Pergamon

Tetrahedron: *Asymmetry* 12 (2001) 2731–2741

TETRAHEDRON: *ASYMMETRY*

Steric constraints against [3,3]-sigmatropic rearrangement of allylic azides. A convenient approach to β-L-4-aminopent-2-eno*glycero* pyranosides

Cristiana Fava, Roberta Galeazzi, Giovanna Mobbili and Mario Orena*

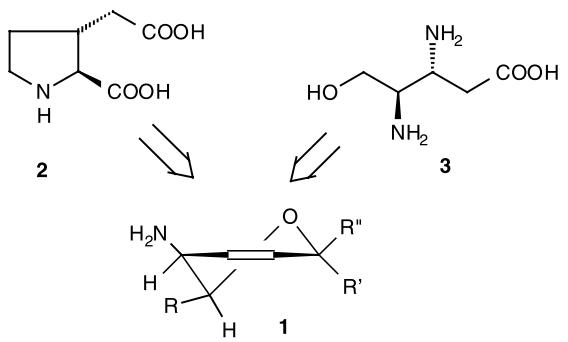
Dipartimento di Scienze dei Materiali e della Terra, Università di Ancona, Via Brecce Bianche, I-60131 Ancona, Italy

Received 4 October 2001; accepted 15 October 2001

Abstract—Starting from alkyl α-D-4-*O*-methanesulphonylpent-2-eno*glycero* pyranosides **13a–c**, nucleophilic substitution carried out with polymer-supported azide ion led to regioisomeric mixtures of the azides **14a–c** and **15a–c**. An analogous result, due to a [3,3]-sigmatropic rearrangement, was observed starting from methyl α-D-hex-2-eno*erythro* pyranoside derivatives **6a** and **6b**. On the contrary, starting from alkyl β-D-4-*O*-methanesulphonylpent-2-eno*glycero* pyranosides **21a–c**, azides **22a–c** were exclusively obtained, and subsequently converted into the corresponding amino derivatives **23a–c**. The behaviour of β-anomers **21a–c** was ascribed to steric interactions in the cyclic transition state, as supported by ab initio calculations.

1. Introduction

In connection with a project directed to preparing non-proteinogenic amino acids and peptide mimetics in enantiomerically pure form,[1] we have devised carbohydrates containing an allylic amine moiety such as **1a** and **1b** which could be the starting material of our synthetic approach proceeding via either C–C[2] or C–heteroatom bond formation,[3] leading to either **2** or **3**, respectively[4] (Scheme 1). Moreover, for introduction of the amino group, we were particularly interested in evaluating the use of polymeric reagents such as solid supported azide ion, in order to avoid aqueous work-up of the reactions.[5]



a. R = $CH_2OTBDMS$ or $CH_2OTBDPS$, R" = H, R' = OAlkyl
b. R = R' = H, R" = OAlkyl

Scheme 1.

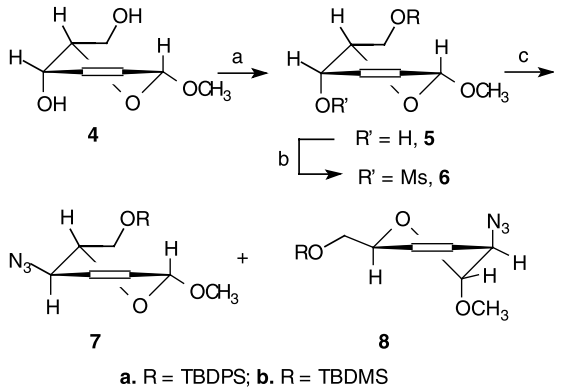
2. Results and discussion

As a first attempt, we focused on the nucleophilic displacement of the mesyl group in 2-hexenopyranosides **6a** and **6b**[6–8] carried out by using Amberlite IRA-900-supported azide ion[9] (Scheme 2). However, the reaction proceeded only in refluxing benzene,[10] and thermal [3,3]-sigmatropic rearrangement of the azido group occurred,[11–13] to give an inseparable mixture of regioisomeric azides **7** and **8**.[10,14,15]

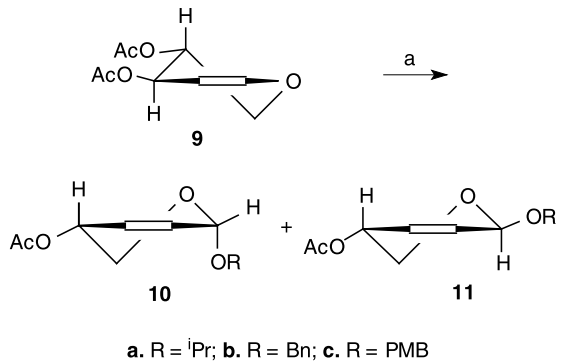
Owing to this result, hex-2-enopyranosides **5a** and **5b** were unsuitable for our aims. In our opinion, however, the [3,3]-sigmatropic rearrangement could be prevented by a sterically demanding β-substituent at C(1), but testing this hypothesis was discarded, due to the difficulty in preparing significant amount of methyl β-D-hex-2-enopyranosides.[8] Thus, we turned our attention to pent-2-enopyranosides **10** and **11**,[16,17] which can be obtained in good yield and high stereoselection starting from 3,4-di-*O*-acetyl-D-xylal, **9**,[18] the β-anomer **11** being the major component of the reaction mixture[16,19] (Scheme 3).

* Corresponding author. Tel.: +39 71 2204720; fax: +39 71 2204714; e-mail: orena@popcsi.unian.it

0957-4166/01/$ - see front matter
PII: S0957-4166(01)00450-5



Scheme 2. (a) TBDPSCl or TBDMSCl, Et_3N, DMAP, DCM (for **5a**, 76%; for **5b**, 69%); (b) MsCl, Et_3N, DMAP, AcOEt (for **6a**, 86%; for **6b**, 88%); (c) IRA 900 in the azide form, refluxing benzene (for **7a**+**8a**, 85%, d.r. 50:50; for **7b**+**8b**, 83%, d.r. 50:50).



Scheme 3. (a) I_2, ROH, Et_2O (79% for **10a**+**11a**, α:β 15:85; 90% for **10b**+**11b**, α:β 15:85; 88% for **10c**+**11c**, α:β 15:85).

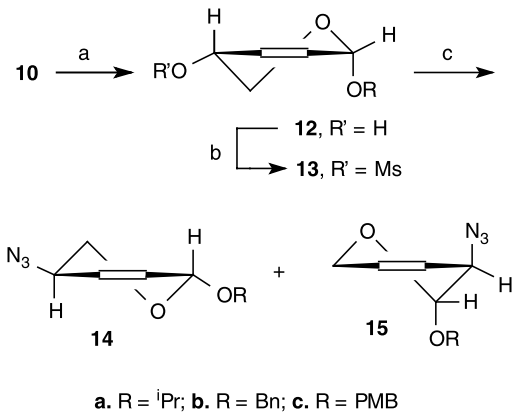
When methanesulphonyl derivatives **13a–c**, having α-configuration at the anomeric centre, were treated in refluxing benzene with azide ion on Amberlite IRA-900, nucleophilic displacement of the methanesulphonyl group occurred, followed by [3,3]-sigmatropic rearrangement, in agreement with the results observed starting from α-D-hex-2-enopyranosides **6a** and **6b**. Therefore, the regioisomeric allylic azides **14** and **15** were obtained and, after chromatographic separation, their structures were assigned by ^1H NMR spectral analysis (Scheme 4).

In order to unambiguously confirm the assigned configurations, the corresponding amines **16** and **18** were prepared by reduction of both **14a** and **15a** with $LiAlH_4$. These compounds were directly converted into the corresponding *p*-iodobenzamides **17** and **19**, whose structures were assigned on the basis of their ^1H NMR spectral data (Scheme 5).

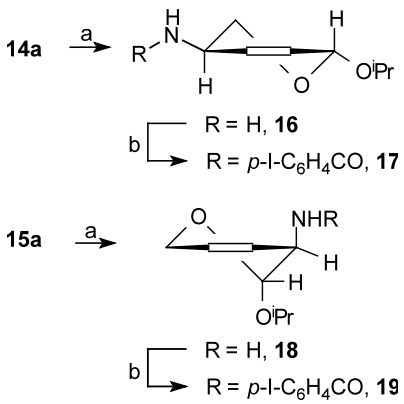
In contrast to the above results, when the methanesulphonyl derivatives **21a–c**, having β-configuration at the anomeric centre, were treated in refluxing benzene with polymer-supported azide ion, a single azido derivative (**22a–c**, respectively) was exclusively obtained in good yield, whose structure was assigned by ^1H NMR data. In this case the product arising from [3,3]-sigmatropic rearrangement was not observed, even after protracted heating of the pure isolated azides **22a–c** (Scheme 6).

Therefore, by reduction of the allylic azides **22** with $LiAlH_4$, the amines **23** were obtained, which were eventually converted into the corresponding amides **24**, useful intermediates to obtain stereoselectively both C–C[1,2] and C–heteroatom[3] bonds (Scheme 7).

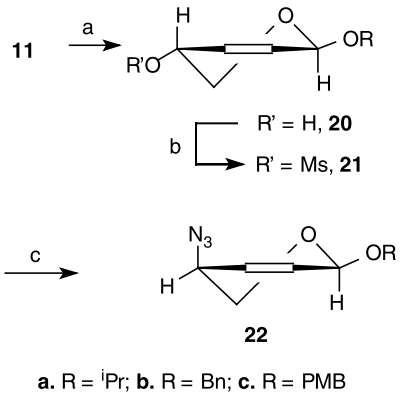
The outcome of the reaction starting from the β-anomer was ascribed to the steric interaction at the transition state between the rearranging azido group and the substituent at C(1). In fact, when this interaction is lacking, as in the α-anomers **14**, the azido group can easily undergo rearrangement to give a mixture of regioisomeric azides **14** and **15**.



Scheme 4. (a) Amberlite IRA-900 in the methoxide form, MeOH (for **12a–c**, 100%); (b) MsCl, Et_3N, DMAP, AcOEt (for **13a**, 89%; for **13b**, 93%; for **13c**, 90%); (c) Amberlite IRA-900 in the azide form, refluxing benzene (for **14a**+**15a**, 85%, d.r. 70:30; for **14b**+**15b**, 91%, d.r. 40:60; for **14c**+**15c**, 89%, d.r. 30:70).

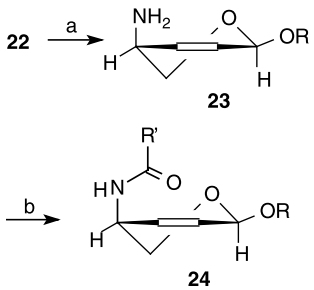


Scheme 5. (a) $LiAlH_4$, THF; (b) *p*-IC_6H_4COCl, Et_3N, DMAP, AcOEt (90% for **17**; 92% for **19**).



a. R = ^{i}Pr; **b.** R = Bn; **c.** R = PMB

Scheme 6. (a) IRA 900 in the methoxide form, MeOH (for **20a**–**c**, 100%); (b) MsCl, Et_3N, DMAP, AcOEt (for **21a**, 95%; for **21b**, 91%; for **21c**, 90%); (c) IRA 900 in the azide form, refluxing benzene (for **22a**, 81%; for **22b**, 89%; for **22c**, 86%).



a. R = ^{i}Pr, R' = ICH_2
b. R = Bn, R' = CH_3OOCCH_2
c. R = PMB, R' = Ph

Scheme 7. (a) $LiAlH_4$, THF (87% for **23a**; 88% for **23b**; 76% for **23c**); (b) R″COCl, Et_3N, DMAP, AcOEt (71% for **24a**; 76% for **24b**; 91% for **24c**).

