$HClO_4$·SiO_2 catalysed synthesis of alkyl 3-deoxy-hex-2-enopyranosides from 2-hydroxy glucal ester: application in the synthesis of a *cis*-fused bicyclic ether and a 4-amino-*C*-glucoside†

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A variety of alcohols react with 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-arabino-hex-1-enopyranose **1** in the presence of a catalytic amount of $HClO_4$ supported on silica gel to give the corresponding alkyl 3-deoxy-hex-2-enopyranosides **2** in high yield, with short reaction times (10–45 mins) and good α-selectivity. Work-up merely involves filtration of the reagent, followed by chromatographic purification of the crude product. This methodology has also been employed in the synthesis of a bicyclic ether, a useful precursor for cyclic polyethers, and a 4-amino-*C*-glucoside.

Introduction

2-Hydroxy glucal ester[1] **1** (Fig. 1) and its analogues are important intermediates in organic synthesis because of the presence of a masked carbonyl group at C-2. These molecules react with alcohols in the presence of a Lewis acid to undergo allylic rearrangement,[2] forming the corresponding 3-deoxy-hex-2-enopyranosides **2** or 3,4-dideoxy-hex-3-enopyranoside-2-uloses **3**. These enosides, in turn, are useful building blocks in organic synthesis since they make provision for substitutions at C-2, C-3, and C-4. This has led to the synthesis of a number of biologically active natural products.[3–10] The Lewis acids that have been used in the allylic rearrangement of 2-hydroxy glycal esters include BF_3·Et_2O,[2] NIS[11] and $SnCl_4$,[12] and depending upon the reaction conditions, enosides **2** or enones **3** are the preferred products.

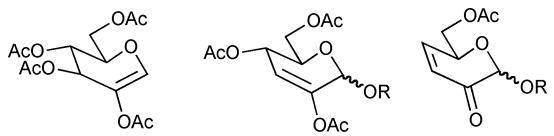

Fig. 1 Allylic rearrangement of **1** to products **2** and **3**.

Despite their importance, there are very few methods for the synthesis of enosides **2** or enones **3** from **1**, and many of these have some drawbacks. Thus, for example, in the synthesis of enone **3** from **1** using *N*-iodosuccinimide (NIS) longer reaction times (2.5–60 h) were generally needed, and most of the time the product **3** was accompanied by a small amount of **2**. With $SnCl_4$, though it gave only the α-anomer, in most of the cases a 2-furaldehyde derivative was formed as a side product.

Furthermore, it was necessary to use a large excess of BF_3·Et_2O in the conversion of **1** to **2**, and the amount varied depending on the glycosyl acceptors. Further, in the literature this reaction has not been reported using allylic alcohols as the glycosyl acceptors where the products could be useful in organic synthesis. Also, only one report is known for this reaction using *p*-methoxy phenol as a glycosyl acceptor in the presence of BF_3·Et_2O. Moreover, the product is formed in only 49% yield.[13]

Also, allylic rearrangements employing thiols are not reported in the literature except for one recent report[14] wherein $LiBF_4$ and BF_3·Et_2O have been used as Lewis acids to obtain S-linked disaccharides and the yields range from 15–60% depending on the Lewis acid used. Keeping these developments in mind it appeared that there is a need to develop methods that can be applicable to a wide range of alcohols and thiols, and give only one of the two products, *viz.* **2** or **3**.

Recently, 'perchloric acid supported on silica gel' ($HClO_4$·SiO_2) has been used for the acetylation of simple alcohols and sugars,[15] one pot acetylation–acylation of sugars,[16] O- and C-Ferrier rearrangement of glycals,[17] glycosylation of disarmed thioglycoside[18] and in the deprotection[19] of terminal isopropylidenes and trityl ethers. In continuation of our efforts[17a,19] to explore the potential of this reagent system, herein we wish to report the reaction of 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-arabino-hex-1-eno-pyranose **1** with various primary, secondary, tertiary, and allylic alcohols, phenols and thiols in the presence of $HClO_4$·SiO_2.

The above methodology has also been used in the synthesis of a *cis*-fused 6/7 membered bicyclic ether **24**. Such types of fused ethers are present in natural products of marine origin[20] such as brevetoxins, ciguatoxins, maitotoxins, halichondrins *etc.* These molecules have a ladder like framework with contiguous *trans*- and/or *cis*- fused five to nine membered polyether rings. Structural complexity, coupled with the impressive biological properties of these natural products, has been the main attraction for the development of new synthetic methods for their construction.[21]

Furthermore, the present methodology has also been extended towards the synthesis of a 4-amino-2,3-diacetoxy-*C*-glucoside **30**. Additionally, the double bond in its precursor *viz.* **29**, can also be easily functionalised into different 4-aminosugars.[22] Very few methods are known in the literature for the synthesis of such compounds, which mostly involve the allyl cyanate-to-isocyanate

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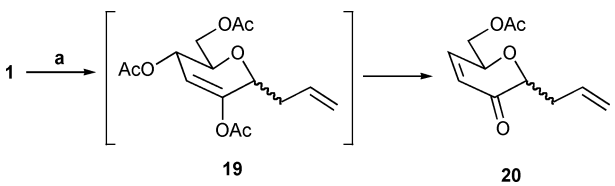
† Electronic supplementary information (ESI) available: Spectroscopic data for new compounds and copies of spectra for compounds **21–30**. See DOI: 10.1039/b810654a

rearrangement of hex-3-enopyranosides and the palladium catalysed allylic substitution by amines or azides of suitable hex-2-enopyranosides.[23] Recently, glycal derived activated allylic aziridines have also been used as precursors for the synthesis of 4-amino-derived-2,3-unsaturated glycosides.[24] In this paper, we have utilised the Overman rearrangement[25] for the stereoselective introduction of nitrogen functionality at the C-4 position of the sugar derivative and later transformed it into an amino sugar.

Results and discussion

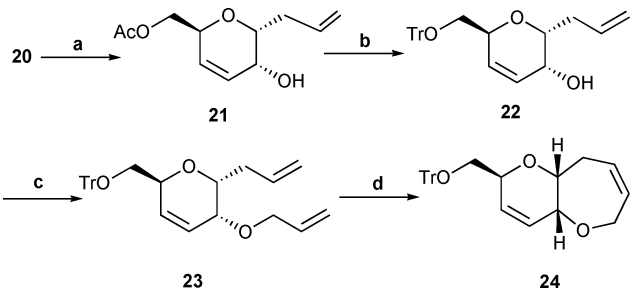
The reaction of 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-arabino-hex-1-enopyranose **1** with various primary, secondary, tertiary, and allylic alcohols, phenols and thiols in the presence of $HClO_4{\cdot}SiO_2$ went smoothly, leading to the corresponding alkyl-3-deoxy-hex-2-enopyranosides **2** in good to excellent yields with high α-selectivity, and required short reaction times (10–45 min). The work-up involved merely filtration of the reagent followed by chromatographic purification. Our results are summarised in Table 1. For aliphatic alcohols (entries 1 to 10, Table 1) 10 mg of $HClO_4{\cdot}SiO_2$ was needed per 100 mg of **1**, and for phenols and thiols (entries 11 to 15, Table 1) 5 mg of the reagent was needed per 100 mg of **1** for optimum yields. As mentioned above, primary and secondary aliphatic thiols do react[14] with **1** using $LiBF_4$ or $BF_3{\cdot}Et_2O$ as Lewis acids. With $BF_3{\cdot}Et_2O$, although α-selectivity was observed, the yields were moderate.[14] On the other hand, in the present study, although we have not used aliphatic thiols, the reactions with aromatic thiols required low catalyst loading and good yields of the products were obtained with reasonably good selectivity. All the products were characterised by ^1H and ^{13}C NMR, IR and mass spectral data and further by comparison with literature data wherever available.

