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Facial selectivities in the nucleophilic additions of 2,3-unsaturated 3-arylsulfinyl pyranosides

Arunima Mukherjee, Narayanaswamy Jayaraman *

Department of Organic Chemistry, Indian Institute of Science, Bangalore 560 012, India

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ABSTRACT

2,3-Unsaturated 3-arylsulfinyl pyranosides undergo nucleophilic additions at C-2, with facial selectivities depending on the nucleophile and the substituent on sulfinyl sulfur. The reactions of such sugar vinyl sulfoxides lead to the addition of nucleophile preferring an axial orientation at C-2, with concomitant formation of an allylic bond at C-3 to C-4. This trend in the addition pattern is observed for primary amine, carbon and sulfur nucleophiles, whereas secondary amines prefer an equatorial addition at C-2. The effect of *p*-tolylthio- versus (*p*-isopropylphenyl)thio vinyl sulfoxide is that the equatorial nucleophilic addition is preferred even more with the latter vinyl sulfoxide.

1. Introduction

1,2-Unsaturated sugars, namely, glycals are excellent examples of a double bond present endocyclic to the sugar ring and its reactivity in varied types of reactions.[1–3] Sugars with exocyclic double bond also find applications in synthesis.[4–7] For example, the utility of *exo*-glycals to incorporate hetero-atoms[8] and synthesis of anomeric azido esters,[9] a useful intermediate for the preparation of anomeric amino acids, were demonstrated. Among unsaturated sugar derivatives, the particular class of 2,3-unsaturated sugars serve as important derivatives for modification of monosaccharides.[10,11] In our efforts to study the reactions of 2,3-unsaturated sugars, having a sulfoxide functionality at C-3, we demonstrated the preparation of such vinyl sulfoxides from 2,3-unsaturated thioglycosides (**I**), in the presence of trifluoromethanesulfonic acid (TfOH) or trimethylsilyl trifluoromethanesulfonate (TMSOTf) (Scheme 1).[12] The reaction led to the regioselective intramolecular transposition of C-1 alkyl/arylthio-moiety to C-3 to afford alkyl 2,3-dideoxy-3-alkyl/arylthio-*arabino*-hexopyranosides (**II**), through formation of 3-alkyl/arylthio-glycal intermediate, followed by glycosylation with an acceptor alcohol. The Pummerer rearrangement reaction on **II** was identified, in order to form 2,3-unsaturated vinyl sulfide (**IV**) from saturated sugar sulfide **II**. Thus, formation of sulfoxide **III**, followed by the Pummerer rearrangement reaction afforded vinyl sulfide **IV**.[13] The resulting vinyl sulfide was elaborated further to vinyl sulfoxides (**V**), suitable for conjugate addition reactions. The steric and electronic influences generally affect the rate of conjugate addition reactions, as well as, stereochemistry of the products.[14–17] Conjugate addition of **V** with alkoxide nucleophiles was verified and the addition afforded derivative **VI**, with axial orientation of the substituent at C-2, as a single diastereomer at sulfinyl sulfur moiety. Realizing the reactivity of new 2,3-unsaturated sulfoxides, namely, vinyl sulfoxides, as acceptors for conjugate addition reactions with alcohols, further studies were undertaken to verify their reactivities with nitrogen, carbon, and sulfur derived nucleophiles. A detailed study of stereoselectivities of conjugate addition reactions of 2,3-unsaturated sulfoxides is presented herein. The nature of nucleophile and the substituent at sulfinyl sulfur plays an important role in these reactions. Whereas conjugate addition reactions of vinyl sulfoxides of organic synthons are known,[18,19] we report herein such reactions on newer vinyl sulfoxides.

2. Results and discussion

Conjugate addition reaction of amines with vinyl sulfoxide **1**[13] was undertaken first with primary amines, namely, *n*-butylamine and cyclohexylamine. The reaction of **1** with amines was conducted in MeOH, under reflux for 8–10 h (Scheme 2). Upon removal of solvents, ^{1}H NMR spectrum of the product was analyzed to establish addition pattern of the nucleophile.

The H-1 nucleus was observed at 5.24 ppm (d, J = 2.6 Hz) for the product of reaction with *n*-butylamine and at 5.42 ppm (app. singlet) for the reaction with cyclohexylamine. A new vinylic proton at 6.50 and 6.39 ppm was also observed in both the reactions. The product of the reaction of **1** with *n*-butylamine

* Corresponding author. Tel.: +91 80 2293 2578; fax: +91 80 2360 0529.
E-mail address: jayaraman@orgchem.iisc.ernet.in (N. Jayaraman).

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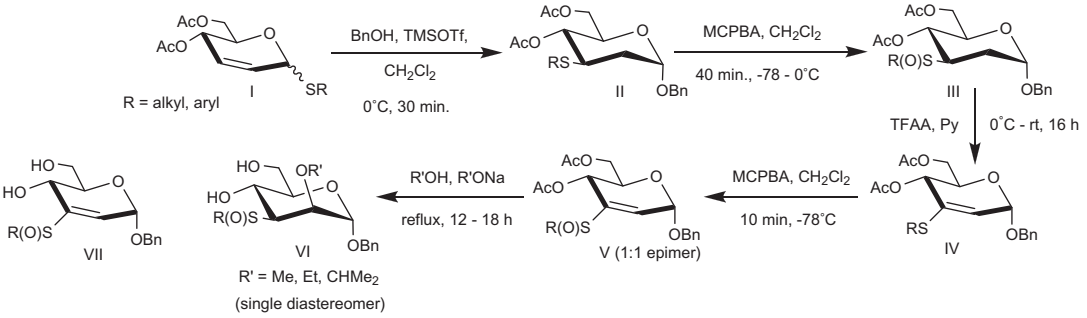
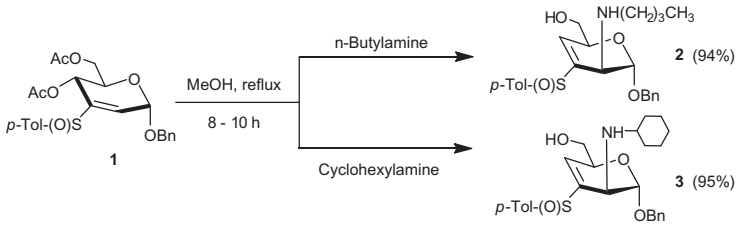


Scheme 1.



Scheme 2.

and cyclohexylamine was a single diastereomer and that a double bond evolved during the addition reaction. The doublet with the coupling constant $J_{H\text{-}1\text{–}H\text{-}2}$ = 2.6 Hz and the apparent singlet nature of the anomeric proton of the product of each reaction suggested *trans*-diequatorial nature of H-1–H-2 protons. The products were characterized further by 1D and 2D NMR techniques. The H-4 at 6.50 ppm (d, J = 1.2 Hz) was identified from cross peak of COSY spectrum to H-5 (3.76–3.72 ppm) for the reaction with *n*-butylamine. Similarly, H-4 at 6.39 ppm was identified from the cross peak of COSY spectrum with H-5 (3.96–3.94 ppm) for the reaction with cyclohexylamine. Cross peaks due to through-bond coupling of remaining protons were also observed in the COSY spectrum. Mass spectral analysis showed *m/z* 452.1872 for the product of the reaction with *n*-butylamine and *m/z* 478.2026 for the reaction with cyclohexylamine, which suggested loss of an acetate moiety, in addition to loss of an acetyl moiety. Combining results of NMR and mass spectral analyses, the constitution of the product was established as **2**, resulting from reaction of **1** with *n*-butylamine, and **3**, resulting from reaction with cyclohexylamine.

