Synthesis of pseudo saccharide precursors through ‘off template site’ Michael –Wittig reaction on sugar derived enal

G. V. M. Sharma*a, A. Subhash Chander*a, Palakodety Radha Krishna*a, K. Krishnudu*a, M. H. V. Ramana Rao*b, and A. C. Kunwarb

a D-211, Discovery Laboratory, Organic Chemistry Division-III, b NMR Group, Indian Institute of Chemical Technology, Hyderabad-500 007, India
E-mail: esmvee@iict.res.in

Dedicated to Dr. A V Rama Rao on his 70th birthday April 2, 2005
(received 12 Dec 03; accepted 03 May 04; published on the web 03 Jun 04)

Abstract
[3+3] Annulation protocol at an ‘off template site’ on the sugar derived enal synthon effectively resulted in the formation of C-C linked pseudo saccharide precursors. Thus, the enolate of phosphorane generated from ethyl acetoacetate first undergoes a Michael reaction on the enal followed by a Wittig reaction to furnish the target saccharides, where the chirality is very effectively translated from the parent sugar.

Keywords: ‘Off template site’, pseudo saccharide precursors, Michael Wittig reaction, [3+3] annulation, nuclear Overhauser effect, molecular mechanics

Introduction

Several antibiotics and compounds of biological interest incorporate glycosides of pseudosugars1-3 or carba-sugars4, since, they are endowed with relatively greater stability towards glycosidase-induced hydrolysis. Besides the application as enzyme inhibitors, the carba-sugars are discussed as synthetic intermediates for the preparation of more efficient drugs in order to substitute carbohydrate moieties5. Thus, development of novel and efficient methods for the enantioselective or enantiospecific construction of carbocycles6 resulted in a variety of useful routes such as Diels-Alder approaches, the double Michael cyclisation, 1,3-dipolar cycloaddition and free radical-induced C-C bond formation. As part of our ongoing efforts on the transformation of monosaccharides into new glycospurstances7-15, herein we describe the synthesis of C-C linked pseudo saccharide precursors 1-5 (Figure 1), adopting a Michael-Wittig reaction on sugar-derived enal.
Results and Discussion

From the retro synthetic analysis of 1-5 (Scheme 1), it was envisaged that, the enones 6a-d are appropriate late stage intermediates, which could be realized from the condensation of α, β-unsaturated aldehyde 7 and Wittig ylide 8 by a Michael-Wittig reaction. The enal 7 in turn could be made from D-glucose through aldehyde 9, while 8 could be prepared from ethyl acetoacetate.

Scheme 1

Scheme 2. a) Ph3=CHCO2Et, C6H6, reflux, b) DIBAL-H, CH2CL2, -23 °C, c)PDC CH2CL2, reflux, d) Ph3P=CHCOCH2CO2Et, NaH, 2 drops water, THF, 50 °C.

Aldehyde 916 was subjected to Wittig olefination (Scheme 2) with (ethoxycarbonyl methylene)triphenylphosphorane in benzene at reflux to give the ester 10, which on reduction with DIBAL-H in CH2Cl2 afforded 11 in 86% yield. Oxidation of 11 with PDC in CH2Cl2 at reflux gave enal 7 (95%), which on reaction with 817 in the presence of NaH and two drops of

Figure 1
water\textsuperscript{18} in THF at 50 °C for 10 min., resulted in the formation of 6a-d as a partially separable mixture of diastereoisomers in (6:1.5:1.5:1) 75% overall yield. The stereochemical outcome of each of the annulated products was unambiguously determined by \textsuperscript{1}H NMR spectra. The formation of 6a as major product, in the present study, indicates that the initial Michael-addition of nucleophile (sodium enolate of 8) on the $\gamma$-alkoxy enal system 7 results in the formation of a syn product\textsuperscript{19} and the aldehyde moiety of the adduct concomitantly undergoes a Wittig reaction in affording the cyclohexenone derivatives 6a-d.

The mixture of diastereoisomers 6a and 6b were separated from 6c and 6d by column chromatography and both the mixtures were independently treated with NaBH\textsubscript{4} in ethanol (Scheme 3) in the presence of CeCl\textsubscript{3}.7H\textsubscript{2}O under Luche’s reaction conditions\textsuperscript{20}. 6a and 6b afforded a mixture of alcohols 12 (major), 13 (minor) and 14 (single isomer) in the ratio of 4:1:2 respectively in a combined yield of 88%, while 6c and 6d furnished 15 as an inseparable mixture of alcohols. Acetylation of alcohols 12-14 with acetic anhydride in pyridine independently gave the corresponding acetates 16, 17 and 18 respectively, while 15 gave 19, 20 and 21a-b. All the acetates were thoroughly identified by spectral data.

\textbf{Scheme 3.} a) NaBH\textsubscript{4}, CeCl\textsubscript{3}.H\textsubscript{2}O, Et OH, 0 °C to RT, b) Ac\textsubscript{2}O-Py, c) OsO\textsubscript{4}-NMO, CH\textsubscript{3}COCH\textsubscript{3}:H\textsubscript{2}O (3:1).
Stereoselective *cis*-hydroxylation of the olefins 16-20 was affected using OsO₄-NMO in acetone-water (3:1) system to afford the diols 22-26. The stereochemical outcome, *anti*-to the -OAc group, is in accordance with literature²¹ precedence. Acetylation of diols 22-26 with acetic anhydride in pyridine afforded the corresponding pseudo saccharide precursors 1-5 in quantitative yields.

The structures of 1-5 were fully confirmed with the help of detailed NMR analysis using the vicinal couplings (J) as well as the data from the NOESY experiments. For compound 1, the characteristic NOE cross peaks (Figure 2) H6-H8, H6-H10a, H8-H10a and H7-H5 and J₅,₆, J₆,₇, J₇,₈ and J₅,₁₀a values of about 10 Hz are in consensus with a chair conformation, C₅, for the carbocycle ring. Interestingly, most of the substituents in this conformation take energetically favored equatorial position. For compound 2, the structure and conformation are supported by strong NOE cross peaks between H5-H9 and H6-H10a as well as large value of about 10 Hz for J₅,₆, J₅,₁₀a and J₉,₁₀a whereas large NOE cross peaks between H5-H7 as well as J₅,₁₀a 13.0 Hz and J₇,₈ 10.8 Hz confirm the structure of compound 3.

![Diagram of NOEs](image)

**Figure 2.** Diagramatic representation of NOEs.

Such a conformation for the carbocycle ring is again energetically favored, as apart from substituent at C-6 and C-9, all the substituents are placed equatorial. For compound 4 the characteristic NOE cross peaks H6-H10a and H5-H9 as well as large value of about 10 Hz for J₀, 10a and J₅, 10a and 9.8 Hz for J₅,₆ are in conformity with a chair conformation, while for 5, the
structure and conformation are supported by strong NOE cross peaks between H5-H7, H8-H10a and J5, 10a and J7, 8 of about 10 Hz. The six membered rings in all these molecules take $^8C_5$ chair conformation. The five membered ring is puckered in all the compounds. Small values of J1,2, J2,3 and J3,4 point out to a twist conformation for the sugar ring. The presence of NOE cross peaks between H1-Me (A), H2-Me (A) and H4-Me (B) implies an envelop conformation for the five membered ring containing isopropylidene group. The relative orientation of the carbocycle and sugar rings is derived with the help of NOESY experiments. For 1-3 the strong NOE cross peaks between H3-H10e, H4-H10a, and weak NOE cross peaks between H3-H10a and H4-H10e and H10e-OMe confirm the structures shown in Figure 2. For 4 and 5, on the other hand, there is change in configuration at C5 and the NOE cross peak between H3-H6 and H4-H6 support relative orientation of the rings. Molecular mechanics study is carried out on 1-5 using Sybyl$^{22}$ and the results obtained agree with the experimental data. Dihedral angle H4-C4-C5-H5 of about 170° for 1-3 and 5 (Figure 3) is consistent with large J4,5 of about 10 Hz. For 4 the calculated dihedral angle H4-C4-C5-H5 of -129° is conformity in experimentally observed J4,5 4.3 Hz.