In order to extend the scope of this methodology, 100 mg of **1** was treated with 3 equivalents of allyl trimethylsilane in the presence of 10 mg of the $HClO_4{\cdot}SiO_2$ reagent system, which led to the formation of the *C*-glycosidic enone **20** instead of the enoside **19** (Scheme 1) in 75% yield. The product was obtained as a 3 : 1 mixture of α and β anomers, which was characterised by spectroscopic means and compared with the literature data.[26] *C*-Glycosyl enones of the type **20** serve as valuable precursors in organic synthesis.[27–31]The reactions of vinyl trimethylsilane and trimethylsilyl cyanide with **1** were extremely sluggish, and the increased amount of $HClO_4{\cdot}SiO_2$ used led to extensive decomposition from which no product could be identified.



Scheme 1 *Reagents and conditions*: (a) $CH_2{=}CH{-}CH_2SiMe_3$, $HClO_4{\cdot}SiO_2$, CH_3CN, reflux, 5 h, 75%.

We have also utilised the enone **20** in the synthesis of a bicyclic ether **24** (Scheme 2). Thus, enone **20**, which was present as an inseparable 3 : 1 mixture of α and β anomers, was treated with $NaBH_4$ in the presence of $CeCl_3{\cdot}7H_2O$ to get a separable mixture of 3 diastereomers in the ratio of 7 : 2 : 1 and 80% combined yield.



Scheme 2 *Reagents and conditions*: (a) $NaBH_4$, $CeCl_3{\cdot}7H_2O$, MeOH, 0 °C, 2 h, 56% (major isomer); (b) (i) NaOMe–MeOH, 0 °C, 1 h; (ii) TrCl, Et_3N, CH_2Cl_2, 0 °C → rt, 8 h, 92% over 2 steps; (c) NaH, allyl bromide, THF, reflux, 3 h, 86%; (d) 1st generation Grubbs' catalyst, toluene, rt, overnight, 88%.

We proceeded further with the major alcohol **21**, but the relative stereochemistry at C-1 and C-2 could not be determined at this stage. Deacetylation of **21** using sodium methoxide in methanol (Zemplén procedure),[32] followed by regioselective protection of the primary alcohol as the trityl ether gave **22** in 92% yield over two steps. Allylation of the secondary alcohol in the presence of allyl bromide and sodium hydride provided triene **23** in 86% yield. The stereochemistry at C-1 and C-2 was confirmed through NOE experiments. Thus, when the signal for H-5 was irradiated the signal for H-1 was not enhanced (Fig. 2) indicating that H-1 and H-5 are *trans* oriented. Furthermore, irradiation of the signal for H-2 led to the enhancement of the signals for H-1 and the olefinic hydrogen H-3 present in the ring, suggesting that H-1 and H-2 are *cis* oriented. Finally the ring closing metathesis of **23**, using Grubbs' 1st generation ruthenium catalyst[33] (6 mol%), proceeded smoothly in toluene at room temperature to furnish the *cis*-fused bicyclic ether **24** which was characterised by ^1H, ^{13}C NMR, COSY experiments. The stereochemistry at the A–B ring junction was further confirmed from the NOE experiments, wherein irradiation of the signal for H-2 led to the enhancement of the signal for H-1, suggesting *cis* stereochemistry at the ring junction and thus supporting its stereochemical assignment. (Fig. 2)

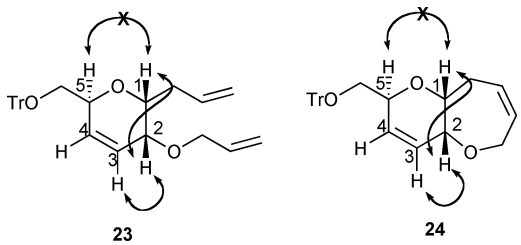


Fig. 2 NOE correlations.

For the synthesis of the 4-amino-*C*-glucoside (Scheme 3) the allyl alcohol **22** was reacted with trichloroacetonitrile in the presence of DBU to afford trichloroacetimidate **25** in 95% yield. This imidate **25** was then subjected to the Overman rearrangement[34] by refluxing in xylene in the presence of K_2CO_3,[35] to provide the corresponding trichloroacetyl amide **26** in 80% yield and with total stereocontrol. The product was well characterised by analysing its ^1H NMR spectral data, in addition to other data, which showed the disappearance of the imine proton singlet at δ 8.27 and the appearance of the amine proton as a doublet at δ 6.73.

Table 1 Reaction of 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-arabino-hex-1-enopyranose **1** with alcohols in the presence of $HClO_4 \cdot SiO_2$

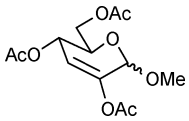
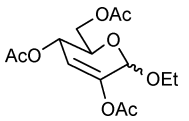
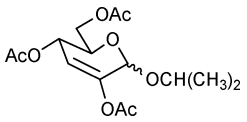
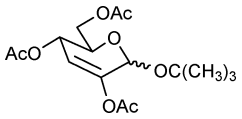
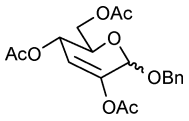
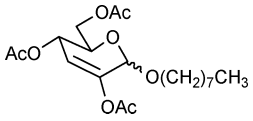
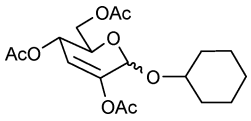
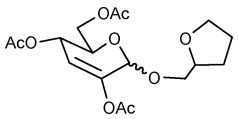
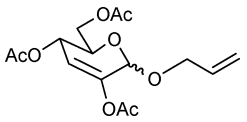
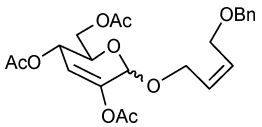
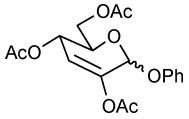
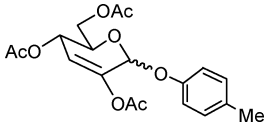
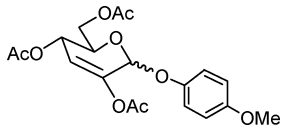
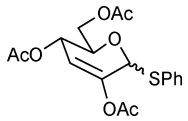
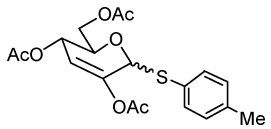
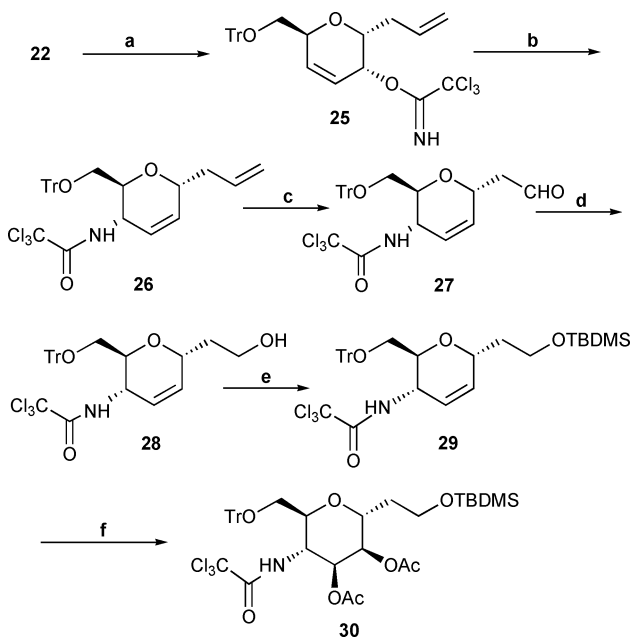
Entry	Product structure	Product no.	Time/min	Yield (%)	α : β
1		**4**	20[a]	90	13 : 2[2]
2		**5**	20[a]	95	4 : 1[11]
3		**6**	20[a]	90	7 : 1[11]
4		**7**	45[a]	86	6 : 1[11]
5		**8**	10[a]	82	5 : 1
6		**9**	20[a]	85	10 : 1
7		**10**	10[a]	93	8 : 1
8		**11**	15[a]	75	3 : 1
9		**12**	10[a]	82	2 : 1
10		**13**	10[a]	80	3 : 1
11		**14**	15[b]	84	8 : 1
12		**15**	30[b]	85	14 : 1

