J*=6.7 Hz, CH_3), 1.17 (d, 3H, *J*=7.3 Hz, CH_3), 1.18–1.48 (m, 8H, $4CH_2$), 1.56–1.72 (m, 2H, H-7, H-7a), 2.42–2.76 (m, 2H, H-3, H-3a), 3.33 (s, 3H, OCH_3), 3.62 (dd, 1H, *J*=9.7, 7.8 Hz, H-6a), 3.82–4.02 (m, 2H, H-2, H-2a), 4.50 (t, 1H, *J*=7.8 Hz, H-6), 4.80 (d, 1H, *J*=4.8 Hz, H-4); *m/z* (FABMS) 256 (M^+).

3.1.28. 6-Hexyl-4-methoxy-3-methyl-(3*R*,3a*S*,4*R*,6-*R*,6a*R*)-perhydrofuro[3,4-*b*]furan-2-one (19a). Reaction of **17a** (0.400 g, 1.65 mmol) in CCl_4:CH_3CN:H_2O (2:2:3, 7 mL) with sodium periodate (2.120 g, 9.91 mmol) and catalytic amount of $RuCl_3 \cdot H_2O$ (0.01 g) as described for **13** gave 6-hexyl-4-methoxy-3-methyl-(3*R*,3a*S*,4*R*,6*R*,6a*R*)-perhydrofuro[3,4-*b*]furan-2-one **19a** (0.265 g) in 63% yield as a colorless syrup; [Found: C, 65.55; H, 9.40. $C_{14}H_{24}O_4$ requires C, 65.60; H, 9.44%]; $[\alpha]_D$=+32.92 (*c* 0.70, $CHCl_3$); ν_{max} (Neat) 1770 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.88 (t, 3H, *J*=6.7 Hz, CH_3), 1.18 (d, 3H, *J*=4.7 Hz, CH_3), 1.20–1.38 (m, 3H, CH_3), $2CH_2$, CH_3), 1.52–1.72 (m, 2H, H-7, H-7a), 2.48–2.96 (m, 2H, H-3, H-3a), 3.48 (dd, 1H, *J*=6.2, 3.5 Hz, H-6a), 3.67 (s, 3H, OCH_3), 4.30 (ddd, 1H, *J*=8.0, 7.2, 3.2 Hz, H-6), 4.88 (d, 1H, *J*=2.2 Hz, H-4); *m/z* (FABMS) 256 (M^+).

3.1.29. 6-Hexyl-4-methoxy-3-methyl-(3*S*,3a*S*,4*R*,6-*R*,6a*R*)-perhydrofuro[3,4-*b*]furan-2-one (20a). A suspension of **18a** (0.500 g, 2.06 mmol) in CCl_4:CH_3CN:H_2O (2:2:3, 7 mL) on reaction with sodium periodate (2.652 g, 12.39 mmol) and catalytic amount of $RuCl_3 \cdot H_2O$ (0.01 g) as described for **13** furnished 6-hexyl-4-methoxy-3-methyl-(3*S*,3a*S*,4*R*,6*R*,6a*R*)-perhydrofuro[3,4-*b*]furan-2-one **20a** (0.305 g) in 58% yield as a colorless syrup; [Found: C, 65.56; H, 9.42. $C_{14}H_{24}O_4$ requires C, 65.60; H, 9.44%]; $[\alpha]_D$=+14.96 (*c* 0.50, $CHCl_3$); ν_{max} (Neat) 1770 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.88 (t, 3H, *J*=6.7 Hz, CH_3), 1.52–1.76 (m, 2H, H-7, H-7a), 2.52 (dq, 1H, *J*=8.0, 7.2 Hz, H-3), 2.64 (dd, 1H, *J*=7.7, 4.5 Hz, H-3a), 3.30 (s, 3H, OCH_3), 3.92 (ddd, 1H, *J*=9.0, 8.2, 3.2 Hz, H-6), 4.74 (dd, 1H, *J*=7.0, 3.5 Hz, H-6a), 4.94 (s, 1H, H-4); *m/z* (FABMS) 256 (M^+).

3.1.30. Conversion of 19a to 2a. Reaction of **19a** (0.215 g, 0.83 mmol) in 60% aq. AcOH (6 mL) containing conc. HCl (catalytic) as described for **15** afforded **15a** (0.154 g) in 76% yield as a syrup. Reaction of **15a** (0.085 g, 0.35 mmol) in dry CH_2Cl_2 (10 mL) with PDC [prepared from CrO_3 (1.053 g, 10.53 mmol) and pyridine (0.92 mL, 11.68 mmol)] as described for **2** furnished **2a** (0.059 g), in 71% yield as a solid, whose spectral data was identical with **2a** prepared from **13a**.

3.1.31. Conversion of 20a to 1a. Reaction of **20a** (0.2 g, 0.78 mmol) in 60% aq. AcOH (6 mL) containing conc. HCl (catalytic) as described for **15** afforded **16a** (0.143 g) in 76% yield as a syrup. Reaction of **16a** (0.125 g, 0.516 mmol) in dry CH_2Cl_2 (10 mL) with PDC [prepared from CrO_3 (1.54 g, 15.49 mmol) and pyridine (1.35 mL, 17.18 mmol)] as described for **2** furnished **1a** (0.083 g) in 67% yield as a solid, which has shown identical spectral properties with **1a** prepared from **14a**.

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