These observations are in agreement with the experimental data supporting the trans stereochemistry across the rings.

Figure 3. Structures obtained from energy minimization for 1-5. (Note: For clarity in visualization the protecting groups are not shown in the figure).
Thus, pseudo saccharide precursors 1-5 were synthesised by adopting an ‘off template site’ stereoselective [3+3] annulation approach, where the chirality of the carbocycle is induced from the sugar template. In this present [3+3] annulation protocol, Michael-Wittig reaction was exploited for the first time in carbohydrate chemistry for the installation of carbocycle ring system at C-5 of sugar synthon. Due to the ready availability of reagents and simple reaction conditions, the present protocol and the pseudo saccharide precursors 1-5 should find a wide use in the synthesis of several C-glycoside mimics towards the bioactive carbohydrates.

Experimental Section

General Procedures. Solvents were dried over standard drying agents and freshly distilled prior to use. $^1$H NMR (200 MHz, 400 MHz, 500 MHz) and $^{13}$C NMR (50 MHz, 100 MHz, 125 MHz) spectra were recorded in deuteriochloroform solution with tetramethylsilane as an internal reference on Varian Gemini-200 MHz, Unity-400 MHz and INOVA-500 MHz spectrometers and J values are given in Hz. Optical rotations were measured with a JASCO DIP-370 instrument and $[\alpha]_D$ values are in units of $10^1$deg cm$^2$g$^{-1}$. Organic solutions were dried over anhydrous Na$_2$SO$_4$ and concentrated below 40°C in vacuo. HRMS were recorded on VG Autospec Mass Spectrometer at 5 or 7 K resolution using perfluoro kerosene as an internal reference. Infrared (IR) are reported in wavenumbers (cm$^{-1}$). The nomenclature mentioned in the experimental section was adopted from ACD/Name version 1.0$\beta$, ACD Inc., Toronto, Canada.

Synthesis

Ethyl 3-[6-methoxy-2,2-dimethyl-(3a$R$,5$R$,6$S$,6a$R$)-perhydrofuro[2,3-d][1,3]dioxol-5-yl]-($E$)-2-propenoate (10). A mixture of 9 (5.0 g, 24.75 mmol) and (ethoxycarbonylmethylene) triphenylphosphorane (10.3 g, 29.60 mmol) in benzene (50 mL) was heated at reflux temperature for 4 h. The reaction mixture was brought to room temperature and solvent evaporated under reduced pressure. The crude product was purified by column chromatography (60-120 mesh Siligel, Ethyl acetate: Pet. ether 1:9) to give the title compound 10 (5.5 g) in 82% yield as a light yellow syrup. $[\alpha]_D^{20}$ -125.38 (c 1.30, CHCl$_3$); $\nu_{\max }$ (Neat): 3020, 1200, 1160, 1080 cm$^{-1}$; $\delta_{\ell}$H(200 MHz, CDCl$_3$): 6.36-6.22 (m, 1H, H-5), 5.96-5.85 (m, 2H, H-1,6), 5.62-5.52 (m, 1H, H-4), 4.55 (d, 1H, J$_{1,2}$ 4.4 Hz, H-2), 4.18 (q, 2H, -OCH$_2$CH$_3$), 4.02 (d, 1H, J$_{3,4}$ 4.0 Hz, H-3), 3.32 (s, 3H, -OMe), 1.52 (s, 3H, CH$_3$), 1.30 (t, 6H, CH$_3$); m/z (FABMS) 273 (100 MH$^+$), 272 (9), 271 (26), 257 (39), 227 (64).

3-[6-Methoxy-2,2-dimethyl- (3a$R$,5$R$,6$S$,6a$R$)-perhydrofuro [2,3-d][1,3]dioxol-5-yl]-($E$)-2-propen-1-ol (11). To a stirred solution of 10 (4.0 g, 14.70 mmol) in dry CH$_2$Cl$_2$ (30 mL), DIBAL-H (29.4 mL, 29.41 mmol, 1M solution in hexane) was added dropwise at $-23^\circ$C (CCl$_4$ + solid CO$_2$) under nitrogen atmosphere for 15 min. After 3 h, methanol (15 mL) was added, stirred for 1 h and brought to room temperature. The separated solid was filtered off and washed with CH$_2$Cl$_2$ (2 x 50 mL). The combined organic layers were washed with brine (50 mL) and
dried (Na₂SO₄). Solvent was evaporated under reduced pressure and purification of the residue by column chromatography (60-120 mesh Si-gel, Ethyl acetate: Pet. ether 1:4) gave the title compound 11 (2.9 g) in 86% yield as a colorless syrup \([\alpha]_D^{20} -84.57 (c 1.40, CHCl₃); \nu_{\text{max}} (\text{Neat}): 3500, 2980, 1760, 1420, 1140 \text{ cm}^{-1}; \delta_H (200 MHz, CDCl₃): 9.98-5.83 (m, 2H, H-1,5), 5.75-5.62 (m, 1H, H-6), 4.92 (dd, 1H, J₃,₄ 3.6 J₄,₅ 8.6 Hz, H-4), 4.56 (d, 1H, J₁,₂ 4.0 Hz, H-2), 4.40-4.10 (m, 2H, H-7, 7'), 3.61 (d, 1H, J₃,₄ 3.6 Hz, H-3), 3.40 (s, 3H, -OMe), 1.95 (br. t, 1H, -OH), 1.50, 1.32 (2s, 6H, CH₃); m/z (FABMS) 253 (15 M⁺+23), 231 (57), 215 (18), 213 (100).

Michael-Wittig reaction on enal 7 (preparation of 6a-d). A solution of 11 (2.5 g, 10.86 mmol) in dry CH₂Cl₂ (25 mL) was treated with PDC (4.9 g, 13.04 mmol) and heated at reflux for 2 h. The reaction mixture was brought to room temperature; CH₂Cl₂ was removed under reduced pressure and filtered through silica gel bed using ether as eluent. Evaporation of solvent gave the title compound 3-[6-methoxy-2,2-dimethyl-(3aR,5R,6S,6aR)-perhydrofuro[2,3-d][1,3]dioxol-5-yl]-(E)-2-propenal (7; 2.36 g) in 95% yield as a light yellow syrup. \([\alpha]_D^{20} -61.91 (c 2.40, \text{CHCl}_3); \delta_H (200 MHz, \text{CDCl}_3): 9.55 (d, 1H, J₆,CHO 8.8 Hz, -CHO), 6.72 (dd, 1H, J₄,₅ 5.8, J₅,₆ 17.6 Hz, H-5), 6.32 (dd, 1H, J₅,₆ 17.6, J₆,CHO 8.8 Hz, H-6), 5.88 (d, 1H, J₁,₂ 4.4 Hz, H-1), 4.85-4.76 (m, 1H, H-4), 4.56 (d, 1H, J₁,₂ 4.4 Hz, H-2), 3.75 (d, 1H, J₃,₄ 4.0 Hz, H-3), 3.35 (s, 3H, -OMe), 1.45, 1.28 (2s, 6H, CH₃).

