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Synthesis of monoglycosides, bisglycosides and open-chain ketoacetals from sugar derived exocyclic enol ethers

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Abstract: Under acidic condition, the reaction of pent-4-enofuranosides with various nucleophiles of mostly alcohol origin furnished bisglycosylated products along with open-chain ketoacetals and monoglycosylated products depending upon the reagents and reaction conditions. The reactions appear to proceed via nucleophilic attack at C-1 and/or C-4 of the reaction intermediates.

Exocyclic vinyl ether derivatives of sugar[1] are formed as intermediates in various biosynthetic pathways, for example during the enzymatic hydrolysis of S-adenosylhomocysteine to adenosine,[2] enzymatic synthesis of 2-deoxy-scyllo-inosose from D-glucose-6-phosphate,[3] formation of dehydroquinate in the shikimic pathway,[4] the synthesis of nucleoside antibiotic angustmycin A,[5] and the biomimetic rearrangement to carbocycles[6] that are key precursors of nucleoside-based natural products neplanocin A and aristeromycin.[7] Several synthetic reports for these vinyl ethers via dehydrohalogenation of 5-halogeno-furanose derivatives,[8] Bamford-Stevens rearrangement of 5-tosylhydrazono-furanose derivatives[9] and Wittig reaction of aldehydes with sugar-based triphenylphosphonium salts[10] have been reported in the literature. Attempts to elaborate the synthetic utility of these ethers in producing glycosides,[11] polyethers,[12] spiroketals[13] and related compounds[14] including heterocycles,[15] carbocyles,[16] and nucleosides[17] using coupling reactions,[18] radical processes[19] and cycloaddition reactions[20] have generated molecules of diverse nature. Nevertheless, the chemistry of these systems is less developed as compared to endocyclic vinyl ethers that allow regio- and stereoselective transformation, glycosylation as well as C–C and C–

heteroatom bond formations at the anomeric centre.[21] However, the methods, which take advantage of the nucleophilic character of these ethers for the direct formation of C–C and C–O bonds during organic synthesis are limited to dimerization,[22] and opening of epi-sulphonium ion[23] and iodonium ion[24] intermediates by nucleophiles. As functionalized tetrahydrofurans are integral components of many biologically significant compounds, the development of more general processes using exocyclic vinyl ethers could find broad application in the synthesis of bioactive molecules.

For a long time, we have been interested in the preparation of various glycoside derivatives via open-chain acetals used as chiral auxiliaries[25] towards asymmetric synthesis of natural products or products useful in drug research.[26] As a part of that programme, we initiated the present work taking a pent-4-enofuranoside derivative (exocyclic enol ether) as the precursor that could deliver the desired products via nucleophilic attack by alcohols at C-1 and/or C-4 under acidic conditions. The oxocarbeniun ions formed at C-1 and C-4 are stabilized, providing scope of nucleophilic attack at these two positions as shown (Figure 1). We herein report the results of the work.

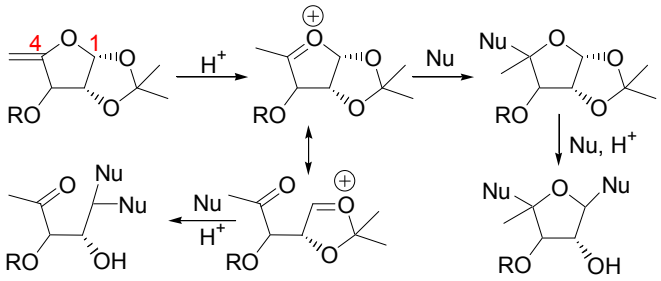
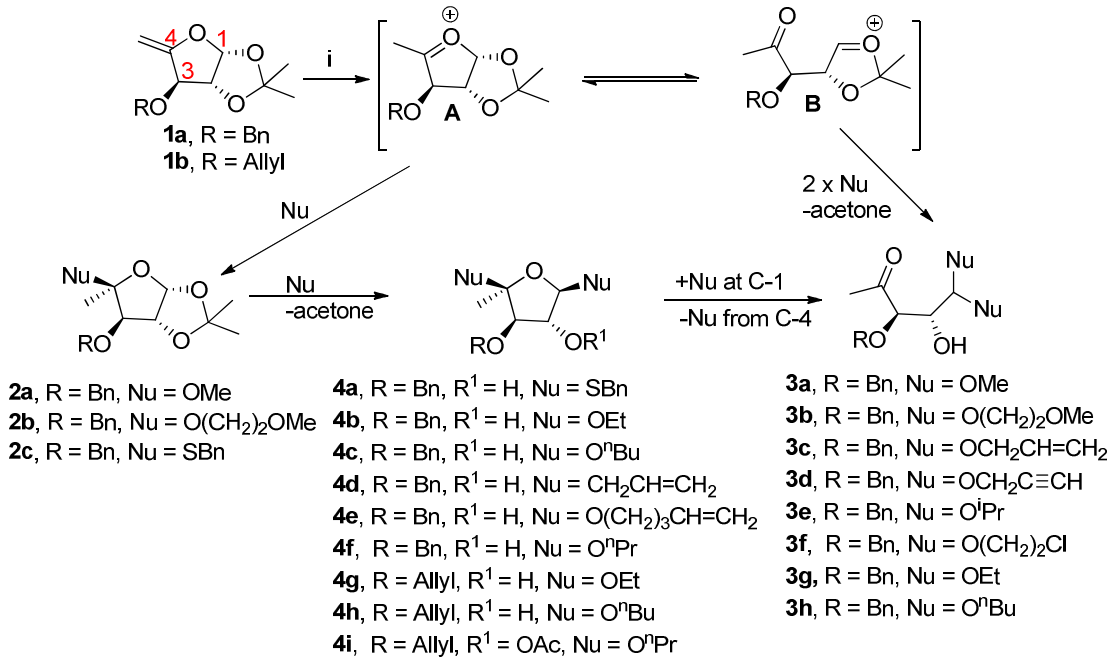


Figure 1. A strategy for the synthesis of monoglycosides, bisglycosides and open-chain ketoacetals