In comparison to conjugate addition with alkoxide nucleophiles which also led to the axial nucleophilic addition, important observation of the reaction of **1** with primary amines is that the additions of nucleophiles lead to a concomitant elimination of acetate at C-4, even when the addition occurred at axial orientation at C-2.[20] No other product formed during the course of the reaction, thereby ruling-out formation of an intermediate, which would then subject itself to an elimination, leading to the reaction being considered as S_N2' reaction. It is pertinent to note that the isolated yields of reactions are excellent and the products were stereochemically pure. The 1:1 epimeric mixture at sulfinyl sulfur of **1** led to only one diastereomerically pure **2** and **3**.

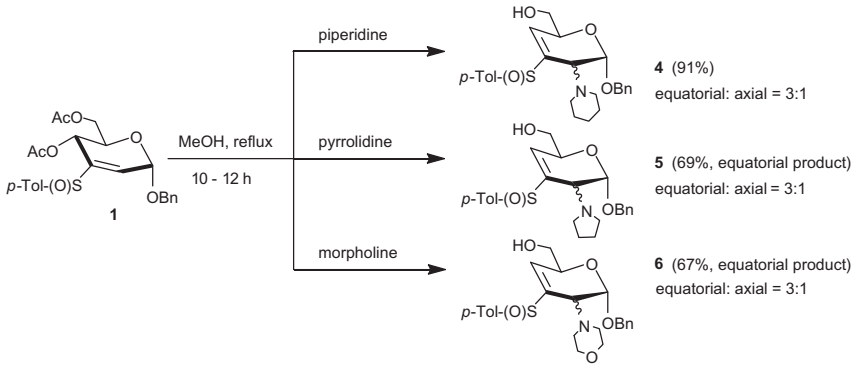
Reactivities of sugar vinyl sulfoxide were assessed with secondary amines, namely, piperidine, pyrrolidine, and morpholine. The reactions were conducted with **1**, in MeOH under reflux condition for 10–12 h (Scheme 3). ^{1}H NMR spectral analysis of products isolated from reaction of **1** with piperidine indicated that the addition occurred to afford products with both equatorial and axial orientations of the substituent at C-2, in a ratio of 3:1. The product with equatorial orientation of the substituents at C-2 showed resonances at 5.10 ppm (d, $J_{1,2}$ = 3.8 Hz, H-1) and at 3.00 ppm (d, $J_{1,2}$ = 3.8 Hz, H-2). On the other hand, product with axial orientation of substituent at C-2 showed resonances at 5.25 ppm (app. s, H-1) and 3.97 ppm (app. s, H-2).

In the case of reaction with pyrrolidine and morpholine, a major product was isolated in each case. ^{1}H NMR analysis of the products revealed that the conjugate addition to amines occurred at the equatorial face of C-2 (~5.12 ppm, J = 4 Hz, H-1). With the inability to isolate the minor product with pyrrolidine and morpholine, the reaction mixture prior to purification was analyzed. The spectrum of the reaction mixture exhibited the presence of a set of peaks in the ^{1}H NMR spectrum, indicating the presence of an epimeric mixture. A comparison of the resonances corresponding to the anomeric proton at 5.25 (app. s) and at 5.13 (d, J = 4 Hz) showed a ratio of 1:3. The resonance at 5.25 ppm as an apparent singlet corresponded to 1,2-*trans*-diequatorial relation of H-1–H-2 protons in **5**, whereas the resonance at 5.13 ppm with J = 4 Hz related to 1,2-equatorial-axial relation of H-1–H-2 protons in **6**. The major products having the *equatorial*-orientation at C-2, namely, *erythro*-epimer of **4**–**6** was characterized further through 2D NMR techniques of COSY, HSQC, and NOESY. The NOESY spectrum showed absence of cross peak between H-2–H-5 protons, in line with the equatorial substituent at C-2.

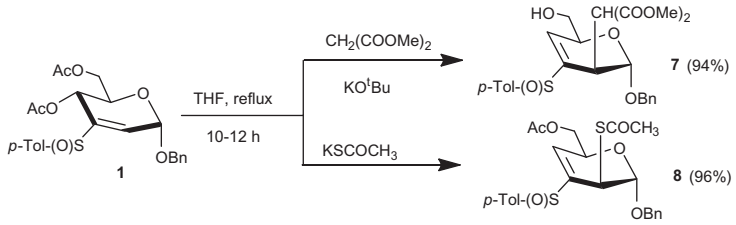
From the above experiments, we observe that whereas conjugate addition to sugar vinyl sulfoxide with primary amines afford the products with axial orientation of the substituent at C-2 diastereoselectively, the reaction with secondary amines lead to an epimeric mixture at C-2, the major product being the epimer with substituent in the equatorial orientation.

Carbon and sulfur nucleophiles were examined next, in order to assess the conjugate addition pattern with the vinyl sulfoxide. For this purpose, dimethyl malonate and potassium thioacetate ($KSCOCH_3$) were chosen as carbon and sulfur nucleophiles, respectively. The reaction of **1** with dimethyl malonate and $KSCOCH_3$ was conducted under reflux overnight (Scheme 4). The malonate and thioacetate derivative **7** and **8** were isolated in good yields after purification.

The H-1 and H-2 nuclei of **7** resonated at 5.01 and 2.74 ppm as a doublet (J = 2 Hz) and doublet of doublet (J = 2, 7.2 Hz), respec-



Scheme 3.



Scheme 4.

tively. The *threo*-configuration of **7** was confirmed further by NOESY experiments, wherein, cross-peaks between H-2–H-5 and H-1–$CH(COOMe)_2$ were observed. In the absence of an external base in the reaction of **1** with thioacetate, the conjugate addition product was found to retain the acetate protecting group at C-6. As observed in the case of reactions with primary amines, the diastereoselectivity of the reaction with carbon and sulfur nucleophiles was retained fully in favor of the axial orientation of the substituent at C-2.

The above set of experiments illustrated that the conjugate addition to nitrogen, carbon, and sulfur derived nucleophiles with vinyl sulfoxide **1** underwent conjugate addition at C-2 with concomitant elimination of acetic acid to form 3,4-unsaturated sugar **2**–**8**. We presume that α-sulfinyl carbanion, formed during the nucleophilic addition, is stabilized further through planar sulfinate anion formation. Subsequent elimination of the acetate accounts the product formation.

It was observed that the conjugate addition to **1** did not proceed when sugar vinyl sulfoxide was having either free hydroxyl groups or the hydroxyl groups protected as benzyl ethers. It is thus likely that the electron withdrawing nature and good leaving group ability of the acetate group may play an important role in the reaction. Such an addition-elimination reaction sequence is known earlier in the conjugate addition to 3-nitro hex-2-enopyranoside with carbon nucleophiles.[21,22] Addition, followed by elimination was suggested occurring through a S_N2' reaction mechanism, although without a chiral induction originating from the vinyl nitrate functionality. Further, we come across the recent report of Pathak and co-workers on 4,6-benzylidene protected vinyl sulfoxide modified hex-2-enopyranosides and their Michael addition reactions.[23] An axial entry of the nucleophile at C-2 of α-anomer and ~2:1 axial and equatorial entry of nucleophile at C-2 of the β-anomer were reported. Only the conjugate addition products were obtained in these instances. The authors presumed a directing influence of sulfoxide when ~2:1 axial and equatorial entry of the nucleophile at C-2 was observed.