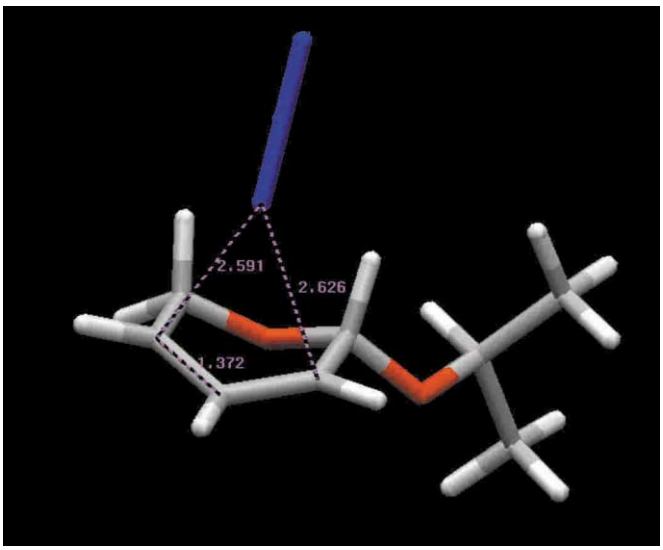


Figure 1. Optimised geometry of **TS-1**.

In order to confirm this suggestion, a quantum mechanical ab initio investigation was performed, with the aim to find out and characterise all the stationary points involved in the rearrangement reactions.[20] The transition structures of the two possible [3,3]-sigmatropic rearrangements, whose geometries are reported in Figs. 1 and 2, were located at B3LYP/6-31G* level of theory[21] together with the structures of the starting reagents and final products.[22]

From the calculations, for pathway 1 (**14a**—**TS-1**) the activation energy ($\Delta E^{\ddagger}$) was found to be 18.57 kcal/mol lower than for pathway 2 (**22a**—**TS-2**) (Scheme 8 and Tables 1 and 2). This large difference could be due to the steric hindrance between the rearranging azido and the isopropyl groups leading to **A**, as it appears from the geometry of **TS-2** (Fig. 2). Moreover, this highly destabilising steric interaction redirects the attack of the azido group so that the correct orientation for the reaction is not reached. This result is in agreement with

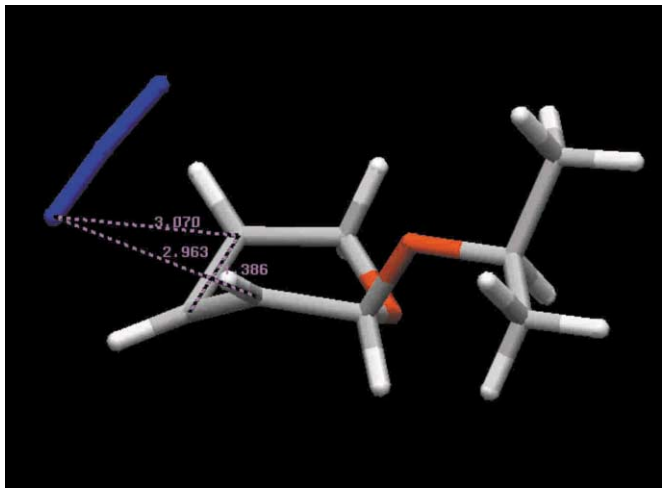
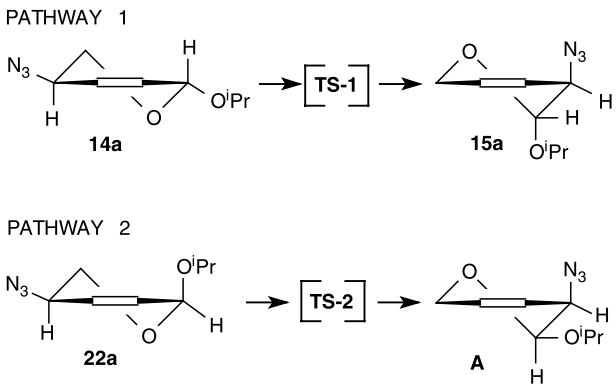


Figure 2. Optimised geometry of **TS-2**.



Scheme 8. Pathways involved in [3,3]-sigmatropic rearrangements.

Table 1. Activation energies ($\Delta E^{\ddagger}$) for pathways 1 and 2

	Level of theory	$\Delta E^{\ddagger}$ (298 K)
Pathway 1	HF/631G*	75.43
	B3LYP/6.31G*	56.99
Pathway 2	HF/6.31G*	97.94
	B3LYP/6.31G*	75.56

Table 2. Total energies (au) of reagents, transition structures and products for pathways 1 and 2

	HF/6-31G* (au)[a]	B3LYP/6-31G* (au)[b]
14a	−623.474617255	−627.275060282
TS-1	−623.354400735	−627.184239474
22a	−623.470863991	−627.270789852
TS-2	−623.314791416	−627.150378038
15a	−623.46633935910	−627.268018548
A	−623.474634447	−627.274399962

[a] Optimised at the same level of theory.
[b] Single point on the RHF/6-31G* geometry.

experimental data, since the azide **A** was never observed in the reaction mixture.[23]

3. Conclusions

From the observed results, supported by quantum-mechanical calculations, we can conclude that [3,3]-sigmatropic rearrangement of the azido group in β-pentenopyranosides **22** is strongly influenced by steric interaction of the anomeric substituent in the transition state. Thus, the easy access to either 4-amino-, **23**, or 4-amido pent-2-enopyranosides, **24**, makes these compounds attractive as key intermediates for the preparation of homochiral bioactive compounds. Applications directed to the synthesis of enantiomerically pure non-proteinogenic amino acids are currently underway in our laboratory.

4. Experimental

4.1. General procedures

Melting points were measured on an Electrothermal IA 9000 apparatus and are uncorrected. IR spectra were recorded in $CHCl_3$ on a Nicolet Fourier-transform infrared 20-SX spectrophotometer. Diastereomeric ratios (d.r.) were determined by GC analysis using a Chrompack 9001 instrument equipped with a Chrompack 7720 capillary column (50 m×0.25 mm i.d.; stationary phase CP-Sil-5 CB). ^{1}H and ^{13}C NMR spectra were recorded at 200 and 50 MHz, respectively, on a Varian Gemini 200 spectrometer, using $CDCl_3$ as a solvent. Chemical shifts (δ) are reported in ppm relative to TMS and coupling constants (J) in Hz. The assignment of all separate signals in the ^{1}H NMR spectra was made on the basis of coupling constants, selective proton–proton homonuclear decoupling experiments, proton–proton COSY experiments and proton–carbon HETCOR experiments. Optical rotations were measured on a Perkin–Elmer 241 polarimeter. Mass spectra (MS) were obtained by electron impact (EI) on a Hewlett–Packard 5989B mass spectrometer. Column chromatography was performed using silica gel 60 (230–400 mesh).

4.2. Methyl α-D-6-*O*-*t*-butyldiphenylsilyl-2,3-dideoxyhex-2-eno*erythro*pyranoside 5a

To a solution containing methyl α-D-2,3-dideoxyhex-2-eno*erythro*pyranoside **4**[8] (2.4 g, 15 mmol), triethylamine (1.5 g, 15 mmol) and DMAP (0.3 g) in dichloromethane (25 mL) *t*-butyldiphenylsilyl chloride (4.1 g, 15 mmol) dissolved in dichloromethane (10 mL) was added at 0°C and the mixture was stirred for 2 h. Water (50 mL) was added and the mixture was extracted with ethyl acetate (3×100 mL). After drying (Na_2SO_4), the solvent was removed under reduced pressure and the residue was purified by silica-gel chromatography (cyclohexane:ethyl acetate 90:10) to give the title compound in 76% yield; colourless viscous oil; IR ($CHCl_3$): 3350 cm^{-1}; ^{1}H NMR: δ 1.08 (s, 9H), 2.58 (d, 1H, J=4.6, OH), 3.39 (s, 3H), 3.72–3.83 (m, 1H), 3.86–3.94 (m, 2H), 4.19–4.30 (m, 1H), 4.85 (br s, 1H), 5.71–5.80 (m, 1H), 5.92–5.99 (m, 1H), 7.37–7.51 (m, 6 ArH), 7.65–7.78 (m, 4 ArH); ^{13}C NMR: δ 19.7, 27.3, 56.2, 66.2, 67.0, 71.0, 95.6, 126.4, 128.3, 130.4, 133.3, 133.5, 136.1; $[\alpha]_D$ +106.4 (c 0.5, $CHCl_3$). Anal. calcd for $C_{23}H_{30}O_4Si$: C, 69.31; H, 7.59. Found: C, 69.24; H, 7.52%.

4.3. Methyl α-D-6-*O*-*t*-butyldimethylsilyl-2,3-dideoxyhex-2-eno*erythro*pyranoside 5b

Following the procedure described for compound **5a**, but using *t*-butyldimethylsilyl chloride, the title compound was obtained in 69% yield; colourless oil; IR ($CHCl_3$): 3345 cm^{-1}; ^{1}H NMR: δ 0.09 (s, 6H), 0.89 (s, 9H), 2.87 (d, 1H, J=3.7, OH), 3.40 (s, 3H), 3.59–3.77 (m, 1H), 3.79 (dd, 1H, J=6.0, J=9.6), 3.89 (dd, 1H, J=4.9, J=9.6), 4.16 (m, 1H), 4.84 (s, 1H), 5.67–5.74 (m, 1H), 5.88–5.97 (m, 1H); ^{13}C NMR: δ −4.6, 18.7, 26.3, 56.1, 65.6, 67.1, 70.9, 95.6, 126.1, 133.6; $[\alpha]_D$ +99.6 (c 0.5, $CHCl_3$). Anal. calcd for $C_{13}H_{26}O_4Si$: C, 56.90; H, 9.55. Found: C, 56.84; H, 9.59%.

4.4. Methyl α-D-6-*O*-*t*-butyldiphenylsilyl-4-*O*-methanesulphonyl-2,3-dideoxyhex-2-eno*erythro*pyranoside 6a

To a solution containing compound **5a** (4.8 g, 12 mmol), triethylamine (1.2 g, 12 mmol) and *N*,*N*-dimethylaminopyridine (DMAP) (0.3 g) in ethyl acetate (70 mL), methanesulphonyl chloride (1.4 g, 12 mmol) dissolved in ethyl acetate (10 mL) was added at 0°C. After stirring for 3 h at 0°C, the suspension was poured into water–ice and extracted with ethyl acetate (3×100 mL). After drying (Na_2SO_4), the solvent was removed at reduced pressure and the residue was purified by silica-gel chromatography (cyclohexane:ethyl acetate 1:1) to give the title compound in 86% yield; colourless oil; ^{1}H NMR: δ 1.09 (s, 9H), 2.93 (s, 3H), 3.67 (s, 3H), 3.85–3.91 (m, 2H), 3.91–4.02 (m, 1H), 4.94 (d, 1H, J=2.6), 5.30 (br d, 1H, J=9.0), 6.85–6.94 (m, 1H), 6.07–6.15 (m, 1H), 7.34–7.48 (m, 6 ArH), 7.66–7.78 (m, 4 ArH); ^{13}C NMR: δ 19.8, 27.3, 56.5, 62.9, 69.6, 71.7, 95.7, 128.1, 128.2, 128.3, 128.4, 129.4, 129.6, 130.1, 130.3, 135.3, 135.7, 136.0, 136.1, 136.2, 136.4; $[\alpha]_D$ +105.6 (c 0.5, $CHCl_3$). Anal. calcd for $C_{24}H_{32}O_6SSi$: C, 60.48; H, 6.77. Found: C, 60.41; H, 6.83%.