To begin with, the key precursor pent-4-enofuranose derivative **1a**,[15a] easily prepared from 3-*O*-benzyl-1,2-*O*-isopropylidene-5-*O*-mesyl-xylofuranose,[27] was exposed to 5% conc. HCl in methanol for 15 min to afford the monoglycosylated product (MGP) **2a** in 45% yield (Scheme 1). Though there was no appreciable change in product formation up to 1 h, continuation of the reaction for 6 h yielded the open-chain acetal (OCA) **3a** (65%). Similar results were obtained when **1a** was treated with 5% conc. HCl in 2-methoxyethanol furnishing the MGP **2b** (42%) and the OCA **3b** (65%). But treatment with 5% conc. HCl in benzyl thiol provided the MGP **2c** (45%) in 15 min and the bisglycosylated product (BGP) **4a** (47%) after 1 h. No OCA product however resulted from this reaction. Reaction of the same

starting material with 5% conc. HCl in allyl alcohol, propargyl alcohol, isopropanol or 2-chloroethanol, surprisingly, did not provide any identifiable product in 15 min -1 h. But all of these reactions afforded the OCAs **3c**–**3f** in 52–67% yields after 6 h. In contrast, addition of 5% conc. HCl in ethanol or *n*-butanol to **1a** did not result in any appreciable change in 15 min. However, it afforded the BGPs **4b** (53%) and **4c** (52%) respectively after 1 h and produced their OCAs **3g** (60%) and **3h** (61%) after 6 h. Further, reaction of the same precursor with 5% conc. HCl in allyltrimethylsilane, pent-4-ene-1-ol, or *n*-propanol did not indicate any appreciable change after 15 min, but furnished the BGPs **4d**–**4f** in 52-58% yields when the reaction time was 1 h. Similar reactions of **1b**[28] with 5% conc. HCl in ethanol, *n*-butanol, or *n*-propanol furnished BGPs **4g**–**4i** as the major products in 46-55% yields after 1 h. The product **4i** was isolated as its acetate derivative. However, these reactions produced intractable mixture of products after 5-6 h.



Scheme 1 Conversion of pent-4-enofuranose to glycosides and open-chain ketoacetals via the proposed pathway

It is apparent from the results that the nucleophiles (also solvents) can solvate the oxocarbenium ion intermediates **A** and **B**, and lower their potential energy. The intermediate **B** can be more solvated, possibly due to smaller in size and difficult for it to escape from the solvents furnishing less reactivity to the nucleophiles and take longer time (6 h) for the

reactions to occur in these solvents (Table 1). 2-Chloroethanol affords lower yield of its OCA product in comparison to 2-methoxyethanol due to the lesser nucleophilicity of the latter (due to electron-withdrawing inductive effect of Cl). On the other hand, the relatively more hindered intermediate **A** appeared to be less solvated and thus attack can even take place by allyltrimethylsilane and pent-4-ene-1-ol having comparatively low nucleophilicity affording their BGP within 1 h of the reactions. The reactions in the solvents like ethanol, *n*-propanol and *n*-butanol produce their BGPs through this intermediate also. The MGPs formed in methanol, benzyl thiol and 2-methoxyethanol solvents after 15 min are expected to be going through this oxocarbenium ion intermediate.

Table 1 Acid induced reactions[a] of pent-4-enofuranoses **1a** and **1b** to MGPs (**2**), OCAs (**3**), and BGPs (**4**)

Entry	Substrate	Reagent: 5% conc. HCl (vol/vol) in	Products (Yield %) after		
			15 min	1 h	6 h
1	**1a**	CH_3OH	**2a** (45)		**3a** (65)
2	**1a**	$MeO(CH_2)_2OH$	**2b** (42)		**3b** (65)
3	**1a**	$PhCH_2SH$	**2c** (45)	**4a** (47)	
4	**1a**	$CH_2=CHCH_2OH$			**3c** (63)
5	**1a**	$CH\equiv CCH_2OH$			**3d** (67)
6	**1a**	$(CH_3)_2CHOH$			**3e** (64)
7	**1a**	$Cl(CH_2)_2OH$			**3f** (52)
8	**1a**	CH_3CH_2OH		**4b** (53)	**3g** (60)
9	**1a**	$CH_3(CH_2)_3OH$		**4c** (52)	**3h** (61)
10	**1a**	$CH_2=CHCH_2SiMe_3$		**4d** (58)	
11	**1a**	$CH_2=CH(CH_2)_3OH$		**4e** (52)	
12	**1a**	$CH_3(CH_2)_2OH$		**4f** (52)	
13	**1b**	CH_3CH_2OH		**4g** (50)	
14	**1b**	$CH_3(CH_2)_3OH$		**4h** (55)	
15	**1b**	$CH_3(CH_2)_2OH$		**4i** (46)[b]	

[a]all reactions carried out at rt; [b]isolated as acetate derivative.

The structures of all the products were confirmed by ^1H and ^{13}C NMR and MS analyses. Anomeric purity of the bisglycosides was provided by their ^1H NMR spectra. The resonance corresponding to the anomeric proton appeared at $\delta \sim 5.0$ as a doublet (J = ~5.0 Hz) indicating the presence of only the β-anomer.[29] The absence of any detectable amount of the

α-anomer was not surprising due to the acid catalyzed attack by nucleophiles at the anomeric carbon from β-face removing the isopropylidene moiety. The relative *syn*-disposition of the incoming nucleophiles at C-1 and C-4 of BGPs was deduced from the NOESY correlation between one of the methylene protons (2 × multiplets at δ 3.86–3.90 and δ 3.65–3.68) of each ethyl group at C-1 and C-4 of **2b**. The methylene carbons (δ 56.8 and 64.2) of the ethyl groups have been identified by HSQC spectrum. The carbon signal at δ 56.8 showed HMBC correlation with the signal at δ 1.40 for the methyl protons at C-4 indicating their propinquity.

Regarding the mechanism of product formation in the reaction, initial protonation of the sugar-derived exocyclic vinyl ether **1a/1b** must have furnished the oxocarbenium intermediates. Attack by nucleophiles at C-4 of the intermediate produced the C-4 MGPs. Apparently, because of the steric hindrance induced by the acetonide group of the intermediate the addition occurred across the double bond from the opposite face.[15a] Further, under acidic condition the cleavage of the isopropylidene group of the MGPs leading to an oxocabenium ion and concomitant attack by a variety of nucleophiles at C-1 furnished the BGPs. The other intermediate, upon nucleophilic addition, afforded the OCAs. The OCAs, however, appeared to be generated also from the corresponding BGPs during the progress of the reaction.