Whereas addition and subsequent elimination occurred, leading to the formation of products with an allylic bond, the addition itself preferred an axial face for primary amines, carbon and sulfur derived nucleophiles. In contrary, secondary amines afforded C-2 addition products with equatorial orientation of the substituent as the major product. Approach of the nucleophile through either axial (*re*) or equatorial (*si*) face of the electron-deficient double bond might encounter a steric influence of the substituent at the sulfinyl functionality. In the light of the observed addition pattern, the following scenario was envisaged (Fig. 1).

Steric influence, arising from the nature of α-substituent to the sufinyl functionality, may play a dominant role in relation to the addition pattern. It is noted that the above model envisaging the role of steric influence of α-substituent is considered un-affected even when the lone pair of electrons on the sulfoxide moiety is co-planer with the *endocyclic* double bond. With this presumption, reactions involving a more bulky (*p*-isopropylphenyl)thio-moiety, installed in place of *p*-tolyl-moiety as in **1**, were undertaken.

Vinyl sulfoxide **13** was synthesized following a similar reaction sequence as in **1**. An 1,3-shift of **9**[24] was initiated by TMSOTf, in the presence of benzyl alcohol to afford glycoside **10** (Scheme 5).[12] Treatment of **10** with MCPBA afforded sulfoxide **11**, as a single diastereomer at sulfinyl sulfur moiety. The Pummerer rearrangement of **11**, in the presence of TFAA and pyridine afforded vinyl sulfide **12**, which upon a controlled oxidation produced vinyl sulfoxide **13**, in ~1:1 epimeric ratio at the sulfinyl sulfur moiety (Scheme 5).

Conjugate addition reactions of vinyl sulfoxide **13** were performed with a primary and a secondary amine. The reactions were performed similar to those in the case of reaction of amines with **1** (Scheme 6). As the reactions were conducted to identify

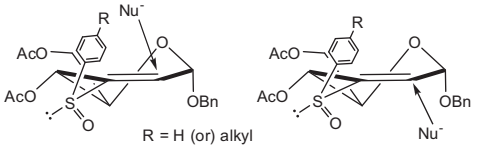
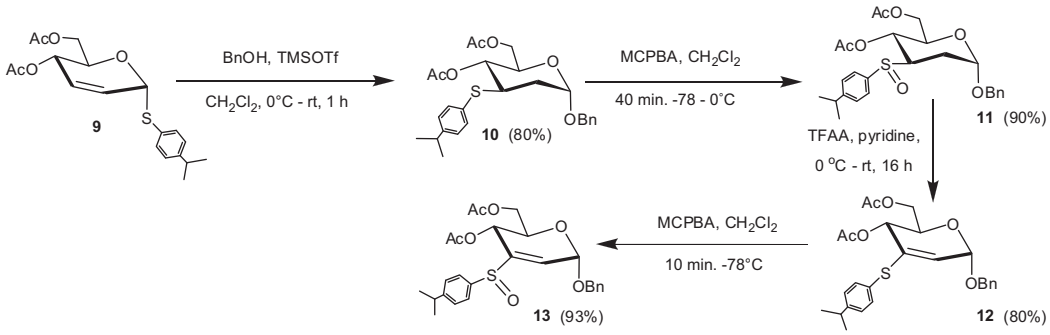


Figure 1. Facial approaches of the nucleophile in the conjugate addition on to vinyl sulfoxide.



Scheme 5.

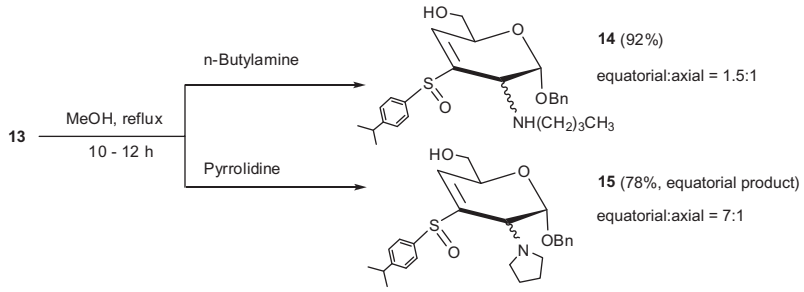
the addition pattern in the product with either axial or equatorial orientation at C-2, 1H NMR analysis of the reaction product prior to purification was conducted. A set of anomeric protons at 5.25 ppm (app. s) and at 5.11 ppm (d, J = 4 Hz) was observed in the ^{1}H NMR spectrum of **14** for the reaction of **13** with *n*-butylamine. The coupling constants with $J_{1,2}$ of 4 Hz indicated the equatorial-axial relationship of H-1 and H-2, whereas, the apparent singlet at 5.25 ppm suggested the *trans*-diequatorial relationship of H-1 and H-2. From the integration of peaks at 5.11 and 5.25 ppm, an epimeric ratio of 1.5:1 was adjudged. Mass spectrometric analysis showed that the product formed as a result of addition-elimination reaction sequence. In comparison to the conjugate addition to primary amines with vinyl sulfoxide **1**, which afforded **2** and **3** exclusively, reaction of **13** with primary amine led to the formation of an epimeric mixture of **14**, in 1.5:1 ratio in favor of product with equatorial orientation of the substituent at C-2.

An ^{1}H NMR analysis of the product formed in the reaction with pyrrolidine showed an H-1 resonance at 5.17 ppm (J = 3.8 Hz) and 5.28 ppm (app. s). From the observed coupling constants and comparison of the integration, the addition product was adjudged to afford equatorial versus axial in 7:1 ratio. The major **15**, with equatorial orientation of the substituent at C-2, was separated through column chromatography and characterized.

The following observations were made when comparing the conjugate addition reaction with alkoxide nucleophiles[13] and conjugate addition-elimination reactions observed with nitrogen, carbon and sulfur nucleophiles in the present work: (i) O-deacetylated vinyl sulfoxide starting material **VII** (Scheme 1) was also recovered in the conjugate addition with alkoxides, whereas vinyl sulfoxide starting material was fully consumed in the addition-elimination reactions; (ii) conjugate addition with alkoxide afforded products with the axial orientation of the substituent at C-2, whereas addition-elimination reaction sequence was found to afford *axial*-orientation at C-2 with primary amines, carbon and sulfur nucleophiles, whereas an epimeric mixtures formed with secondary amines and (iii) with (*p*-isopropylphenyl)vinyl sulfoxide **13**, formation of C-2 *equatorial* epimer was observed in higher ratio, when compared to the *p*-tolyl vinyl sulfoxide **1**, with both primary and secondary amines.

Conjugate addition across vinyl sulfoxide occurs in a conformer in which sulfoxide oxygen is co-planar with respect to the double bond. In the absence of severe steric crowding, the nucleophiles would preferably approach *anti*- to the lone pair of electrons on sulfur, or to bulky substituent on aryl sulfinyl sulfur.[18,25] Thus, the preference of an *axial* attack was observed with alkoxide nucleophiles, as well as, primary amine, carbon and sulfur nucleophiles to vinyl sulfoxide **1**. With secondary amines, the *equatorial* approach would originate to avoid the steric crowding between the incoming nucleophiles and the aryl substituent on the sulfoxide, in a preferred conformation of vinyl sulfoxide, as shown in Figure 1. The steric hindrance was even more pronounced, when the *p*-tolyl group was replaced by *p*-isopropylphenyl group.