4.5. Methyl α-D-6-*O*-*t*-butyldimethylsilyl-4-*O*-methanesulphonyl-2,3-dideoxyhex-2-eno*erythro* pyranoside 6b

Following the procedure described for compound **6a**, but starting from **5b**, the title compound was obtained in 88% yield; colourless oil; ^{1}H NMR: δ 0.10 (s, 6H), 0.91 (s, 9H), 3.08 (s, 3H), 3.44 (s, 3H), 3.74–3.95 (m, 3H), 4.89 (s, 1H), 5.19 (d, 1H, $J=10.3$), 5.81–5.92 (m, 1H), 6.05–6.14 (m, 1H); ^{13}C NMR: δ −4.9, 18.8, 26.4, 39.5, 56.4, 62.3, 69.4, 71.9, 95.7, 129.3, 129.6; $[\alpha]_D$ +114.3 (*c* 0.5, $CHCl_3$). Anal. calcd for $C_{14}H_{28}O_6SSi$: C, 47.70; H, 8.01. Found: C, 47.64; H, 7.97%.

4.6. Methyl α-D-4-azido-6-*O*-*t*-butyldiphenylsilyl-2,3,4-trideoxyhex-2-eno*threo* pyranoside 7a and methyl α-D-2-azido-6-*O*-*t*-butyldiphenylsilyl-2,3,4-trideoxyhex-3-eno-*glycero* pyranoside 8a

To a solution containing the methanesulphonate **6a** (1.8 g, 4.0 mmol) in benzene (40 mL), Amberlite IRA-900 in the azide form[9] (5.0 g, 3.0 mequiv./g) was added and the suspension was stirred under reflux for 2 h. The resin was then filtered off and the solvent removed under reduced pressure. The residue was purified by silica-gel chromatography (cyclohexane:ethyl acetate 80:20), to give as a 1:1 inseparable mixture the regioisomeric azides **7a** and **8a** in 85% overall yield which gave however distinct signal patterns in the ^{1}H and ^{13}C NMR spectra. Colourless oil; IR ($CHCl_3$): 2098 cm^{-1}. Anal. calcd for $C_{23}H_{29}N_3O_3Si$: C, 65.22; H, 6.90; N, 9.92. Found: C, 65.16; H, 6.85; N, 9.86%.

4.7. Methyl α-D-4-azido-6-*O*-*t*-butyldiphenylsilyl-2,3,4-trideoxyhex-2-eno*threo* pyranoside 7a

^{1}H NMR: δ 1.10 (s, 9H), 3.35–3.42 (m, 1H), 3.43 (s, 3H), 3.90 (d, 2H, $J=7.1$), 4.21–4.34 (m, 1H), 4.94 (d, 1H, $J=1.5$), 6.07–6.21 (m, 2H), 7.36–7.52 (m, 6 ArH), 7.65–7.79 (m, 4 ArH); ^{13}C NMR: δ 19.7, 27.3, 52.8, 56.1, 63.9, 71.1, 90.5, 125.3, 128.2, 130.3, 131.0, 133.8, 136.1, 136.2.

4.8. Methyl α-D-2-azido-6-*O*-*t*-butyldiphenylsilyl-2,3,4-trideoxyhex-3-eno*glycero* pyranoside 8a

^{1}H NMR: δ 1.11 (s, 9H), 3.35–3.41 (m, 1H), 3.45 (s, 3H), 3.72 (dd, 1H, $J=7.0$, $J=10.0$), 3.91 (dd, 1H, $J=6.1$, $J=10.0$), 4.41–4.35 (m, 1H), 4.84 (s, 1H), 5.78–5.89 (m, 1H), 6.29–6.38 (m, 1H), 7.36–7.52 (m, 6 ArH), 7.65–7.79 (m, 4 ArH); ^{13}C NMR: δ 19.8, 27.3, 55.5, 56.4, 66.7, 69.2, 100.4, 119.5, 128.2, 130.3, 131.1, 133.1, 136.1, 136.2.

4.9. Methyl α-D-4-azido-6-*O*-*t*-butyldimethylsilyl-2,3,4-trideoxyhex-2-eno*threo* pyranoside 7b and methyl α-D-2-azido-6-*O*-*t*-butyldimethylsilyl-2,3,4-trideoxyhex-3-eno-*glycero* pyranoside 8b

Following the same procedure as for compounds **4a** and **5a**, but starting from the methanesulphonate **6b**, an inseparable 1:1 mixture of the regioisomeric azides **7b** and **8b** was obtained in 83% overall yield which gave however distinct signal patterns in the ^{1}H and ^{13}C NMR spectra. Colourless oil; IR ($CHCl_3$): 2093 cm^{-1}. Anal. calcd for $C_{13}H_{25}N_3O_3Si$: C, 52.14; H, 8.42; N, 14.03. Found: C, 52.08; H, 6.81; N, 14.07%.

4.10. Methyl α-D-4-azido-6-*O*-*t*-butyldimethylsilyl-2,3,4-trideoxyhex-2-eno*threo* pyranoside 7b

^{1}H NMR: δ 1.11 (s, 9H), 3.32–3.41 (m, 1H), 3.44 (s, 3H), 3.81 (d, 2H, $J=7.0$), 4.07–4.25 (m, 1H), 4.90 (d, 1H, $J=1.4$), 6.03–6.16 (m, 2H); ^{13}C NMR: δ −4.8, 18.6, 26.3, 52.7, 56.0, 63.0, 71.1, 95.6, 125.2, 131.0.

4.11. Methyl α-D-2-azido-6-*O*-*t*-butyldimethylsilyl-2,3,4-trideoxyhex-3-eno*glycero* pyranoside 8b

^{1}H NMR: δ 1.09 (s, 9H), 3.39–3.40 (m, 1H), 3.61 (dd, 1H, $J=6.1$, $J=10.2$), 3.47 (s, 3H), 3.79 (dd, 1H, $J=4.9$, $J=10.2$), 4.15–4.26 (m, 1H), 4.83 (s, 1H), 5.75–5.87 (m, 1H), 6.20–6.28 (m, 1H); ^{13}C NMR: δ −4.9, 18.4, 26.3, 55.5, 56.5, 66.2, 69.3, 100.4, 119.2, 133.1.

4.12. Isopropyl α-D-4-*O*-acetyl-2,3-dideoxypent-2-eno-*glycero* pyranoside 10a and isopropyl β-D-4-*O*-acetyl-2,3-dideoxypent-2-eno*glycero* pyranoside 11a

A solution containing di-*O*-acetyl-D-xylal **9**[18] (4.0 g, 20 mmol) and isopropyl alcohol (3.0 mL) in diethyl ether (40 mL) was added at rt to a solution containing iodine (1.5 g, 6 mmol) in diethyl ether (40 mL) and the mixture was stirred for 3 h. An aqueous saturated solution of $Na_2S_2O_4$ (30 mL) was then added, the mixture was extracted with ethyl acetate (3×100 mL) and the organic layer was subsequently washed with 10% aqueous $NaHCO_3$ (50 mL) and brine (150 mL). After drying (Na_2SO_4), the solvent was removed under reduced pressure to give a residue which was purified by silica-gel column chromatography (cyclohexane:ethyl acetate 4:1) to give compounds **10a** and **11a** (15:85 d.r.) in 79% overall yield.

4.12.1. Isopropyl α-D-4-*O*-acetyl-2,3-dideoxypent-2-eno-*glycero* pyranoside 10a. Colourless oil; IR ($CHCl_3$): 1741 cm^{-1}; ^{1}H NMR: δ 1.17 (d, 6H, 50%, $J=6.2$), 1.24 (d, 6H, 50%, $J=6.2$), 2.06 (s, 3H), 3.82 (d, 2H, $J=7.0$), 3.97 (m, 1H, $J=6.2$), 5.03 (s, 1H), 5.28 (m, 1H), 5.77–5.98 (m, 2H); ^{13}C NMR: δ 21.4, 22.3, 24.0, 60.2, 65.5, 70.6, 92.7, 129.0, 130.2, 170.8; $[\alpha]_D$ +97.1 (*c* 0.5, $CHCl_3$); MS *m*/*z*: 200 (M^+), 185, 141, 82, 60. Anal. calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 60.04; H, 7.99%.

4.12.2. Isopropyl β-D-4-*O*-acetyl-2,3-dideoxypent-2-eno-*glycero* pyranoside 11a. Colourless oil; IR ($CHCl_3$): 1738 cm^{-1}; ^{1}H NMR: δ 1.17 (d, 6H, 50%, $J=6.2$), 1.22 (d, 6H, 50%, $J=6.2$), 2.08 (s, 3H), 3.80 (d, 1H, $J=13.1$), 3.97 (m, 1H, $J=6.2$), 4.18 (dd, 1H, $J=2.9$, $J=13.1$), 4.91–4.97 (m, 1H), 5.10 (d, 1H, $J=2.4$), 5.95–6.09 (m, 2H); ^{13}C NMR: δ 21.4, 22.2, 23.9, 61.4, 63.9, 70.3, 91.5, 125.1, 131.9, 170.8; $[\alpha]_D$ +120.4 (*c* 0.5, $CHCl_3$); MS *m*/*z*: 200 (M^+), 185, 141, 82, 60. Anal. calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 59.94; H, 8.00%.

4.13. Benzyl α-D-4-*O*-acetyl-2,3-dideoxypent-2-eno-*glycero* pyranoside 10b and benzyl β-D-4-*O*-acetyl-2,3-dideoxypent-2-eno*glycero* pyranoside 11b

Following the same procedure described for compounds **10a** and **11a**, but starting from di-*O*-acetyl-D-xylal **9** and benzyl alcohol, compounds **10b** and **11b** were obtained in 90% overall yield (d.r. 15:85).

4.13.1. Benzyl α-D-4-*O*-acetyl-2,3-dideoxypent-2-eno-*glycero* pyranoside 10b. Colourless oil; IR ($CHCl_3$): 1738 cm^{-1}; ^1H NMR: δ 2.08 (s, 3H), 3.83–3.94 (m, 2H), 4.58 (d, 1H, $J=11.7$), 4.83 (d, 1H, $J=11.7$), 5.04 (m, 1H), 5.25–5.36 (m, 1H), 5.82–5.93 (m, 1H), 5.94–6.01 (m, 1H), 7.23–7.41 (m, 5 ArH); ^{13}C NMR: δ 21.4, 60.6, 65.5, 70.5, 93.8, 128.2, 128.5, 128.9, 129.5, 129.6, 138.3, 170.8; $[\alpha]_D$ +77.1 (*c* 0.5, $CHCl_3$); MS *m*/*z*: 248 (M^+), 189, 141, 107, 91, 82. Anal. calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.68; H, 6.44%.