To a stirred solution of 7 (2.0 g, 8.77 mmol) and ylide 8 (3.42 g, 8.77 mmol) in dry THF (25 mL), NaH (0.8 g, 17.54 mmol, 60% suspension in paraffin oil) was added in portions at 50 °C under nitrogen atmosphere followed by 2 drops of water and stirred for 15 min. at the same temperature. The reaction mixture was brought to room temperature, acidified with 5% aq. HCl solution (pH~6) and extracted into ether (2 × 50 mL). The organic layer was washed with water (50 mL), brine (50 mL) and dried (Na₂SO₄). Evaporation of solvent under reduced pressure and purification of the residue by column chromatography (finer than 200 mesh Si-gel, Ethyl acetate: Pet. ether 1:4) gave the title compounds 6a-d (2.23 g) in 75% yield as partially separable mixtures 6a, b (1.66 g, 56%) and 6c, d (0.56 g, 19%). However, the mixture was separated by HPLC (ODS-preparative column, MeOH: H₂O, 7:3; UV: 225 nm) to afford 6a-d in 6:1.5:1.5:1 ratio respectively. First eluted was ethyl 6-[6-methoxy-2,2-dimethyl-(3aR,5R,6S,6aR)-perhydrofuro[2,3-d][1,3]dioxol-5-yl]-(E)-2-oxo-(1S,6R)-3-cyclohexene-1-carboxylate (6a) as a light yellow syrup. \([\alpha]_D^{20} -88.55 (c 1.16, \text{CHCl}_3); \delta_H (200 MHz, \text{CDCl}_3): 7.00-6.86 (m, 1H, H-9), 6.14-6.02 (m, 1H, H-8), 5.81 (d, 1H, J₁,₂ 4.6 Hz, H-1), 4.52 (d, 1H, J₁,₂ 4.6 Hz, H-2), 4.20 (q, 2H, -OCH₂CH₃), 4.02 (dd, 1H, J₃,₄ 4.4, J₄,₅ 9.3 Hz, H-4), 3.62 (d, 1H, J₃,₄ 4.4 Hz, H-3), 3.45 (d, 1H, J₅,₆ 9.3 Hz, H-6), 3.40 (s, 3H, -OMe), 3.12-2.96 (m, 1H, H-5), 2.70-2.51 (m, 1H, H-10), 2.34-2.14 (m, 1H, H-10'), 1.42 (s, 3H, CH₃), 1.30-1.20 (m, 6H, CH₃); m/z (FABMS) 341 (29 MH⁺), 295 (43), 133 (85), 87 (100), 43 (94); HRMS(FAB): MH⁺ found 340.150527. C₁₇H₂₄O₇ required 340.152203.

Second eluted was ethyl 6-[6-methoxy-2,2-dimethyl-(3aR,5R,6S,6aR)-perhydrofuro[2,3-d][1,3]dioxol-5-yl]-2-oxo-(1R,6R)-3-cyclohexene-1-carboxylate (6b) as a pale yellow syrup. \([\alpha]_D^{20} -60.24 (c 0.80, \text{CHCl}_3); \delta_H (200 MHz, \text{CDCl}_3): 7.05-6.92 (m, 1H, H-9), 6.12-6.00 (m, 1H, H-8), 5.82 (d, 1H, J₁,₂ 4.0 Hz, H-1), 4.55 (d, 1H, J₁,₂ 4.0 Hz, H-2), 4.20 (q, 2H, -OCH₂CH₃), 4.18
issue in honor of dr. rama rao arkivoc 2005 (iii) 12-26

(dd, 1H, J_{3,4} 4.0, J_{4,5} 8.5 Hz, H-4), 3.62 (d, 1H, J_{3,4} 4.0 Hz, H-3), 3.45-3.35 (m, 4H, H-6, -OMe),
3.15-3.00 (m, 1H, H-5), 2.75-2.62 (m, 1H, H-10), 2.32-2.10 (m, 1H, H-10'), 1.44 (s, 3H, CH₃),
1.35-1.20 (m, 6H, CH₃); m/z (FABMS) 363 (M⁺+23, 28), 341 (42), 295 (44), 55 (100), 41 (85);
HRMS (FAB): MH⁺, found 340.151054. C_{17}H_{24}O_{7} requires 340.152203.

Third eluted was ethyl 6-[6-methoxy-2,2-dimethyl-(3aR,5R,6S,6aR)-perhydrofuro[2,3-d][1,3]dioxol-5-yl]-2-oxo-(1R,6S)-3-cyclohexene-1-carboxylate (6c) as a light yellow syrup.

[α]D^{20} +94.40 (c 0.70, CHCl₃); δH (200 MHz, CDCl₃): 7.00-6.90 (m, 1H, H-9), 6.12-6.03 (m, 1H, H-8),
5.82 (d, 1H, J_{1,2} 3.7 Hz, H-1), 4.54 (d, 1H, J_{1,2} 3.7 Hz, H-2), 4.21 (q, 2H, -OCH₂CH₃), 4.00
(dd, 1H, J_{3,4} 3.2, J_{4,5} 9.3 Hz, H-4), 3.60 (d, 1H, J_{3,4} 3.2 Hz, H-3), 3.41 (s, 3H, -OMe), 3.30 (d, 1H, J_{5,6} 6.9 Hz, H-6),
3.10-2.95 (m, 1H, H-5), 2.85-2.50 (m, 2H, H-10, 10'), 1.44 (s, 3H, CH₃), 1.36-1.22 (m, 6H, CH₃); m/z (FABMS): 341 (17 MH +), 295 (35), 133 (100). 55 (45); HRMS (FAB) MH⁺, found 340.154248. C_{17}H_{24}O_{7} requires 340.152203.

Fourth eluted was ethyl 2-hydroxy-6-[6-methoxy-2,2-dimethyl-(3aR,5R,6S,6aR)-perhydrofuro[2,3-d][1,3]dioxol-5-yl]-(1S,2R,6S)-3-cyclohexene-1-carboxylate (6d) as a colorless solid, m. p. 105-107 °C; [α]D^{20} +72.64 (c 0.65, CHCl₃);
νmax (Neat): 3040, 1680, 1080 cm⁻¹; δH (200 MHz, CDCl₃): 7.15-7.02 (m, 1H, H-9), 6.12-6.02 (m, 1H, H-8),
5.82 (d, 1H, J_{1,2} 3.7 Hz, H-1), 4.55 (d, 1H, J_{1,2} 3.7 Hz, H-2), 4.18 (q, 2H, -OCH₂CH₃), 4.05
(dd, 1H, J_{3,4} 3.2, J_{4,5} 4.6 Hz, H-6), 2.75-2.55 (m, 3H, H-5, 10, 10'), 1.45 (s, 3H, CH₃), 1.32-1.20 (m, 6H, CH₃); m/z (FABMS) 363 (19 M⁺+23), 341 (13 MH⁺), 133 (57), 43 (100); HRMS(FAB): MH⁺, found 340.153724. C_{17}H_{24}O_{7} requires 340.152203.

Reduction of enones 6a and 6b. Preparation of 12-14. To a stirred solution of 6a-b (0.8 g, 2.35 mmol) and CeCl₃.7H₂O (1.75 g, 4.70 mmol) in ethanol (10 mL), NaBH₄ (0.08 g, 2.35 mmol) was added in portions at 0 °C. The reaction mixture was brought to room temperature and stirred for 1h. Ethanol was removed under reduced pressure, diluted with water (25 mL) and extracted into ether (3 × 25 mL). The combined ether layers were washed with water (50 mL), brine (50 mL) and dried (Na₂SO₄). Solvent was evaporated under reduced pressure and residue purified by column chromatography (finer than 200 mesh Si -gel, Ethyl acetate: Pet. ether 1:4) gave a mixture of title diastereoisomers 12, 13 and 14 (0.7 g) in 88% yield in 4:1:2 ratio respectively.

First eluted was ethyl 2-hydroxy-6-[6-methoxy-2,2-dimethyl-(3aR,5R,6S,6aR)-perhydrofuro[2,3-d][1,3]dioxol-5-yl]-(1S,2R,6R)-3-cyclohexene-1-carboxylate (13; 0.7 g) in 13% yield as a colorless solid, m. p. 84-86 °C; [α]D^{20} -123.22 (c 1.30, CHCl₃), νmax (Neat) 3560, 2960, 1140 cm⁻¹; δH (200 MHz, CDCl₃): 5.92-5.70 (m, 3H, H-1,8,9), 4.50 (d, 1H, J_{1,2} 4.5 Hz, H-2),
4.40-4.05 (m, 3H, H-7, -OCH₂CH₃), 4.00 (dd, 1H, J_{3,4} 4.2, J_{4,5} 5.8 Hz, H-4), 3.56 (d, 1H, J_{3,4} 4.2 Hz, H-3),
3.40 (s, 3H, -OMe), 2.86-2.62 (m, 2H, H-5,6), 2.32-2.14 (m, 1H, H-10), 1.84-1.66 (m, 1H, H-10'), 1.46 (s, 3H, CH₃), 1.35-1.25 (m, 6H, CH₃); m/z (FABMS): 365 (15 M⁺+23), 343 (14 MH⁺), 325 (28), 281 (29), 221 (50), 147 (100), 109 (75); HRMS (FAB): MH⁺, found 343.175791. C_{17}H_{27}O_{7} requires 343.175679.