Another important observation of the study was that whereas conjugate additions were feasible with alkoxide nucleophiles even when sugar hydroxyl groups remained in the anionic form, the reaction did not proceed with amine, carbon and sulfur derived nucleophiles when free-hydroxyl group containing sugar vinyl sulfoxide (**VII**) was used. Rather, the acetate group underwent facile elimination, so as to afford product with C-3 to C-4 unsaturation. The vinyl sulfoxide starting materials were 1:1 diastereomeric ratio at the sulfoxide functionality. In the earlier work with alkoxide nucleophiles, it was found that one of the sulfoxide epimers was more reactive than the other. The electrostatic repulsion between sugar alkoxide anion and sulfur lone pair of electrons was probably accountable for the slow inversion at sulfoxide moiety in the case of alkoxide nucleophiles. Such a situation is absent in the conjugate addition-elimination reaction involving nitrogen, carbon and sulfur nucleophiles, studied herein. On the other hand, an influence by the nature of the α-substituent of sulfoxide moiety was observed in the stereochemical preference of the nucleophile



Scheme 6.

addition. Whereas S_N2' reactions are known in vinyl nitrates of sugars,[21,22] the present study establishes stereochemical preferences for such S_N2' reactions on chiral vinyl sulfoxides of sugars.

3. Conclusion

The present study establishes the diastereoselective addition pattern of nitrogen, carbon, and sulfur derived nucleophiles reacting with newer sugar vinyl sulfoxides, where the nature of the nucleophile and the substituent α- to the sulfinyl sulfur moiety play a role in the facial preference of the addition reaction. Whereas, primary amine, carbon and sulfur nucleophiles afford product with axial orientation of the substituent at C-2, secondary amines provide conjugate addition product with equatorial orientation of the substituent at C-2, with concomitant formation of an allylic bond at C-3 to C-4. Secondary amines undergo pronounced steric interactions with the bulkier (*p*-isopropylphenyl)vinyl sulfoxide when compared to *p*-tolylvinyl sulfoxide, leading to the conjugate addition product with higher levels of facial differentiation. The present study demonstrates the reaction of varied nucleophiles with sugar vinyl sulfoxides in conjunction with that reported by us previously, involving alkoxide nucleophiles. The method of vinyl sulfoxide conjugate addition opens-up further possibilities of enriching functionalization of monosaccharides.

4. Experimental

4.1. General methods

Chemicals were purchased from commercial sources and were used without further purification. Solvents were dried and distilled according literature procedures. Analytical TLC was performed on commercial plates coated with silica gel GF254 (0.25 mm). Silica gel (230–400 mesh) was used for column chromatography. Optical rotations were recorded on a polarimeter at the sodium D line at 24 °C. High-resolution mass spectra were obtained from Q-TOF instrument by electron spray ionization (ESI) technique. NMR spectral analyses were performed on a spectrometer operating at 400 MHz for ^{1}H nucleus and 100 MHz spectrometer for ^{13}C nucleus, with residual solvent signal acting as the internal standard. COSY and HMQC analyses were performed on a 400 MHz NMR spectrometer. Standard abbreviations s, d, t, dd, br, app., m, and band refer to singlet, doublet, triplet, doublet of doublet, broad, apparent, multiplet, and set of resonances, respectively.

4.2. Benzyl 2,3,4-trideoxy-2-*N*-butylamino-3-(*p*-tolylsulfinyl)-α-D-*threo*-hex-3-eno-pyranoside (2)

A solution of **1** (0.05 g, 0.1 mmol) in MeOH (8 mL) was treated with *n*-butylamine (0.06 mL, 0.65 mmol), refluxed for 8 h, solvents were removed in vacuo, and the residue was purified (SiO_2) (76% EtOAc/pet. ether) to afford **2** (0.043 g, 94%), as a gum.

R_f = 0.5 (85% EtOAc/pet. ether). $[\alpha]_D$ +46 (*c* 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38–7.26 (band, 9H, Aromatic), 6.50 (d, 1H, *J* = 1.2 Hz, H-4), 5.24 (d, 1H, *J* = 2.6 Hz, H-1), 4.76 (d, 1H, *J* = 12 Hz, PhCH_{2a}), 4.62 (d, 1H, *J* = 12 Hz, PhCH_{2b}), 3.88–3.86 (band, 1H, H-6_b), 3.82 (dd, 1H, *J* = 3.6, 12 Hz, H-6_a), 3.76–3.72 (band, 2H, H-5, H-2), 2.38 (s, 3H, –$C_6H_4CH_3$), 2.32–2.30 (band, 2H, –NH(CH_2)$_3$CH$_3$), 1.23 (br, 4H, –NH(CH_2)$_3$CH$_3$), 0.84–0.80 (band, 3H, –NH(CH$_2$)$_3$CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.6, 141.9. 138.8, 137.5, 137.1, 129.9, 128.3, 127.9, 126.5, 125.7, 124.1 (Aromatic, C-3, C-4), 94.1 (C-1), 71.8, (PhCH$_2$), 70.8, (C-5), 69.5 (C-6), 63.4 (C-2), 61.6 (–NH(CH$_2$)$_3$CH$_3$), 54.3 (–NH(CH$_2$)$_3$CH$_3$), 46.4 (–NH(CH$_2$)$_3$CH$_3$), 21.3 (–$C_6H_4CH_3$), 20.1 (–NH(CH$_2$)$_3$CH$_3$). HRMS: *m*/*z* calcd for $C_{24}H_{31}NO_4S$: 452.1872 $[M+Na]^+$; found 452.1872.

4.3. Benzyl 2,3,4-trideoxy-2-*N*-cyclohexylamino-3-(*p*-tolylsulfinyl)-α-D-*threo*-hex-3-enopyranoside (3)

A solution of **1** (0.05 g, 0.1 mmol) in MeOH (8 mL) was treated with cyclohexylamine (0.08 mL, 0.65 mmol), refluxed for 10 h, solvents were removed in vacuo, and the residue was purified (SiO_2) (72% EtOAc/pet. ether) to afford **3** (0.046 g, 95%), as a gum.

R_f = 0.4 (80% EtOAc/pet. ether). $[\alpha]_D$ +33 (*c* 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48–7.30 (band, 9H, Aromatic), 6.39 (app. s, 1H, H-4), 5.42 (app. s, 1H, H-1), 4.65–4.51 (band, 2H, PhCH_2), 3.94 (dd, 1H, *J* = 3, 12 Hz, H-6_a), 3.96–3.94 (m, 1H, H-5), 3.92–3.88 (band, 2H, H-2, H-6_b), 2.43 (s, 3H, –$C_6H_4CH_3$), 1.72–1.44 (band, 11H, –NHC$_6H_{11}$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.2, 137.4, 137.0, 136.8, 130.2, 128.5, 128.4, 128.2, 128.0, 127.9 (Aromatic, C-3, C-4), 93.2 (C-1), 72.1 (PhCH$_2$), 70.9 (C-5), 70.5 (C-6), 70.1 (C-2), 69.6 (–NHC$_6H_{11}$), 53.6, 51.3 (–NHC$_6H_{11}$), 34.7, 31.7 (–NHC$_6H_{11}$), 24.7 (–NHC$_6H_{11}$), 21.4 (–$C_6H_4CH_3$). HRMS: *m*/*z* calcd for $C_{26}H_{33}NO_4S$: 478.2028 $[M+Na]^+$; found 478.2026.