4.13.2. Benzyl β-D-4-*O*-acetyl-2,3-dideoxypent-2-eno-*glycero* pyranoside 11b. Colourless oil; IR ($CHCl_3$): 1732 cm^{-1}; ^1H NMR: δ 2.09 (s, 3H), 3.86 (d, 1H, $J=13.0$), 4.21 (dd, 1H, $J=2.8$, $J=13.0$), 4.58 (d, 1H, $J=11.7$), 4.80 (d, 1H, $J=11.7$), 4.93–4.99 (m, 1H), 5.10 (d, 1H, $J=2.0$), 5.95–6.15 (m, 2H), 7.25–7.39 (m, 5 ArH); ^{13}C NMR: δ 21.6, 61.8, 63.8, 70.3, 92.5, 125.6, 128.3, 128.8, 129.0, 131.4, 138.1, 171.0; $[\alpha]_D$ +137.7 (*c* 0.5, $CHCl_3$); MS *m*/*z*: 248 (M^+), 189, 141, 107, 91, 82. Anal. calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.67; H, 6.53%.

4.14. *p*-Methoxybenzyl α-D-4-*O*-acetyl-2,3-dideoxypent-2-eno*glycero* pyranoside 10c and *p*-methoxybenzyl β-D-4-*O*-acetyl-2,3-dideoxypent-2-eno*glycero* pyranoside 11c

The title compounds were prepared in 88% overall yield (d.r. 15:85) as described for **10a** and **11a**, starting from di-*O*-acetyl-D-xylal, **9**, and *p*-methoxybenzyl alcohol.

4.14.1. *p*-Methoxybenzyl α-D-4-*O*-acetyl-2,3-dideoxypent-2-eno*glycero* pyranoside 10c. Colourless oil; IR ($CHCl_3$): 1743 cm^{-1}; ^1H NMR: δ 2.07 (s, 3H), 3.80 (s, 3H), 3.83–3.87 (m, 2H), 4.63 (ABq, 2H, $J=11.4$), 5.02 (br s, 1H), 5.25–5.36 (m, 1H), 5.81–5.97 (m, 2H), 6.87 (d, 2 ArH, $J=8.6$), 7.28 (d, 2 ArH, $J=8.6$); ^{13}C NMR: δ 21.2, 55.5, 60.4, 65.5, 70.0, 93.4, 114.2, 129.3, 129.8, 130.1, 130.2, 130.3, 159.7, 170.6; $[\alpha]_D$ +63.4 (*c* 0.5, $CHCl_3$); MS *m*/*z*: 278 (M^+), 263, 219, 189, 141, 122, 121, 81, 60. Anal. calcd for $C_{15}H_{18}O_5$: C, 64.74; H, 6.52. Found: C, 64.69; H, 6.56%.

4.14.2. *p*-Methoxybenzyl β-D-4-*O*-acetyl-2,3-dideoxypent-2-eno*glycero* pyranoside 11c. Colourless oil; IR ($CHCl_3$): 1743 cm^{-1}; ^1H NMR: δ 2.09 (s, 3H), 3.80 (s, 3H), 3.85 (d, 1H, $J=13.0$), 4.19 (dd, 1H, $J=2.8$, $J=13.0$), 4.61 (ABq, 2H, $J=11.4$), 4.91–4.98 (m, 1H), 5.07 (d, 1H, $J=2.4$), 5.96–6.11 (m, 2H), 6.85 (d, 2 ArH, $J=8.6$), 7.37 (d, 2 ArH, $J=8.6$); ^{13}C NMR: δ 21.5, 55.6, 61.7, 63.8, 69.9, 92.2, 114.3, 125.4, 130.1, 130.2, 131.5, 159.8, 170.9; $[\alpha]_D$ +58.3 (*c* 0.5, $CHCl_3$); MS *m*/*z*: 278 (M^+), 263, 219, 189, 141, 122, 121, 81, 60. Anal. calcd for $C_{15}H_{18}O_5$: C, 64.74; H, 6.52. Found: C, 64.69; H, 6.56%.

4.15. Preparation of alcohols 12a–c and 20a–c. General procedure

A solution containing **10a–c** or **11a–c** (20 mmol) in methanol (30 mL) was added to the resin IRA 900 (5.0 g) in the methoxide form prepared in methanol (30 mL).[24] The mixture was stirred at rt for 1 h, then the resin was filtered off and washed with methanol (10 mL). The solvent was removed under reduced pressure and the residue was purified by silica-gel chromatography (cyclohexane:ethyl acetate 7:3) to give **12a–c** or **20a–c**.

4.15.1. Isopropyl α-D-2,3-dideoxypent-2-eno*glycero*-pyranoside 12a. The title compound was prepared in quantitative yield starting from isopropyl α-D-4-*O*-acetyl-2,3-dideoxypent-2-eno*glycero* pyranoside **10a**. Colourless oil; IR ($CHCl_3$): 3411 cm^{-1}; ^1H NMR: δ 1.17 (d, 6H, 50%, $J=6.2$), 1.24 (d, 6H, 50%, $J=6.2$), 1.81 (br d, 1H, $J=6.5$, OH), 3.71 (dd, 1H, $J=7.8$, $J=11.0$), 3.79 (dd, 1H, $J=5.5$, $J=11.0$), 3.97 (m, 1H, $J=6.2$), 4.11–4.32 (m, 1H), 5.04 (s, 1H), 5.69–5.77 (m, 1H), 5.96–6.05 (m, 1H); ^{13}C NMR: δ 22.4, 24.1, 63.6, 64.0, 70.8, 93.1, 128.5, 133.4; $[\alpha]_D$ +37.9 (*c* 0.5, $CHCl_3$); MS *m*/*z*: 158 (M^+), 140, 99, 82, 81. Anal. calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.69; H, 8.86%.

4.15.2. Benzyl α-D-2,3-dideoxypent-2-eno*glycero* pyranoside 12b. The title compound was prepared in quantitative yield starting from benzyl α-D-4-*O*-acetyl-2,3-dideoxypent-2-eno*glycero* pyranoside **10b**. Low melting solid; IR ($CHCl_3$): 3401 cm^{-1}; ^1H NMR: δ 2.48 (br s, 1H, OH), 3.70 (dd, 1H, $J=8.3$, $J=11.0$), 3.79 (dd, 1H, $J=5.6$, $J=11.0$), 4.12–4.28 (m, 1H), 4.56 (d, 1H, $J=11.7$), 4.80 (d, 1H, $J=11.7$), 5.01 (br s, 1H), 5.76 (ddd, 1H, $J=1.7$, $J=2.5$, $J=10.3$), 5.95–6.06 (m, 1H), 7.35 (m, 5 ArH); ^{13}C NMR: δ 63.5, 64.0, 70.5, 93.9, 127.6, 128.3, 129.0, 134.0, 138.0; $[\alpha]_D$ +73.3 (*c* 0.5, $CHCl_3$); MS *m*/*z*: 206 (M^+), 188, 115, 91, 81, 77. Anal. calcd for $C_{12}H_{14}O_3$: C, 69.89; H, 6.84. Found: C, 69.84; H, 6.79%.

4.15.3. *p*-Methoxybenzyl α-D-2,3-dideoxypent-2-eno-*glycero* pyranoside 12c. The title compound was prepared in a quantitative yield starting from *p*-methoxybenzyl α-D-4-*O*-acetyl-2,3-dideoxypent-2-eno*glycero*-pyranoside **10c**. Colourless oil; IR ($CHCl_3$): 3347 cm^{-1}; ^1H NMR: δ 2.05 (br s, 1H, OH), 3.71 (dd, 1H, $J=8.1$, $J=11.0$), 3.79 (dd, 1H, $J=5.6$, $J=11.$), 3.80 (s, 3H), 4.15–4.28 (m, 1H), 4.62 (ABq, 2H, $J=11.3$), 4.98 (br s, 1H), 5.69–5.79 (m, 1H), 5.94–6.04 (m, 1H), 6.86 (d, 2 ArH, $J=8.6$), 7.27 (d, 2 ArH, $J=8.6$); ^{13}C NMR: δ 55.7, 63.4, 63.8, 70.1, 93.5, 114.3, 127.6, 130.1, 130.3, 134.0, 146.9, 159.8; $[\alpha]_D$ +31.0 (*c* 0.5, $CHCl_3$); MS *m*/*z*: 236 (M^+), 221, 218, 206, 189, 121, 103, 81, 77. Anal. calcd for $C_{13}H_{16}O_4$: C, 66.09; H, 6.83. Found: 66.12; H, 6.79%.

4.15.4. Isopropyl β-D-2,3-dideoxypent-2-eno*glycero*-pyranoside 20a. The title compound was prepared in a quantitative yield starting from isopropyl β-D-4-*O*-acetyl-2,3-dideoxypent-2-eno*glycero* pyranoside **11a**. Colourless oil; IR ($CHCl_3$): 3410 cm^{-1}; ^1H NMR: δ

1.17 (d, 6H, 50%, $J=6.1$), 1.22 (d, 6H, 50%, $J=6.1$), 2.15 (br d, 1H, $J=7.2$, OH), 3.75 (d, 1H, $J=12.4$), 3.76–3.87 (m, 1H), 3.97 (m, 1H, $J=6.1$), 4.14 (dd, 1H, $J=2.6$, $J=12.4$), 5.03 (d, 1H, $J=3.4$), 5.84 (dd, 1H, $J=3.4$, $J=9.9$), 6.12 (dd, 1H, $J=5.3$, $J=9.9$); ^{13}C NMR: δ 22.3, 24.0, 61.9, 64.6, 91.7, 129.3, 129.5; $[\alpha]_D$ +101.4 (*c* 0.5, $CHCl_3$); MS *m*/*z*: 158 (M^+), 140, 99, 82, 81. Anal. calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.69; H, 8.97%.

4.15.5. Benzyl β-D-2,3-dideoxypent-2-eno*glycero*pyranoside 20b. The title compound was prepared in a quantitative yield starting from benzyl β-D-4-*O*-acetyl-2,3-dideoxypent-2-eno*glycero*pyranoside **11b**. Low melting solid; IR ($CHCl_3$): 3411 cm^{-1}; ^{1}H NMR: δ 3.81 (d, 1H, $J=8.8$, OH), 3.81 (d, 1H, $J=12.7$), 4.16 (dd, 1H, $J=2.3$, $J=12.7$), 4.57 (d, 1H, $J=11.8$), 4.79 (d, 1H, $J=11.8$), 5.01 (d, 1H, $J=3.1$), 5.87 (dd, 1H, $J=3.1$, $J=10.0$), 6.11 (dd, 1H, $J=5.3$, $J=10.0$), 7.36 (m, 5 ArH); ^{13}C NMR: δ 61.8, 65.0, 70.2, 92.6, 128.3, 128.6, 129.0, 129.9, 138.1; $[\alpha]_D$ +99.2 (*c* 0.5, $CHCl_3$); MS *m*/*z*: 206 (M^+), 188, 115, 91, 82, 77. Anal. calcd for $C_{12}H_{14}O_3$: C, 69.89; H, 6.84. Found: C, 69.95; H, 6.78%.

