Carbohydrate Research 345 (2010) 457–461

Contents lists available at ScienceDirect

Carbohydrate Research

journal homepage: www.elsevier.com/locate/carres

Synthesis of densely functionalised C-glycosides by a tandem oxy Michael addition–Wittig olefination pathway

R. Senthil Kumar [a], K. Karthikeyan [a], B. V. N. Phani Kumar [b], D. Muralidharan [a], P. T. Perumal [a,*]

[a] Organic Chemistry Division, Central Leather Research Institute, Adyar, Chennai 600 020, India
[b] Chemical Physics Division, Central Leather Research Institute, Adyar, Chennai 600 020, India

ARTICLE INFO

Article history:
Received 21 September 2009
Received in revised form 19 November 2009
Accepted 14 December 2009
Available online 16 December 2009

Keywords:
Tandem cyclisation
C-Vinyl glycosides
Oxy Michael addition
Wittig olefination

ABSTRACT

Wittig olefination of 5,6-dideoxy-5,6-anhydro-6-nitro-D-glucofuranose (**5**) triggered a concomitant cyclisation via oxy Michael addition of the C2-hydroxyl group resulting in the formation of *C*-vinyl glycosides with *Z*-olefinic geometry.

1. Introduction

The vital role played by carbohydrates in various biological processes is evident from the recent advances made in glycobiology.[1–6] Because carbohydrates occur as constituents of various glycoproteins and glycolipids the development of carbohydrate-based drugs will be of much use in the treatment of various diseases such as obesity and diabetes.[7] However, the task remains elusive mainly because of the hydrolytic lability of O-linked carbohydrates, the glycosides, towards enzyme and chemicals. However, replacement of the anomeric oxygen with a carbon substituent confers the C-glycoside molecules' tremendous stability towards enzymes and chemicals with minimal loss or enhancement in biological activity with respect to the parent O-glycosides.[8–13] This is mainly attributed to the nearly similar conformation of the O- and C-glycosides in the solution state.[14,15] C-Glycosides are also found in number of natural products such as the antibiotics vineomycin,[16] elfamycin, aurodox and efrotomycin.[17] As a consequence, a number of strategies have been developed for the syntheses of C-glycosides by various research groups.[18–27]

C-Vinyl glycosides form a unique class of C-glycosides that assumes importance on account of their unsaturation, which is further amenable to a myriad of chemical reactions. However, only a handful of reports on their synthesis exist in the literature. For example, Taylor and co-workers[28,29] developed two approaches for the stereoselective synthesis of either α or β-*C*-vinyl glycosides from a common chiron derived from D-glucose. The addition of organometallic reagents to epoxides derived from carbohydrates has been reported in two instances. Wipf and co-workers [30] reported the addition of alkenyl zirconocenes to glycal epoxides and Haudrechy and co-workers[31] reported the addition of metal acetylides to carbohydrate-derived epoxides. Wittig olefination, the most sought after reaction in olefin synthesis, has been used in the synthesis of *C*-vinyl glycosides. Wittig olefination has been carried out both at the C-1 of a formyl furanose[32–34] and at the anomeric carbon of a suitably modified furanose.[35,36] The latter approach is a simple and straightforward method especially when ring closure happens in one-pot. However the process occurs by oxy Michael addition on the newly formed olefin by C-4 alkoxide and hence the olefin is saturated and therefore the end product is *C*-alkyl glycoside and not *C*-alkenyl glycoside.

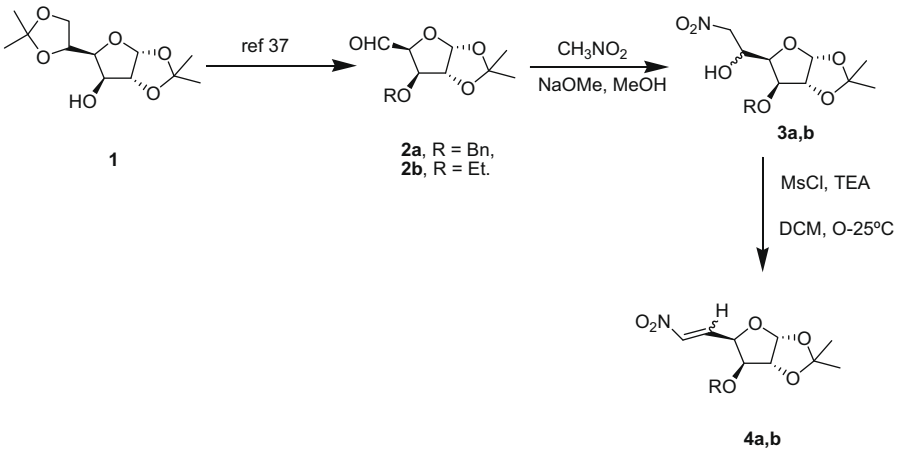
2. Results and discussion

2.1. Synthesis of C-glycosides

We envisioned that by installing a powerful Michael acceptor moiety in the substrate we could drive the cyclisation to the other side and thereby retain the newly formed olefinic moiety. To this end, we wanted to prepare the chiral diene (**6**) and to selectively cyclise it using appropriate base taking advantage of the difference in Michael acceptor power of the nitrovinyl and carbethoxy vinyl groups. Thus, our synthesis began with the preparation of the 1,2-*O*-isopropylidene-5,6-dideoxy-5,6-dehydro-6-nitro-D-glucofuranose (**4**) from the known aldehyde[37] (**2**) using modified reaction conditions[38,39] (Scheme 1).