4.4. Benzyl 2,3,4-trideoxy-2-*N*-piperidino-3-(*p*-tolylsulfinyl)-α-D-*erythro*/*threo*-hex-3-enopyranoside (4)

A solution of **1** (0.04 g, 0.08 mmol) in MeOH (6 mL) was treated with piperidine (0.06 mL, 0.52 mmol), refluxed for 10 h, solvents were removed in vacuo, and the residue was purified (SiO_2) (76% EtOAc/pet. ether) to afford **4**, as a gum.*erythr*o-isomer: Yield: 0.026 g, 68%. R_f = 0.2 (85% EtOAc/pet. ether). $[\alpha]_D$ +63 (*c* 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50–7.22 (band, 9H, Aromatic), 6.68 (app. s, 1H, H-4), 5.10 (d, 1H, *J* = 3.8 Hz, H-1), 4.78 (d, 1H, *J* = 12 Hz, PhCH_{2a}), 4.58 (d, 1H, *J* = 12 Hz, PhCH_{2b}), 4.48 (br, 1H, H-5), 3.74–3.71 (band, 2H, H-6_a, H-6_b), 3.00 (d, 1H, *J* = 3.8 Hz, H-2), 2.76–2.73 (band, 2H, –NCH_2), 2.51–2.48 (band, 2H, –NCH_2), 2.38 (s, 3H, –$C_6H_4CH_3$), 1.64 (br, 2H, –NCH$_2$CH_2), 1.47 (br, 4H, –NCH$_2$-CH_2CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.1, 143.4, 141.7, 137.4, 130.1, 128.4, 127.9, 127.8, 126.4, 126.3, (Aromatic, C-3, C-4), 94.1 (C-1), 71.7 (PhCH$_2$), 70.5 (C-5), 69.2 (C-6), 64.5 (C-2), 60.7 (–NCH$_2$), 50.6 (–NCH$_2$CH$_2$), 24.6 (–NCH$_2$CH$_2$CH$_2$), 21.4 (–$C_6H_4CH_3$). HRMS: *m*/*z* calcd for $C_{25}H_{31}NO_4S$: 464.1872 $[M+Na]^+$; found 464.1873.*threo*epimer: Yield: 9 mg, 23%. R_f = 0.26 (85% EtOAc/pet. ether). $[\alpha]_D$ +48 (*c* 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38–7.22 (band, 9H, Aromatic), 6.52 (app. s, 1H, H-4), 5.25 (app. s, 1H, H-1), 4.78 (band, 2H, PhCH_2), 4.65–4.60 (band, 1H, H-5), 3.97 (app. s, 1H, H-2), 3.95–3.83 (band, 2H, H-6_a, H-6_b), 2.76–2.73 (m, 4H, –NHCH_2CH_2), 2.51–2.38 (m, 4H, –NHCH_2CH_2), 2.39 (s, 3H, –$C_6H_4CH_3$), 2.04–2.00 (m, 2H, –NHCH$_2$CH$_2$CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.2, 142.1, 141.6, 137.4, 130.2, 130.1, 128.4, 128.0,126.2, 125.6, (Aromatic, C-4, C-3), 95.7 (C-1), 71.7 (PhCH$_2$), 70.5 (C-5), 69.3 (C-6), 64.6 (C-2), 60.8 (–NHCH$_2$), 50.6 (–NHCH$_2$CH$_2$), 26.4 (–NHCH$_2$CH$_2$CH$_2$), 21.6 (–$C_6H_4CH_3$). HRMS: *m*/*z* calcd for $C_{25}H_{31}NO_4S$: 464.1872 $[M+Na]^+$; found 464.1873.

4.5. Benzyl 2,3,4-trideoxy-2-*N*-pyrrolidino-3-(*p*-tolylsulfinyl)-α-D-*erythro*-hex-3-enopyranoside (5)

A solution of **1** (0.04 g, 0.08 mmol) in MeOH (8 mL) was treated with pyrrolidine (0.04 mL, 0.52 mmol), refluxed for 12 h, solvents were removed in vacuo, and the residue was purified (SiO_2) (78% EtOAc/pet. ether) to afford **5** (0.021 g, 69%), as a gum.

R_f = 0.3 (82% EtOAc/pet. ether). $[\alpha]_D$ +53 (*c* 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, 2H, *J* = 8 Hz, Aromatic), 7.44–7.25 (band, 7H, Aromatic), 6.60 (app. s, 1H, H-4), 5.13 (d, 1H, *J* = 4 Hz, H-1), 4.76 (d, 1H, *J* = 12 Hz, PhCH_{2a}), 4.52 (d, 1H, *J* = 12 Hz, PhCH_{2b}), 4.50 (br, 1H, H-5), 3.72 (dd, 1H, *J* = 3.2, 11.6 Hz H-6_a), 3.66 (dd, 1H, *J* = 6, 11.6 Hz, H-6_b), 3.22 (d, 1H, *J* = 4 Hz, H-2), 2.71 (br, 4H, –NCH_2), 2.34 (s, 3H, –$C_6H_4CH_3$), 1.63 (br, 4H, –NCH_2CH$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.5, 137.2, 129.8, 129.6, 128.5, 128.4,

127.8, 125.6, 125.3 (Aromatic, C-3, C-4), 95.6 (C-1), 70.5 (C-5), 69.4 (PhCH$_2$), 64.6 (C-6), 54.7 (C-2), 48.1 (–NCH$_2$), 24.1 (–NCH$_2$CH$_2$), 21.4 (–C$_6$H$_4$CH$_3$). HRMS: *m*/*z* calcd for $C_{24}H_{29}NO_4S$: 450.1715 [M+Na]$^+$; found 450.1718.

4.6. Benzyl 2,3,4-trideoxy-2-*N*-morpholino-3-(*p*-tolylsulfinyl)-α-D-*erythro*-hex-3-enopyranoside (6)

A solution of **1** (0.035 g, 0.08 mmol) in MeOH (6 mL) was treated with morpholine (0.05 mL, 0.53 mmol), refluxed for 10 h, solvents were removed in vacuo, and the residue was purified (SiO_2) (70% EtOAc/pet. ether) to afford **6** (0.023 g, 67%), as a gum.

R_f = 0.4 (78% EtOAc/pet. ether). $[\alpha]_D$ +87 (*c* 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40–7.22 (band, 9H, Aromatic), 6.46 (app. s, 1H, H-4), 5.12 (d, 1H, *J* = 4 Hz, H-1), 4.84 (d, 1H, *J* = 12 Hz, PhC*H*$_{2a}$), 4.58 (d, 1H, *J* = 12 Hz, PhC*H*$_{2b}$), 4.54–4.47 (br-m, 1H, H-5), 3.70–3.68 (band, 2H, H-6$_a$, H-6$_b$), 3.60 (d, 1H, *J* = 4 Hz, H-2), 3.40–3.35 (band, 2H, –NC*H*$_2$), 3.24–3.21 (band, 2H, –NC*H*$_2$), 2.82–2.71 (m, 4H, –NCH$_2$C*H*$_2$), 2.41 (s, 3H, –C$_6$H$_4$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.3, 141.9, 139.3, 137.0, 132.0, 12.8, 129.6, 128.4, 128.3, 128.1, 127.9, 126.7 (Aromatic, C-3, C-4), 94.2 (C-1), 72.6 (C-5), 70.1 (PhCH$_2$), 67.1(C-6), 64.5 (C-2), 60.3 (–NCH$_2$CH$_2$), 50.4 (–NCH$_2$CH$_2$), 21.4 (–C$_6$H$_4$CH$_3$). HRMS: *m*/*z* calcd for $C_{24}H_{29}NO_5S$: 466.1664 [M+Na]$^+$; found 466.1664.