In conclusion, sugar-derived exocyclic vinyl ether derivatives are important biosynthetic intermediates in various metabolic pathways in biological processes and could also be regarded as synthetic intermediates for the synthesis of important bioactive molecules. We have demonstrated that the 4-methylidenefuranoside derivative, the key precursor of the reaction, can be utilized to synthesize mono- and bis-glycosides of diverse structures through nucleophilic attack at C-1 and C-4 under acidic condition. Many of these reactions produced open-chain γ-keto acetals as the sole products when the solvents were miscible with conc. HCl. These acetals could be used as chiral auxiliaries in asymmetric synthesis of appropriate organic molecules. On the other hand, immiscible and partially miscible solvents furnished bisglycosides as the major products.

Experimental

General Experimental: Melting points were taken in open capillaries and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ as solvent using TMS as internal standard. Mass spectra were recorded using ESI mode. Specific rotations were measured at 589 nm.

Pre-coated plates (0.25 mm, silica gel 60 F_{254}) were used for TLC. All the solvents were distilled and purified as necessary

(3a*S*,5*R*,6*R*,6a*R*)-6-(Benzyloxy)-5-methoxy-2,2,5-trimethyltetrahydrofuro[2,3-*d*]dioxole (2a)

A solution (10 mL) of a mixture of conc. HCl - MeOH (1:19) was added to **1a** (150 mg, 0.57 mmol) and stirred at room temperature for 15 min. The reaction mixture was neutralized by slow addition of a saturated $NaHCO_3$ solution, the solvent was evaporated and the product was extracted by DCM (3 x 10 mL). The solvent was washed with water (2 x 5 mL), dried (Na_2SO_4) and concentrated to an oil, which was purified on a silica gel (230 – 400 mesh) column using petroleum ether – EtOAc (23: 2) as eluent to furnish **2a** (75 mg, 45%) as colourless liquid. $[\alpha]_D^{25}$ + 195.6 (*c* 0.5 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.41 (s, 3H), 1.42 (s, 3H), 1.46 (s, 3H), 3.32 (s, 3H), 3.78 (d, 1H, *J* = 3.0 Hz), 4.61 (d, 1H, *J* = 12.0 Hz), 4.78 (t, 1H, *J* = 3.6 Hz), 4.84 (d, 1H, *J* = 12.0 Hz), 5.75 (d, 1H, *J* = 4.8 Hz), 7.29 – 7.40 (m, 5H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 19.9 (CH_3), 27.8 (CH_3), 28.0 (CH_3), 48.6 (CH_3), 72.2 (CH_2), 86.2 (CH), 88.2 (CH), 103.6 (CH), 105.8 (C), 114.5 (C), 127.9 – 128.4 (5 x CH), 137.2 (C); ESIMS, *m/z*: 317 $(M + Na)^+$.

(3a*S*, 5*R*, 6*R*, 6a*R*)-6-(Benzyloxy)-5-(2-methoxyethoxy)-2,2,5-trimethyltetrahydrofuro [2,3-*d*][1,3] dioxole (2b)

Following the procedure as described for **2a**, the reaction was done using **1a** (150 mg, 0.57 mmol) and conc. HCl – 2-methoxy ethanol (1:19) solution (10 mL) at room temperature for 15 min. Work up and purification on a silica gel (230 – 400 mesh) column using a mixture of petroleum ether – EtOAc (23:2) as eluent furnished **2b** (80 mg, 42%) as colourless liquid. $[\alpha]_D^{25}$ – 175.9 (*c* 0.34 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.30 (s, 3H), 1.49 (s, 3H), 1.54 (s, 3H), 3.36 (s, 3H), 3.48 – 3.61 (m, 2H), 3.67 – 3.80 (m, 2H), 3.97 (s, 1H), 4.56 (d, 1H, *J* = 11.7 Hz), 4.64 (d, 1H, *J* = 4.8 Hz), 4.70 (d, 1H, *J* = 11.7 Hz), 5.94 (d, 1H, *J* = 4.8 Hz), 7.27 – 7.38 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 18.3 (CH_3), 26.1 (CH_3), 26.4 (CH_3), 58.9 (CH_3), 60.8 (CH_2), 71.8 (CH_2), 72.1 (CH_2), 83.9 (CH), 87.5 (CH), 106.0 (CH), 112.2 (C), 112.5 (C), 127.5 (2 x CH), 127.8 (CH), 128.4 (2 x CH), 137.5 (C); HRMS (ESI, positive ion) calcd for $C_{18}H_{26}NaO_6$, *m/z* 361.1627, found 361.1642.

(3a*S*, 5*R*, 6*R*, 6a*R*)-6-(Benzyloxy)-5-(benzylthio)-2,2,5-trimethyltetrahydrofuro[2,3-*d*] [1,3] dioxole (2c)

A solution of a mixture of conc. HCl - BnSH (1:19, 10 mL) was added to **1a** (150 mg, 0.57 mmol) and the mixture was stirred at room temperature for 15 min. Usual work up and purification on a silica gel (230 – 400 mesh) column using a mixture of petroleum ether – EtOAc (93:7) as eluent furnished **2c** (100 mg, 45%) as yellowish liquid. $[\alpha]_D^{25}$ + 195.6 (*c* 0.5 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.43 (s, 3H), 1.52(s, 3H), 1.74 (s, 3H), 3.84 (brs, 2H), 3.93 (d, 1H, *J* = 3.0 Hz), 4.66 (d, 1H, *J* = 12.0 Hz), 4.75 – 4.79 (m, 2H), 5.86 (d, 1H, *J* = 4.5 Hz), 7.20 – 7.39 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 27.7 (CH_3), 27.9 (2 x CH_3), 31.4 (CH_2), 72.4 (CH_2), 86.8 (CH), 90.9 (CH), 93.1 (C), 104.2 (CH), 114.8 (C), 126.8 – 129.3 (10 x CH), 137.1 (C), 138.5 (C); HRMS (ESI, positive ion) calcd for $C_{22}H_{26}NaO_4S$, *m/z* 409.1449, found 409.1465.