Table 1 (*Contd.*)

Entry	Product structure	Product no.	Time/min	Yield (%)	α : β
13		**16**	30[b]	87	10 : 1[13]
14		**17**	30[b]	80	4 : 1
15		**18**	30[b]	82	5 : 1

[a] 10 mg, [b] 5 mg of $HClO_4{\cdot}SiO_2$ used per 100 mg of 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-arabino-hex-1-enopyranose **1**.



Scheme 3 *Reagents and conditions*: (a) Cl_3CCN, DBU, CH_2Cl_2, 0 °C → rt, 30 min, 95%; (b) K_2CO_3, xylene, reflux, 12 h, 80%; (c) (i) OsO_4 cat., NMO, acetone : water (1 : 2), rt, 3 h; (ii) $NaIO_4$, MeOH, 0 °C → rt, 30 min, 71% over 2 steps (based on starting material recovered); (d) $NaBH_4$, MeOH, 0 °C → rt, 30 min, 95%; (e) TBDMSCl, Et_3N, DMAP cat., CH_2Cl_2, reflux, 5 h, 94%; (f) (i) OsO_4 cat., NMO, *t*-BuOH : acetone : water (1 : 2 : 2), rt, 12 h; (ii) Ac_2O, Et_3N, DMAP cat., CH_2Cl_2, 0 °C → rt, 3 h, 89% over 2 steps.

Regioselective dihydroxylation of the terminal olefin in **26**, followed by oxidation with sodium periodate, produced the aldehyde **27** in 71% combined yield. Reduction using sodium borohydride gave alcohol **28** whose protection as a *tert*-butyldimethylsilyl ether furnished **29** in 94% yield after chromatographic purification. The exposure of **29** to a catalytic amount of OsO_4 in the presence of NMO, followed by acetylation, afforded **30** as the major diastereomer in 89% yield. As expected, the dihydroxylation of **29** took place from the less hindered side of the double bond. The configuration of **30** was assigned based on the coupling constant values, where $J_{3,4} = 10.76$ Hz, and $J_{2,3} = 2.92$ Hz were observed. Since H-2 and H-3 have to be *cis* to each other because of the *cis* dihydroxylation, and the larger coupling of $J = 10.76$ Hz must be due to the coupling of protons H-3 and H-4, a diaxial disposition of H-3 and H-4 is suggested and thus the *trans* relationship between them confirmed.

Conclusion

In conclusion, we have developed an efficient method for the allylic rearrangement of 2-hydroxy glucal ester **1** leading to 3-deoxy-hex-2-enopyranosides **2**. Furthermore, only enopyranosides **2** are formed in the present work and no trace of **3** was seen to form. Also, a specific *C*-glucoside **20** could be readily formed under these conditions. The advantages of this method are the ease of handling, short reaction times, high yields and good anomeric selectivity. This methodology also provides easy access to a bicyclic ether **24** and a highly functionalised 4-amino-*C*-glucoside, which can serve as chiral building blocks allowing a variety of synthetic transformations.

Experimental

Infrared spectra were recorded on a Bruker FT/IR Vector 22 spectrophotometer. ^1H and ^{13}C NMR spectra were recorded on a JEOL LA-400 (400 and 100 MHz respectively) spectrometer in solutions of $CDCl_3$ as a solvent. Chemical shifts are reported in δ units (ppm) with reference to tetramethylsilane as an internal standard and J values are given in Hz. The mass spectra were recorded on a Micromass Quattro II triple quadrupole mass spectrometer. Rotation values were recorded on an Autopol II automatic polarimeter at the wavelength of the sodium D-line (589 nm) at 25 °C. Elemental analyses were carried out on a Thermoquest CE-instruments EA-1110C, H, N, S analyser. Column chromatography was performed on silica gel (100–200 mesh) and thin layer chromatography (TLC) was performed on silica gel plates made by using grade G silica gel obtained from

S. D. Fine-Chem Ltd., Mumbai or precoated plates (E. Merck, Germany). The visualisation of spots on TLC plates was effected by exposure to iodine and spraying with 10% aqueous H_2SO_4, followed by charring. Melting points were determined using a Fischer-John melting point apparatus and are uncorrected. The reactions were carried out in oven-dried glassware under a N_2 atmosphere. In extractive work-up, aqueous solutions were always extracted thrice with the appropriate organic solvent. The combined organic extracts were washed with water and brine, dried over anhydrous sodium sulfate, then evaporated under reduced pressure. All solvents and common reagents were purified by established procedures. The $HClO_4{\cdot}SiO_2$ reagent system was prepared by following the literature procedure.[15a]

General experimental procedure for the synthesis of 3-deoxy-hex-2-enopyranosides

To a stirred mixture of 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-arabino-hex-1-enopyranose **1** (100 mg, 0.33 mmol) and an alcohol [1 equiv. (2 equiv. in the case of the methyl, ethyl and allyl alcohols)] in anhydrous acetonitrile (1.5 mL), was added "$HClO_4{\cdot}SiO_2$" (10 mg in the case of entries 1–10; 5 mg in the case of entries 11–15). The reaction mixture was refluxed for the appropriate time (Table 1) and completion of the reaction was monitored by TLC analysis. The reaction mixture was then filtered, washed with acetonitrile, and then the combined organic extracts were concentrated under vacuum. The products were purified by silica gel column chromatography.