Second eluted was ethyl 2-hydroxy-6-[6-methoxy-2,2-dimethyl-(3aR,5R,6S,6aR)-perhydrofuro[2,3-d][1,3]dioxol-5-yl]-(1R,2S,6R)-3-cyclohexene-1-carboxylate (14; 0.2 g) in
25% yield as a colorless solid, m. p. 103-105 °C. $[\alpha]_D^{20}$ -37.20 (c 2.20, CHCl$_3$), $\delta_H$ (200 MHz, CDCl$_3$): 5.78 (d, 1H, J$_{1,2}$ 4.0 Hz, H-1), 5.70-5.62 (m, 2H, H-8,9), 4.48 (d, 1H, J$_{1,2}$ 4.0 Hz, H-2), 4.40-4.25 (m, 2H, H-4,7), 4.14 (q, 2H, -OCH$_2$CH$_3$), 3.49 (d, 1H, J$_{3,4}$ 3.7 Hz, H-3), 3.35 (s, 3H, -OME), 3.15 (dd, 1H, J$_{5,6}$, J$_{6,7}$ 4.1 Hz, H-6), 2.48-2.30 (m, 1H, H-5), 1.95-1.86 (m, 2H, H-10,10'), 1.42 (s, 3H, CH$_3$), 1.30-1.20 (m, 6H, CH$_3$); m/z (FABMS) 343 (75 MH$^+$), 342 (45, M+), 325 (100), 221 (70), 154 (89), 136 (86); HRMS(FAB): MH$^+$, found 343.176421. C$_{17}$H$_{27}$O$_7$ requires 343.175679.

Third eluted was ethyl 2-hydroxy-6-[6-methoxy-2,2-dimethyl-(3aR,5R,6S,6aR)-perhydrofuro[2,3-d][1,3]dioxol-5-yl]-(1S,2S,6R)-3-cyclohexene-1-carboxylate (12); 0.4 g in 50% yield as a colorless solid, m. p. 78-80 °C. $[\alpha]_D^{20}$ -56.80 (c 2.00, CHCl$_3$); $\nu$$_{max}$ (Neat): 3540, 2950, 1120 cm$^{-1}$; $\delta_H$ (200 MHz, CDCl$_3$): 5.79 (d, 1H, J$_{1,2}$ 4.4 Hz, H-1), 5.68 (br. s, 2H, H-8,9), 4.62-4.52 (m, 1H, H-7), 4.48 (d, 1H, J$_{1,2}$ 4.4 Hz, H-2), 4.28-4.05 (m, 2H, -OCH$_2$CH$_3$), 3.98 (dd, 1H, J$_{3,4}$ 4.0, J$_{4,5}$ 9.5 Hz, H-4), 3.55 (d, 1H, J$_{3,4}$ 4.0 Hz, H-3), 3.36 (s, 3H, -OMe), 2.42-2.26 (m, 2H, H-5,6), 2.20-2.00 (m, 1H, H-10), 1.95-1.76 (m, 1H, H-10'), 1.46 (s, 3H, CH$_3$), 1.35-1.22 (m, 6H, CH$_3$); m/z (FABMS): 343 (52 MH$^+$), 327 (18), 325 (100), 297 (31), 221 (70); HRMS(FAB): MH$^+$, found 343.176149. C$_{17}$H$_{27}$O$_7$ requires 343.175679.

6-Ethyloxycarbonyl-5-[6-methoxy-2,2-dimethyl-(3aR,5R,6S,6aR)-perhydrofuro[2,3-d][1,3]dioxol-5-yl]-(1S,5R,6R)-2-cyclohexenyl acetate (16). A solution of 12 (0.075 g, 0.219 mmol) in pyridine (0.5 mL) containing DMAP (catalytic) was treated with Ac$_2$O (0.02 g, 0.219 mmol) at 0 °C and stirred for 1 h at room temperature. The reaction mixture was diluted with sat. aq. NaHCO$_3$ solution (15 mL) and extracted into CH$_2$Cl$_2$ (2 × 15 mL). The combined organic layers were washed with sat. CuSO$_4$ solution (10 mL), water (10 mL), brine (15 mL) and dried (Na$_2$SO$_4$). Solvent was evaporated under reduced pressure and residue purified by column chromatography (60-120 mesh Si-gel, Ethyl acetate: Pet. ether 1:4) to give the title compound 16 (0.075 g) in 90% yield as a colorless solid, m. p. 86-88 °C. $[\alpha]_D^{20}$  -19.90 (c 0.75, CHCl$_3$); $\nu$$_{max}$ (Neat): 2960, 1730, 1230 cm$^{-1}$; $\delta_H$ (400 MHz, CDCl$_3$): 5.84 (d, 1H, J$_{1,2}$ 4.0 Hz, H-1), 5.83-5.81 (m, 1H, H-8), 5.74-5.70 (m, 1H, H-9), 5.64-5.61 (m, 1H, H-7), 4.54 (d, 1H, J$_{1,2}$ 4.0 Hz, H-2), 4.20-4.10 ( m, 3H, H-4, -OCH$_2$CH$_3$), 3.55 (d, 1H, J$_{3,4}$ 9.5 Hz, H-4), 3.55 (d, 1H, J$_{3,4}$ 9.5 Hz, H-4), 3.36 (s, 3H, -OMe), 2.59-2.51 (m, 1H, H-5), 2.25-2.18 (m, 1H, H-10), 2.04 (s, 3H, -OAc), 1.91-1.84 (m, 1H, H-10'), 1.48, 1.38 (2s, 6H, CH$_3$), 1.26 (t, 3H, CH$_3$); $\delta_C$ NMR (50 MHz, CDCl$_3$): 172.54, 170.36, 128.68, 125.27, 111.19, 104.63, 83.68, 80.65, 80.54, 69.67, 60.76, 57.26, 47.34, 33.57, 26.62, 26.20, 25.62, 21.03, 13.94; m/z (FABMS): 385 (6 MH$^+$), 325 (84), 297 (31), 221 (70); HRMS(FAB): MH$^+$, found 385.184093. C$_{19}$H$_{29}$O$_8$ requires 385.186243.

6-Ethyloxycarbonyl-5-[6-methoxy-2,2-dimethyl-(3aR,5R,6S,6aR)-perhydrofuro[2,3-d][1,3]dioxol-5-yl]-(1S,5R,6R)-2-cyclohexenyl acetate (17). A solution of 13 (0.02 g, 0.058 mmol) in pyridine (0.3 mL) containing DMAP (catalytic) was treated with Ac$_2$O (0.006 g, 0.058 mmol) at 0 °C and stirred for 1 h at room temperature. The reaction mixture was diluted with sat. aq. NaHCO$_3$ solution (15 mL) and extracted into CH$_2$Cl$_2$ (2 × 15 mL). The combined organic layers were washed with sat. CuSO$_4$ solution (10 mL), water (10 mL), brine (15 mL) and dried (Na$_2$SO$_4$). Solvent was evaporated under reduced pressure and residue purified by column chromatography (60-120 mesh Si-gel, Ethyl acetate: Pet. ether 1:4) to give the title compound 17 (0.021 g) in 94% yield as a pale yellow syrup. $[\alpha]_D^{20}$ -144.60 (c 1.65, CHCl$_3$); $\delta_H$ (400 MHz, CDCl$_3$): 5.96-5.91 (m, 1H, H-8); 5.86 (d, 1H, J$_{1,2}$ 4.0 Hz, H-1), 5.77-5.72 (m, 1H, H-9), 5.56 (br. t, 1H, H-7), 4.52 (d, 1H, J$_{1,2}$ 4.0 Hz, H-2), 4.15-4.06 (m, 3H, H-4, -OCH$_2$CH$_3$), 3.57 (d, 1H, J$_{3,4}$ 2.8 Hz, H-3), 3.37 (s, 3H, -OMe),
2.92 (dd, 1H, J5,6 9.2, J6,7 7.2 Hz, H-6), 2.74-2.69 (m, 1H, H-5), 2.45-2.38 (m, 1H, H-10), 2.04 (s, 3H, -OAc), 1.96-1.89 (m, 1H, H-10'), 1.46, 1.30 (2s, 6H, CH3), 1.24 (t, 3H, CH3), δc (50 MHz, CDCl3): 171.48, 170.43, 131.00, 123.75, 111.31, 104.87, 84.38, 80.87, 80.45, 65.65, 60.47, 57.28, 45.28, 31.18, 26.73, 26.20, 25.80, 21.10, 14.05; m/z (FABMS): 369 (7), 325 (29), 301 (18), 221 (100); HRMS (FAB): MH+, found 385.186374. C19H29O8 requires 385.186243.