(3*R*, 4*R*)-3-(Benzyloxy)-4-hydroxy-5, 5-dimethoxypentan-2-one (3a)

Using the same protocol as described above in **2a** the reaction was carried out for 6 h. Work up and purification on a silica gel (230 – 400 mesh) column furnished **3a** (164 mg, 65%) as colourless gummy material using petroleum ether – EtOAc (19:1). $[\alpha]_D^{25}$ + 26.3 (*c* 0.24 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.24 (s, 3H), 2.40 (brs, 1H), 3.29 (s, 3H), 3.42 (s, 3H), 3.88 (dd, 1H, *J* = 2.1, 6.6 Hz), 3.99 (d, 1H, *J* = 2.7 Hz), 4.40 (d, 1H, *J* = 6.9 Hz), 4.46 (d, 1H, *J* = 11.4 Hz), 4.72 (d, 1H, *J* =11.4 Hz), 7.32-7.38 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 27.3 (CH_3), 54.1 (CH_3), 55.3 (CH_3), 72.0 (CH), 73.4 (CH_2), 83.7 (CH), 103.5 (CH), 128.2 (CH), 128.4 (2 x CH), 128.5 (2 x CH), 136.9 (C), 209.8 (C); HRMS (ESI, positive ion) calcd for $C_{14}H_{20}NaO_5$, *m/z* 291.1208, found 291.1236.

Preparation of 2a and 3a (Scale up to 20 fold): To **1a** (3.0 g, 11.4 mmol) was added a mixture of conc. HCl - MeOH (1:19) (200 mL) and stirred at room temperature for 15 min. Usual work up and purification yielded **2a** (1.6 g, 48%). This reaction was repeated and after 6 h it afforded **3a** (3.20 g, 63%) upon work up and purification.

(3*R*, 4*R*)- 3-(Benzyloxy)-4-hydroxy-5,5-bis(2-methoxyethoxy)pentan-2–one (3b)

Another set of reaction was performed using **1a** (250 mg, 0.95 mmol) and conc. HCl – 2-methoxy ethanol (1:19) solution (20 mL) at room temperature for 6 h, following the procedure as described in the preparation of **2a**. Usual work up and purification by column chromatography over silica gel (230 – 400 mesh) using petroleum ether – EtOAc (23:2) as eluent afforded **3b** (219 mg, 65%) as colourless liquid. $[\alpha]_D^{25}$ + 57.1 (*c* 0.36 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.25 (s, 3H), 3.32 (s, 3H), 3.37 (s, 3H), 3.40 − 3.42 (m, 3H), 3.53

(t, 3H, J = 4.2 Hz), 3.62 − 3.69 (m, 1H), 3.72 − 3.80 (m, 1H), 3.87 − 3.94 (m, 2H), 4.02 (d, 1H, J = 2.1 Hz), 4.47 (d, 1H, J = 11.4 Hz), 4.65 (d, 1H, J = 7.5 Hz), 4.71 (d, 1H, J = 11.4 Hz), 7.32 − 7.36 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 27.5 (CH_3), 58.9 (2 x CH_3), 65.4 (CH_2), 67.1 (CH_2), 71.5 (CH_2), 71.9 (CH_2), 72.2 (CH), 73.5 (CH_2), 84.2 (CH), 102.8 (CH), 128.0 (CH), 128.4 (2 x CH), 128.4 (2 x CH), 137.3 (C), 210.7 (C); ESIMS, *m/z*: 379 $(M + Na)^+$.

(3*R*, 4*R*)-5,5-Bis(allyloxy)-3-(benzyloxy)-4-hydroxypentan-2-one (3c)

Compound **1a** (250 mg, 0.95 mmol) was allylated using conc. HCl – allyl alcohol (1:19) solution (20 mL) at room temperature for 6 h, following the procedure as described in the preparation of **2a**. Usual work up and purification by column chromatography over silica gel (230 – 400 mesh) using petroleum ether – EtOAc (19:1) as eluent furnished **3c** (190 mg, 63%) as colourless liquid. $[\alpha]_D^{25}$ + 70.1 (*c* 0.23 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.24 (s, 3H), 3.89 (dd, 1H, J = 5.4, 12.6 Hz), 3.93 (m, 1H), 4.04 (d, 1H, J = 2.4 Hz), 4.11 − 4.20 (m, 3H), 4.47 (d, 1H, J = 11.4 Hz), 4.65 (d, 1H, J = 6.6 Hz), 4.71 (d, 1H, J = 11.4 Hz), 5.15 (dd, 1H, J = 1.2, 10.2 Hz), 5.19 (dd, 1H, J = 1.2, 10.2 Hz), 5.24 (dd, 1H, J = 1.2, 16.8 Hz), 5.30 (dd, 1H, J = 1.2, 16.8 Hz), 5.78 − 5.84 (m, 1H), 5.89 − 5.95 (m, 1H), 7.32 − 7.36 (m, 5H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 27.4 (CH_3), 68.0 (CH_2), 68.8 (CH_2), 72.6 (CH), 73.5 (CH_2), 83.7 (CH), 101.2 (CH), 117.4 (2 x CH_2), 128.2 – 128.5 (5 x CH), 133.9 (CH), 134.1 (CH), 137.0 (C), 209.8 (C); HRMS (ESI, positive ion) calcd for $C_{18}H_{24}NaO_5$, *m/z* 343.1521, found 343.1507.

