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Synthesis of some carbahexopyranoses using Mn/$CrCl_3$ mediated domino reactions and ring closing metathesis

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ABSTRACT

An efficient and common method for the synthesis of 5a-carba-α-D-mannopyranose **5**, 5a-carba-β-D-mannopyranose **6**, (+) methyl shikimate **9**, (+) methyl-5-*epi*-shikimate **10**, validamine analogue **15** and valiolamine analogue **16** from D-mannose, formal synthesis of Tamiflu **17** from D-ribose and also synthesis of 5a-carba-α-D-glucopyranose **1**, 5a-carba-β-D-glucopyranose **2**, 5a-carba-β-L-altropyranose **7** and 5a-carba-α-L-altropyranose **8** from D-xylose is described using Nozaki–Hiyama–Kishi (NHK) condition and ring closing metathesis (RCM). In this transformation 5-deoxy-5-halo-manno/ribo/xylo furanoside undergoes reductive elimination in the presence of Mn/$CrCl_3$ to give corresponding olefin-aldehyde which was trapped by nucleophile under the same condition to afford diolefinic species which on metathesis reaction with appropriate Grubbs catalyst produced required carbocycles.

1. Introduction

Carbasugars or pseudosugars are carbocyclic analogues of monosaccharides in which the ring oxygen is replaced by methylene.[1] If C-1 OH in carbasugars is replaced by amino group then they are called as aminocarbasugars. These compounds are excellent glycosidase inhibitors and shows interesting biological activity such as *anti*-cancer, *anti*-diabetic, *anti*-HIV, etc.[1,2]

Some of the important carbasugars and their derivatives are depicted in Fig. 1. Racemic pseudo-α-D-glucopyranose **1** shows inhibition of glucose stimulated-insulin release and islet glucokinase activity.[3] (±) Carbasugar **2** is a substrate of the cellobioside phosphorylase of *cellvibro gilvuse*,[4] and also the taste of (±) carba-β-DL-glucopyranose **2** is same as that of D-glucose.[5] Carba-glucotropaeolin **3** is a 5a-carba analogue of β-D-glucopyranose and is a good inhibitor of myrosinase.[6] Pseudo-sergliflozin **4** is a carba analogue of sergliflozin, a phase II drug and is a potent and selective inhibitor of sodium-dependent glucose cotransporter 2 (SGLT2) for the treatment of Type 2 diabetes and its IC_{50}=2.45 nm.[7] Shikimic acid is a key intermediate in the synthesis of aromatic amino acids by plants, fungi and microorganisms. Shikimic acid and their derivatives such as methyl shikimate **9** and methyl-5-*epi*-shikimate **10** are biologically important compounds.[8] Moreover several carbasugars and aminocarbasugars have been synthesised starting from shikimic acid and their intermediates.[1a]

Some of the important aminocarbasugars are depicted in Fig. 2. These are valienamine **11,** validamine **12** and valiolamine **13**, which are secondary metabolites of various microorganisms showing glycosidase inhibitory activity. Valiolamine **13** shows activity against maltase and sucrase.[9] Voglibose **14** is the chemical modification of valiolamine currently used for the treatment of diabetes.[10] Tamiflu **17** is related to aminocarbasugar structure and is widely used for the treatment of H5N1 influenza as well as H1N1 influenza.[11]

In continuation of our efforts towards the synthesis of carbohydrate mimics such as carbasugars,[12] aminocarbasugars[13] and iminosugars,[14] herein we report the synthesis of 5a-carba-α-D-mannopyranose **5**,[15] 5a-carba-β-D-mannopyranose **6**,[15b,c,d,h] (+) methyl shikimate **9**,[16] (+) methyl-5-*epi*-shikimate **10**,[16] validamine analogue **15**[13b,17a,b] and valiolamine analogue **16**[13b,17c,d] from D-mannose and formal synthesis of Tamiflu[18] from D-ribose. Also we present here synthesis of 5a-carba-α-D-glucopyranose **1**,[15a,b,c,19] 5a-carba-β-D-glucopyranose **2**,[9c,9e,15a,19g] 5a-carba-β-L-altropyranose **7**[19d,20] and 5a-carba-α-L-altropyranose **8**[21] from D-xylose. The key step in the synthesis of above molecules is one pot reductive ring opening of 5-deoxy-5-iodomanno/ribo/xylo furanoside and C–C bond formation using allyl bromide under NHK[22] condition to get the diene precursor for RCM reaction.[23]