4.7. Benzyl 2,3,4-trideoxy-2-C-bis(methoxycarbonyl)methyl-3-(*p*-tolylsulfinyl)-α-D-*threo*-hex-3-enopyranoside (7)

A solution of **1** (0.04 g, 0.098 mmol) in THF (4 mL) was added drop-wise to the stirred solution of dimethyl malonate (0.02 mL, 0.19 mmol) and ^{t}BuOK (0.011 g, 0.098 mmol) in THF (4 mL), refluxed under N_2 atmosphere for 11 h, solvents were removed in vacuo, and the residue was purified (SiO_2) (60% EtOAc/pet. ether) to afford **7** (0.039 g, 94%) as a gum.

R_f = 0.4 (65% EtOAc/pet. ether). $[\alpha]_D$ +56 (*c* 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42–7.29 (band, 5H, Aromatic), 7.18 (d, 2H, *J* = 8 Hz, Aromatic), 7.12–7.07 (band, 2H, Aromatic), 6.81 (d, 1H, *J* = 2 Hz, H-4), 5.01 (d, 1H, *J* = 2 Hz, H-1), 4.65 (d, 1H, *J* = 12 Hz, PhC*H*$_{2a}$), 4.47–4.42 (br-m, 1H, H-5), 4.40 (d, 1H, *J* = 12 Hz, PhC*H*$_{2b}$), 3.88 (dd, 1H, *J* = 3.6, 11.6 Hz, H-6$_a$), 3.79 (s, 3H, CH(COO*Me*)$_2$), 3.78–3.73 (band, 2H, H-6$_b$, C*H*(COOMe)$_2$), 3.68 (s, 3H, CH(COO*Me*)$_2$), 2.74 (dd, 1H, *J* = 2, 7.2 Hz, H-2), 2.37 (s, 3H, –C$_6$H$_4$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.1, 167.6 (CO), 142.6, 140.8, 137.9, 137.2, 130.2, 129.9, 128.2, 127.9, 127.5, 127.2, 127.0, 126.6 (Aromatic, C-3, C-4), 97.0 (C-1), 71.6 (PhCH$_2$), 70.2 (C-5), 69.6 (C-6), 64.1 (C-2), 53.9 (CH(COO*Me*)$_2$), 53.1 (CH(COO*Me*)$_2$), 38.0 (*C*H(COOMe)$_2$), 21.5 (–C$_6$H$_4$CH$_3$). HRMS: *m*/*z* calcd for $C_{25}H_{28}O_8S$: 511.1403 [M+Na]$^+$; found 511.1401.

4.8. Benzyl 6-*O*-acetyl-2,3,4-trideoxy-2-thioacetyl-3-(*p*-tolylsulfinyl)-α-D-*threo*-hex-3-eno-pyranoside (8)

A solution of **1** (11 mg, 0.1 mmol) in THF (5 mL) was added drop-wise to a solution of CH_3COSK (0.04 g, 0.1 mmol) in THF (5 mL) at rt, refluxed under N_2 atmosphere for 12 h, solvents were removed in vacuo, and the residue was purified (SiO_2) (20% EtOAc/pet. ether) to afford **8** (0.039 g, 96%), as a gum.

R_f = 0.3 (30% EtOAc/pet. ether). $[\alpha]_D$ +32 (*c* 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.31 (m, 9H, Aromatic), 6.77 (d, 1H, *J* = 2.4 Hz, H-4), 5.32 (d, 1H, *J* = 2.4 Hz, H-1), 4.80 (d, 1H, *J* = 12 Hz, PhC*H*$_{2a}$), 4.61 (d, 1H, *J* = 12 Hz, PhC*H*$_{2b}$), 4.16–4.11 (band, 1H, H-5), 4.26–4.23 (band, 1H, H-6$_a$), 4.02 (dd, 1H, *J* = 4.8, 11.2 Hz, H-6$_b$) 3.89 (d, 1H, *J* = 2.4 Hz, H-2), 2.62 (s, 3H, SCOCH$_3$), 2.42 (s, 3H, –C$_6$H$_4$CH$_3$), 1.99 (s, 3H, –OCOCH$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.5 (SCO), 169.3 (OCO), 143.5, 142.2, 139.7, 137.0, 136.9, 129.7, 128.1, 128.0, 127.9, 126.9 (Aromatic, C-3, C-4), 95.6 (C-1), 70.2 (PhCH$_2$), 70.1 (C-5), 69.8 (C-6), 67.7 (C-2), 30.0 (SCOCH$_3$), 21.5 (–C$_6$H$_4$CH$_3$), 20.7 (OCOCH$_3$). HRMS: *m*/*z* calcd for $C_{24}H_{26}O_6S_2$: 497.1060 [M+Na]$^+$; found 497.1067.

4.9. *p*-Isopropylphenyl 4,6-di-*O*-acetyl-2,3-dideoxy-1-thio-α-D-*erythro*-hex-2-enopyrano-side (9)

A mixture of tri-*O*-acetyl glucal[26] (2 g, 73 mmol) and CAN (0.4 g, 73 mmol) in MeCN (10 mL) was stirred at 0 °C for 15 min. A solution of *p*-isopropylthiophenol (9 mL, 59 mmol) was added drop-wise to the reaction mixture, stirring was continued for 16 h at room temperature, and the reaction mixture concentrated in vacuo. The resulting crude product was purified (SiO_2) (12% EtOAc/pet. ether) to afford **9** (2.1 g, 79%), as a foamy solid.

R_f = 0.4 (15% EtOAc/pet. ether). $[\alpha]_D$ −78 (*c* 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (d, 2H, *J* 8 Hz, Aromatic), 7.17 (d, 2H, *J* = 8 Hz, Aromatic), 6.06 (dd, 1H, *J* = 1.6, 10 Hz, H-3), 5.84 (app. d, 1H, *J* = 10 Hz, H-2), 5.70 (app. s, 1H, H-1), 5.38 (dd, 1H, *J* = 1.6, 9.6 Hz, H-4), 4.51–4.47 (band, 1H, H-5), 4.31–4.21 (band, 2H, H-6$_a$, H-6$_b$), 2.92–2.81 (m, 1H, C*H*Me$_2$), 2.11 (s, 3H, COCH$_3$), 2.09 (s, 3H, COCH$_3$), 1.25 (d, 3H, *J* = 6.8 Hz CH*Me*$_2$), 1.23 (d, 3H, *J* = 6.8 Hz, CH*Me*$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.7, 170.2 (CO), 148.7, 133.1, 132.3, 131.2, 128.6, 127.3, 127.0, 126.8 (C-2, C-3, Aromatic), 83.9 (C-1), 67.1 (C-4), 65.1 (C-5), 63.0 (C-6), 33.7, (*C*HMe$_2$), 23.8 (CH*Me*$_2$), 20.9, 20.7 (CO*C*H$_3$). HRMS: *m*/*z* calcd for $C_{19}H_{24}O_5S$: 387.1242 [M+Na]$^+$; found 387.1240.

4.10. Benzyl 4,6-di-*O*-acetyl-2,3-dideoxy-3-(*p*-isopropylphenyl) thio-α-D-arabino-hexopyranoside (10)

TMSOTf (70 mol % in CH_2Cl_2) was added to a stirred solution of 9 (0.2 g, 0.54 mmol) and BnOH (0.4 mL, 0.44 mmol) in CH_2Cl_2 (6 mL) and stirred at 0 °C for 1 h. The reaction mixture was concentrated in vacuo and purified (SiO_2) (10% EtOAc/pet. ether) to afford **10** (0.2 g, 80%), as a gum.