* Corresponding author. Tel.: +91 44 24913289; fax: +91 44 24911589.
E-mail address: ptperumal@gmail.com (P.T. Perumal).

0008-6215/$ - see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.carres.2009.12.014



Scheme 1. Synthesis of nitrovinyl glucofuranose.

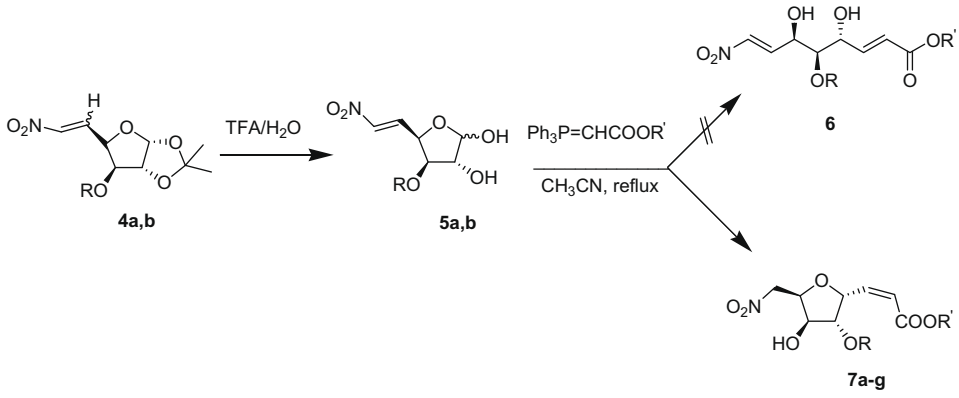
The 1,2-*O*-isopropylidine group was removed with TFA–H_2O and the anomeric mixture of hemiacetals, after coevaporation of TFA with toluene, was heated at reflux with the phosphorane in acetonitrile for the appropriate time to obtain the diene (**6**) (Scheme 2). However, the proton NMR spectrum of the isolated product did not conform to the expected diene structure. Only two olefinic protons were observed instead of four. In addition, D_2O exchange experiments confirmed the presence of single hydroxy group. These two facts together with the nature of splitting pattern of the individual protons led us to arrive at the cyclic structure, the *C*-vinyl glycoside **7a** for the product. Thus, indeed a fortitutious reaction had occurred towards our synthetic endeavour as our synthetic scheme was shortened by one step. Having obtained this potential compound, we next varied the reaction conditions in order to increase the yield of **7a** from its initial modest yield. Solvent screening with THF, Et_2O, toluene and DCM instead of acetonitrile did not show any significant improvement on the yield (Table 1, entries 1–3). Additives such as LiBr and LiCl also did not have any substantial effect on the reaction (Table 1, entries 3 and 7). On the other hand, the use of bases such as Et_3N and K_2CO_3 for prolonged reaction times and reflux conditions led to a decrease of product spot intensity as detected by TLC, with the formation of a mixture of more polar compounds[40] (Table 1, entry 8). However, increasing the stoichiometry of the phosphorane from 1.2 to 2.5 equiv significantly increased the yield to nearly 75% over two steps. A further increase in the phosphorane did not show any improvement. To elucidate the generality of this methodology various other phosphoranes were reacted under this optimised conditions and in all cases, the reaction followed a similar path and resulted in the corresponding *C*-vinyl furanoside (Table 2). Replacement of bulkier 3-*O*-benzyl group with ethyl group in the substrate did not show any marked difference with regard to either yield or stereochemical outcome of the reaction (Table 2, entry 7).

Table 1

Entry	Product	Solvent	Ylide (equiv)	Time (h)	Yield[a] (%)
1	**7a**	CH_3CN	1.2	10	45
2	**7a**	THF	1.2	10	42
3	**7a**	THF	1.2	10	40[b]
4	**7a**	Et_2O	1.2	10	30
5	**7a**	Toluene	1.2	10	20
6	**7a**	DCM	1.2	10	35
7	**7a**	CH_3CN	1.2	10	48[c]
8	**7a**	CH_3CN	1.2	24	Trace[d]
9	**7a**	CH_3CN	2.5	4	75

[a] Isolated yield after column chromatography.
[b] LiCl 0.5 equiv was added.
[c] LiBr 0.5 equiv was added.
[d] NEt_3 or K_2CO_3 0.5 equiv was added.

A tentative mechanism to account for the formation of the C-glycoside is given in Scheme 3. Thus, it is likely that the Wittig reagent deprotonates[41] the hydroxyl protons of the hemiacetal and triggers the tandem cyclisation by oxy Michael addition. This is further supported by the above observation that increasing the stoichiometry of the Wittig reagent increases the yield.