Benzyl 2,4,6-tri-*O*-acetyl-3-deoxy-α/β-D-erythro-hex-2-eno-pyranoside (8)

Yield: 82% (5 : 1 mixture of α : β anomers). Found: C, 60.39; H, 5.82. Calc. for $C_{19}H_{22}O_8$ C, 60.31; H, 5.86%; R_f 0.5 (hexane : ethyl acetate, 7 : 3); IR (neat) ν_{max}/cm^{-1} 2925, 1740; δ_H (400 MHz, $CDCl_3$) (α-anomer) 1.99 (3H, s, $COCH_3$), 2.02 (3H, s, $COCH_3$), 2.04 (3H, s, $COCH_3$), 4.04–4.18 (3H, m, H-5, H-6, H-6′), 4.54 (2H, s, $OCH_2C_6H_5$), 5.05 (1H, br s, H-1), 5.39 (1H, dd, J = 2.2, 9.5 Hz, H-4), 5.64 (1H, d, J = 2.0 Hz, H-3), 7.21–7.29 (5H, m, $OCH_2C_6H_5$); (β-anomer) 5.23 (1H, s, H-1), 5.26 (1H, dd, J = 4.4, 8.6 Hz, H-4), 5.73 (1H, d, J = 4.6 Hz, H-3); δ_C (100 MHz, $CDCl_3$) (α-anomer) 20.7, 20.8, 20.9, 29.6, 62.4, 65.2, 67.3, 70.5, 72.6, 93.0, 115.4, 112.1, 127.8, 128.6, 137.2, 146.3, 168.1, 170.0, 170.7; MSES$^+$: 401 $[M + Na]^+$

Tetrahydrofurfuryl 2,4,6-tri-*O*-acetyl-3-deoxy-α/β-D-erythro-hex-2-enopyranoside (11)

Yield: 75% (3 : 1 mixture of α : β anomers). Found: C, 54.79; H, 6.55. Calc. for $C_{17}H_{24}O_9$ C, 54.83; H, 6.50%; R_f 0.6 (hexane : ethyl acetate, 7 : 3); IR (neat) ν_{max}/cm^{-1} 2925, 1746; δ_H (400 MHz, $CDCl_3$) (α-anomer) 1.56–2.05 (4H, m, H-3′, H-3″, H-4′, H-4″), 2.08 (3H, s, $COCH_3$), 2.10 (3H, s, $COCH_3$), 2.17 (3H, s, $COCH_3$), 3.46–3.59 (1H, m, H-2′), 3.74–3.81 (2H, m, H-5′,H-5″), 3.83–3.89 (1H, m, H-1′), 4.06–4.11 (1H, m, H-1″), 4.19–4.32 (3H, m, H-5, H-6, H-6′), 5.31 (1H, s, H-1), 5.46 (1H, br d, J = 9.3 Hz, H-4), 5.73 (1H, d, J = 2.2 Hz, H-3); (β-anomer) 5.78 (1H, d, J = 4.1 Hz, H-3); δ_C (100 MHz, $CDCl_3$) (α-anomer) 20.7, 20.9, 25.5, 25.7, 27.9, 28.2, 62.5, 65.2, 67.1, 68.3, 71.6, 94.1, 115.2, 146.3, 168.2, 170.1, 170.7; MSES$^+$: 390 $[M + NH_4]^+$, 271 $[M - 101]^+$.

Allyl 2,4,6-tri-*O*-acetyl-3-deoxy-α/β-D-erythro-hex-2-eno-pyranoside (12)

Yield: 82% (2 : 1 mixture of α : β anomers). Found: C, 54.92; H, 6.11. Calc. for $C_{15}H_{20}O_8$ C, 54.87; H, 6.14%; R_f 0.5 (hexane : ethyl acetate, 7 : 3); IR (neat) ν_{max}/cm^{-1} 1749; δ_H (400 MHz, $CDCl_3$) (α-anomer) 2.07 (3H, s, $COCH_3$), 2.10 (3H, s, $COCH_3$), 2.17 (3H, s, $COCH_3$), 4.07–4.34 (5H, m, H-1′, H-1″, H-5, H-6, H-6′), 5.10 (1H, s, H-1), 5.19–5.34 (2H, m, $CH{=}CH_2$), 5.47 (1H, br d, J = 8.6 Hz, H-4), 5.75 (1H, d, J = 2.2 Hz, H-3), 5.87–5.97 (1H, m, $CH{=}CH_2$); (β-anomer) 5.78 (1H, d, J = 4.9 Hz, H-3); δ_C (100 MHz, $CDCl_3$) (α-anomer) 20.9, 29.6, 31.8, 62.4, 65.2, 67.1, 69.3, 92.9, 115.3, 117.7, 133.6, 146.3, 168.1, 170.1, 170.6; MSES$^+$: 351 $[M + Na]^+$.

p-Methylphenyl 2,4,6-tri-*O*-acetyl-3-deoxy-α/β-D-erythro-hex-2-enopyranoside (15)

Yield: 85% (14 : 1 mixture of α : β anomers). Found: C, 60.37; H, 5.82. Calc. for $C_{19}H_{22}O_8$ C, 60.31; H, 5.86%; R_f 0.5 (hexane : ethyl acetate, 7 : 3); IR (neat) ν_{max}/cm^{-1} 2923, 1741; δ_H (400 MHz, $CDCl_3$) (α-anomer) 2.01 (3H, s, $COCH_3$), 2.10 (3H, s, $COCH_3$), 2.18 (3H, s, $COCH_3$), 2.29 (3H, s, pCH_3-C_6H_4), 4.16–4.34 (3H, m, H-5, H-6, H-6′), 5.52 (1H, dd, J = 2.0, 9.5 Hz, H-4), 5.62 (1H, s, H-1), 5.87 (1H, d, J = 2.2 Hz, H-3), 6.96–7.11 (4H, m, C_6H_4); (β-anomer) 5.79 (1H, s, H-1), 5.34 (1H, m, H-4), 5.95 (1H, d, J = 5.4 Hz, H-3); δ_C (100 MHz, $CDCl_3$) (α-anomer) 20.5, 20.6, 20.9, 22.6, 29.6, 62.2, 65.1, 67.8, 93.1, 116.0, 117.2, 129.9, 132.4, 145.6, 154.8, 164.3, 168.1, 170.0, 170.6; MSES$^+$: 401 $[M + Na]^+$.

Thiophenyl 2,4,6-tri-*O*-acetyl-3-deoxy-α/β-D-erythro-hex-2-enopyranoside (17)

Yield: 80% (4 : 1 mixture of α : β anomers). Found: C, 56.79; H, 5.31; S, 8.42. Calc. for $C_{18}H_{20}O_7S$ C, 56.83; H, 5.30; S, 8.43%; R_f 0.6 (hexane : ethyl acetate, 7 : 3); IR (neat) ν_{max}/cm^{-1} 2928, 1746; δ_H (400 MHz, $CDCl_3$) (α-anomer) 2.07 (3H, s, $COCH_3$), 2.11 (3H, s, $COCH_3$), 2.20 (3H, s, $COCH_3$), 4.23–4.33 (2H, m, H-6, H-6′), 4.48–4.52 (1H, m, H-5), 5.48 (1H, br d, J = 9.5 Hz, H-4), 5.72 (1H, d, J = 2.2 Hz, H-3), 5.75 (1H, s, H-1), 7.27–7.34 (3H, m, C_6H_4), 7.53–7.55 (2H, m, C_6H_4); (β-anomer) 5.81 (1H, s, H-1); δ_C (100 MHz, $CDCl_3$) (α-anomer) 20.7, 20.9, 62.6, 64.7, 67.5, 67.6, 83.4, 115.3, 127.8, 128.9, 129.0, 131.9, 132.0, 133.8, 146.4, 167.9, 170.1, 170.6; MSES$^+$: 403 $[M + Na]^+$, 271 $[M - 109]^+$.