(3*R*, 4*R*)-3-(Benzyloxy)-4-hydroxy-5,5-bis(prop-2-ynyloxy)pentan-2-one (3d)

To **1a** (250 mg, 0.95 mmol) was added conc. HCl – propargyl alcohol (1:19) solution (20 mL) and the mixture was stirred at room temperature for 6 h, following the procedure as described in the preparation of **2a**. Usual work up and purification by column chromatography over silica gel (230 – 400 mesh) using petroleum ether – EtOAc (19:1) as eluent afforded **3d** (200 mg, 67%) as colourless liquid. $[\alpha]_D^{25}$ + 36.0 (*c* 0.31 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) : δ 2.22 (s, 3H), 2.50 (brs, 2H), 3.94 – 4.00 (m, 1H), 4.08 (d, 1H, J = 2.4 Hz), 4.23 – 4.41 (m, 4H), 4.56 (d, 1H, J = 11.1 Hz), 4.70 (d, 1H, J = 11.1 Hz), 4.92 (d, 1H, J = 6.6 Hz), 7.35 – 7.61 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 27.4 (CH_3), 54.8 (CH_2), 55.0 (CH_2), 72.6 (CH), 73.6 (CH_2), 75.2 (2 x CH), 78.9 (C), 79.3 (C), 83.4 (CH), 100.2 (CH),

128.2 – 128.5 (5 x CH), 136.8 (C), 209.9 (C); HRMS (ESI, positive ion) calcd for $C_{18}H_{20}NaO_5$, *m/z* 339.1208, found 339.1227.

(3*R*, 4*R*)-3-(Benzyloxy)-5,5-diisopropoxy-4-hydroxypentan-2-one (3e)

Compound **1a** (250 mg, 0.95 mmol) was treated with conc. HCl – *i*-PrOH mixture (1:19, 20 mL) at room temperature for 6 h, following the procedure as described in the preparation of **2a**. Usual work up and purification by column chromatography over silica gel (230 – 400 mesh) using petroleum ether – EtOAc (19:1) as eluent gave **3e** (195 mg, 64%) as colourless liquid. $[\alpha]_D^{25}$ + 16.5 (*c* 0.27 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.14 − 1.25 (m, 12H), 2.24 (s, 3H), 2.48 (d, 1H, *J* = 5.7 Hz), 3.77 − 3.97 (m, 3H), 4.06 (d, 1H, *J* = 3.0 Hz), 4.52 (d, 1H, *J* = 11.4 Hz), 4.66 (d, 1H, *J* = 11.4 Hz), 4.71 (d, 1H, *J* = 6.0 Hz), 7.32 − 7.41 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.9 (CH_3), 22.8 (CH_3), 23.2 (CH_3), 23.4 (CH_3), 27.4 (CH_3), 69.1 (CH), 70.1 (CH), 73.3 (CH, CH_2), 83.7 (CH), 98.8 (CH), 128.0 – 128.6 (5 x CH), 137.2 (C), 209.9 (C); HRMS (ESI, positive ion) calcd for $C_{18}H_{28}NaO_5$, *m/z* 347.1834, found 347.1851.

(3*R*, 4*R*)-3-(Benzyloxy)-5,5-bis-(2-chloroethoxy)-4-hydroxypentan-2-one (3f)

A mixture of conc. HCl – chloro ethanol (1:19, 20 mL) was added to **1a** (250 mg, 0.95 mmol) and the mixture was stirred at room temperature for 6 h, following the procedure as described in the preparation of **2a**. Usual work up and purification by column chromatography over silica gel (230 – 400 mesh) using petroleum ether – EtOAc (19:1) as eluent produced **3f** (220 mg, 64%) as colourless liquid. $[\alpha]_D^{25}$ + 107.1 (*c* 0.16 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.25 (s, 3H), 2.52 (brs, 1H), 3.50 – 3.57 (m, 2H), 3.66 (t, 3H, *J* = 5.4 Hz), 3.81 – 3.99 (m, 4H), 4.47 (d, 1H, *J* = 11.4 Hz), 4.65 (d, 1H, *J* = 7.2 Hz), 4.75 (d, 1H, *J* = 11.4 Hz), 7.36 (s, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 27.4 (CH_3), 42.8 (CH_2), 43.2 (CH_2), 66.3 (CH_2), 67.7 (CH_2), 72.0 (CH), 73.3 (CH_2), 83.4 (CH), 101.8 (CH), 128.2 (CH), 128.4 (2 x CH), 128.5 (2 x CH), 136.8 (C), 209.9 (C); HRMS (ESI, positive ion) calcd for $C_{16}H_{22}Cl_2NaO_5$, *m/z* 387.0742, found 387.0760.

(3*R*, 4*R*)-3-(Benzyloxy)-5,5-diethoxy-4-hydroxypentan-2-one (3g)

The reaction was carried out following the procedure as described for **2a**, using the same protocol at room temperature for 6 h. Work up and purification by column chromatography over silica gel (230 – 400 mesh) using petroleum ether – EtOAc (19:1) as eluent afforded **3g**

(170 mg, 60%) as colourless liquid. $[\alpha]_D^{25}$ + 153.1 (*c* 0.31 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.12 (t, 3H, *J* = 7.2 Hz), 1.22 (t, 3H, *J* = 7.2Hz), 2.25 (s, 3H), 2.40 (d, 1H, *J* = 4.2 Hz), 3.34 (quint, 1H, *J* = 7.2 Hz), 3.59 − 3.65 (m, 1H), 3.66 − 3.76 (m, 2H), 3.85(brt, 1H, *J* = 3.0 Hz), 4.01 (d, 1H, *J* = 2.4 Hz), 4.46 (d, 1H, *J* = 11.4 Hz), 4.53 (d, 1H, *J* = 6.6 Hz), 4.72 (d, 1H, *J* = 12.0 Hz), 7.29 − 7.36 (m, 5H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 15.2 (CH_3), 15.4 (CH_3), 27.4 (CH_3), 63.1 (CH_2), 63.7 (CH_2), 72.6 (CH), 73.4 (CH_2), 83.8 (CH), 102.0 (CH), 127.9, 128.1, 128.2, 128.4, and 128.5 (5 x CH), 137.0 (C), 209.8 (C); HRMS (ESI, positive ion) calcd for $C_{16}H_{24}NaO_5$, *m/z* 319.1521, found 319.1493.