6-Ethyloxycarbonyl-5-[6-methoxy-2,2-dimethyl-(3aR,5R,6S,6aR)-perhydrofuro[2,3-d] [1,3]dioxol-5-yl]-(1R,5R,6S)-2-cyclohexenyl acetate (18). A solution of 14 (0.05 g, 0.14 mmol) in pyridine (0.5 mL) containing DMAP (catalytic) was treated with Ac2O (0.014 g, 0.14 mmol) at 0 °C, worked up and purified as described for 16, to give the title compound 18 (0.044 g) in 79% yield as a colorless solid, m. p. 102-104 °C. [α]D20 -32.14 (c 1.40, CHCl3); δH (400 MHz, CDCl3): 5.94-5.89 (m, 1H, H-8), 5.86 (d, 1H, J1,2 4.0 Hz, H-1), 5.59-5.57 (m, 2H, H-7,9), 4.54 (d, 1H, J 1,2 4.0 Hz, H-2), 4.20-4.00 (m, 2H, -OCH2CH3), 3.92 (dd, 1H, J3,4 2.8, J4,5 9.0 Hz, H-4), 3.57 (d, 1H, J3,4 2.8 Hz, H-3), 3.49 (dd, 1H, J5,6 7.2, J6,7 3.6 Hz, H-6), 3.40 (s, 3H, -OMe), 2.47-2.40 (m, 1H, H-5), 2.34-2.24 (m, 1H, H-10), 2.04 (s, 3H, -OAc), 2.00-1.93 (m, 1H, H-10'), 1.42, 1.31 (2s, 6H, CH3), 1.26 (t, 3H, CH3); δc NMR (50 MHz, CDCl3): 170.85, 170.07, 129.38, 124.43, 111.38, 104.58, 83.30, 80.88, 80.52, 69.33, 60.08, 57.48, 42.28, 33.38, 26.83, 26.30, 24.10, 20.92, 14.31; m/z (FABMS): 407 (M+23, 17), 385 (MH+, 17), 370 (13), 326 (72), 173 (100), 135 (68); HRMS (FAB): MH+, found 385.186298. C19H29O8 requires 385.186243.

Reduction of enones 6c and 6d. A solution of 6c-d (0.40 g, 1.17 mmol) and CeCl3·7H2O (0.87 g, 2.35 mmol) in ethanol (5 mL), was treated with NaBH4 (0.04 g, 1.17 mmol), worked up and purified as described for 12-14 to give 15 (0.31 g) in 78% yield as an inseparable mixture of isomers. A solution of above alcohols 15 (0.20 g, 0.58 mmol) in pyridine (0.5 mL) was treated with Ac2O (0.05 g, 0.58 mmol), worked up and purified as described for 16 to give 19, 20 and 21a-b (0.20 g) in 89% yield in 1:1:1.7 ratio respectively, after purification by column chromatography (finer than 200 mesh Si-gel, Ethyl acetate: Pet. ether 1:9). First eluted was 6-ethyloxycarbonyl-5-[6-methoxy-2,2-dimethyl-(3aR,5R,6S,6aR)-perhydrofuro[2,3-d][1,3]dioxol-5-yl]-(1R,5S,6S)-2-cyclohexenyl acetate (20; 0.054 g) in 24% yield as a pale yellow syrup. [α]D20 +116.33 (c 0.60, CHCl3); δH (400 MHz, CDCl3): 6.00-5.96 (m, 1H, H-8), 5.85 (d, 1H, J1,2 4.0 Hz, H-1), 5.73-5.68 (m, 1H, H-9), 5.51-5.49 (m, 1H, H-7), 4.54 (d, 1H, J1,2 4.0 Hz, H-2), 4.17 (dd, 1H, J3,4 3.6, J4,5 5.0 Hz, H-5), 4.14-4.08 (m, 2H, -OCH2CH3), 3.75 (d, 1H, J3,4 3.6 Hz, H-3), 3.43 (s, 3H, -OMe), 2.96 (dd, 1H, J5,6 4.8, J6,7 9.2 Hz, H-6), 2.63-2.53 (m, 1H, H-5), 2.50-2.48 (m, 1H, H-10), 2.32-2.25 (m, 1H, H-10'), 2.03 (s, 3H, -OAc), 1.43, 1.31 (2s, 6H, CH3), 1.24 (t, 3H, -CH2CH3); δc (50 MHz, CDCl3): 171.52, 170.38, 152.38, 132.48, 122.38, 111.35, 104.38, 85.62, 81.61, 79.78, 67.00, 60.49, 57.62, 45.88, 30.83, 26.71, 26.29, 25.14, 21.01, 14.12; m/z (FABMS): 385 (14 MH+), 383 (18), 369 (46), 325 (97), 173 (100), 147 (50); HRMS (FAB): MH+, found 385.186112. C19H29O8 requires 385.186243.

Second eluted was 6-ethyloxycarbonyl-5-[6-methoxy-2,2-dimethyl-(3aR,5R,6S,6aR)-perhydrofuro[2,3-d][1,3]dioxol-5-yl]-(1R,5S,6S)-2-cyclohexenyl acetate (19; 0.054 g) in 24% yield as a pale yellow syrup. [α]D20 +15.99 (c 0.65, CHCl3); δH (400 MHz, CDCl3): 5.98-
5.948 (m, 1H, H-8), 5.87 (d, 1H, -OCH2CH3), 3.90 (dd, 1H, J1,2 3.6 Hz, H-2), 3.77 (d, 1H, J3,4 3.6 Hz, H-3), 3.45 (s, 3H, -OMe), 3.09 (dd, 1H, J5,6 3.6 Hz, H-5), 2.48-2.41 (m, 1H, H-10,10'), 2.06 (s, 3H, -OAc), 1.44, 1.31 (2s, 6H, CH3), 1.26 (t, 3H, -OCH2CH3); δc (50 MHz, CDCl3): 170.47, 170.04, 130.37, 123.63, 111.30, 104.57, 83.28, 81.80, 69.68, 60.22, 57.57, 42.70, 33.60, 26.61, 26.19 (2C), 21.05, 14.31; m/z (FABMS): 385 (10 MH+), 383 (14), 369 (29), 325 (100), 173 (63), 133 (49); HRMS(FAB): MH+, found 385.186972. C19H29O8 requires 385.186243.

Further eluted was 21a-b (0.092 g) in 41% yield as an inseparable mixture.