Allyl 6-*O*-acetyl-3,4-dideoxy-α/β-D-glycero-hex-3-eno-pyranoside-2-ulose (20)

To a stirred mixture of 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-arabino-hex-1-enopyranose **1** (0.100 g, 0.33 mmol) and allyl trimethylsilane (0.113 g, 0.16 mL, 0.99 mmol) in anhydrous acetonitrile (2 mL), was added $HClO_4{\cdot}SiO_2$ (10 mg). The reaction mixture was refluxed for 5 h. After completion of the reaction, the reaction mixture was filtered, washed with acetonitrile, and then the combined organic extracts were concentrated under vacuum. Purification by silica gel chromatography (hexane : ethyl acetate = 4 : 1) afforded compound **20** (0.048 g, 75%, 3 : 1 mixture of α : β anomers) as a colourless viscous liquid. Found: C, 62.89; H, 6.69. Calc. for $C_{11}H_{14}O_4$ C, 62.85; H, 6.71%; R_f 0.5 (hexane : ethyl acetate, 7 : 3); δ_H (400 MHz, $CDCl_3$) 2.10 (3H, s, $COCH_3$), 2.52

(2H, m, H-1′, H-1″), 4.11 (1H, dd, J = 4.2, 11.7 Hz, H-6), 4.34–4.44 (2H, m, H-6′, H-1), 4.67 (1H, m, H-5), 5.12–5.19 (2H, m, H-3′, H-3″), 5.79–5.89 (1H, m, H-2′), 6.15 (1H, dd, J = 2.2, 10.5 Hz, H-3), 6.91 (1H, dd, J = 2.7, 10.5 Hz, H-4); (β-anomer) 6.19 (1H, dd, J = 2.6, 10.3 Hz, H-3), 6.95 (1H, dd, J = 1.6, 10.3 Hz, H-4); δ_C (100 MHz, $CDCl_3$) (α-anomer) 20.8, 34.0, 63.7, 68.7, 77.5, 117.9, 127.4, 133.3, 146.2, 170.7, 195.3; MSES$^+$: 228 $[M + NH_4]^+$.

((2*S*,5*R*,6*R*)-6-Allyl-5-hydroxy-5,6-dihydro-2*H*-pyran-2-yl)methyl acetate (21)

To a solution of enone **20** (1.20 g, 5.71 mmol, 3 : 1 diastereomeric mixture) in methanol (10 mL) was added $CeCl_3{\cdot}7H_2O$ (2.552 g, 6.85 mmol) at 0 °C. The mixture was stirred for 5 min at 0 °C followed by the addition of $NaBH_4$ (0.260 g, 6.85 mmol). The resulting mixture was stirred for 2 h at the same temperature and then quenched with saturated NH_4Cl solution (10 mL). The reaction mixture was concentrated under high vacuum to remove methanol. The aqueous phase was extracted with ethyl acetate (3 × 30 mL), then the combined organic extracts were washed with brine and dried over anhydrous Na_2SO_4. After concentration, the residue was purified by silica gel chromatography (hexane : ethyl acetate = 3 : 1) to afford alcohol **21** (0.678 g, 56%) as a colourless viscous liquid along with other diastereomers in 16% (0.194 g) and 8% (0.097 g) yield respectively. Found: C, 62.23; H, 7.64. Calc. for $C_{11}H_{16}O_4$ C, 62.25; H, 7.60%; R_f 0.5 (hexane : ethyl acetate, 3 : 2); $[\alpha]_D^{25}$ −186.1 (*c* 2.4, CH_2Cl_2); IR (neat) ν_{max}/cm^{-1} 3442, 3076, 2919, 1742, 1642, 1040; δ_H (400 MHz, $CDCl_3$) 2.10 (3H, s, $COCH_3$), 2.34 (1H, br s, O*H*), 2.41 (2H, t, J = 7.0 Hz, H-1′, H-1″), 3.76–3.82 (2H, m, H-1, H-2), 3.98 (1H, dd, J = 3.6, 11.7 Hz, H-6), 4.35 (1H, dd, J = 8.2, 11.7 Hz, H-6′), 4.43–4.46 (1H, m, H-5), 5.09 (1H, bd, J = 10.4 Hz, H-3′), 5.18 (1H, dd, J = 1.7, 17.3 Hz, H-3″), 5.82–5.89 (2H, m, H-4, H-2′), 6.17 (1H, ddd, J = 1.9, 5.3, 10.0 Hz, H-3); δ_C (100 MHz, $CDCl_3$) 20.7, 34.8, 62.5, 62.6, 71.3, 72.0, 117.1, 127.9, 129.4, 134.3, 170.8; MSES$^+$: 213.2 $[M + H]^+$.

(2*R*,3*R*,6*S*)-2-Allyl-6-(trityloxymethyl)-3,6-dihydro-2*H*-pyran-3-ol (22)

To a solution of compound **21** (0.200 g, 0.94 mmol) in dry methanol (5 mL) at 0 °C was added a catalytic amount of sodium methoxide. The mixture was stirred for 1 h at the same temperature. Evaporation of the solvent under vacuum gave a residue which was passed through a short pad of silica gel (eluent ethyl acetate) to afford diol as a yellowish oil, which was subjected to trityl protection without any further purification. To a solution of crude diol in CH_2Cl_2 (2 mL) at 0 °C were added Et_3N (0.286 g, 0.4 mL, 2.82 mmol) and TrCl (0.288 g, 1.03 mmol). The reaction mixture was stirred for 8 h at room temperature and then extraction with CH_2Cl_2 followed by the usual work up gave a crude product which after purification by column chromatography (hexane : ethyl acetate = 4 : 1) afforded compound **22** (0.358 g, 92%) as a colourless liquid. Found: C, 81.48; H, 6.87. Calc. for $C_{28}H_{28}O_3$ C, 81.52; H, 6.84%; R_f 0.5 (hexane : ethyl acetate, 4 : 1); $[\alpha]_D^{25}$ −112.2 (*c* 1.2, CH_2Cl_2); IR (neat) ν_{max}/cm^{-1} 3431, 3059, 2919, 1641, 1075; δ_H (400 MHz, $CDCl_3$) 1.66 (1H, br s, O*H*), 2.48 (2H, t, J = 7.0 Hz, H-1′, H-1″), 3.05 (1H, dd, J = 3.9, 9.7 Hz, H-6), 3.33 (1H, dd, J = 7.0, 9.7 Hz, H-6′), 3.72 (1H, br s, H-2), 3.78 (1H, dt, J = 1.9, 7.0 Hz, H-1), 4.44–4.47 (1H, m, H-5), 5.09 (1H, bd, J = 10.0 Hz, H-3′), 5.19 (1H, dd, J = 1.6, 17.0 Hz, H-3″), 5.81–5.91 (2H, m, H-4, H-2′), 6.11 (1H, ddd, J = 2.2, 5.6, 10.0 Hz, H-3), 7.21–7.32 (9H, m, $C(C_6H_5)_3$), 7.41–7.47 (6H, m, $C(C_6H_5)_3$); δ_C (100 MHz, $CDCl_3$) 35.3, 62.7, 63.4, 72.4, 73.1, 86.5, 117.3, 126.9, 127.7, 128.1, 128.6, 130.1, 134.4, 143.7; MSES$^+$: 435.4 $[M + NH_4]^+$.