(3*R*, 4*R*)-3-(Benzyloxy)-5,5-dibutoxy-4-hydroxypentan-2-one (3h)

The reaction was carried out using **1a** (250 mg, 0.95 mmol) and conc. HCl – *n*-BuOH (1:19) solution (20 mL) at room temperature for 6 h, following the procedure as described in the preparation of **2a**. Work up and purification by column chromatography over silica gel (230 – 400 mesh) using petroleum ether – EtOAc (93:7) as eluent gave **3h** (205 mg, 61%) as colourless liquid. $[\alpha]_D^{25}$ + 153.1 (*c* 0.31 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.90 (t, 3H, *J* = 7.8 Hz), 0.92 (t, 3H, *J* = 7.8 Hz), 1.30 − 1.39 (m, 4H), 1.44 − 1.49 (m, 2H), 1.55 − 1.59 (m, 2H), 2.25 (s, 3H), 3.28 (dd, 1H, *J* = 6.6, 15.6 Hz), 3.54 (dd, 1H, *J* = 6.6, 15.6 Hz), 3.61 − 3.68 (m, 2H), 3.87 (dd, 1H, *J* = 3.0, 7.2 Hz), 4.04 (d, 1H, *J* = 2.4 Hz), 4.46 (d, 1H, *J* = 11.4 Hz), 4.53 (d, 1H, *J* = 6.6 Hz), 4.70 (d, 1H, *J* = 11.4 Hz), 7.28 − 7.36 (m, 5H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 13.8 (2 x CH_3), 19.3 (2 x CH_2), 27.4 (CH_3), 31.8 (CH_2), 31.9 (CH_2), 67.1 (CH_2), 67.9 (CH_2), 72.6 (CH), 73.4 (CH_2), 83.8 (CH), 102.0 (CH), 128.3 (CH), 128.4 (2 x CH), 128.5 (2 x CH), 137.1 (C), 210.0 (C); HRMS (ESI, positive ion) calcd for $C_{20}H_{32}NaO_5$, *m/z* 375.2147, found 375.2125.

(2*S*, 3*R*, 4*R*, 5*R*)-4-(Benzyloxy)-2,5-bis-(benzylthio)-5-methyl-tetrahydrofuran-3-ol (4a)

The same reaction was carried out using **1a** (250 mg, 0.95 mmol) and conc. HCl – BnSH (1: 19) solution (20 mL) at room temperature for 1 h, following the procedure as described in the preparation of **2a**. Subsequent work up and purification by column chromatography over silica gel (230 – 400 mesh) using petroleum ether – EtOAc (23:2) as eluent afforded **4a** (200 mg, 47%) as yellowish liquid; $[\alpha]_D^{25}$ −16.5 (*c* 0.12 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.73 (s, 3H), 2.54 (brd, 1H *J* = 7.5 Hz), 3.71 (d, 1H, *J* = 3.3 Hz), 3.77 – 3.91 (m, 4H), 4.06 – 4.11 (m, 1H), 4.60 (d, 1H, *J* = 12.0 Hz), 4.66 (d, 1H, *J* = 12.0 Hz), 4.83 (d, 1H, *J* = 6.0 Hz), 7.26 – 7.36 (m, 15H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 24.2 (CH_3), 33.0 (CH_2), 35.1 (CH_2),

72.2 (CH_2), 80.6 (CH), 86.9 (CH), 89.1 (CH), 93.5 (C), 127.1 – 129.0 (15 x CH), 137.4 (C), 137.5 (C), 137.8 (C); HRMS (ESI, positive ion) calcd for $C_{26}H_{28}NaO_3S_2$, *m/z* 475.1378, found 475.1366.

(2*R*, 3*R*, 4*R*, 5*S*)-4-(Benzyloxy)-2,5-diethoxy-5-methyl-tetrahydrofuran-3-ol (4b)

As described in **2a**, compound **1a** (250 mg, 0.95 mmol) was dissolved in conc. HCl - EtOH (1:19) solution (20 mL) and the reaction mixture was stirred at room temperature for 1 h. Work up and purification on a silica gel (230 – 400 mesh) column using a mixture of petroleum ether – EtOAc (19:1) as eluent to furnish **4b** (150 mg, 53%) as colourless liquid. $[\alpha]_D^{25}$ + 72.7 (*c* 0.33 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.21 (t, 3H, *J* = 6.9 Hz), 1.41 – 1.46 (m , 6H), 3.53 – 3.61 (m, 2H), 3.64 – 3.74 (m, 2H) , 3.76 (d, 1H, *J* = 3.6 Hz) , 4.62 (d, 1H, *J* = 12.0 Hz), 4.79 (t, 1H, *J* = 4.2 Hz), 4.84 (d, 1H, *J* = 12.0 Hz), 5.77(d, 1H, *J* = 4.5 Hz), 7.28 – 7.41(m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.7 (2 x CH_3) 21.1 (CH_3), 56.8 (CH_2), 63.7 (CH_2), 72.0 (CH_2), 86.3 (CH), 88.2 (CH), 103.6 (CH), 105.9 (C), 127.8 – 128.3 (5 x CH), 137.37(C); HRMS (ESI, positive ion) calcd for $C_{16}H_{24}NaO_5$, *m/z* 319.1521, found 319.1509.

(2*R*, 3*R*, 4*S*, 5*R*)-4-(Benzyloxy)-2,5-dibutoxy-5-methyl-tetrahydrofuran-3-ol (4c)

Treatment of **1a** (250 mg, 0.95 mmol) with conc. HCl – *n*-BuOH (1:19) solution (20 mL) at room temperature for 1 h, following the procedure as described in the preparation of **2a** and subsequent work up and purification by column chromatography over silica gel (230 – 400 mesh) using petroleum ether – EtOAc (19:1) as eluent furnished **4c** (175 mg, 52%) as colourless liquid. $[\alpha]_D^{25}$ + 14.5 (*c* 0.22 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.89 – 0.95 (m, 6H), 1.30 – 1.65 (m, 11H, including a 's, 3H' at δ 1.42), 3.44 – 3.65 (m, 3H), 3.67 – 3.85 (m, 1H) , 3.91 (d, 1H, *J* = 5.7 Hz) , 4.02 – 4.16 (m, 1H), 4.67 (d, 1H, *J* = 12.0 Hz), 4.72 (d, 1H, *J* = 11.7 Hz), 4.98 (d, 1H, *J* = 4.8 Hz), 7.28 – 7.41(m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.9 (2 x CH_3), 19.3 (CH_2), 19.4 (CH_2), 20.2 (CH_3), 31.5 (CH_2), 32.1 (CH_2), 61.1 (CH_2), 68.6 (CH_2), 72.0 (CH_2), 75.7 (CH), 87.1 (CH), 100.4 (CH), 107.9 (C), 127.5 – 128.3 (5 x CH), 138.0 (C); HRMS (ESI, positive ion) calcd for $C_{20}H_{32}NaO_5$, *m/z* 375.2147, found 375.2125.