Ethyl 3,4-dihydroxy-6-[6-methoxy-2,2-dimethyl-(3aR,5R,6S,6aR)-perhydrofuro-[2,3-d][1,3]dioxol-5-yl]-2-methylcarbonyloxy-(1S,2R,3R,4R,6R)-cyclohexane-1-carboxylate (22). To a stirred solution of 16 (0.059 g, 0.15 mmol) and NMO (0.036 g, 0.30 mmol, 50% aq. solution) in acetone: water (3:1, 4 mL), OsO4 in toluene (catalytic) was added and stirred for 12 h at room temperature in dark. Excess solid NaHSO3 (100 mg) was added, stirred for 20 min., diluted with water (10 mL) and extracted into ethyl acetate (2 × 15 mL). The combined ethyl acetate layers were washed with brine (15 mL) and dried (Na2SO4). Evaporation of solvent under reduced pressure and purification of residue by column chromatography (60-120 mesh Si-gel, Ethyl acetate: Pet. ether, 1:1) gave the title compound 22 (0.052 g) in 82% yield as a colorless solid, m. p. 158-160 0C. [α]D20 -82.35 (c 0.85, CHCl3); δH (200 MHz, CDCl3): 5.74 (d, 1H, J1,2 4.0 Hz, H-1), 5.30 (dd, 1H, J6,7 12.0, J7,8 12.0 Hz, H-7), 4.45 (d, 1H, J1,2 4.0 Hz, H-2), 4.20-4.00 (m, 3H, H-9, -OCH2CH3), 3.82 (dd, 1H, J3,4 3.6, J4,5 10.0 Hz, H-4), 3.55 (d, 1H, J3,4 3.6 Hz, H-3), 3.46 (dd, 1H, J7,8 12.0, J8,9 4.0 Hz, H-8), 3.40 (s, 3H, -OMe), 2.80-2.55 (m, 1H, H-5), 2.38 (dd, 1H, J5,6 12.0, J6,7 10.5 Hz, H-6), 2.05 (s, 3H, -OAc), 1.98-1.82 (m, 1H, H-10'), 1.45 (s, 3H, CH3), 1.31-1.18 (m, 6H, CH3); m/z (FABMS): 419 (26 MH+), 375 (17), 373 (100); HRMS(FAB): MH+, found 419.190253. C19H31O10 requires 419.191723.

Ethyl 3,4-dihydroxy-6-[6-methoxy-2,2-dimethyl-(3aR,5R,6S,6aR)-perhydrofuro-[2,3-d][1,3]dioxol-5-yl]-2-methylcarbonyloxy-(1R,2R,3R,4R,6R)-cyclohexane-1-carboxylate (23). To a stirred solution of 17 (0.02 g, 0.05 mmol) and NMO (0.012 g, 0.10 mmol, 50% aqueous solution) in acetone: water (3:1, 4 mL), OsO4 in toluene (catalytic) was added, worked up and purified as described for 22, to give the title compound 23 (0.018 g) in 86% yield as a pale yellow syrup. [α]D20 -36.00 (c 0.80, CHCl3); δH (200 MHz, CDCl3): 5.74 (d, 1H, J1,2 4.4 Hz, H-1), 5.30 (dd, 1H, J6,7 12.0, J7,8 9.0 Hz, H-7), 4.45 (d, 1H, J1,2 4.4 Hz, H-2), 4.20-4.00 (m, 5H, H-4,8,9, -OCH2CH3), 3.60 (d, 1H, J3,4 4.0 Hz, H-3), 3.40 (s, 3H, -OMe), 2.90 (dd, 1H, J5,6 4.5, J6,7 9.0 Hz, H-6), 2.52-2.36 (m, 1H, H-5), 2.05 (s, 3H, -OAc), 1.92-1.72 (m, 2H, H-10, -OH), 1.60-1.45 (m, 1H, H-10'), 1.40 (s, 3H, CH3), 1.30-1.15 (m, 6H, CH3); m/z (FABMS): 419 (100 MH+), 375 (17), 373 (100); HRMS(FAB): MH+ found 419.192053. C19H31O10 requires 419.191723.

Ethyl 3,4-dihydroxy-6-[6-methoxy-2,2-dimethyl-(3aR,5R,6S,6aR)-perhydrofuro-[2,3-d][1,3]dioxol-5-yl]-2-methylcarbonyloxy-(1R,2R,3R,4R,6R)-cyclohexane-1-carboxylate (24). To a stirred solution of 18 (0.044 g, 0.11 mmol) and NMO (0.026 g, 0.22 mmol, 50% aq. solution) in acetone: water (3:1, 4 mL), OsO4 in toluene (catalytic) was added, worked up and purified as
described for 22, gave the title compound 24 (0.039 g) in 83% yield as a colorless solid, m. p. 154-156 °C. [α]D20 -73.90 (c 2.20, CHCl3); νmax (Neat): 3470, 2960, 1725, 1230, 1080 cm⁻¹; δH (200 MHz, CDCl3): 5.76 (d, 1H, J1,2 4.4 Hz, H-1), 5.10 (dd, 1H, J6,7 6.0, J7,8 10.0 Hz, H-7), 4.45 (d, 1H, J1,2 4.4 Hz, H-2), 4.20-4.00 (m, 4H, H-8,9, -OCH2CH3), 3.72 (dd, 1H, J3,4 4.0, J4,5 11.3 Hz, H-4), 3.50 (d, 1H, J3,4 4.0 Hz, H-3), 3.45-3.30 (m, 4H, H-6, -OMe), 2.75-2.50 (m, 1H, H-5), 2.15-1.86 (m, 4H, H-10, -OAc), 1.65-1.50 (m, 1H, H-10'), 1.35 (s, 3H, CH3), 1.32-1.20 (m, 6H, CH3); m/z (FABMS) 419 (100 MH⁺), 403 (6), 373 (86), 87 (32), 43 (57); HRMS(FAB): MH⁺ found 419.194050. C19H31O10 requires 419.191723.

Ethyl 3,4-dihydroxy-6-[6-methoxy-2,2-dimethyl-(3aR,5R,6S,6aR)-perhydrofuro[2,3-d][1,3]dioxol-5-yl]-2-methylcarbonyloxy-(1R,2R,3R,4R,6S)-cyclohexane-1-carboxylate (25). To a stirred solution of 19 (0.035 g, 0.09 mmol) and NMO (0.021 g, 0.18 mmol, 50% aq. solution) in acetone: water (3:1, 4 mL), OsO4 in toluene (catalytic) was added, worked up and purified as described for 22, to give the title compound 25 (0.03 g) in 79% yield as a colorless solid, m. p. 140-142 °C. [α]D20 +21.90 (c 1.05, CHCl3); νmax (Neat): 3490, 1735, 1230, 1070 cm⁻¹; δH (200 MHz, CDCl3): 5.82 (d, 1H, J1,2 4.0 Hz, H-1), 5.15 (dd, 1H, J6,7 5.5, J7,8 9.3 Hz, H-7), 4.55 (d, 1H, J1,2 4.0 Hz, H-2), 4.32 (dd, 1H, J 3,4 3.7, J 4,5 9.3 Hz, H-4), 4.24-4.04 (m, 3H, H-8, -OCH2CH3), 3.78-3.68 (m, 2H, H-3,9), 3.45 (s, 3H, -OMe), 3.05 (dd, 1H, J 5,6 5.5, J6,7 7.0 Hz, H-6), 2.74-2.40 (m, 1H, H-5), 2.19-1.86 (m, 5H, H-10,10', -OAc), 1.42 (s, 3H, CH3), 1.34-1.22 (m, 6H, CH3); m/z (FABMS): 419 (135 MH⁺), 373 (47), 361 (33), 154 (100); HRMS(FAB): MH⁺ found 419.190928. C19H31O10 requires 419.191723.