2. Results and discussions

Reductive elimination of 5-deoxy-5-halofuranosides under Bernet-Vasella[24] protocol giving chiral 4-pentenals, has many

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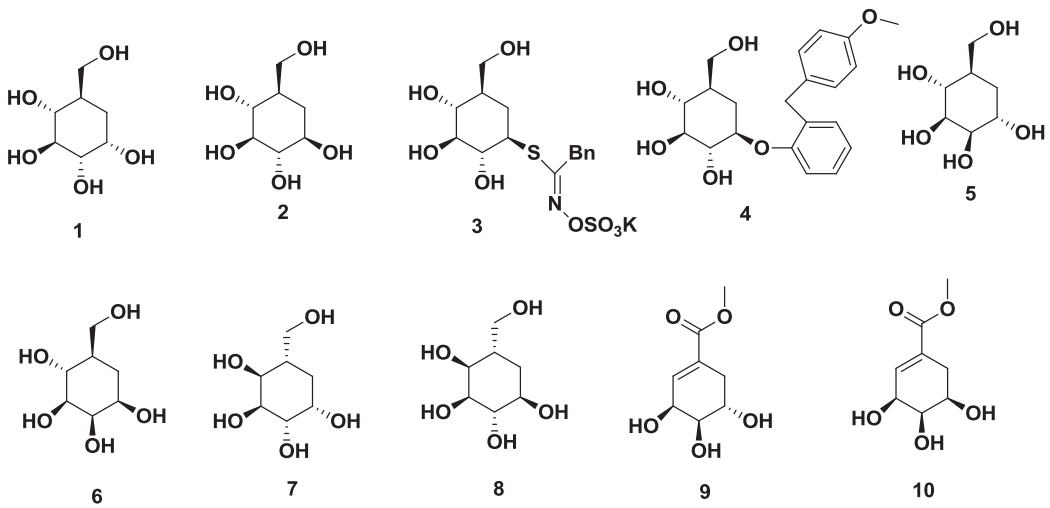


Fig. 1. Carbasugars and their derivatives.

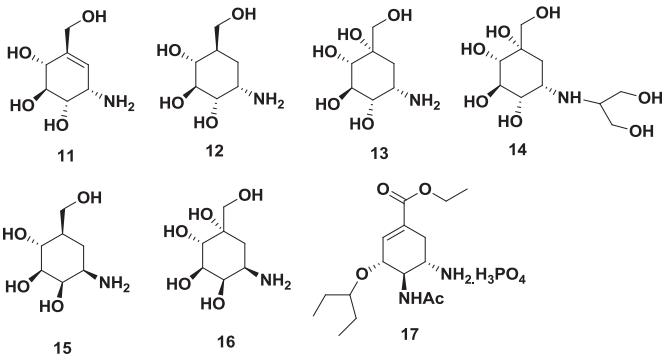
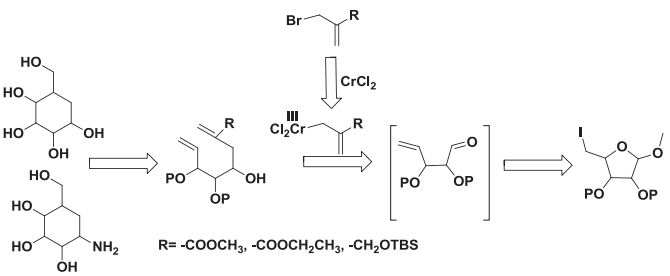


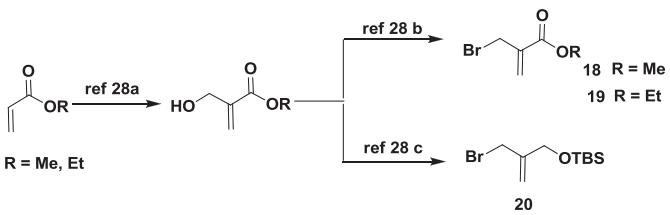
Fig. 2. Some important aminocarbasugars.