(2*R*,3*R*,6*S*)-2-Allyl-3-(allyloxy)-6-(trityloxymethyl)-3,6-dihydro-2*H*-pyran (23)

To a stirred suspension of NaH (0.015 g, 0.36 mmol, 60% suspension in mineral oil) in dry THF (2 mL) was added compound **22** (0.100 g, 0.24 mmol). The reaction mixture was stirred at room temperature for 30 min followed by reflux for 1 h. It was cooled to room temperature, allyl bromide added (0.035 g, 0.025 mL, 0.29 mmol) and again it was refluxed for 2 h. The reaction was cooled to room temperature and quenched with saturated NH_4Cl solution, extracted with ethyl acetate (3 × 10 mL) and the combined organic extracts were washed with water, brine and dried over anhydrous Na_2SO_4. After concentration, the residue was purified by silica gel chromatography (hexane : ethyl acetate = 9 : 1) to furnish **23** (0.095 g, 86.6%) as a colourless liquid. Found: C, 82.30; H, 7.11. Calc. for $C_{31}H_{32}O_3$ C, 82.27; H, 7.13%; R_f 0.6 (hexane : ethyl acetate, 9 : 1); $[\alpha]_D^{25}$ −133.0 (*c* 1.0, CH_2Cl_2); IR (neat) ν_{max}/cm^{-1} 3060, 2923, 1642, 1072; δ_H (400 MHz, $CDCl_3$) 2.48 (2H, t, J = 7.0 Hz, H-1′, H-1″), 3.05 (1H, dd, J = 4.6, 9.5 Hz, H-6), 3.28 (1H, dd, J = 6.6, 9.5 Hz, H-6′), 3.70 (1H, br s, H-2), 3.89 (1H, dt, J = 2.9, 7.0 Hz, H-1), 4.02 (1H, dd, J = 5.6, 12.6 Hz, H-7), 4.15 (1H, dd, J = 5.6, 12.6 Hz, H-7′), 4.45 (1H, br s, H-5), 5.08 (1H, dd, J = 1.2, 10.0 Hz, H-3′), 5.15 (1H, d, J = 1.2 Hz, H-3″), 5.18 (1H, dd, J = 1.4, 6.6 Hz, H-9), 5.29 (1H, dd, J = 1.4, 17.0 Hz, H-9′), 5.83–5.97 (3H, m, H-4, H-2′, H-8), 6.04 (1H, ddd, J = 1.9, 4.4, 10.2 Hz, H-3), 7.21–7.31 (9H, m, $C(C_6H_5)_3$), 7.44–7.46 (6H, m, $C(C_6H_5)_3$); δ_C (100 MHz, $CDCl_3$) 34.4, 64.2, 68.8, 69.6, 72.0, 72.5, 86.4, 116.7, 117.0, 125.3, 126.9, 127.7, 128.6, 131.0, 135.0, 135.1, 143.8; MSES$^+$: 475.2 $[M + Na]^+$.

(2*S*,4a*R*,9a*R*,*Z*)-2-(Trityloxymethyl)-4a,6,9,9a-tetrahydro-2*H*-pyrano[3,2-*b*]oxepine (24)

Bis-(tricyclohexylphosphine)benzylidine ruthenium(IV) dichloride (0.011 g, 6 mol%) was added to a stirred solution of **23** (0.100 g, 0.22 mmol) in toluene (5 mL) under a nitrogen atmosphere. The reaction mixture was stirred at room temperature for 8 h and then filtered through a pad of celite and concentrated *in vacuo*. Purification by silica gel chromatography (hexane : ethyl acetate = 9 : 1) gave **24** (0.083 g, 88%) as a colourless solid, mp 136 °C. Found: C, 82.09; H, 6.69. Calc. for $C_{29}H_{28}O_3$ C, 82.05; H, 6.65%; R_f 0.5 (hexane : ethyl acetate, 9 : 1); $[\alpha]_D^{25}$ −104.8 (*c* 0.7, CH_2Cl_2); IR (neat) ν_{max}/cm^{-1} 3057, 2923, 1597, 1091, 1072; δ_H (400 MHz, $CDCl_3$) 2.43–2.46 (1H, m, H-10), 2.74–2.77 (1H, m, H-10′), 3.01 (1H, dd, J = 4.3, 9.7 Hz, H-6), 3.28 (1H, dd, J = 6.8, 9.7 Hz, H-6′), 3.97 (1H, t, J = 4.1 Hz, H-2), 4.13 (1H, br d, J = 16.6 Hz, H-7), 4.17–4.21 (1H, m, H-1), 4.42–4.46 (2H, m, H-5, H-7′), 5.57–5.60 (1H, m, H-8), 5.68–5.71 (1H, m, H-9), 5.87 (1H, ddd, J = 2.2, 4.1, 10.4 Hz, H-3), 6.00 (1H, ddd, J = 1.5, 3.5, 10.4 Hz, H-4), 7.21–7.32 (9H, m, $C(C_6H_5)_3$), 7.45–7.47 (6H, m, $C(C_6H_5)_3$); δ_C (100 MHz, $CDCl_3$) 30.0, 64.1, 68.2, 71.0, 71.1, 72.9, 86.5, 125.0, 125.1, 126.9, 127.7, 128.6, 129.9, 130.8, 143.9; MSES$^+$: 447.5 $[M + Na]^+$.

(2*R*,3*R*,6*S*)-2-Allyl-6-(trityloxymethyl)-3,6-dihydro-2*H*-pyran-3-yl 2,2,2-trichloroacetimidate (25)

Alcohol **22** (0.100 g, 0.24 mmol) was dissolved in CH_2Cl_2 (2 mL) and cooled to 0 °C. DBU (0.04 mL, 0.24 mmol) was added to it, followed by trichloroacetonitrile (0.03 mL, 0.29 mmol). The reaction mixture was stirred at the same temperature for 1 h and then the CH_2Cl_2 evaporated. The crude product was purified by column chromatography (hexane : ethyl acetate = 4 : 1) to afford trichloroacetimidate **25** (0.1283 g, 95%) as a viscous liquid. Found: C, 64.74; H, 5.09; N, 2.49. Calc. for $C_{30}H_{28}Cl_3NO_3$ C, 64.70; H, 5.07; N, 2.52%; R_f 0.7 (hexane : ethyl acetate, 4 : 1); $[\alpha]_D^{25}$ −35.1 (*c* 0.6, CH_2Cl_2); IR (neat) ν_{max}/cm^{-1} 3340, 2924, 1660, 1002; δ_H (400 MHz, $CDCl_3$) 2.51–2.59 (2H, m, H-1′, H-1″), 3.10 (1H, dd, J = 3.9, 10.0 Hz, H-6), 3.34 (1H, dd, J = 6.8, 10.0 Hz, H-6′), 4.06 (1H, dt, J = 2.4, 7.0 Hz), 4.56 (1H, t, J = 2.9 Hz), 5.08–5.10 (2H, m), 5.17 (1H, dd, J = 1.7, 17.1 Hz), 5.78–5.88 (1H, m), 6.02 (1H, dd, J = 3.1, 10.2 Hz), 6.22 (1H, ddd, J = 2.4, 5.3, 10.2 Hz), 7.22–7.32 (9H, m, $C(C_6H_5)_3$), 7.45–7.47 (6H, m, $C(C_6H_5)_3$), 8.27 (1H, s, N*H*); δ_C (100 MHz, $CDCl_3$) 34.9, 63.9, 69.2, 71.2, 72.6, 86.6, 91.5, 117.7, 122.5, 127.0, 127.7, 128.6, 133.2, 133.9, 143.8, 162.1; MSES$^+$: 578.4 $[M + Na]^+$.