4.15.6. *p*-Methoxybenzyl β-D-2,3-dideoxypent-2-eno*glycero*pyranoside 20c. The title compound was prepared in a quantitative yield starting from *p*-methoxybenzyl β-D-4-*O*-acetyl-2,3-dideoxypent-2-eno*glycero*-pyranoside **11c**. White solid; mp 59–60°C; IR ($CHCl_3$): 3351 cm^{-1}; ^{1}H NMR: δ 1.86 (d, 1H, OH, $J=8.5$), 3.75–3.92 (m, 1H), 3.81 (s, 3H), 3.82 (d, 1H, $J=12.1$), 4.16 (dd, 1H, $J=2.8$, $J=12.1$), 4.62 (ABq, 2H, $J=11.4$), 5.14 (d, 1H, $J=3.1$), 5.87 (dd, 1H, $J=3.1$, $J=9.9$), 6.13 (dd, 1H, $J=5.2$, $J=9.9$), 6.99 (d, 2 ArH, $J=8.7$), 7.27 (d, 2 ArH, $J=8.7$); ^{13}C NMR: δ 55.7, 61.8, 65.0, 69.7, 92.3, 114.3, 128.7, 129.8, 130.2, 130.3, 159.8; $[\alpha]_D$ +68.4 (*c* 0.5, $CHCl_3$); MS *m*/*z*: 236 (M^+), 221, 218, 206, 189, 121, 103, 81, 77. Anal. calcd for $C_{13}H_{16}O_4$: C, 66.09; H, 6.83. Found: C, 66.03; H, 6.87%.

4.16. Preparation of methanesulphonates 13a–c and 21a–c. General procedure

To a solution containing the alcohols **12a**–**c** or **20a**–**c** (6.4 mmol), triethylamine (0.64 g, 6.4 mmol) and DMAP (0.3 g) in ethyl acetate (70 mL), methanesulphonyl chloride (0.7 g, 6.4 mmol) dissolved in ethyl acetate (10 mL) was added at 0°C. After 3 h the suspension was poured in ice–water and extracted with ethyl acetate (3×100 mL). After drying (Na_2SO_4), the residue was purified by chromatography on silica gel (cyclohexane:ethyl acetate 1:1) to give the methanesulphonates **13a**–**c** or **21a**–**c**.

4.16.1. Isopropyl α-D-4-*O*-methanesulphonyl-2,3-dideoxypent-2-eno*glycero*pyranoside 13a. The title compound was obtained in 89% yield starting from isopropyl α-D-2,3-dideoxypent-2-eno*glycero*pyranoside **12a**. Colourless oil; ^{1}H NMR: δ 1.05 (d, 6H, 50%, $J=6.2$), 1.21 (d, 6H, 50%, $J=6.2$), 3.07 (s, 3H), 3.87–4.06 (m, 1H, $J=6.2$), 3.90 (dd, 1H, $J=5.9$, $J=15.1$), 3.99 (dd, 1H, $J=9.0$, $J=15.1$), 5.03 (br s, 1H), 5.14–5.26 (m, 1H), 5.84–5.95 (m, 1H), 5.96–6.05 (m, 1H); ^{13}C NMR: δ 22.3, 24.0, 39.1, 60.6, 61.8, 71.1, 92.6, 127.7, 131.9; $[\alpha]_D$ +98.2 (*c* 0.5, $CHCl_3$). Anal. calcd for $C_9H_{16}O_5S$: C, 45.75; H, 6.83. Found: C, 45.69; H, 6.77%.

4.16.2. Benzyl α-D-4-*O*-methanesulphonyl-2,3-dideoxypent-2-eno*glycero*pyranoside 13b. The title compound was prepared in 93% yield starting from benzyl α-D-2,3-dideoxypent-2-eno*glycero*pyranoside **12b**. White solid; mp 53–55°C; ^{1}H NMR: δ 3.06 (s, 3H), 3.95 (dd, 1H, $J=6.0$, $J=11.2$), 4.03 (dd, 1H, $J=7.8$, $J=11.2$), 4.58 (d, 1H, $J=11.7$), 4.82 (d, 1H, $J=11.7$), 5.04 (br s, 1H), 5.19–5.28 (m, 1H), 5.95 (ddd, 1H, $J=1.5$, $J=3.5$, $J=10.3$), 5.99–6.81 (m, 1H), 7.35 (m, 5 ArH); ^{13}C NMR: δ 39.1, 60.9, 70.7, 71.0, 93.5, 128.2, 128.6, 129.0, 129.3, 129.4, 129.9, 131.2 $[\alpha]_D$ +84.2 (*c* 0.5, $CHCl_3$). Anal. calcd for $C_{13}H_{16}O_5S$: C, 54.92; H, 5.67. Found: C, 54.86; H, 5.72%.

4.16.3. *p*-Methoxybenzyl α-D-4-*O*-methanesulphonyl-2,3-dideoxypent-2-eno*glycero*pyranoside 13c. The title compound was prepared in 90% yield starting from *p*-methoxybenzyl α-D-2,3-dideoxypent-2-eno*glycero*pyranoside **12c**. White solid; mp 74–76°C; ^{1}H NMR: δ 3.06 (s, 3H), 3.81 (s, 3H), 3.94 (dd, 1H, $J=5.9$, $J=11.2$), 4.02 (dd, 1H, $J=7.9$, $J=11.2$), 4.63 (ABq, 2H, $J=11.4$), 5.02 (br s, 1H), 5.15–5.35 (m, 1H), 5.87–5.96 (m, 1H), 5.98–6.07 (m, 1H), 6.89 (d, 2 ArH, $J=8.7$), 7.29 (d, 2 ArH, $J=8.7$); ^{13}C NMR: δ 39.1, 55.8, 60.9, 70.4, 70.9, 93.2, 114.4, 128.1, 129.9, 130.3, 130.4, 131.4, 159.9; $[\alpha]_D$ +61.2 (*c* 0.5, $CHCl_3$). Anal. calcd for $C_{14}H_{18}O_6S$: C, 53.49; H, 5.77. Found: C, 53.54; H, 5.73%.

4.16.4. Isopropyl β-D-4-*O*-methanesulphonyl-2,3-dideoxypent-2-eno*glycero*pyranoside 21a. Compound **21a** was prepared in 95% yield starting from isopropyl β-D-2,3-dideoxypent-2-eno*glycero*pyranoside **20a**. Colourless oil; ^{1}H NMR: δ 1.08 (d, 6H, 50%, $J=6.2$), 1.13 (d, 6H, 50%, $J=6.2$), 3.04 (s, 3H), 3.82 (dd, 1H, $J=1.2$, $J=13.5$), 3.88 (m, 1H, $J=6.2$), 4.13 (dd, 1H, $J=2.3$, $J=13.5$), 4.75 (br s, 1H), 5.01–5.12 (m, 1H), 5.96–6.02 (m, 2H); ^{13}C NMR: δ 22.2, 23.9, 39.3, 61.5, 70.1, 70.6, 91.3, 123.9, 133.6; $[\alpha]_D$ +102.0 (*c* 0.5, $CHCl_3$); MS *m*/*z*: 236 (M^+). Anal. calcd for $C_9H_{16}O_5S$: C, 45.75; H, 6.83. Found: C, 45.69; H, 6.77%.

4.16.5. Benzyl β-D-4-*O*-methanesulphonyl-2,3-dideoxypent-2-eno*glycero*pyranoside 21b. Compound **21b** was prepared in 91% yield as reported for **6a**, but starting from benzyl β-D-2,3-dideoxypent-2-eno*glycero*pyranoside **20b**. Colourless oil; ^{1}H NMR: δ 3.06 (s, 3H), 4.06 (d, 1H, $J=13.3$), 4.25 (dd, 1H, $J=2.6$, $J=13.5$), 4.59 (d, 1H, $J=11.7$), 4.79 (d, 1H, $J=11.7$), 4.85–4.92 (m, 1H), 5.11 (d, 1H, $J=1.6$), 6.04–6.19 (m, 2H), 7.36 (m, 5 ArH); ^{13}C NMR: δ 39.5, 61.9, 69.8, 70.6, 92.3, 124.4, 128.6, 128.9, 129.0, 133.0, 137.8; $[\alpha]_D$ +81.4 (*c* 0.5, $CHCl_3$); MS *m*/*z*: 284 (M^+). Anal. calcd for $C_{13}H_{16}O_5S$: C, 54.92; H, 5.67. Found: C, 54.85; H, 5.71%.

4.16.6. *p*-Methoxybenzyl β-D-4-*O*-methanesulphonyl-2,3-dideoxypent-2-eno*glycero*pyranoside 21c. Compound **21c** was prepared in 90% yield starting from *p*-methoxybenzyl β-D-2,3-dideoxypent-2-eno*glycero*pyranoside **20c**. White solid; mp 67–69°C; ^{1}H NMR: δ 3.07 (s, 3H), 3.81 (s, 3H), 4.05 (d, 1H, $J=13.5$), 4.24 (dd, 1H, $J=2.5$, $J=13.5$), 4.62 (ABq, 2H, $J=11.3$), 4.85–4.91 (m, 1H), 5.09 (d, 1H, $J=1.6$), 6.04–6.16 (m, 2H), 6.89 (d, 2 ArH, $J=8.8$), 7.28 (d, 2 ArH, $J=8.8$); ^{13}C NMR: δ 39.4, 55.7, 61.8, 69.7, 70.1, 91.9, 114.3, 124.3, 129.8, 130.3, 133.1, 159.9; $[\alpha]_D$ +77.6 (*c* 0.5, $CHCl_3$); MS: 314 (M^+). Anal. calcd for $C_{14}H_{18}O_6S$: C, 53.49; H, 5.77. Found: C, 53.44; H, 5.72%.

4.17. Preparation of azides 14a–c, 15a–c and 22a–c. General procedure

To a solution containing the methanesulphonates **13a–c** and **21a–c** (4.0 mmol) in benzene (40 mL), Amberlite IRA-900 in the azide form[9] (5.0 g, 3.0 mequiv./g) was added and the suspension was refluxed for 2 h. The resin was then filtered off and the solvent removed under reduced pressure. The residue was purified by silica-gel chromatography (cyclohexane:ethyl acetate 4:1), to give pure isolated azides **14a–c**, **15a–c** and **22a–c**.

4.17.1. Isopropyl α-L-4-azido-2,3,4-trideoxypent-2-eno*glycero*pyranoside 14a and isopropyl α-2-azido-2,3,4-trideoxypent-3-enopyranoside 15a. Starting from methanesulphonyl derivative **13a**, the title compounds were obtained in 85% overall yield and 7:3 d.r.

4.17.1.1. Isopropyl α-L-4-azido-2,3,4-trideoxypent-2-eno*glycero*pyranoside 14a. Colourless oil; IR ($CHCl_3$): 2097 cm^{-1}; ^{1}H NMR: δ 1.18 (d, 6H, 50%, $J=6.2$), 1.23 (d, 6H, 50%, $J=6.2$), 3.28–3.37 (m, 1H), 3.90 (d, 1H, $J=12.2$), 3.89–4.09 (m, 1H, $J=6.2$), 4.21 (dd, 1H, $J=2.9$, $J=12.2$), 5.08 (d, 1H, $J=2.2$), 5.98–6.13 (m, 2H); ^{13}C NMR: δ 24.0, 22.3, 52.3, 62.7, 70.6, 91.6, 124.4, 131.8; $[\alpha]_D$ −53.6 (*c* 0.5, $CHCl_3$); MS *m*/*z*: 182 (M^+), 154, 123, 107, 95. Anal. calcd for $C_8H_{13}N_3O_2$: C, 52.74; H, 6.64. Found: C, 52.78; H, 6.59%.