Scheme 2. Wittig olefination of nitrovinyl glucofuranose

Table 2
Synthesis of *C*-vinyl furanoside

Entry	R	R′	Product **7**	Time (h)	Yield[a] (%)
1	Bn	Et	**7a**	4.0	75
2	Bn	^{i}Pr	**7b**	5.0	68
3	Bn	^{t}Bu	**7c**	5.0	65
4	Bn	^{n}Bu	**7d**	4.5	70
5	Bn	Bn	**7e**	5.0	75
6	Bn	^{n}Oct	**7f**	9.0	68
7	Et	^{n}Oct	**7g**	9.5	65

[a] Isolated yield after column chromatography.

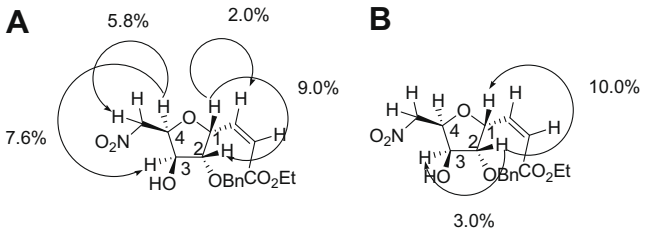


Figure 1. NOE studies of the *C*-vinyl glycoside **7a**.

2.2. Stereochemical assignment of C-glycosides

The relative stereochemistry of the product was established by NOE studies and coupling constant values (Fig. 1). A coupling constant value of 11.5 Hz between the vinylic protons indicated *Z*-geometry at olefinic carbons. The α-anomeric configuration and the cis relationship of C1–H and C2–H (furanoside numbering) protons are clearly indicated by the presence of an NOE (9%) and the coupling constant values. Similar compounds have been reported earlier.[28,29] Also the presence of an NOE between C3–H and C4–H (7.6%) shows the cis relationship of these protons and the absence of an NOE interaction between C1–H and C4–H clearly indicates the trans relationship between the C1 and C4 substituents. This is further confirmed by the irradiation of C2–H which showed an NOE of 10% with C1–H and only 3% with C3–H thereby indicating the trans relationship between protons C2–H and C3–H. Finally, the structure was unambiguously confirmed by single crystal X-ray diffraction of the benzyl ester derivative (**7e**,[42] Fig. 2). It is also evident from the above observation that epimerisation about C4 and C2 (1,2:5,6-di-*O*-isoproylidene-D-glucofuranose numbering) had taken place under the basic nature of Wittig reaction condition. This is clear from the fact that C1–H and C2–H are syn in the product whereas they are anti (C2–H and C3–H of D-glucofuranose) in the reactant. Similarly the hydrogens on C2 and C3 are anti in the product and are syn in the starting compound (C3–H and C4–H of D-glucofuranose).

2.3. Conclusions

In summary, we report a novel tandem Michael–Wittig reaction sequence for the synthesis of *C*-vinyl furanosides. Though the above sequence has the literature precedence in C-glycoside synthesis, the end products of such reactions were *C*-alkyl glycosides and not *C*-alkenyl glycosides. This is essentially because the formed olefin is consumed in situ in the subsequent Michael addition. However, in our case, due to the presence of powerful Michael acceptor moiety in the substrate, the oxy Michael addition precedes Wittig olefination and hence the newly formed olefin is intact in the product. Because the obtained C-glycosides has dense functionalities viz. acidic methylene, nitro group, conjugated ester and partially protected hydroxyl groups in stereochemically pure form, the reported reaction sequence constitutes a powerful method for the stereoselective synthesis of functionalised *C*-vinyl furanosides. Further, these C-glycosides, due to the presence of these synthetic handles, would serve as versatile intermediates in various chiron approach-based synthesis of natural and unnatural products.

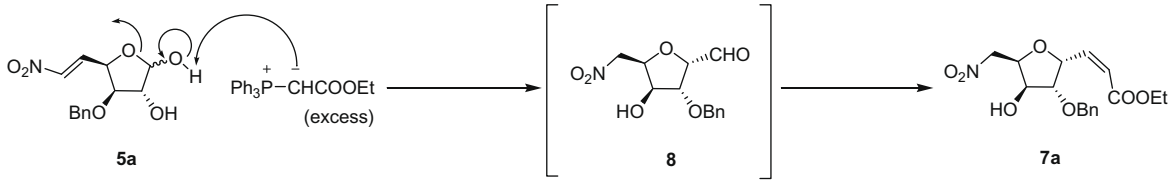
3. Experimental

3.1. General methods

Melting points were determined in capillary tubes and are uncorrected. IR spectra were taken as neat for liquid compound and as KBr pellets for solids on a Perkin–Elmer Spectrometer RXI FT-IR. ^{1}H NMR (500 and 400 MHz) and ^{13}C NMR (125 and 100 MHz) spectra were recorded in $CDCl_3$ with TMS as an internal standard on a JEOL or Bruker Spectrometer. HRMS were recorded on a JEOL JMS600 and Q-TOF Mass spectrometer. Specific rotation was recorded on a RUDOLPH AUTOPOL II, Automatic Polarimeter.