synthetic applications.[25] The reductive elimination can be carried out with different metallic reagents such as Zn,[24a,b] In,[25d] $CrCl_2$,[26a] SmI_2,[26b] $Mn/PbCl_2$,[26c] BuLi[24a,b] and acetyliron.[24g] Reductive ring opening of 5-deoxy-5-halofuranosides followed by intermolecular C–C bonding coupling in one pot have been performed by using Zn[25c–f] and In[25d] under ultrasonication. Our group has earlier developed $CrCl_3/Zn$ condition for the generation of olefin-aldehyde in which Zn is used for the conversion of $CrCl_3$ to $CrCl_2$ and the aldehyde was trapped by vinyl chromium (NHK reaction) to form diene precursor for the RCM, which was carried further for the synthesis of carbafuranoses.[12a] Later for this purpose,[12b] we utilized Furstner's modified NHK condition for the generation of $CrCl_2$ from $CrCl_3$ using Mn as reductant which remains inert throughout the reaction.[27] Herein we wish to describe the synthetic utility of our domino NHK and RCM strategy for the synthesis of various carbapyranoses from 5-deoxy-5-halo manno/ribo/xylo furanosides. The retrosynthetic analysis was depicted in Scheme 1.



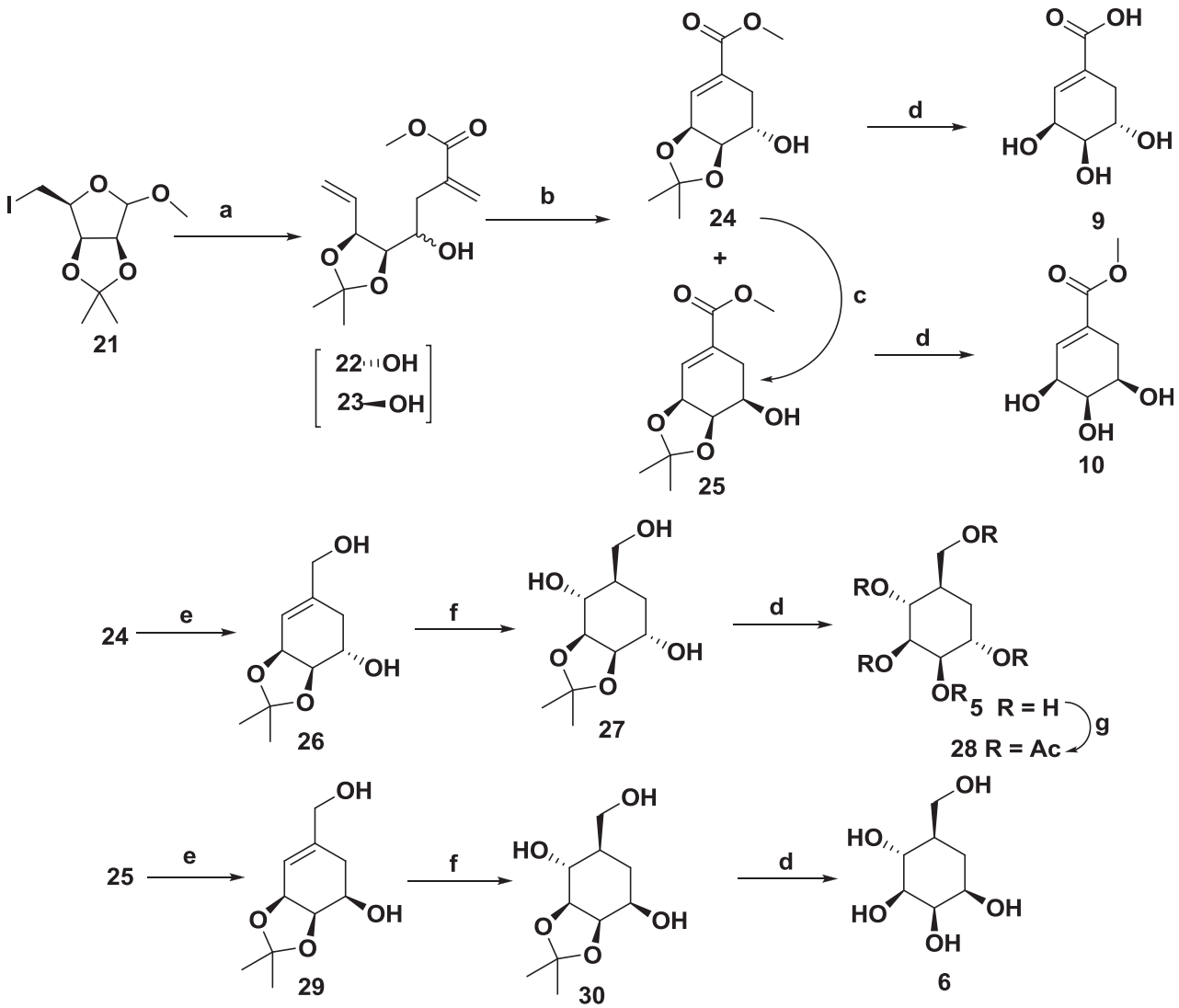
Scheme 1. Retrosynthetic analysis.