(2*S*, 3*S*, 4*S*, 5*R*)-2,5-diallyl-4-(benzyloxy)-5-methyltetrahydrofuran-3-ol (4d)

To **1a** (150 mg, 0.57 mmol) were added allyltrimethylsilane (10 mL) and conc. HCl (0.5 mL) and the reaction mixture as stirred at room temperature for 60 min. following the procedure as described in **2a**. Work up and purification on a silica gel (230 – 400 mesh) column using a mixture of petroleum ether – EtOAc (19:1) as eluent afforded **4d** (95 mg, 58%) as colourless liquid. $[\alpha]_D^{25}$ + 27.8 (*c* 0.43 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.22 (s, 3H), 2.27 – 2.48 (m, 4H), 3.66 – 3.69 (m, 1H), 3.99 – 4.17 (m, 2H), 4.54 – 4.71 (m, 2H), 4.98 – 5.23 (m, 4H), 5.74 – 5.94 (m, 2H), 7.29 – 7.36 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.2 (CH_3), 33.6 (CH_2), 45.6 (CH_2), 72.4 (CH_2), 77.3 (CH), 77.4 (CH), 82.9 (C), 89.2 (CH), 117.1 (CH_2), 118.5 (CH_2), 127.3 – 128.6 (5 x CH), 134.0 (CH), 134.7 (CH), 138.2 (C); ESIMS, *m/z*: 311 $(M + Na)^+$.

(2*R*, 3*R*, 4*R*, 5*S*)-4-(Benzyloxy)-5-methyl-2,5-bis(pent-4-enyloxy)tetrahydrofuran-3-ol (4e)

The reaction was carried out using the protocol, viz. **1a** (250 mg, 0.95 mmol), conc. HCl – 4-penten-1-ol (1 : 19) solution (20 mL) and stirring at room temperature for 1 h, following the procedure as described in the preparation of **2a**. Work up and purification by column chromatography over silica gel (230 – 400 mesh) using petroleum ether – EtOAc (19:1) as eluent afforded **4e** (185 mg, 52%) as colourless liquid. $[\alpha]_D^{25}$ + 34.5 (*c* 0.21 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.42 (s, 3H), 1.60 – 1.77 (m, 4H), 2.09 – 2.25 (m, 4H), 3.45 – 3.92 (m, 5H), 4.03 – 4.13 (m, 1H), 4.67 (d, 1H, *J* = 12.0 Hz), 4.72 (d, 1H, *J* = 12.0 Hz), 4.96 – 5.05 (m, 5H), 5.74 – 5.86 (m, 2H), 7.27 – 7.45 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.2 (CH_3), 28.6 (CH_2), 29.1 (CH_2), 30.2 (CH_2), 30.3 (CH_2), 60.8 (CH_2), 68.2 (CH_2), 72.0 (CH_2), 75.8 (CH), 87.1 (CH), 100.4 (CH), 107.9 (C), 114.7 (CH_2), 114.9 (CH_2), 127.5 – 128.3 (5 x CH), 137.9 (CH), 138.0 (C), 138.2 (CH); HRMS (ESI, positive ion) calcd for $C_{22}H_{32}NaO_5$, m/z 399.2147, found 399.2150.

***(2R, 3R, 4R, 5S)*-4-(Benzyloxy)-5-methyl-2,5-dipropoxy-tetrahydrofuran-3-ol (4f)**

Treatment of **1a** (250 mg, 0.95 mmol) with conc. HCl – *n*-PrOH (1:19) solution (20 mL), at room temperature for 60 min, following the procedure as described in the preparation of **2a**, followed by work up and purification by column chromatography over silica gel (230 – 400 mesh) using petroleum ether – EtOAc (19:1) as eluent furnished **4f** (160 mg, 52%) as colourless liquid. $[\alpha]_D^{25}$ + 86.7 (*c* 0.26 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.91 (t, 3H, *J* = 7.2 Hz), 0.94 (t, 3H, *J* = 7.2 Hz), 1.42 (s, 3H), 1.53 – 1.59 (m, 2H), 1.60 – 1.66 (m, 2H),

2.73(d, 1H, *J* = 10.8 Hz), 3.42 – 3.48 (m, 2H), 3.49 – 3.52 (m, 1H), 3.75 – 3.79 (m, 1H), 3.92 (d, 1H, *J* = 5.4 Hz), 4.12 (quint, 1H, *J* = 4.8 Hz), 4.68 (d, 1H, *J* = 12.0 Hz), 4.72 (d, 1H, *J* = 12.0 Hz), 4.99 (d, 1H, *J* = 5.4 Hz), 7.27 – 7.36 (m, 5H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 10.6 (CH_3), 10.6 (CH_3), 20.3 (CH_3), 22.7 (CH_2), 23.2 (CH_2), 63.0 (CH_2), 70.4 (CH_2), 72.0 (CH_2), 75.8 (CH), 87.2 (CH), 100.4 (CH), 107.9 (C), 127.5 (2 x CH), 127.6 (CH), 128.3 (2 x CH), 138.1 (C); HRMS (ESI, positive ion) calcd for $C_{18}H_{28}NaO_5$, m/z 347.1834, found 347.1881.