3.2. Experimental procedure for (3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-2,2-dimethyl-5-((*E*)-2-nitrovinyl)tetrahydrofuro[2,3-*d*][1,3]dioxole 4a

To a solution of aldehyde **2a** (1.30 g, 4.67 mmol) in dry CH_3OH (10 mL) was added nitromethane (2.91 g, 47.7 mmol) followed by $NaOCH_3$ (0.302 g, 5.60 mmol) and stirred for 1.5 h. The pH of the mixture was brought to 2 by the addition of glacial HOAc and the solvent was evaporated under reduced pressure. The residue was dissolved in CH_2Cl_2 and was given brine wash, dried (Na_2SO_4) and concentrated under reduced pressure. Column chromatography of the obtained residue gave the C-5 epimeric mixture of nitro alcohols **3a** as viscous oil. To a stirred solution of **3a** (1.33 g, 3.93 mmol) of nitro alcohol dissolved in dry dichloromethane (10 mL) at 0 °C was added methanesulfonyl chloride (0.97 mL, 12.60 mmol) followed by triethylamine (2.35 mL, 16.94 mmol) and stirred further for 45 min. After completion, the reaction mixture was diluted with dichloromethane and was given a bicarbonate wash, dried with Na_2SO_4, filtered and concentrated under reduced pressure. Column chromatography 0.8:9.2 (EtOAc–petroleum ether) of the residue gave 1.15 g (92%) of the compound **4a** as yellow oil. A similar procedure with **2b** gives compound **4b**.



Scheme 3. Tentative mechanism for the formation of *C*-vinyl glycoside.

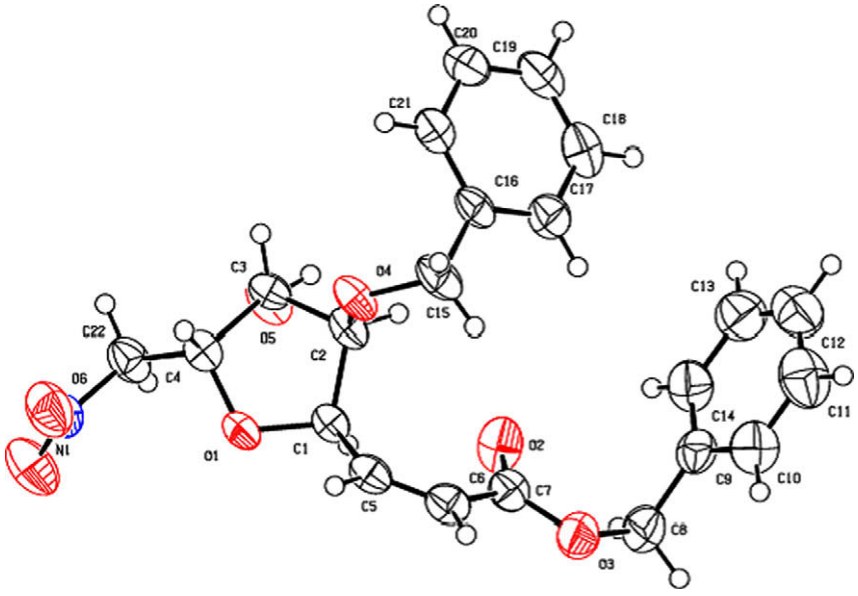


Figure 2. ORTEP diagram of compound **7e**.

3.2.1. (3a*R*,5*R*,6*S*,6a*R*)-6-(Benzyloxy)-2,2-dimethyl-5-((*E*)-2-nitrovinyl)tetrahydrofuro[2,3-*d*][1,3]dioxole 4a

Viscous oil; IR (neat): 2981, 1660, 1524, 1347, 1218 cm^{-1}; R_f = 0.31 (20% EtOAc–petroleum ether); $[\alpha]_D$ −76.0 (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 1.33 (s, 3H, isopropylidene-C*H*$_3$), 1.48 (s, 3H, isopropylidene-C*H*$_3$), 4.04 (d, *J* = 3.1 Hz,1H, *H*-3), 4.45 (d, *J* = 12.2 Hz, 1H, OCH*H*Ph), 4.63–4.67 (m, 2H, *H*-2, OC*H*HPh), 4.88–4.90 (m, 1H, *H*-4), 5.99 (d, *J* = 3.8 Hz, 1H, *H*-1), 7.16 (dd, *J* = 13.7, 3.8 Hz, 1H, CH=C*H*NO_2) 7.18–7.25 (m, 3H, C*H*=CHNO_2, Ar-*H*), 7.29–7.36 (m, 3H, Ar–*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ 26.3, 26.9, 72.3, 77.1, 82.4, 82.5, 105.2, 112.5, 128.0, 128.5, 128.8, 136.1, 136.7, 141.0; HRMS: Found 344.1107 $C_{16}H_{19}NO_6Na$ $[M+Na]^+$ calcd 344.1110.

3.2.2. (3a*R*,5*R*,6*S*,6a*R*)-6-Ethoxy-2,2-dimethyl-5-((*E*)-2-nitrovinyl)tetrahydrofuro[2,3-*d*][1,3]dioxole 4b

Viscous oil; IR (neat): 2981, 1660, 1528, 1354, 1376, 1214 cm^{-1}; R_f = 0.30 (20% EtOAc–petroleum ether); $[\alpha]_D$ −65.8 (*c* 3.5, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 1.16 (t, *J* = 6.8 Hz, 3H, OCH_2CH_3), 1.34 (s, 3H, isopropylidene-C*H*$_3$), 1.50 (s, 3H, isopropylidene-C*H*$_3$), 3.42–3.45 (m, 1H, OCH*H*CH_3), 3.59–3.67 (m, 1H, OC*H*HCH_3), 3.97 (d, *J* = 3.2 Hz, 1H, *H*-3), 4.62 (d, *J* = 4.0 Hz, 1H, *H*-2), 4.93 (d, *J* = 3.2 Hz, 1H, *H*-4), 5.97 (d, *J* = 4.0 Hz, 1H, *H*-1), 7.24 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.3, 27.5, 28.2, 67.7, 78.4, 84.3, 84.9, 106.4, 113.6, 137.1, 142.4.; HRMS: Found: 282.0947 $C_{11}H_{17}NO_6Na$ $[M+Na]^+$ calcd 282.0954.