Ethyl 3,4-dihydroxy-6-[6-methoxy-2,2-dimethyl-(3aR,5R,6S,6aR)-perhydrofuro[2,3-d][1,3]dioxol-5-yl]-2,3,4-tri(methylcarbonyloxy)-(1S,2S,3S,4S,6S)-cyclohexane-1-carboxylate (1). Ac2O (0.016 g, 0.16 mmol) was added to a stirred solution of diol 22 (0.036 g, 0.086 mmol) in pyridine (0.32 mL) containing DMAP (catalytic), worked up and purified as described for 22, to give the title compound 1 (0.03 g) in 75% yield as a colorless solid, m. p. 95-97 °C. [α]D20 -53.41 (c 1.70, CHCl3); δH (400 MHz, CDCl3): 5.80 (d, 1H, J1,2 4.0 Hz, H-1), 5.28 (br. t, 1H, H-7), 4.51 (d, 1H, J1,2 4.0 Hz, H-2), 4.28-3.94 (m, 5H, H-8, -OCH2CH3), 3.78-3.68 (m, 2H, H-3,9), 3.45 (s, 3H, -OMe), 3.05 (dd, 1H, J5,6 5.5, J6,7 7.0 Hz, H-6), 2.56-2.38 (m, 1H, H-5), 2.08 (s, 3H, -OAc), 2.04-1.80 (m, 2H, H-10,10'), 1.45 (s, 3H, CH3), 1.34-1.18 (m, 6H, CH3); m/z (FABMS): 419 (100 MH⁺), 401 (10), 373 (95), 154 (31); HRMS(FAB): MH⁺ found 419.191573. C19H31O10 requires 419.191723.

Ethyl 6-[6-methoxy-2,2-dimethyl-(3aR,5R,6S,6aR)-perhydrofuro[2,3-d][1,3]dioxol-5-yl]-2,3,4-tri(methylcarbonyloxy)-(1S,2R,3R,4R,6R)-cyclohexane-1-carboxylate (1). Ac2O (0.016 g, 0.16 mmol) was added to a stirred solution of diol 22 (0.036 g, 0.086 mmol) in pyridine (0.32 mL) containing DMAP (catalytic), worked up and purified as described for 16, gave the title compound 1 (0.03 g) in 75% yield as a colorless solid, m. p. 95-97 °C. [α]D20 -53.41 (c 1.70, CHCl3); δH (400 MHz, CDCl3): 5.80 (d, 1H, J1,2 3.9 Hz, H-1), 5.60 (t, 1H, H-7), 5.33 (m, 1H, J9,10a 2.3, J9,10c 4.2 Hz, H-9), 4.88 (dd, 1H, J7,8 9.9, J8,9 3.1 Hz, H-8), 4.51 (d, 1H, J1,2 3.9 Hz, H-2), 4.13 (q, 2H, J 7.1 Hz, -OCH2CH3), 3.93 (dd, 1H, J3,4 2.9, J4,5 8.8 Hz, H-4), 3.60 (d, 1H, J3,4 2.9 Hz, H-3), 3.35 (s, 3H, -OMe), 2.65 (m, 1H, J5,10e 3.5 Hz, H-5), 2.56 (dd, 1H, J5,6 11.3, J6,7 10.5 Hz, H-6), 2.15-1.86 (m, 4H, H-10, -OAc), 1.65-1.50 (m, 1H, H-10'), 1.35 (s, 3H, CH3), 1.32-1.20 (m, 6H, CH3); m/z (FABMS): 419 (100 MH⁺), 401 (10), 373 (95), 154 (31); HRMS(FAB): MH⁺ found 419.191573. C19H31O10 requires 419.191723.
Hz, H-6), 2.13 (s, 3H, -OAc), 2.02 (dt, 1H, H-10e), 1.99 (s, 3H, -OAc), 1.98 (s, 3H, -OAc), 1.52 (ddd, 1H, J_{5,10a} 12.4, J_{10a,10c} 13.6, J_{9,10a} 2.3 Hz, H-10a), 1.45 (s, 3H, CH₃), 1.28 (s, 3H, CH₃), 1.25 (t, 3H, J 7.1 Hz, -OCH₂CH₃);

δ_{c}(50 MHz, CDCl₃): 170.88, 170.24, 170.18, 168.11, 111.38, 104.56, 85.32, 81.06, 80.85, 72.32, 70.37, 68.62, 60.38, 57.20, 47.08, 33.16, 29.53, 28.02, 26.83, 26.17, 20.98, 20.64, 13.31; m/z (FABMS): 503 (36 MH⁺), 487 (12), 457 (100), 443 (27); HRMS(FAB): MOEt⁺, found 457.169200. C₂₁H₂₉O₁₁ requires 457.170987.

Ethyl 6-[6-methoxy-2,2-dimethyl-(3aR,5R,6S,6aR)-perhydrofuro[2,3-d][1,3]dioxol-5-yl]-2,3,4-tri(methylcarbonyloxy)-(1S,2S,3S,4S,6R)-cyclohexane-1-carboxylate (2). Ac₂O (0.006 g, 0.06 mmol) was added to a stirred solution of diol 23 (0.014 g, 0.033 mmol) in pyridine (0.3 mL) containing DMAP (catalytic), worked up and purified as described for 16, to give the title compound 2 (0.012 g) in 75% yield as a pale yellow syrup. [α]_D²⁰ +3.20 (c 0.50, CHCl₃);

δ_{H} (400 MHz, CDCl₃): 5.83 (d, 1H, J₁,₂ 3.8 Hz, H-1), 5.42 (dd, 1H, J₆,₇ 3.5, J₇,₈ 6.0 Hz, H-7), 5.34 (dd, 1H, J₇,₈ 6.0, J₉,₉ 3.2 Hz, H-9), 4.55 (d, 1H, J₁,₂ 3.8 Hz, H-2), 4.11 (dd, 1H, J₃,₄ 3.0, J₄,₅ 9.1 Hz, H-4), 4.10 (qd, 2H, J 7.1 Hz, -OCH₂CH₃), 3.57 (d, 1H, J₃,₄ 3.0 Hz, H-3), 3.40 (s, 3H, -OMe), 2.92 (dd, 1H, J₅,₆ 9.1, J₆,₇ 3.5 Hz, H-6), 2.67 (dq, 1H, J₅,₁₀e 4.8 Hz, H-5), 2.10, 2.08, 2.03 (3s, 9H, -OAc), 1.99 (dt, 1H, J₁₀a,₁₀e 13.2, J₉,₁₀e 4.2, J₅,₁₀e 4.8 Hz, H-10e), 1.64 (dt, 1H, J₁₀a,₁₀c 13.2 Hz, H-10a), 1.49 (s, 3H, CH₃), 1.31 (s, 3H, CH₃), 1.24 (t, 3H, J 7.1 Hz, -OCH₂CH₃); δ_{c} (50 MHz, CDCl₃): 171.18, 160.80, 160.33 (2C), 111.54, 104.50, 83.73, 81.30, 80.66, 68.59, 68.21, 67.70, 60.81, 57.32, 44.71, 32.85, 28.62, 26.74, 26.27, 26.21, 20.83, 20.77, 13.85; m/z (FABMS): 503 (100), 457 (52), 443 (22); HRMS (FAB): MH⁺, found 503.210874. C₂₃H₃₅O₁₂ requires 503.212852.