***(2R, 3R, 4R, 5S)*-4-(Allyloxy)-2,5-diethoxy-5-methyl-tetrahydrofuran-3-ol (4g)**

Compound **1b** (250 mg, 1.18 mmol) was treated with a solution (20 mL) of conc. HCl – EtOH (1:19) at room temperature for 1 h, following the procedure as described in the preparation of **2a** followed by work up and purification by column chromatography over silica gel (230 – 400 mesh) using petroleum ether – EtOAc (23:2) as eluent furnished **4g** (145 mg, 50%) as colourless liquid. $[\alpha]_D^{25}$ + 160.3 (*c* 0.18 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.18 (t, 3H, *J* = 6.9 Hz), 1.26 (t, 3H, *J* = 6.9 Hz), 1.38 (s, 3H), 2.76 (d, 1H, *J* = 10.5 Hz), 3.51 – 3.70 (m, 3H), 3.82 – 3.93 (m, 2H), 4.03 – 4.11 (m, 1H), 4.15 (t, 2H, *J* = 5.4 Hz), 5.00 (d, 1H, *J* = 5.1 Hz), 5.19 (d, 1H, *J* = 10.5 Hz), 5.32 (d,1H, *J* = 17.4 Hz), 5.86 – 5.99 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.1 (CH_3), 15.6 (CH_3), 20.0 (CH_3), 56.8 (CH_2), 64.2 (CH_2), 71.1 (CH_2), 75.9 (CH), 87.3 (CH), 100.3 (CH), 108.0 (C), 117.0 (CH_2), 134.4 (CH); HRMS (ESI, positive ion) calcd for $C_{12}H_{22}NaO_5$, m/z 269.1365, found 269.1382.

***(2R, 3R, 4R, 5S)*-4-(Allyloxy)-2,5-dibutoxy-5-methyl-tetrahydrofuran-3-ol (4h)**

A solution (20 mL) of conc. HCl – *n*-BuOH (1:19) was added to **1b** (250 mg, 1.18 mmol) and the mixture was stirred at room temperature for 1 h, following the procedure as described in the preparation of **2a**. Work up and purification by column chromatography over silica gel (230 – 400 mesh) using petroleum ether – EtOAc (19:1) as eluent furnished **4h** (195 mg, 55%) as colourless liquid. $[\alpha]_D^{25}$ + 21.3 (*c* 0.37 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.92 (t, 3H, *J* = 7.5 Hz), 0.95 (t, 3H, *J* = 7.2 Hz), 1.32 (s, 3H), 1.13 – 1.42 (m, 4H), 1.47 – 1.66 (m, 4H), 3.45 – 3.75 (m, 3H), 3.78 – 3.84 (m, 2H) , 4.01 – 4.10 (m, 1H), 4.14 – 4.16 (m, 2H), 4.96 (d, 1H, *J* = 5.1 Hz), 5.20 (d, 1H, *J* = 10.5 Hz), 5.32 (dd, 1H, *J* = 1.5, 17.1 Hz), 5.86 – 5.99 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.9 (CH_3), 14.0 (CH_3), 19.3 (CH_2), 19.4 (CH_2), 20.2 (CH_3), 31.6 (CH_2), 32.1 (CH_2), 61.2 (CH_2), 68.6 (CH_2), 71.1 (CH_2), 75.8 (CH), 87.0 (CH), 100.4 (CH), 107.9 (C), 117.0 (CH_2), 134.4 (CH). HRMS (ESI, positive ion) calcd for $C_{16}H_{30}NaO_5$, *m/z* 325.1991, found 325.1980.

***(2R, 3R, 4R, 5S)*-2-Acetoxy-4-Allyloxy-5-methyl-2,5-dipropoxy-tetrahydrofuran (4i)**

To **1b** (250 mg, 1.18 mmol) was added a mixture of conc. HCl – *n*-PrOH (1:19) (20 mL) at room temperature for 1 h, following the procedure as described in the preparation of **2a** and subsequent work up and purification led to an inseparable mixture (230 mg). To a solution of the mixture in pyridine (8 mL) at 0 ^{o}C, was added Ac_2O (0.17 mL, 1.8 mmol) and the solution was stirred at 0 ^{0}C for 60 min and then at 25 ^{0}C for 6 h. The solvent was removed, crushed ice was added to the residue and the crude product was extracted with DCM (3 x 20 mL). The solvent was successively washed with 1(N) HCl (10 mL), a saturated $NaHCO_3$ solution (2 x 15 mL), brine (2 x 15 mL), dried (Na_2SO_4), and evaporated to a residue, which was purified by column chromatography on silica gel (230 – 400 mesh) using petroleum ether – EtOAc (24:1) as eluent to afford **4i** (170 mg, 46%) as colourless liquid. $[\alpha]_D^{25}$ + 30.5 (*c* 0.28 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.86 – 0.96 (m, 6H), 1.39 (s, 3H), 1.57 (q-like, 4H, *J* = 6.9 Hz), 2.11 (s, 3H), 3.45 – 3.57 (m, 3H), 3.64 – 3.73 (m, 2H), 4.06 – 4.22 (m, 2H), 4.99 (dd-like, 1H, *J* = 1.8, 4.8 Hz), 5.13 (d, 1H, *J* = 4.8 Hz), 5.16 – 5.34 (m, 2H), 5.82 – 5.97 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 10.5 (CH_3), 10.6 (CH_3), 20.7 (CH_3), 21.5 (CH_3), 22.6 (CH_2), 23.3 (CH_2), 63.3 (CH_2), 70.2 (CH_2), 71.3 (CH_2), 77.0 (CH), 83.1 (CH), 97.9 (CH), 106.5 (C), 117.1 (CH_2), 134.2 (CH), 170.6 (C). HRMS (ESI, positive ion) calcd for $C_{16}H_{28}NaO_6$, m/z 339.1784, found 339.1809.

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Supporting materials. ^{1}H- and ^{13}C-NMR spectra of all new compounds; NOESY, HSQC and HMBC spectra of **2b**.

Table of contents

Pent-4-enofuranoside derivative has been converted to glycosides and open-chain ketoacetals on treatment with various alcohols under acidic conditions.

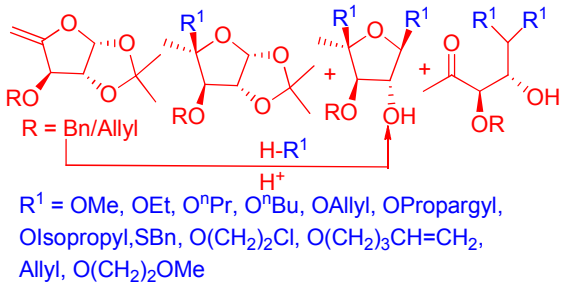

Table of contents

Pent-4-enofuranoside derivative has been converted to glycosides and open-chain ketoacetals on treatment with various alcohols under acidic conditions.