3.3. Representative procedure for C-glycosides 7a–g

To the nitro compound **4a** 0.142 g (0.44 mmol) was added TFA–H_2O (3 mL, 3:2) at room temperature and stirred for 3 h. After completion, the TFA was coevaporated with toluene and the sticky mass of hemiacetals was directly used in the next step. A solution of carbethoxymethylene triphenylphosphorane (0.326 g, 0.96 mmol) in dry acetonitrile was added to the solution of hemiacetal in dry acetonitrile (2 mL), and the mixture was stirred in an oil bath at 85 °C for 4.0 h. After completion of the reaction, the solvent was evaporated under reduced pressure and the residue was dissolved in EtOAc, given a water wash, dried (Na_2SO_4) filtered and concentrated under reduced pressure. Column chromatography 2:8 (EtOAc–petroleum ether) of the crude compound yielded **7a** as a colourless viscous oil 0.115 g (75%).

3.3.1. (*Z*)-Ethyl 3-((2*R*,3*R*,4*S*,5*R*)-3-(benzyloxy)-4-hydroxy-5-(nitromethyl)tetrahydrofuran-2-yl)acrylate 7a

Yield: 0.115 g (75%); viscous oil; IR (neat): 3463, 2910, 1712, 1553, 1372 cm^{-1}; R_f = 0.23 (30% EtOAc–petroleum ether); $[\alpha]_D$ +206.0 (*c* 1.5, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 1.25 (t, *J* = 7.6 Hz, 3H, OCH_2CH_3), 3.22 (br s, exchanges with D_2O, 1H, O*H*), 4.08 (q, *J* = 7.6 Hz, 2H, OCH_2CH_3), 4.24 (d, *J* = 3.1 Hz, 1H, *H*-2), 4.43 (br s, becomes doublet on D_2O exchange, 1H, *H*-3), 4.52 (ABq, *J* = 11.5 Hz, $\Delta\nu$ = 46 Hz, 2H, OCH_2Ph), 4.59–4.66 (m, 2H, CH_2NO_2), 4.88–4.91 (m, 1H, *H*-4), 5.65–5.67 (m, 1H, *H*-1), 5.91 (dd, *J* = 11.5, 1.5 Hz, 1H, CH=C*H*–COOEt), 6.39 (dd, *J* = 11.5, 6.9 Hz, 1H, C*H*=CH–COOEt), 7.23–7.31 (m, 5H, Ar–H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 14.2, 60.7, 72.6, 74.7, 74.9, 77.6, 78.6, 86.0, 120.9, 127.8, 128.0, 128.5, 137.6, 147.1, 166.3; HRMS: Found 352.1376; $C_{17}H_{21}NO_7$ $[M+H]^+$ calcd 351.1318.

3.3.2. (*Z*)-Isopropyl 3-((2*R*,3*R*,4*S*,5*R*)-3-(benzyloxy)-4-hydroxy-5-(nitromethyl) tetrahydrofuran-2-yl)acrylate 7b

Yield: 0.116 g (68%); viscous oil; IR neat: 3464, 2981, 1710, 1555 cm^{-1}; R_f = 0.24 (30% EtOAc–petroleum ether); $[\alpha]_D$ +303.5 (*c* 0.6, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 1.22 (d, *J* = 6.1 Hz, 3H, isopropyl-C*H*$_3$), 1.25 (d, *J* = 6.9 Hz, 3H, isopropyl-C*H*$_3$), 2.58 (br s, 1H, O*H*), 4.25 (d, *J* = 3.8 Hz, 1H, *H*-2), 4.43 (br s, 1H, *H*-3), 4.53 (ABq, *J* = 12.2 Hz, $\Delta\nu$ = 28.8 Hz, 2H, OCH_2Ph), 4.59–4.67 (m, 2H, CH_2NO_2), 4.87–4.90 (m, 1H, *H*-4), 4.95 (septet, *J* = 6.1 Hz, 1H, C*H*$(CH_3)_2$), 5.65–5.67 (m, 1H, *H*-1), 5.88 (dd, *J* = 12.2, 1.5 Hz, 1H, CH=C*H*–COO*i*Pr), 6.36 (dd, *J* = 11.5, 6.9 Hz, 1H, C*H*=CH–COO*i*Pr), 7.24 (d, *J* = 7.6 Hz, 1H, Ar–H), 7.27–7.33 (m, 4H, Ar–H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.8, 21.9, 68.2, 72.7, 74.4, 75.2, 77.5, 78.5, 86.1, 121.5, 127.7, 128.1, 128.5, 137.5, 146.5, 165.6; HRMS: Found 388.1379; $C_{18}H_{23}NO_7Na$ $[M+Na]^+$ calcd 388.1372.