Ethyl 6-[6-methoxy-2,2-dimethyl-(3aR,5R,6S,6aR)-perhydrofuro[2,3-d][1,3]dioxol-5-yl]-2,3,4-tri(methylcarbonyloxy)-(1R,2R,3R,4R,6R)-cyclohexane-1-carboxylate (3). Ac₂O (0.018 g, 0.18 mmol) was added to a stirred solution of diol 24 (0.04 g, 0.095 mmol) in pyridine (0.3 mL) containing DMAP (catalytic), worked up and purified as described for 16, to give the title compound 3 (0.04 g) in 83% yield as a colorless solid, m. p. 95-97 °C. [α]_D²⁰ -54.54 (c 2.30, CHCl₃), δ_{H} (400 MHz, CDCl₃): 5.85 (d, 1H, J₁,₂ 3.8 Hz, H-1), 5.40 (dd, 1H, J₇,₈ 10.8, J₈,₉ 3.3 Hz, H-8), 5.44 (m, 1H, J₈,₉ 3.3 Hz, H-9), 5.36 (dd, 1H, J₇,₈ 10.8 Hz, H-7), 4.54 (d, 1H, J₁,₂ 3.8 Hz, H-2), 4.25-4.11 (m, 2H, -OCH₂CH₃), 3.83 (dd, 1H, J₃,₄ 2.9, J₄,₅ 10.5 Hz, H-4), 3.54 (d, 1H, J₃,₄ 3.0 Hz, H-3), 3.53 (t, 1H, H-6), 3.36 (s, 3H, -OMe), 2.58 (m, 1H, J₄,₅ 10.5, J₅,₆ 4.2, J₅,₁₀e 3.3 Hz, H-5), 2.23 (m, 1H, J₉,₁₀e 2.5, J₅,₁₀a 13.0 Hz, H-10a), 2.00, 2.01, 2.09 (3s, 9H, -OAc), 1.64 (dt, 1H, J₉,₁₀e 5.8, J₅,₁₀e 3.3, J₉,₁₀a 14.2 Hz, H-10e), 1.41, 1.31 (2s, 6H, CH₃), 1.28 (t, 3H, J 7.1 Hz, -OCH₂CH₃); δ_{c} (50 MHz, CDCl₃): 171.30, 170.19, 169.97, 169.75, 111.48, 104.60, 83.23, 80.97, 79.93, 69.68, 69.57, 69.16, 60.60, 57.66, 45.15, 31.30, 29.64, 26.61, 26.40, 26.25, 20.76, 20.69, 14.31; m/z (FABMS): 503 (36 MH⁺), 457 (52), 457 (72); HRMS(FAB): MH⁺ found 503.214328. C₂₃H₃₅O₁₂ requires 503.212852.

Ethyl 6-[6-methoxy-2,2-dimethyl-(3aR,5R,6S,6aR)-perhydrofuro[2,3-d][1,3]dioxol-5-yl]-2,3,4-tri(methylcarbonyloxy)-(1R,2R,3R,4R,6R)-cyclohexane-1-carboxylate (4). Ac₂O (0.009 g, 0.09 mmol) was added to a stirred solution of diol 25 (0.02 g, 0.048 mmol) in pyridine (0.3 mL) containing DMAP (catalytic), worked up and purified as described for 16, to give the title
compound 4 (0.022 g) in 94% yield as a colorless solid, m. p. 150-152 °C. \([\alpha]_D^{20}+185.71\) (c 0.35, CHCl3); \(\delta_H\) (400 MHz, CDCl3): 5.85 (d, 1H, J\(_{1,2}\) 3.8 Hz, H-1), 5.36 (dd, 1H, J\(_{6,7}\) 3.5, J\(_{7,8}\) 5.6 Hz, H-7), 5.32 (dd, 1H, J\(_{7,8}\) 5.6, J\(_{8,9}\) 2.7 Hz, H-8), 5.25 (dt, 1H, J\(_{8,9}\) 2.7 Hz, H-9), 4.53 (d, 1H, J\(_{1,2}\) 3.8 Hz, H-2), 4.18-4.13 (m, 3H, H-4, -OCH\(_2\)CH\(_3\)), 3.71 (d, 1H, J\(_{3,4}\) 3.5 Hz, H-3), 3.43 (s, 3H, -OMe), 3.01 (dd, 1H, J\(_{5,6}\) 9.8, J\(_{6,7}\) 3.5 Hz, H-6), 2.65 (tt, 1H, J\(_{4,5}\) 4.3, J\(_{5,6}\) 9.8 Hz, H-5), 2.13 (dt, 1H, J\(_{5,10e}\) 4.4, J\(_{9,10e}\) 4.2 Hz, H-10e), 2.10, 2.08, 2.01 (3s, 9H, -OAc), 1.97 (dt, 1H, J\(_{5,10a}\) 10.3, J\(_{9,10a}\) 10.3, J\(_{10a,10e}\) 13.6 Hz, H-10a), 1.45, 1.32 (2s, 6H, CH\(_3\)), 1.24 (t, 3H, -OCH\(_2\)CH\(_3\)); \(\delta_c\) (100 MHz, CDCl3): 171.49, 170.14, 169.46, 169.37, 111.29, 104.45, 85.76, 81.36, 79.83, 69.20, 68.90, 67.77, 60.94, 57.68, 45.14, 31.73, 26.68, 26.15, 24.90, 20.98, 20.81, 20.74, 14.05; m/z (FABMS): 525 (10 M\(^+\)+23, 10), 445 (18), 207 (35), 73 (61), 57 (100), 55 (96); HRMS (FAB): MH\(^+\) found 503.213914. C\(_{23}\)H\(_{35}\)O\(_{12}\) requires 503.212852.

Ethyl 6-[6-methoxy-2,2-dimethyl-(3aR,5R,6S,6aR)-perhydrofuro[2,3-d][1,3]dioxol-5-yl]-2,3,4-tri(methylcarbonyloxy)-(1S,2S,3S,4S,6S)-cyclohexane-1-carboxylate (5). Ac\(_2\)O (0.02 g, 0.2 mmol) was added to a stirred solution of diol 26 (0.045 g, 0.107 mmol) in pyridine (0.3 mL) containing DMAP (catalytic), worked up and purified as described for 16, to give the title compound 5 (0.052 g) in 98% yield as a pale yellow syrup. \([\alpha]_D^{20} -27.12\) (c 2.50, CHCl\(_3\)); \(\delta_H\) (400 MHz, CDCl3): 5.86 (d, 1H, J\(_{1,2}\) 4.0 Hz, H-1), 5.69 (dd, 1H, J\(_{7,8}\) 10.7, J\(_{8,9}\) 3.5 Hz, H-8), 5.57 (m, 1H, J\(_{8,9}\) 3.5 Hz, H-9), 5.32 (dd, 1H, J\(_{6,7}\) 6.1, J\(_{7,8}\) 10.7 Hz, H-7), 4.59 (d, 1H, J\(_{1,2}\) 4.0 Hz, H-2), 4.25, 4.14 (2dq, 2H, -OCH\(_2\)CH\(_3\)), 3.77 (dd, 1H, J\(_{3,4}\) 3.1, J\(_{4,5}\) 9.6 Hz, H-4), 3.74 (d, 1H, J\(_{3,4}\) 3.1 Hz, H-3), 3.46 (s, 3H, -OMe), 3.18 (t, 1H, J\(_{5,6}\) 4.7, J\(_{6,7}\) 6.1 Hz, H-6), 2.56 (tt, 1H, J\(_{4,5}\) 9.6, J\(_{5,6}\) 4.7 Hz, H-5), 2.16 (m, 1H, J\(_{5,10a}\) 12.7, J\(_{9,10a}\) 2.5 Hz, H-10a), 2.10 (s, 3H, -OAc), 2.09 (dt, 1H, J\(_{5,10e}\) 4.3, J\(_{9,10e}\) 4.2 Hz, H-10e), 2.03, 1.98 (2s, 6H, -OAc), 1.43, 1.31 (2s, 6H, CH\(_3\)), 1.29 (t, 3H, -OCH\(_2\)CH\(_3\)); \(\delta_c\) (100 MHz, CDCl3): 170.46, 170.12, 170.10, 169.97, 111.34, 104.44, 83.24, 80.93, 80.69, 69.72, 69.28, 68.58, 60.91, 57.59, 45.15, 31.44, 28.16, 26.50, 26.06, 21.06, 20.82, 20.74, 14.27; m/z (FABMS): 503 (12 MH\(^+\)), 457 (20), 154 (50), 133 (79), 89 (68), 77 (100); HRMS (FAB): MH\(^+\) found 503.211435. C\(_{23}\)H\(_{35}\)O\(_{12}\) requires 503.212852.

**Acknowledgments**

A S C and M H V R R are thankful to CSIR, New Delhi for financial support. This work was supported by a Grant-in-Aid project (CSIR Young Scientist Award to Dr G V M Sharma).

**References**

22. The energy minimization was carried out using Sybyl 6.8 with default Tripose force field Parameters. Minimization was done first with steepest descent followed by conjugate gradient methods for a maximum of 2000 iteration each or RMS deviation of 0.005 Kcal/mole which ever was earlier.

# IICT Communication No. 4656