***N*-((2*S*,3*S*,6*R*)-6-Allyl-2-(trityloxymethyl)-3,6-dihydro-2*H*-pyran-3-yl)-2,2,2-trichloroacetamide (26)**

A mixture of imidate **25** (0.100 g, 0.18 mmol) and K_2CO_3 (10 mg) in xylene (5 mL) was refluxed (150 °C) for 12 h. The reaction mixture was cooled to room temperature and the solvent evaporated, followed by silica gel chromatography (hexane : ethyl acetate = 4 : 1) giving **26** (0.080 g, 80%) as a white solid along with recovered starting material (0.008 g, 8%). Found: C, 64.66; H, 5.10; N, 2.54. Calc. for $C_{30}H_{28}Cl_3NO_3$ C, 64.70; H, 5.07; N, 2.52%; R_f 0.6 (hexane : ethyl acetate, 4 : 1); $[\alpha]_D^{25}$ −56.17 (*c* 1.2, CH_2Cl_2); IR (neat) ν_{max}/cm^{-1} 3409, 3325, 2925, 1711, 1597, 1082; δ_H (400 MHz, $CDCl_3$) 2.30–2.40 (2H, m, H-1′, H-1″), 3.22 (1H, dd, J = 4.8, 9.7 Hz, H-6), 3.35 (1H, dd, J = 6.8, 9.7 Hz, H-6′), 3.97–4.01 (1H, m, H-5), 4.08–4.11 (1H, m, H-1), 4.28–4.30 (1H, m, H-4), 5.12–5.18 (2H, m, H-3′, H-3″), 5.74–5.88 (3H, m, H-2, H-2′, H-3), 6.72 (1H, d, J = 8.5 Hz, N*H*), 7.21–7.31 (9H, m, $C(C_6H_5)_3$), 7.45–7.47 (6H, m, $C(C_6H_5)_3$); δ_C (100 MHz, $CDCl_3$) 38.2, 45.7, 62.3, 69.8, 73.7, 86.7, 92.3, 118.1, 122.9, 127.0, 127.8, 128.6, 133.1, 133.6, 143.6, 161.1; MSES$^+$: 578.4 $[M + Na]^+$.

2,2,2-Trichloro-*N*-((2*S*,3*S*,6*R*)-6-(2-oxoethyl)-2-(trityloxymethyl)-3,6-dihydro-2*H*-pyran-3-yl)acetamide (27)

To a stirred solution of compound **26** (0.100 g, 0.18 mmol) in acetone : water (1 : 2, 1.5 mL) at room temperature, were added NMO·H_2O (0.027 g, 0.198 mmol) and OsO_4 (a 25 mg ml^{-1} solution in ^{t}BuOH, 9 μL, 0.005 eq.). After stirring for 3 h, a solution of $Na_2S_2O_5$ (0.041 g, 0.216 mmol dissolved in water) was added and the resulting mixture was stirred for 10 min. After removal of the acetone, the residue was extracted with ethyl acetate (3 × 15 mL) and washed with brine solution. The combined organic layers were dried and concentrated *in vacuo*, and the residual oil was purified by silica gel chromatography to give diol (0.066 g, 62%) as a colourless liquid along with recovered starting material **26** (0.020 g, 20%).

To a solution of diol (0.060 g, 0.10 mmol) in methanol (2 mL) was added $NaIO_4$ (0.032 g, 0.15 mmol) dissolved in water, at 0 °C. The reaction mixture was stirred for 30 min and quenched with water. Evaporation *in vacuo* gave a residue which was extracted with ethyl acetate (3 × 10 mL) and the combined organic layers were washed with water, brine and concentrated. The residual oil was purified by silica gel chromatography (hexane : ethyl acetate = 7 : 3) to give the aldehyde **27** (0.052 g, 91.5%) as a colourless oil. Found: C, 62.36; H, 4.66; N, 2.49. Calc. for $C_{29}H_{26}Cl_3NO_4$ C, 62.32; H, 4.69; N, 2.51%; R_f 0.6 (hexane : ethyl acetate, 3 : 2); $[\alpha]_D^{25}$ + 48.4 (*c* 0.5, CH_2Cl_2); IR (neat) ν_{max}/cm^{-1} 3332, 2924, 1714, 1596, 1079; δ_H (400 MHz, $CDCl_3$) 2.65–2.75 (2H, m, H-1′, H-1″), 3.26 (1H, dd, J = 4.8, 10.0 Hz, H-6), 3.35 (1H, dd, J = 7.0, 10.0 Hz, H-6′), 3.93–3.97 (1H, m), 4.35 (1H, dd, J = 3.2, 8.3 Hz), 4.44–4.45 (1H, m), 5.82 (2H, s), 7.06 (1H, d, J = 8.5 Hz, N*H*), 7.21–7.32 (9H, m, $C(C_6H_5)_3$), 7.44–7.46 (6H, m, $C(C_6H_5)_3$), 9.78 (1H, s, C*H*O); δ_C (100 MHz, $CDCl_3$) 45.6, 47.0, 62.2, 66.1, 73.7, 86.9, 92.4, 123.7, 127.1, 127.8, 128.6, 131.8, 143.6, 161.3, 199.4; HRMS (ESI): 556.0843 $[M - H]^-$. Calc. for $C_{29}H_{26}Cl_3NO_4$ $[M - H]^-$: 556.0849.

2,2,2-Trichloro-*N*-((2*S*,3*S*,6*R*)-6-(2-hydroxyethyl)-2-(trityloxymethyl)-3,6-dihydro-2*H*-pyran-3-yl)acetamide (28)