R_f = 0.5 (15% EtOAc/pet. ether). $[\alpha]_D$ −57 (*c* 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.30 (band, 9H, Aromatic), 4.98 (app. d, 1H, *J* = 1.6 Hz, H-1), 4.82 (dd, 1H, *J* = 3, 11.6 Hz, H-4), 4.60 (d, 1H, *J* = 12 Hz, PhCH$_{2a}$), 4.55 (d, 1H, *J* = 12 Hz, PhCH$_{2b}$), 4.35–4.11 (band, 3H, H-5, H-6$_a$, H-6$_b$), 4.05–3.97 (m, 1H, H-3), 2.91–2.83 (m, 1H, *C*HMe$_2$), 2.45–2.31 (band, 1H, H-2), 2.11 (s, 2H, COCH$_3$), 2.09 (s, 2H, COCH$_3$), 2.07 (s, 2H, COCH$_3$), 2.03–1.97 (band, 1H, H-2), 1.23 (d, 3H, *J* = 6.8 Hz, CH*Me*$_2$), 1.21 (d, 3H, *J* = 6.8 Hz, CH*Me*$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.7, 170.2 (CO), 147.8, 137.5, 131.8, 128.4, 128.3, 127.9, 127.5, 126.9 (Aromatic), 93.6 (C-1), 69.4 (C-4), 69.1 (C-5), 67.0 (PhCH$_2$), 65.2 (C-6), 44.7 (C-3), 35.2 (C-2), 33.6 (*C*HMe$_2$), 23.8 (CH*Me*$_2$), 20.9, 20.7 (COCH$_3$). HRMS: *m*/*z* calcd for $C_{26}H_{32}O_6S$: 495.1817 [M+Na]$^+$; found 495.1814.

4.11. Benzyl 4,6-di-*O*-acetyl-2,3-dideoxy-3-(*p*-isopropylphenyl)sulfinyl-α-D-arabino-hexopyranoside (11)

A mixture of **10** (0.15 g, 0.31 mmol) and MCPBA (0.054 g, 0.31 mmol) in CH_2Cl_2 (8 mL) was stirred at −78 °C under N_2 atmosphere for 40 min. The reaction mixture was diluted with CH_2Cl_2 (10 mL), washed with satd aq $NaHCO_3$ solution (2 × 5 mL), dried (Na_2SO_4), concentrated in vacuo, and purified (SiO_2) (35% EtOAc/pet. ether) to afford **11** (0.14 g, 90%), as a foamy solid.

R_f = 0.4 (40% EtOAc/pet. ether). $[\alpha]_D$ −26 (*c* 1 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (d, 2H, *J* = 8 Hz), 7.42 (d, 2H, *J* = 8 Hz), 7.39–7.31 (band, 4H, Aromatic), 7.29–7.27 (band, 1H, Aromatic), 5.94–5.01 (band, 2H, H-1, H-4), 4.80 (d, 1H, *J* = 12 Hz, PhCH$_{2a}$), 4.63 (d, 1H, *J* = 12 Hz, PhCH$_{2b}$), 4.30–4.26 (band, 1H, H-5), 4.22 (dd, 1H, *J* = 6, 12 Hz, H-6$_b$), 4.01 (dd, 1H, *J* = 3, 12 Hz, H-6$_a$), 3.50–3.46 (m, 1H, H-3), 2.99–2.92 (m, 1H, *C*HMe$_2$), 2.71–2.65 (band, 1H, H-2), 2.30–2.23 (band, 1H, H-2), 2.01 (s, 3H, COCH$_3$), 1.60 (s,

3H, $COCH_3$), 1.26 (d, 3H, J = 6.8 Hz, CHMe_2), 1.24 (d, 3H, J = 6.8 Hz, CHMe_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.5, 169.5, 153.2, 141.5, 137.3, 128.3, 127.6, 127.5, 126.0 (Aromatic), 95.8 (C-1), 69.4 (PhCH_2) 67.8 (C-5), 67.4 (C-4), 62.6 (C-6), 59.8 (C-3), 34.1 ($CHMe_2$), 26.9 (C-2), 23.7, 23.6 (CHMe_2), 20.6, 20.1 ($COCH_3$). HRMS: m/z calcd for $C_{26}H_{32}O_7S$: 511.1756. Found 511.1766.

4.12. Benzyl 4,6-di-*O*-acetyl-2,3-dideoxy-3-(*p*-isopropylphenyl)thio-α-D-*erythro*-hex-2-enopyranoside (12)

TFAA (0.2 mL, 1.43 mmol) was added drop-wise to a solution of **11** (0.14 g, 0.28 mmol) and pyridine (0.23 mL, 2.86 mmol) in CH_2Cl_2 (5 mL), under N_2 atmosphere and at 0 °C. The reaction mixture was stirred for 16 h at rt, concentrated in vacuo and purified (SiO_2) (10% EtOAc/pet. ether) to afford **12** (0.107 g, 80%), as a gum.

R_f = 0.4 (12% EtOAc/pet. ether). $[\alpha]_D$ +34 (c 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42–7.31 (band, 6H, Aromatic), 7.23–7.21 (band, 3H, Aromatic), 5.69 (d, 1H, J = 9 Hz, H-4), 5.33 (d, 1H, J = 2 Hz, H-2), 5.10 (d, 1H, J = 2 Hz, H-1), 4.74 (d, 1H, J = 12 Hz, PhCH_{2a}), 4.54 (d, 1H, J = 12 Hz, PhCH_{2b}), 4.27–4.23 (band, 2H, H-5, H-6$_a$), 4.05 (app. d, 1H, J = 10.8 Hz, H-6$_b$), 2.94–2.87 (m, 1H, CHMe$_2$), 2.10 (s, 3H, $COCH_3$), 2.07 (s, 3H, $COCH_3$), 1.26 (d, 3H, J = 6.8 Hz, CHMe_2), 1.24 (d, 3H, J = 6.8 Hz, CHMe_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.6, 170.0, (CO), 149.9, 140.2, 137.4, 134.6, 128.4, 128.0, 127.6, 121.8 (C-2, C-3, Aromatic), 94.5 (C-1), 70.0 (C-4), 68.0 (C-5), 66.2 (PhCH_2), 62.6 (C-6), 33.8 (CHMe$_2$), 23.7 (CHMe_2), 20.7, 20.5 ($COCH_3$). HRMS: m/z calcd for $C_{26}H_{30}O_6S$: 493.1661 [M+Na]$^+$; found 493.1657.

4.13. Benzyl 4,6-di-*O*-acetyl-2,3-dideoxy-3-(*p*-isopropylphenyl)sulfinyl-α-D-*erythro*-hex-2-enopyranoside (13)

A mixture of vinyl sulfide **12** (0.107 g, 0.22 mmol) and MCPBA (0.04 g, 0.22 mmol) in CH_2Cl_2 (8 mL) was stirred at −78 °C for 10 min. The reaction mixture was then diluted with CH_2Cl_2 (15 mL), washed with satd aq $NaHCO_3$ solution (2 × 10 mL), dried (Na_2SO_4), concentrated in vacuo, and purified (SiO_2) (40% EtOAc/pet. ether) to afford **13** (0.103 g, 93%), as an epimer (1:1) and as a foamy solid.