3.3.3. (*Z*)-*tert*-Butyl 3-((2*R*,3*R*,4*S*,5*R*)-3-(benzyloxy)-4-hydroxy-5-(nitromethyl) tetrahydrofuran-2-yl)acrylate 7c

Yield: 0.108 g (65%); viscous oil; IR (neat): 3458, 2880, 1709, 1558, 1369 cm^{-1}; R_f = 0.31 (30% EtOAc–petroleum ether); $[\alpha]_D$ +172.2 (*c* 0.5, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 1.44 (s, 9H, $C(CH_3)_3$), 2.72 (d, *J* = 4.5 Hz, 1H, O*H*), 4.23 (d, *J* = 3.8 Hz, 1H, *H*-2), 4.43 (br s, 1H, *H*-3), 4.53 (ABq,, *J* = 11.5 Hz, $\Delta\nu$ = 26.6 Hz, 2H, OCH_2Ph), 4.62–4.68 (m, 2H, CH_2NO_2), 4.87–4.92 (m, 1H, *H*-4), 5.64–5.66 (m, 1H, *H*-1), 5.84 (dd, *J* = 11.5, 1.5 Hz, 1H, CH=C*H*–COOC$(CH_3)_3$), 6.29 (dd, *J* = 12.2, 6.9 Hz, 1H, C*H*=CH–COOC$(CH_3)_3$),

7.24–7.33 (m, 5H, Ar–H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 28.2, 72.7, 74.5, 75.1, 77.5, 78.4, 81.1, 86.0, 123.0, 127.7, 128.1, 128.6, 137.6, 145.2, 165.5; HRMS: Found: 380.1603 $C_{19}H_{25}NO_7$ $[M+H]^+$ calc 379.1631.

3.3.4. (*Z*)-Butyl 3-((2*R*,3*R*,4*S*,5*R*)-3-(benzyloxy)-4-hydroxy-5-(nitromethyl)tetrahydrofuran-2-yl)acrylate 7d

Yield: 0.117 g (70%); viscous oil; IR (neat): 3460, 2894, 1715, 1551, 1375 cm^{-1}; R_f = 0.27 (30% EtOAc–petroleum ether); $[\alpha]_D$ +136.7 (*c* 0.2, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.92 (t, *J* = 7.6 Hz, 3H, CH_2CH_3), 1.29–1.44 (m, 2H, CH_2CH_3), 1.50–1.62 (m, 2H, $CH_2CH_2CH_3$), 2.52 (br s, 1H, O*H*), 4.05 (t, *J* = 5.3 Hz, 2H, $CH_2CH_2CH_2CH_3$), 4.25 (d, *J* = 3.8 Hz, 1H, *H*-2), 4.42 (br s, 1H, *H*-3), 4.52 (ABq, *J* = 12.2 Hz, $\Delta\nu$ = 29.6 Hz, 2H, OCH_2Ph), 4.59–4.67 (m, 2H, CH_2NO_2), 4.87–4.90 (m, 1H, *H*-4), 5.65–5.66 (m, 1H, *H*-1), 5.92 (dd, *J* = 11.5, 1.5 Hz, 1H, CH=C*H*–COO*n*-But), 6.37 (dd, *J* = 11.5, 4.2 Hz, 1H, C*H*=CH–COO*n*-But), 7.23–7.33 (m, 5H, Ar–H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 13.8, 19.2, 30.7, 64.5, 72.8, 74.4, 75.2, 77.5, 78.6, 86.1, 120.9, 127.8, 128.1, 128.5, 137.5, 146.8; 166.2; HRMS: Found: 380.1648 $C_{19}H_{25}NO_7$ $[M+H]^+$ calcd 379.1631.

3.3.5. (*Z*)-Benzyl 3-((2*R*,3*R*,4*S*,5*R*)-3-(benzyloxy)-4-hydroxy-5-(nitromethyl) tetrahydrofuran-2-yl)acrylate 7e

Yield: 0.136 g (75%); white solid mp 97–99 °C; IR (neat): 3462, 2920, 1713, 1551, 1369 cm^{-1}; R_f = 0.28 (30% EtOAc–petroleum ether); $[\alpha]_D$ +158.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.52 (br s, 1H, O*H*), 4.20 (d, *J* = 3.8 Hz, 1H, *H*-2), 4.39 (br s, 1H, *H*-3), 4.46 (ABq, *J* = 12.2 Hz, $\Delta\nu$ = 39 Hz, 2H, OCH_2Ph), 4.58–4.66 (m, 2H, CH_2NO_2), 4.87–4.90 (m, 1H, *H*-4), 5.08 (s, 2H, $COOCH_2Ph$), 5.64–5.66 (m, 1H, *H*-1), 5.97 (dd, *J* = 11.5, 1.5 Hz, 1H, CH=C*H*–$COOCH_2Ph$), 6.42 (dd, *J* = 11.5, 6.9 Hz, 1H, C*H*=CH–$COOCH_2Ph$), 7.21 (d, *J* = 6.9 Hz, 2H, Ar–H), 7.22 –7.36 (m, 8H, Ar–H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 66.5, 72.7, 74.4, 75.0, 77.5, 78.6, 85.9, 120.6, 127.8, 128.1, 128.4, 128.5, 128.6, 128.7, 135.7, 137.5, 147.7, 165.8; HRMS: Found: 414.1481 $C_{22}H_{23}NO_7$ $[M+H]^+$ calcd 413.1474.