4.17.1.2. Isopropyl α-2-azido-2,3,4-trideoxypent-3-enopyranoside 15a. Colourless oil; IR ($CHCl_3$): 2097 cm^{-1}; ^{1}H NMR: δ 1.19 (d, 6H, 50%, $J=6.2$), 1.24 (d, 6H, 50%, $J=6.2$), 3.41–3.53 (m, 1H), 3.87–4.08 (m, 1H, $J=6.2$), 4.12 (ddd, 1H, $J=2.1$, $J=4.0$, $J=17.2$), 4.25 (ddd, 1H, $J=2.4$, $J=4.6$, $J=17.2$), 4.88 (d, 1H, $J=2.6$), 5.69–5.81 (m, 1H), 6.06–6.16 (m, 1H); ^{13}C NMR: δ 22.1, 23.8, 56.6, 61.2, 70.8, 97.7, 119.9, 131.4; $[\alpha]_D$ −71.4 (*c* 0.5, $CHCl_3$); MS *m*/*z*: 182 (M^+), 154, 123, 107, 95. Anal. calcd for $C_8H_{13}N_3O_2$: C, 52.74; H, 6.64. Found: C, 52.68; H, 6.70%.

4.17.2. Benzyl α-L-4-azido-2,3,4-trideoxypent-2-eno*glycero*pyranoside 14b and benzyl α-2-azido-2,3,4-trideoxypent-3-enopyranoside 15b. Starting from methanesulphonyl derivative **13b**, the title compounds were obtained in 91% overall yield and 40:60 d.r.

4.17.2.1. Benzyl α-L-4-azido-2,3,4-trideoxypent-2-eno*glycero*pyranoside 14b. Colourless oil; IR ($CHCl_3$): 2099 cm^{-1}; ^{1}H NMR: δ 3.31–3.41 (m, 1H), 3.94 (d, 1H, $J=12.1$), 4.23 (dd, 1H, $J=2.3$, $J=12.1$), 4.59 (d, 1H, $J=11.8$), 4.80 (d, 1H, $J=11.8$), 5.08 (d, 1H, $J=2.6$), 6.06 (dd, 1H, $J=5.1$, $J=10.0$), 6.15 (dd, 1H, $J=2.6$, $J=10.0$), 7.36 (m, 5 ArH); ^{13}C NMR: δ 53.8, 61.5, 70.4, 93.5, 123.4, 128.5, 128.7, 128.8, 129.0, 130.0, 138.7; $[\alpha]_D$ −66.8 (*c* 0.5, $CHCl_3$); MS *m*/*z*: 231 (M^+), 203, 107, 96, 91, 77. Anal. calcd for $C_{12}H_{13}N_3O_2$: C, 62.33; H, 5.67; N, 18.17. Found: C, 62.37; H, 5.62; N, 18.24%.

4.17.2.2. Benzyl α-2-azido-2,3,4-trideoxypent-3-enopyranoside 15b. Colourless oil; IR ($CHCl_3$): 2100 cm^{-1}; ^{1}H NMR: δ 3.47–3.54 (m, 1H), 4.09–4.34 (m, 2H), 4.63 (d, 1H, $J=11.9$), 4.84 (d, 1H, $J=11.9$), 4.93 (d, 1H, $J=1.4$), 5.74–5.87 (m, 1H), 6.12–6.22 (m, 1H), 7.37 (m, 5 ArH); ^{13}C NMR: δ 55.9, 60.9, 70.5, 98.3, 119.4, 128.5, 128.7, 128.9, 131.5, 138.7; $[\alpha]_D$ +68.8 (*c* 0.5, $CHCl_3$); MS *m*/*z*: 231 (M^+), 203, 107, 96, 91, 81, 77. Anal. calcd for $C_{12}H_{13}N_3O_2$: C, 62.33; H, 5.67; N, 18.17. Found: C, 62.26; H, 5.73; N, 18.22%.

4.17.3. *p*-Methoxybenzyl α-L-4-azido-2,3,4-trideoxypent-2-eno*glycero*pyranoside 14c and *p*-methoxybenzyl α-2-azido-2,3,4-trideoxypent-3-enopyranoside 15c. Starting from the methanesulphonyl derivative **13c**, the title compounds were obtained in 89% overall yield and 3:7 d.r.

4.17.3.1. *p*-Methoxybenzyl α-L-4-azido-2,3,4-trideoxypent-2-eno*glycero*pyranoside 14c. Colourless oil; IR ($CHCl_3$): 2098 cm^{-1}; ^{1}H NMR: δ 3.28–3.35 (m, 1H), 3.80 (s, 3H), 3.93 (dd, 1H, $J=1.0$, $J=12.2$), 4.21 (dd, 1H, $J=2.7$, $J=12.2$), 4.62 (ABq, 2H, $J=11.4$), 5.05 (d, 1H, $J=2.6$), 6.02 (dd, 1H, $J=5.0$, $J=10.9$), 6.09 (dd, 1H, $J=2.6$, $J=10.9$), 6.89 (d, 2 ArH, $J=8.6$), 7.29 (d, 2 ArH, $J=8.6$); ^{13}C NMR: δ 52.2, 55.7, 62.9, 70.0, 92.2, 114.4, 124.6, 130.1, 130.3, 131.4, 159.9; $[\alpha]_D$ −136.1 (*c* 0.5, $CHCl_3$); MS *m*/*z*: 261 (M^+), 246, 233, 124, 121, 96, 81, 77. Anal. calcd for $C_{13}H_{15}N_3O_3$: C, 59.76; H, 5.79; N, 16.08. Found: C, 59.71; H, 5.74; N, 16.13%.

4.17.3.2. *p*-Methoxybenzyl α-2-azido-2,3,4-trideoxypent-3-enopyranoside 15c. Colourless oil; IR ($CHCl_3$): 2098 cm^{-1}; ^{1}H NMR: δ 3.44–3.51 (m, 1H), 3.81 (s, 3H), 4.15 (ddd, 1H, $J=2.4$, $J=3.8$, $J=17.1$), 4.27 (ddd, 1H, $J=2.3$, $J=4.7$, $J=17.1$), 4.66 (ABq, 2H, $J=11.4$), 5.71–5.83 (m, 1H), 6.08–6.19 (m, 1H), 6.89 (d, 2 ArH, $J=8.7$), 7.29 (d, 2 ArH, $J=8.7$); ^{13}C NMR: δ 55.7, 55.9, 60.8, 70.1, 98.0, 114.4, 124.6, 130.1, 130.3, 131.4, 159.9; $[\alpha]_D$ +181.3 (*c* 0.5, $CHCl_3$); MS *m*/*z*: 261 (M^+), 246, 233, 124, 121, 96. Anal. calcd for $C_{13}H_{15}N_3O_3$: C, 59.76; H, 5.79; N, 16.08. Found: C, 59.74; H, 5.75; N, 16.12%.

4.17.4. Isopropyl β-L-4-azido-2,3,4-trideoxypent-2-eno*glycero*pyranoside 22a. Starting from the methanesulphonyl derivative **21a**, the title compound was obtained in 81% yield; colourless oil; IR ($CHCl_3$): 2101 cm^{-1}; ^{1}H NMR: δ 1.17 (d, 6H, 50%, $J=6.1$), 1.24 (d, 6H, 50%, $J=6.1$), 3.71–3.83 (m, 2H), 3.87–4.06 (m, 1H, $J=6.1$), 3.88–3.93 (m, 1H), 5.04 (s, 1H), 5.82–6.03 (m,

2H); ^{13}C NMR: δ 22.4, 24.1, 53.6, 61.1, 70.7, 92.6, 128.4, 130.5; $[\alpha]_D$ −132.2 (*c* 0.5, $CHCl_3$); MS *m*/*z*: 183 (M^+), 182, 107, 154, 123, 95. Anal. calcd for $C_8H_{13}N_3O_2$: C, 52.45; H, 7.15; N, 22.94. Found: C, 52.39; H, 7.19; N, 22.89%.

4.17.5. Benzyl β-L-4-azido-2,3,4-trideoxypent-2-eno-*glycero*pyranoside 22b. Starting from the methanesulphonyl derivative **21b**, the title compound was obtained in 89% yield; colourless oil; IR ($CHCl_3$): 2101 cm^{-1}; ^{1}H NMR: δ 3.82–3.89 (m, 2H), 3.90–4.03 (m, 1H), 4.59 (d, 1H, *J*=11.8), 4.83 (d, 1H, *J*=11.8), 5.05 (s, 1H), 5.89–5.98 (m, 1H), 5.99–6.07 (m, 1H), 7.36 (m, 5 ArH); ^{13}C NMR: δ 53.8, 61.6, 70.4, 93.6, 128.5, 128.7, 129.0, 129.1, 130.1, 138.2; $[\alpha]_D$ −140.4 (*c* 0.5, $CHCl_3$); MS *m*/*z*: 231 (M^+), 203, 107, 96, 91, 77. Anal. calcd for $C_{12}H_{13}N_3O_2$: C, 62.33; H, 5.67; N, 18.17. Found: C, 62.27; H, 5.64; N, 18.21%.

4.17.6. *p*-Methoxybenzyl β-L-4-azido-2,3,4-trideoxypent-2-eno*glycero*pyranoside 22c. Starting from the methanesulphonyl derivative **21c**, the title compound was obtained in 86% yield; colourless oil; IR ($CHCl_3$): 2097 cm^{-1}; ^{1}H NMR: δ 3.80 (s, 3H), 3.78–4.01 (m, 3H), 4.64 (ABq, 2H, *J*=11.5), 5.03 (br s, 1H), 5.87–5.96 (m, 1H), 5.96–6.04 (m, 1H), 6.90 (d, 2 ArH, *J*=8.7), 7.30 (d, 2 ArH, *J*=8.7); ^{13}C NMR: δ 53.8, 54.8, 55.7, 70.0, 93.3, 114.4, 114.7, 128.5, 130.2, 130.3, 159.9; $[\alpha]_D$ −137.5 (*c* 0.5, $CHCl_3$); MS *m*/*z*: 261 (M^+), 246, 233, 166, 122, 121, 96, 81, 77. Anal. calcd for $C_{13}H_{15}N_3O_3$: C, 59.76; H, 5.79; N, 16.08. Found: C, 59.72; H, 5.75; N, 16.13%.

4.18. Preparation of amides 17 and 19. General procedure

To a solution of the azides **14a** or **15a** (1.5 g, 8.0 mmol) in dry THF (30 mL), $LiAlH_4$ (0.31 g, 8.0 mmol) was added at 0°C under an argon atmosphere and the mixture was stirred for 2 h. Then, methanol (1 mL) was added, followed by a 4 M NaOH solution (30 mL), and the mixture was extracted with ethyl acetate (3×150 mL). After drying (Na_2SO_4), the solvent was removed under reduced pressure to give the corresponding amines which were directly acylated: A solution containing the amines **16** or **18** (1.1 g, 3.6 mmol), triethylamine (0.4 g, 4 mmol) and DMAP (0.3 g) in ethyl acetate (70 mL) was treated by slow addition of a solution of 4-iodobenzoyl chloride (1.0 g, 3.7 mmol) in ethyl acetate (20 mL) at 0°C. After stirring for 1 h, water (40 mL) was added and the mixture was extracted with ethyl acetate. After drying (Na_2SO_4), the solvent was removed under reduced pressure and the residue was purified by silica-gel chromatography (cyclohexane:ethyl acetate 7:3), to give pure isolated **9** or **10**.