R_f = 0.3 (45% EtOAc/pet. ether). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.32 (band, 18H, Aromatic), 6.83 (br, 2H, H-2), 5.75 (d, 1H, J = 9.8 Hz, H-4), 5.38 (br, 2H, H-1), 5.15 (d, 1H, J 9.8 Hz, H-4), 4.82 (d, 2H, J = 12 Hz, PhCH_2), 4.69–4.64 (band, 2H, PhCH_2), 4.20–4.16 (band, 3H, H-5, H-6$_a$, H-6$_b$), 4.12–4.04 (band, 3H, H-5, H-6$_a$, H-6$_b$), 2.98–2.93 (band, 2H, CHMe$_2$), 2.08 (s, 6H, $COCH_3$), 2.07 (s, 6H, $COCH_3$), 1.28 (br, 12H, CHMe_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.5, 170.4, 169.9, 169.7 (CO), 153.7, 146.9, 145.6, 139.3, 138.4, 137.0, 136.9, 130.6, 128.5, 128.0, 127.9, 127.7, 127.5, 127.1, 125.9, 125.5 (Aromatic, C-2, C-3), 93.7 (C-1), 93.5 (C-1), 72.9 (PhCH_2), 72.7 (PhCH_2), 70.5 (C-5), 70.0 (C-5), 68.1 (C-4), 63.6 (C-4), 63.5 (C-6), 60.5 (C-6), 34.1 (CHMe$_2$), 23.6 (CHMe_2), 20.6, 20.5, 20.0 ($COCH_3$). HRMS: m/z calcd for $C_{26}H_{30}O_7S$: 509.1610 [M+Na]$^+$; found 509.1607.

4.14. Benzyl 2,3,4-trideoxy-2-*N*-butylamino-3-(*p*-isopropylphenyl)sulfinyl-α-D-*erythro*/*threo*-hex-3-enopyranoside (14)

A solution of **13** (0.045 g, 0.09 mmol) in MeOH (6 mL) was treated with *n*-butylamine (0.05 mL, 0.55 mmol), refluxed for 10 h, solvents were removed in vacuo, and the residue was purified (SiO_2) (76% EtOAc/pet. ether) to afford **14**, as a gum.

erythro-isomer: Yield: 0.022 g, 55%. R_f = 0.6 (85% EtOAc/pet. ether). $[\alpha]_D$ +45 (c 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.28 (band, 9H, Aromatic), 6.70 (app. s, 1H, H-4), 5.11 (d, 1H, J = 4 Hz, H-1), 4.82 (d, 1H, J = 12 Hz, PhCH_{2a}) 4.60–4.51 (band, 2H, PhCH_{2b}, H-5), 3.87–3.83 (dd, 2H, J 3.6, 11.6 Hz H-6$_a$, H-6$_b$), 3.26–3.21 (band, 2H, H-2, CHMe$_2$), 2.31–2.26 (band, 2H, –NCH_2), 1.25 (d, 3H, J = 6.8 Hz, CHMe_2), 1.23 (d, 3H, J = 6.8 Hz, CHMe_2), 0.94–0.86 (band, 7H, –N$(CH_2)_3CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.2, 137.5, 137.0, 128.4, 128.3, 128.0, 127.7, 127.4 (Aromatic, C-3, C-4), 93.0 (C-1), 71.1 (PhCH_2), 70.8 (C-5), 69.7 (C-6), 69.5 (C-2), 64.5 (–NCH_2), 54.3 (–N$(CH_2)_3CH_3$), 46.4 (–N$(CH_2)_3CH_3$), 34.0 (CHMe$_2$), 23.7, 23.2 (CHMe_2), 19.8 (–N$(CH_2)_3CH_3$). HRMS: m/z calcd for $C_{26}H_{35}NO_4S$: 458.2365 [M+Na]$^+$; found 458.2368.

threo-isomer: Yield: (0.015 g, 37%). R_f = 0.67 (85% EtOAc/pet. ether). $[\alpha]_D$ +76 (c 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.27 (band, 9H, Aromatic), 6.52 (app. s, 1H, H-4), 5.25 (app. s, 1H, H-1), 4.79 (d, 1H, J = 12 Hz, PhCH_{2a}), 4.55 (d, 1H, J = 12 Hz, PhCH_{2b}), 4.52 (br, 1H, H-5), 3.75–3.71 (m, 2H, H-6$_a$, H-6$_b$), 3.95–3.90 (band, 2H, H-2, CHMe$_2$), 2.30–2.26 (band, 2H, –NCH_2), 1.96–1.89 (band, 2H, –N$(CH_2)_3CH_3$), 1.26 (d, 3H, J 6.8 Hz, CHMe_2), 1.24 (d, 3H, J = 6.8 Hz, CHMe_2), 0.94–0.82 (band, 5H, –N$(CH_2)_3CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.5, 137.1, 128.4, 128.1, 127.8, 126.8 (Aromatic, C-3, C-4), 94.1 (C-1), 71.6 (PhCH_2), 70.8 (C-5), 70.4 (C-6), 69.7 (C-2), 64.4 (–N$(CH_2)_3CH_3$), 54.3 (–N$(CH_2)_3CH_3$), 46.4 (–N$(CH_2)_3CH_3$), 34.3 (CHMe$_2$), 23.7, 23.6 (CHMe_2), 20.2 (–N$(CH_2)_3$-CH_3). HRMS: m/z calcd for $C_{26}H_{35}NO_4S$: 458.2365 [M+Na]$^+$; found 458.2368.

4.15. Benzyl 2,3,4-trideoxy-2-*N*-pyrrolidino-3-(*p*-isopropylphenyl)sulfinyl-α-D-*erythro*-hex-3-enopyranoside (15)

A solution of **13** (0.04 g, 0.08 mmol) in MeOH (6 mL) was treated with pyrrolidine (0.04 mL, 0.49 mmol), refluxed for 12 h, solvents were removed in vacuo, and the residue was purified (SiO_2) (68% EtOAc/pet. ether) to afford **15** (0.029 g, 78%), as a gum.

R_f = 0.5 (72% EtOAc/pet. ether). $[\alpha]_D$ +22 (c 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 7.35–7.27 (9H, band, Aromatic), 6.64 (app. s, 1H, H-4), 5.17 (d, 1H, J = 3.6 Hz, H-1), 4.80 (d, 1H, J = 12 Hz, PhCH_{2a}), 4.56 (d, 1H, J = 12 Hz, PhCH_{2b}), 4.51 (br, 1H, H-5), 3.82 (dd, 1H, J = 3.2, 12 Hz, H-6a), 3.76–3.72 (band, 1H, H-6$_b$), 3.27 (d, 1H, J = 3.6 Hz, H-2), 2.95–2.89 (m, 1H, CHMe$_2$), 2.75 (br, 4H, –NCH_2), 1.67 (br, 4H, –NCH_2CH_2), 1.26 (d, 3H, J = 6.8 Hz, CHMe_2), 1.24 (d, 3H, J = 6.8 Hz, CHMe_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.5, 137.1, 128.4, 128.3, 127.9, 127.8, 127.6, 127.5 (Aromatic, C-3, C-4), 94.1 (C-1), 70.5 (PhCH_2), 69.4 (C-5), 64.6 (C-6), 54.6 (C-2), 48.0 (–NCH_2), 34.0 (CHMe$_2$), 24.1 (–NCH_2CH_2), 23.7 (CHMe_2). HRMS: m/z calcd for $C_{26}H_{33}NO_4S$: 456.2209 [M+Na]$^+$; found 456.2209.

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Supplementary data

Supplementary data (spectral data for all new compounds, COSY, HMQC spectra of **2**, **5** and **11** and NOESY spectra of **5** and **7**) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.carres.2013.07.002.

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