To a stirred solution of compound **27** (0.100 g, 0.18 mmol) in methanol (2 mL), cooled to 0 °C, was added $NaBH_4$ (0.008 g, 0.198 mmol). The reaction mixture was stirred at the same temperature for 30 min and then quenched with saturated NH_4Cl solution. The reaction mixture was concentrated under high vacuum to remove methanol. The aqueous phase was extracted with ethyl acetate (3 × 15 mL), the combined organic extracts were washed with water and brine, then dried over anhydrous Na_2SO_4. After concentration, the residue was purified by silica gel chromatography (hexane : ethyl acetate = 1 : 1) to afford alcohol **28** (0.095 g, 95%) as a colourless viscous liquid. Found: C, 62.14; H, 5.05; N, 2.51. Calc. for $C_{29}H_{28}Cl_3NO_4$ C, 62.10; H, 5.03; N, 2.50%; R_f 0.5 (hexane : ethyl acetate, 1 : 1); $[\alpha]_D^{25}$ +54.4 (*c* 0.7, CH_2Cl_2); IR (neat) ν_{max}/cm^{-1} 3410, 3322, 3033, 1701, 1597, 1033; δ_H (400 MHz, $CDCl_3$) 1.78–1.85 (2H, m, H-1′, H-1″), 2.40 (1H, br s, O*H*), 3.27 (1H, dd, J = 4.4, 10.4 Hz, H-6), 3.35 (1H, dd, J = 7.6, 10.4 Hz, H-6′), 3.83–3.86 (2H, m), 3.91–3.95 (1H, m), 4.25–4.28 (2H, m), 5.71–5.74 (1H, m), 5.82 (1H, bd, J = 10.4 Hz), 6.82 (1H, d, J = 8.4 Hz, N*H*), 7.21–7.32 (9H, m, $C(C_6H_5)_3$), 7.44–7.46 (6H, m, $C(C_6H_5)_3$); δ_C (100 MHz, $CDCl_3$) 35.7, 45.8, 60.5, 62.6, 70.1, 73.3, 87.1, 92.8, 123.1, 127.1, 127.8, 128.6, 133.3, 143.6, 161.3.

***N*-((2*S*,3*S*,6*R*)-6-(2-(*tert*-Butyldimethylsilyloxy)ethyl)-2-(trityloxymethyl)-3,6-dihydro-2*H*-pyran-3-yl)-2,2,2-trichloroacetamide (29)**

tert-Butyldimethylsilyl chloride (0.025 g, 0.165 mmol) was added to a solution of alcohol **28** (0.060 g, 0.11 mmol), triethylamine (0.02 mL, 0.165 mmol) and 4-dimethylaminopyridine (catalytic amount) in CH_2Cl_2 (4 mL). The reaction mixture was refluxed for 5 h and then cooled to room temperature. The resultant solution was diluted with CH_2Cl_2 and washed with water and brine then dried over anhydrous Na_2SO_4. Concentration *in vacuo*, followed by silica gel chromatography (hexane : ethyl acetate = 9 : 1) gave **29**

(0.068 g, 94.3%) as a colourless liquid. Found: C, 62.28; H, 6.30; N, 2.04. Calc. for $C_{35}H_{42}Cl_3NO_4Si$ C, 62.26; H, 6.27; N 2.07%; R_f 0.6 (hexane : ethyl acetate, 9 : 1); $[\alpha]_D^{25}$ + 40.2 (*c* 1.7, CH_2Cl_2); IR (neat) ν_{max}/cm^{-1} 3326, 2952, 1697, 1958, 1019; δ_H (400 MHz, $CDCl_3$) 0.01 (s, 6H, Si(CH_3)$_2$), 0.84 (s, 9H, C(CH_3)$_3$), 1.67–1.70 (m, 1H, H-1′), 1.74–1.78 (m, 1H, H-1″), 3.17 (dd, 1H, J = 4.4, 10.0 Hz, H-6), 3.31 (dd, 1H, J = 6.8, 10.0 Hz, H-6′), 3.72–3.82 (m, 3H), 4.23–4.28 (m, 2H), 5.64 (ddd, 1H, J = 2.2, 3.2, 10.2 Hz), 5.83 (bd, 1H, J = 10.2 Hz), 6.53 (d, 1H, J = 8.5 Hz, NH), 7.15–7.26 (m, 9H, C(C_6H_5)$_3$), 7.40–7.42 (m, 6H, C(C_6H_5)$_3$); δ_C (100 MHz, $CDCl_3$) –5.3, 18.2, 25.9, 36.6, 46.2, 59.3, 62.9, 68.0, 72.5, 86.8, 92.3, 122.9, 127.0, 127.8, 128.6, 134.0, 143.6, 161.2; HRMS (ESI): 672.1875 $[M - H]^-$. Calc. for $C_{35}H_{42}Cl_3NO_4Si$ $[M - H]^-$: 672.1870.

(2*R*,5*R*,6*S*)-2-(2-(*tert*-Butyldimethylsilyloxy)ethyl)-5-(2,2,2-trichloroacetamido)-6- (trityloxymethyl)tetrahydro-2*H*-pyran-3,4-diyl diacetate (30)

To a stirred solution of compound **29** (0.100 g, 0.148 mmol) in acetone : water : *t*-BuOH (4 mL, 1 : 1 : 0.5) at ambient temperature, were added NMO·H_2O (0.024 g, 0.178 mmol) and OsO_4 (a 25 mg ml^{-1} solution in ^{t}BuOH, 6 µL, 0.004 equiv.). The reaction mixture was stirred for 12 h and then it was treated with $Na_2S_2O_5$ (0.036 g, 0.192 mmol). The reaction mixture was stirred for a further 0.5 h and extracted with ethyl acetate (3 × 15 mL). The organic layer was washed with water and finally with brine. Evaporation of the organic layer gave a crude product which was dissolved in CH_2Cl_2 and treated with Ac_2O (0.04 mL, 0.444 mmol), Et_3N (0.06 mL, 0.444 mmol) and a catalytic amount of DMAP. The reaction mixture was stirred for 3 h and then extracted with CH_2Cl_2. The usual work up gave a crude product which after purification by column chromatography (hexane : ethyl acetate = 9 : 1) afforded **30** (0.104 g, 89%) as the major isomer along with 7% minor isomer. Found: C, 59.09; H, 6.11; N, 1.74. Calc. for $C_{39}H_{48}Cl_3NO_8Si$ C, 59.05; H, 6.10; N 1.77%; R_f 0.5 (hexane : ethyl acetate, 9 : 1); $[\alpha]_D^{25}$ + 19.3 (*c* 1.5, CH_2Cl_2); IR (neat) ν_{max}/cm^{-1} 3422, 2924, 1754, 1722, 1093; δ_H (400 MHz, $CDCl_3$) 0.00 (3H, s, SiCH_3), 0.01 (3H, s, SiCH_3), 0.83 (9H, s, C(CH_3)$_3$), 1.72–1.75 (1H, m, H-1′), 1.95 (3H, s, COCH_3), 1.97–2.01 (1H, m, H-1″), 2.08 (3H, s, COCH_3), 3.17 (1H, dd, J = 2.2, 10.4 Hz, H-6), 3.25 (1H, dd, J = 6.0, 10.4 Hz, H-6′), 3.71–3.79 (3H, m, H-5, H-2′, H-2″), 4.09–4.18 (2H, m, H-4, H-1), 5.16 (1H, br s, H-2), 5.30 (1H, dd, J = 2.9, 10.7 Hz, H-3), 6.31 (1H, d, J = 8.7 Hz, NH), 7.12–7.23 (9H, m, C(C_6H_5)$_3$), 7.38–7.40 (6H, m, C(C_6H_5)$_3$); δ_C (100 MHz, $CDCl_3$) –5.3, 18.2, 20.6, 20.9, 25.8, 31.5, 50.1, 58.7, 63.6, 68.2, 71.0, 71.9, 73.1, 86.7, 92.0, 127.0, 127.8, 128.6, 143.7, 161.7, 170.1, 170.7; HRMS (ESI): 790.2138 $[M - H]^-$. Calc. for $C_{39}H_{48}Cl_3NO_8Si$ $[M - H]^-$: 790.2137.

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