4.18.1. Isopropyl α-L-4-(*p*-iodobenzamido)-2,3,4-trideoxypent-2-eno*glycero*pyranoside 17. Starting from **14a**, the title compound was obtained in 90% yield; white solid; mp 66–68°C; IR ($CHCl_3$): 3338, 1651 cm^{-1}; ^{1}H NMR: δ 1.12 (d, 6H, 50%, *J*=6.1), 1.17 (d, 6H, 50%, *J*=6.1), 3.69 (d, 1H, *J*=12.1), 3.84–3.98 (m, 1H, *J*=6.1), 4.17 (dd, 1H, *J*=3.2, *J*=12.1), 4.31–4.22 (m, 1H), 5.00 (d, 1H, *J*=2.9), 5.85 (dd, 1H, *J*=2.9, *J*=10.0), 6.01 (dd, 1H, *J*=5.3, *J*=10.0), 7.05 (d, 1H, *J*=7.9, NH), 7.45 (d, 2 ArH, *J*=8.6), 7.76 (d, 2 ArH, *J*=8.6); ^{13}C NMR: δ 22.1, 23.8, 42.8, 62.6, 70.6, 91.9, 99.1, 127.4, 129.1, 129.9, 131.7, 138.1, 167.2; $[\alpha]_D$ −48.2 (*c* 0.5, $CHCl_3$); MS *m*/*z*: 387 (M^+), 357, 328, 303, 302, 299, 248, 231, 203, 161, 127, 101, 87, 81. Anal. calcd for $C_{15}H_{18}NO_3I$: C, 46.53; H, 4.69; N, 3.62. Found: C, 46.47; H, 4.64; N, 3.67%.

4.18.2. Isopropyl α-2-(*p*-iodobenzamido)-2,3,4-trideoxypent-3-enopyranoside 19. Starting from **15a**, the title compound was obtained in 92% yield; white solid; mp 71–73°C; IR ($CHCl_3$): 3340, 1648 cm^{-1}; ^{1}H NMR: δ 1.23 (d, 6H, 50%, *J*=6.1), 1.26 (d, 6H, 50%, *J*=6.1), 3.87–4.05 (m, 1H, *J*=6.1), 4.06 (ddd, 1H, *J*=2.3, *J*=2.3, *J*=16.8), 4.28 (ddd, 1H, *J*=2.2, *J*=4.4, *J*=16.8), 4.38–4.49 (m, 1H), 4.95 (s, 1H), 5.79–5.92 (m, 1H), 5.98–6.09 (m, 1H), 6.16 (d, 1H, *J*=8.1), 7.51 (d, 2 ArH, *J*=8.5), 7.79 (2 ArH, *J*=8.5); ^{13}C NMR: δ 22.2, 23.7, 46.9, 97.1, 99.1, 121.9, 129.1, 130.5, 138.3, 166.4; $[\alpha]_D$ −61.6 (*c* 0.5, $CHCl_3$); MS *m*/*z*: 387 (M^+), 357, 328, 300, 299, 248, 232, 231, 203, 177, 149, 127, 81. Anal. calcd for $C_{15}H_{18}NO_3I$: C, 46.53; H, 4.69; N, 3.62. Found: C, 46.49; H, 4.75; N, 3.66%.

4.19. Preparation of amines 23a–c. General procedure

To a solution containing the azides **22a**–**c** (11 mmol) in dry THF (40 mL), $LiAlH_4$ (0.4 g, 10 mmol) was added at 0°C under an argon atmosphere and the mixture was stirred for 2 h. Then, methanol (1 mL) was added, followed by a 4 M NaOH solution (30 mL), and the mixture was extracted with ethyl acetate (3×150 mL). After drying (Na_2SO_4), the solvent was removed under reduced pressure and the residue was purified by silica-gel chromatography (cyclohexane:ethyl acetate 1:4).

4.19.1. Isopropyl β-L-4-amino-2,3,4-trideoxypent-2-eno*glycero*pyranoside 23a. Starting from **22a**, the title compound was obtained in 87% yield; colourless oil; IR ($CHCl_3$): 3346 cm^{-1}; ^{1}H NMR: δ 1.17 (d, 6H, 50%, *J*=6.2), 1.22 (d, 6H, 50%, *J*=6.2), 1.45 (br s, 2H, NH), 3.42–3.51 (m, 1H), 3.48–3.75 (m, 2H), 3.84–4.08 (m, 1H, *J*=6.2), 5.01 (s, 1H), 5.65–5.68 (m, 1H), 5.86–5.98 (m, 1H); ^{13}C NMR: δ 22.3, 24.1, 45.8, 64.9, 70.2, 92.4, 127.0, 135.7; $[\alpha]_D$ −83.2 (*c* 0.5, $CHCl_3$); MS *m*/*z*: 158 (M^++1), 157, 114, 98, 69. Anal. calcd for $C_8H_{15}NO_2$: C, 61.62; H, 9.62; N, 8.91. Found: C, 61.58; H, 9.67; N, 8.94%.

4.19.2. Benzyl β-L-4-amino-2,3,4-trideoxypent-2-eno-*glycero*pyranoside 23b. Starting from **22b**, the title compound was obtained in 88% yield; colourless oil; IR ($CHCl_3$): 3348 cm^{-1}; ^{1}H NMR: δ 1.16 (br s, 2H, NH), 3.46 (dd, 1H, *J*=9.5, *J*=9.5), 3.78 (dd, 1H, *J*=4.4, *J*=9.5), 4.05–4.25 (m, 1H), 4.56 (d, 1H, *J*=11.8), 4.81 (d, 1H, *J*=11.8), 5.01 (br s, 1H), 5.70–5.81 (m, 1H), 5.89–6.01 (m, 1H), 7.35 (m, 5 ArH); ^{13}C NMR: δ 45.7, 62.2, 65.1, 70.2, 93.4, 126.4, 128.3, 128.4, 128.8, 136.0, 138.4; $[\alpha]_D$ −63.6 (*c* 0.5, $CHCl_3$); MS *m*/*z*: 206 (M^++1), 205, 115, 107, 98, 99, 77. Anal. calcd for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.17; H, 7.33; N, 6.86%.

4.19.3. *p*-Methoxybenzyl β-L-4-amino-2,3,4-trideoxypent-2-eno*glycero*pyranoside 23c. Starting from **22c**, the title compound was obtained in 76% yield; colourless oil; IR ($CHCl_3$): 3345 cm^{-1}; ^1H NMR: δ 1.89 (br s, 2H, NH_2), 3.41–3.56 (m, 2H), 3.69–3.83 (m, 1H), 3.78 (s, 3H), 4.59 (ABq, 2H, $J=11.4$), 4.97 (br s, 1H), 5.64–5.76 (m, 1H), 5.86–5.96 (m, 1H), 6.86 (d, 2 ArH, $J=8.6$), 7.27 (d, 2 ArH, $J=8.6$); ^{13}C NMR: δ 45.7, 55.7, 65.0, 69.8, 93.1, 114.3, 126.6, 130.1, 130.2, 135.7, 159.7; $[\alpha]_D$ +77.4 (*c* 0.5, $CHCl_3$); MS *m*/*z*: 236 (M^++1), 235, 221, 220, 166, 112, 107, 99, 77. Anal. calcd for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28; N, 5.95. Found: C, 66.31; H, 7.24; N, 5.89%.

4.20. Preparation of amides 24a–c. General procedure

To a solution containing the amine **23a**–**c** (10 mmol), triethylamine (1.1 g, 11 mmol) and DMAP (0.3 g) in ethyl acetate (70 mL) at 0°C, a solution containing the appropriate acyl chloride (11 mmol) in ethyl acetate (20 mL) was slowly added. After 1 h, water (40 mL) was added and the mixture was extracted with ethyl acetate (3×150 mL). After drying (Na_2SO_4), the solvent was removed under reduced pressure and the residue was purified by silica-gel chromatography (cyclohexane:ethyl acetate 7:3) to give the amides **24a**–**c**.

4.20.1. Isopropyl β-L-4-iodoacetamido-2,3,4-trideoxypent-2-eno*glycero*pyranoside 24a. Starting from iodoacetyl chloride and **23a**, the title compound was obtained in 71% yield; colourless oil; IR ($CHCl_3$): 1674 cm^{-1}; ^1H NMR: δ 1.17 (d, 6H, 50%, $J=6.2$), 1.23 (d, 6H, 50%, $J=6.2$), 3.65 (dd, 1H, $J=8.1$, $J=11.0$), 3.88 (s, 2H), 3.82 (dd, 1H, $J=5.4$, $J=11.0$), 3.88–4.06 (m, 1H, $J=6.2$), 4.49–4.64 (m, 1H), 5.05 (s, 1H), 5.72–5.94 (m, 2H), 6.12 br d, 1H, $J=8.1$, NH); ^{13}C NMR: δ 22.4, 24.1, 44.4, 61.9, 71.0, 93.1, 129.8, 130.3, 167.5; $[\alpha]_D$ −81.3 (*c* 0.5, $CHCl_3$); MS *m*/*z*: 325 (M^+), 267, 132, 120, 114, 69. Anal. calcd for $C_{10}H_{16}NO_3I$: C, 36.94; H, 4.96; N, 4.31. Found: C, 36.87; H, 4.92; N, 4.25%.

4.20.2. Benzyl β-L-4-methoxycarbonylacetamido-2,3,4-trideoxypent-2-eno*glycero*pyranoside 24b. Starting from methylmalonyl chloride and **23b**, the title compound was obtained in 76% yield; colourless oil; IR ($CHCl_3$): 3346, 1743, 1685 cm^{-1}; ^1H NMR: δ 3.31 (s, 2H), 3.67 (dd, 1H, $J=9.3$, $J=11.0$), 3.71 (s, 3H), 3.87 (dd, 1H, $J=5.5$, $J=11.0$), 4.56 (d, 1H, $J=11.7$), 4.57–4.80 (m, 1H), 4.80 (d, 1H, $J=11.7$), 5.04 (br s, 1H), 5.75–6.02 (m, 2H), 7.10 (d, 1H, NH, $J=8.1$), 7.21–7.39 (m, 5 ArH); ^{13}C NMR: δ 41.7, 43.8, 52.9, 61.7, 70.4, 93.7, 128.2, 128.3, 128.5, 128.9, 131.0, 138.1, 165.7, 169.8; $[\alpha]_D$ −38.8 (*c* 0.5, $CHCl_3$); MS *m*/*z*: 306 (M^++1), 305, 290, 275, 198, 184, 169, 118, 101, 98, 91, 77. Anal. calcd for $C_{16}H_{19}NO_5$: C, 62.94; H, 6.27; N, 4.59. Found: C, 62.89; H, 6.32; N, 4.63%.