3.3.6. (*Z*)-Octyl 3-((2*R*,3*R*,4*S*,5*R*)-3-(benzyloxy)-4-hydroxy-5-(nitromethyl)tetrahydrofuran-2-yl)acrylate 7f

Yield: 0.137 g (68%); semi solid; IR (neat): 3461, 2922, 1712, 1553, 1376 cm^{-1}; R_f = 0.38 (30% EtOAc–petroleum ether); $[\alpha]_D$ +114.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, *J* = 6.8 Hz, 3H, *n*-Oct), 1.27 (br s, 10H, *n*-Oct), 1.61 (br s, 2H, *n*-Oct), 2.30 (s, 1H, O*H*), 4.06 (t, *J* = 6.0 Hz, 2H, *n*-Oct), 4.27 (d, *J* = 3.6 Hz, 1H, *H*-2), 4.43 (br s, 1H, *H*-3), 4.54 (ABq, *J* = 12.0 Hz, $\Delta\nu$ = 24.2 Hz, 2H, OCH_2Ph), 4.60–4.70 (m, 2H, CH_2NO_2), 4.88–4.92 (m, 1H, *H*-4), 5.66–5.69 (m, 1H, *H*-1), 5.93 (dd, *J* = 12.0, 1.6 Hz, 1H, CH=C*H*–COO*n*-Oct), 6.38 (dd, *J* = 11.6, 6.8 Hz, 1H, C*H*=CH–COO*n*-Oct), 7.24–7.33 (m, 5H, Ar–H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0, 22.6, 25.9, 28.5, 29.1, 29.2, 31.8, 64.7, 72.7, 74.1, 75.1, 77.2, 78.4, 85.9, 120.9, 127.6, 127.9, 128.4, 137.3, 146.6, 165.9; HRMS: Found: 458.2143 $C_{23}H_{33}NO_7Na$ $[M+Na]^+$ calcd 458.2155.

3.3.7. (*Z*)-Octyl 3-((2*R*,3*R*,4*S*,5*R*)-3-ethoxy-4-hydroxy-5-(nitromethyl)tetrahydrofuran-2-yl)acrylate 7g

Yield: 0.106 g (65%); viscous oil; IR (neat): 3461, 2929, 1716, 1554, 1417, 1384 cm^{-1}; R_f = 0.37 (30% EtOAc–petroleum ether); $[\alpha]_D$ +161.4 (*c* 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, *J* = 7.2 Hz, 3H, *n*-Oct), 1.12 (t, *J* = 6.8 Hz, 3H, OCH_2CH_3), 1.27–1.37 (br s, 10H, *n*-Oct), 1.65 (quintet, *J* = 6.4 Hz, 2H, *n*-Oct), 2.35 (br s, 1H, O*H*), 3.42–3.49 (m, 1H, $OCHHCH_3$), 3.54–3.61 (m, 1H, $OCHHCH_3$), 4.09–4.14 (m, 3H, *H*-2), 4.42 (br s, 1H, *H*-3), 4.60–4.71 (m, 2H, CH_2NO_2), 4.83–4.87 (m, 1H, *H*-4), 5.63–5.66 (m, 1H, *H*-1), 5.92 (dd, *J* = 12.0, 2.0 Hz, 1H, CH=C*H*–COO*n*-Oct), 6.32 (dd, *J* = 12.0, 7.2 Hz, 1H, C*H*=CH–COO*n*-Oct); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.9, 15.1, 22.5, 25.9, 28.5, 29.11, 29.16, 31.7, 64.6, 66.4, 74.1, 75.3, 77.2, 78.3, 86.5, 120.7, 146.5, 166.0; HRMS: Found: 374.2184 $C_{18}H_{32}NO_7$ $[M+H]^+$ calcd 374.2179.

Acknowledgement

The authors R.S.K and K.K are thankful to the Council of Scientific and Industrial Research, New Delhi, India, for research fellowships.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2009.12.014.