4.20.3. *p*-Methoxybenzyl β-L-4-benzamido-2,3,4-trideoxypent-2-eno*glycero*pyranoside 24c. Starting from benzoyl chloride and **23c**, the title compound was obtained in 91% yield; white crystals; mp 72–74°C; IR ($CHCl_3$): 3344, 1658 cm^{-1}; ^1H NMR: δ 3.74 (s, 3H), 3.76 (dd, 1H, $J=8.1$, $J=11.0$), 3.95 (dd, 1H, $J=5.5$, $J=11.0$), 4.59 (ABq, 2H, $J=11.3$), 4.77–4.91 (m, 1H), 5.01 (s, 1H), 5.79 (m, 1H,), 5.90 (m, 1H), 6.73 (d, 1H, NH), 6.83 (d, 2 ArH, $J=8.7$), 7.24 (d, 2 ArH, $J=8.7$), 7.25–7.53 (m, 3 ArH), 7.68–7.78 (m, 2 ArH); ^{13}C NMR: δ 44.2, 55.7, 62.1, 70.1, 93.6, 114.3, 127.7, 128.8, 128.9, 129.8, 129.9, 130.2, 130.3, 130.5, 131.2, 132.1, 134.5, 159.8, 167.9; $[\alpha]_D$ −80.0 (*c* 0.5, $CHCl_3$) MS *m*/*z*: 339 (M^+), 204, 203, 166, 112, 107, 105, 99, 77. Anal. calcd for $C_{20}H_{21}NO_4$: C, 70.78; H, 6.24; N, 4.13. Found: C, 70.74; H, 6.20; N, 4.17%.

4.21. Computational methods

Ab initio molecular orbitals and DFT calculations were carried out using the GAUSSIAN 94 program package.[20] For DFT calculations the hybrid functional B3LYP which contains gradient corrections for both exchange and correlation was chosen. The geometry of the reactants, products and transition structures were fully optimised at RHF/6-31G* theory level. The calculated stationary points (local minima and saddle points) were characterised by harmonic vibrational frequency calculations at both HF/6-31G* and B3LYP/6-31G* levels.[21,22,25] Transition structures were characterised by a single imaginary frequency whereas reactant and products had none. The Becke3LYP method is found to predict activation barriers for closed- and open-shell pathways of pericyclic reactions in excellent agreement with the available experimental data.[26]

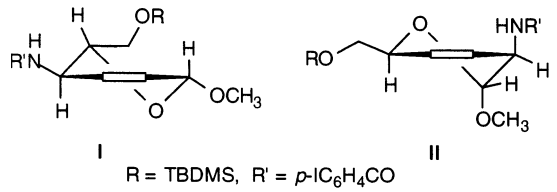
Acknowledgements

We thank M.I.U.R. (Roma, Italy) for a grant (PRIN 2000) and Dr. Luca Santini for valuable technical support.

References

1. (a) Galeazzi, R.; Mobbili, G.; Orena, M. *Tetrahedron* **1996**, *52*, 1069–1084; (b) Galeazzi, R.; Geremia, S.; Mobbili, G.; Orena, M. *Tetrahedron: Asymmetry* **1996**, *7*, 79–88; (c) Galeazzi, R.; Mobbili, G.; Orena, M. *Tetrahedron: Asymmetry* **1997**, *8*, 133–137.
2. (a) Galeazzi, R.; Geremia, S.; Mobbili, G.; Orena, M. *Tetrahedron: Asymmetry* **1996**, *7*, 3573–3584; (b) Galeazzi, R.; Mobbili, G.; Orena, M. *Tetrahedron* **1999**, *55*, 261–270; (c) Galeazzi, R.; Mobbili, G.; Orena, M. *Tetrahedron* **1999**, *55*, 4029–4042; (d) Fava, C.; Galeazzi, R.; Gonzalez-Rosende, M. E.; Orena, M. *Tetrahedron Lett*. **2000**, *41*, 8577–8580.
3. (a) Jordá-Gregori, J. M.; González-Rosende, M. E.; Sepúlveda-Arques, J.; Galeazzi, R.; Orena, M. *Tetrahedron: Asymmetry* **1999**, *10*, 1135–1143; (b) Jordà-Gregori, J. M.; Gonzalez-Rosende, M. E.; Cava-Montesinos, P.; Sepulveda-Arques, J.; Galeazzi, R.; Orena, M. *Tetrahedron: Asymmetry* **2000**, *11*, 3769–3777.
4. A similar product, prepared in low yield starting from D-serine, was recently used for the synthesis of acyclic analogs of kainoids. See: Hashimoto, M.; Hashimoto, K.; Shirahama, H. *Tetrahedron* **1996**, *52*, 1931–1942.
5. Bhalay, G.; Dunstan, A.; Glen, A. *Synlett* **2000**, 1846–1859.

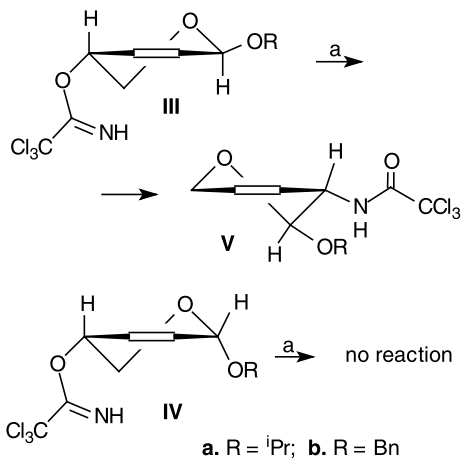
6. Fraser Reid, B. *Acc. Chem. Res.* **1975**, *8*, 192–201.
7. Fraser Reid, B. *Acc. Chem. Res.* **1985**, *18*, 347–354.
8. Ferrier, R. J.; Prasad, N. *J. Chem. Soc. (C)* **1969**, 570–575.
9. The polymeric reagent was prepared by reaction of sodium azide with the resin Amberlite IRA-900 in chloride form. Amberlyst A 26 in the azide form, purchased from Fluka, gave similar results.
10. Iriarte Capaccio, C. A.; Varela, O. *Tetrahedron: Asymmetry* **2000**, *11*, 4945–4954.
11. Gagneux, A.; Winstein, S.; Young, W. G. *J. Am. Chem. Soc.* **1960**, *82*, 5956–5957.
12. VanderWerf, C. A.; Heasley, V. L. *J. Org. Chem.* **1966**, *31*, 3534–3537.
13. Trost, B. M.; Pulley, S. R. *Tetrahedron Lett.* **1995**, *36*, 8737–8740.
14. Ferrier, R. J.; Vetaviyaser, N. *J. Chem. Soc. (C)* **1971**, 1907–1913.
15. The structural assignment was confirmed by conversion of both **7b** and **8b** into the corresponding *p*-iodobenzamides **I** and **II** (R = TBDMS, R′ = *p*-IC_6H_4CO), which were easily separated and characterised.



Compound **I**: white solid; mp 66–68°C; IR ($CHCl_3$): 3345, 1654 cm^{-1}; ^1H NMR: δ 0.06 (s, 3H), 0.07 (s, 3H), 0.90 (s, 9H), 3.49 (s, 3H), 3.78 (d, 2H, $J=4.5$), 4.19–4.28 (m, 1H), 4.47–4.61 (m, 1H), 4.80 (s, 1H), 5.86–6.08 (m, 2H), 6.16 (d, 1H, $J=8.7$, NH), 7.48 (d, 2 ArH, $J=8.4$), 7.77 (d, 2 ArH, $J=8.4$); ^{13}C NMR: δ −4.75, 18.9, 26.4, 46.0, 56.4, 65.5, 69.2, 99.1, 100.5, 123.0, 129.2, 131.5, 134.0, 138.1, 166.5; $[\alpha]_D$ −58.2 (*c* 0.5, $CHCl_3$).

Compound **II**: white solid; mp 58–60°C; IR ($CHCl_3$): 3345, 1654 cm^{-1}; ^1H NMR: δ 0.05 (s, 6H), 0.88 (s, 9H), 3.47 (s, 3H), 3.74 (dd, 1H, $J=6.6$, $J=11.1$), 3.86 (dd, 1H, $J=4.4$, $J=11.1$), 4.08–4.26 (m, 1H), 4.52–4.62 (m, 1H), 3.94 (d, 1H, $J=2.9$), 5.92 (dd, 1H, $J=2.9$, $J=9.9$), 6.16 (dd, 1H, $J=5.7$, $J=9.9$), 6.39 (d, 1H, $J=8.8$, NH), 7.48 (d, 2 ArH, $J=8.5$), 7.78 (d, 2 ArH, $J=8.5$); ^{13}C NMR: δ −4.8, 18.8, 26.3, 43.7, 55.9, 63.6, 70.5, 94.6, 96.0, 128.6, 129.0, 129.1, 138.3, 166.6; $[\alpha]_D$ −78.4 (*c* 0.5, $CHCl_3$).

16. Fraser-Reid, B.; McLean, A.; Usherwood, E. W.; Yunker, M. *Can. J. Chem.* **1970**, *48*, 2877–2884.
17. Fraser-Reid, B.; Carthy, B. J.; Holder, N. L.; Yunker, M. *Can. J. Chem.* **1971**, *49*, 3038–3044.
18. Weygand, F. *Methods Carbohydr. Chem.* **1962**, *1*, 182.
19. Koreeda, M.; Houston, T. A.; Shull, B. K.; Klemke, E.; Tuinman, R. J. *Synlett* **1995**, 90–91. Diethyl ether was used instead of THF since significant amounts of 4-iodobutanol were observed among the reaction products, due to ring opening of THF under the described reaction conditions.
20. *Gaussian 94*; Frish, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keth, T. A.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. Gaussian, Inc.: Pittsburg, PA, 1995.
21. (a) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785–789; (b) Becke, A. D. *Phys. Rev. A* **1988**, *38*, 3098–3100; (c) Miehlich, B.; Savin, A.; Stoll, H.; Preuss, H. *Chem. Phys. Lett.* **1989**, *157*, 200–206; (d) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648–5652.
22. Imaginary frequency corresponding to the expected reaction coordinate for **TS-1**: 188.31*i* cm^{-1}. Imaginary frequency corresponding to the expected reaction coordinate for **TS-2**: 402.49*i* cm^{-1}
23. The same behaviour was observed by us for [3,3]-sigmatropic thermal rearrangement of 4-*O*-imidoyl derivatives **IIIa**,**b** and **IVa**,**b**. In fact, **IIIa**,**b**, where steric constraints are missing, gave the corresponding trichloroacetamides **Va**,**b** in moderate yield. On the contrary, only traces of decomposition products, together with unchanged starting material, were observed after protracted heating of **IVa**,**b** (Scheme 9). A similar effect was already observed for 1-trichloroacetimidoylpent-2-enopyranosides. See: Dyong, I.; Weygand, J.; Thiem, J. *Liebigs Ann. Chem.* **1986**, 577–599.



Scheme 9. (a) Refluxing toluene, 36 h (40% for **IIa**; 38% for **IIb**).

24. Reed, III, I. A.; Risbood, P. A.; Goodman, L. *J. Chem. Soc., Chem. Commun.* **1981**, 760–761.
25. (a) Roothan, C. C. *Rev. Mod. Phys.* **1951**, *23*, 69–88; (b) For a description of the basis set, see: Hehre, W.; Radom, L.; Schleyer, P.v. R.; Pople, J. A. *Ab initio Molecular Orbital Theory*; Wiley: New York, 1986.
26. (a) Jursic, B. S. *J. Mol. Struct. (THEOCHEM)* **1995**, *358*, 139–143; (b) Houk, K. N.; Beno, B. R.; Nendel, M.; Black, K.; Yoo, H. Y.; Wilsey, S.; Lee, J. K. *J. Mol. Struct. (THEOCHEM)* **1997**, *398–399*, 169–179.