References

1. Dwek, R. A. *Chem. Rev.* **1996**, *96*, 683–792.
2. Dwek, R. A.; Butters, T. D. *Chem. Rev.* **2002**, *102*, 283–284.
3. Rudd, P. M.; Elliott, T.; Cresswell, P.; Wilson, I. A.; Dwek, R. A. *Science* **2001**, *291*, 2370–2376.
4. Fraser Reid, B.; Tatsuta, K.; Thiem, J. *Glycoscience: Chemistry and Chemical Biology*; Springer: Heidelberg, Germany, 2001.
5. Varki, A. *Glycobiology* **1993**, *3*, 97–130.
6. Hotha, S.; Kashyap, S. *J. Am. Chem. Soc.* **2006**, *128*, 9620–9621.
7. Wong, C.-H. *Carbohydrate Based Drug Discovery*; Wiley-VCH: Weinheim, Germany, 2003.
8. Du, Y.; Linhardt, R. J.; Vlahov, I. R. *Tetrahedron* **1998**, *54*, 9913–9959.
9. Pellissier, H. *Tetrahedron* **2005**, *61*, 2947–2993.
10. Schmieg, J.; Yang, G.; Franck, R. W.; Tsuji, M. O. *J. Exp. Med.* **2003**, *198*, 1631–1641.
11. Taylor, E. A.; Clinch, K.; Kelly, P. M.; Li, L.; Evans, G. B.; Tyler, P. C.; Schramn, V. L. *J. Am. Chem. Soc.* **2007**, *129*, 6984–6985.
12. Levy, W.; Chang, D. *The Chemistry of C-Glycosyl Compounds*; Elsevier: Cambridge, UK, 1995.
13. Yuasa, H.; Hashimoto, H. *Rev. Heteroat. Chem.* **1998**, *19*, 35–65.
14. Wei, A.; Boy, K. M.; Kishi, Y. *J. Am. Chem. Soc.* **1995**, *117*, 9432–9436.
15. Espinosa, J.-F.; Canada, F. J.; Asensio, J. L.; Martin-Pastor, M.; Dietrich, H.; Martin-Lomas, M.; Schmidt, R. R.; Jimenez-Barbero, J. *J. Am. Chem. Soc.* **1996**, *118*, 10862–10871.
16. Omura, S.; Tanaka, H.; Oiwa, R.; Awaya, J.; Masuma, R.; Tanaka, K. *J. Antibiot.* **1977**, *30*, 908–916.
17. Dolle, R. E.; Nicolaou, K. C. *J. Am. Chem. Soc.* **1985**, *107*, 1691–1694.
18. Crisostomo, F. R. P.; Carrillo, R.; Martin, T.; Garcia-Tellado, F.; Martin, V. *J. Org. Chem.* **2005**, *70*, 10099–10101.
19. Kaliappan, K. P.; Subrahmanyam, A. V. *Org. Lett.* **2007**, *9*, 1121–1124.
20. Masson, G.; Compain, P.; Martin, O. R. *Org. Lett.* **2000**, *2*, 2971–2974.
21. Moreno, B.; Quehen, C.; Rose-Helene, M.; Leclerc, E.; Quirion, J.-C. *Org. Lett.* **2007**, *9*, 2477–2480.
22. Liu, Y.; Gallagher, T. *Org. Lett.* **2004**, *6*, 2445.
23. Parrish, J. D.; Little, R. D. *Org. Lett.* **2002**, *4*, 1439–1442.
24. Schweizer, F.; Inazu, T. *Org. Lett.* **2001**, *3*, 4115–4118.
25. Terauchi, M.; Abe, H.; Matsuda, A.; Shuto, S. *Org. Lett.* **2004**, *6*, 3751–3754.
26. Leonelli, F.; Capuzzi, M.; Calcagno, V.; Passacantilli, P.; Piancatelli, G. *Eur. J. Org. Chem.* **2005**, *13*, 2671–2676.
27. Chjara, J. L.; Sesmilo, E. *Angew. Chem., Int. Ed.* **2002**, *41*, 3242–3246.
28. Jeanmart, S.; Taylor, R. J. K. *Tetrahedron Lett.* **2005**, *46*, 9043–9048.
29. McAllister, G.; Paterson, D. E.; Taylor, R. J. K. *Angew. Chem., Int. Ed.* **2003**, *42*, 1387–1391.
30. Wipf, P.; Pierce, J. G.; Zhuang, N. *Org. Lett.* **2005**, *7*, 483–485.
31. Guillarme, S.; Ple, K.; Haudrechy, A. *J. Org. Chem.* **2006**, *71*, 1015–1017.
32. Rothman, J. H. *J. Org. Chem.* **2007**, *72*, 3945–3948.
33. Dondoni, A.; Zuurmond, H. M.; Boscarato, A. *J. Org. Chem.* **1997**, *62*, 8114–8124.
34. Kozlowski, J. S.; Marzabadi, C. H.; Rath, N. P.; Spilling, C. D. *Carbohydr. Res.* **1997**, *300*, 301–313.
35. Ohrui, H.; Jones, G. H.; Moffatt, G. J.; Maddox, M. L.; Christensen, A. T.; Byram, S. K. *J. Am. Chem. Soc.* **1975**, *97*, 4602–4613.
36. Egron, D.; Durand, T.; Roland, A.; Vidal, J.-P.; Rossi, J.-C. *Synlett* **1999**, 435–437.
37. Wolform, M. L.; Hanessian, S. *J. Org. Chem.* **1962**, *27*, 1800–1804.
38. Iida, T.; Funabashi, M.; Yoshimura, J. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 3203.
39. Torii, S.; Inokuchi, T.; Oi, R.; Kondo, K.; Kobayashi, T. *J. Org. Chem.* **1986**, *51*, 254.
40. In addition to epimerisation base also promotes retro Michael reaction: Zou, W.; Wu, A.-T.; Bhasin, M.; Sandbhor, M.; Wu, S.-H. *J. Org. Chem.* **2007**, *72*, 2686–2689.
41. Johnson, W. *Ylide Chemistry*; Academic Press: New York, NY, 1966.
42. Crystallographic data of the structure of compound **7e** have been deposited with the Cambridge Crystallographic Data centre as supplementary publication no. CCDC-675835.