The 5-deoxy-5-iodo furanosides can be obtained from respective sugar such as mannose, ribose and xylose. The nucleophiles **18, 19** and **20** required for the NHK reaction are prepared from methyl/ethyl acrylate[28] (Scheme 2).



Scheme 2. Allyl nucleophiles for NHK reaction.

For the synthesis of (+) methyl shikimate **9**, (+) methyl-5-*epi*-shikimate **10**, pseudo-α-D-mannopyranose **5** and pseudo-β-D-mannopyranose **6** (Scheme 3), the iodo compound **21**[29] obtained from D-mannose was treated with $Mn/CrCl_3$ (20:1) for 8 h in THF/DMF. The change in colour from violet to pale blue confirmed the formation of $CrCl_2$. After the consumption of starting iodo compound (confirmed by TLC), catalytic amount of $NiCl_2$, methyl 2-(bromomethyl)acrylate **18** followed by TMSCl at 50 °C were added to carry out the NHK reaction. The reaction completed in 5 h and gave an inseparable mixture of diastereomers **22** and **23** in 1:1 ratio in 75% yield (over 2 steps). Mixture of **22** and **23** were reacted with Hoveyda-Grubbs second generation catalyst to afford compounds **24** and **25** in 96% yield which were separated using column chromatography. The compound **24** on oxidation with Dess–Martin periodinane followed by stereo selective reduction with $NaBH_4$ produced compound **25** exclusively. Though NHK reaction gave two diastereomeric alcohols in 1:1 ratio, the oxidation and reduction strategy provided a way for obtaining the single diastereomeric compound **25**. Deprotection of **24** and **25** independently using aqueous TFA afforded (+) methyl shikimate **9** and (+) methyl-5-*epi*-shikimate **10,** respectively. The physical and spectral data of compound **9**[16i,j] and **10**[16h] are in accordance with the reported values. For the synthesis of pseudo-α-D-mannopyranose **5** and pseudo-β-D-mannopyranose **6**, first the ester functionalities in compounds **24** and **25** were reduced using DIBALH to furnish alcohols **26** and **29**, respectively. Next the compounds **26** and **29** on stereoselective hydroboration/oxidation afforded triol compounds **27** and **30**, respectively. Deprotection of acetonide functionality in



Scheme 3. Synthesis of (+) methyl shikimate (9), (+) methyl-5-*epi*-shikimate (10), 5a-carba-α-D-mannopyranose (5) and 5a-carba-β-D-mannopyranose (6). Reagents and conditions: (a) $Mn/CrCl_3$ (20:1), THF:DMF (5:1), 8 h then $NiCl_2$ (cat), 18, TMSCl, 50 °C, 5 h, TBAF, rt, 5 h, 75%; (b) Hoveyda-Grubbs second generation catalyst, 1,2 dichloroethane, reflux, 3 h, 96%; (c) (i) Dess–Martin periodinane, DCM, rt, 1 h (ii) $NaBH_4$, MeOH, 0 °C, 1 h; (d) 50% aqueous CF_3COOH, rt, 4 h, 95% for (5) and (6), 98% for (9) and (10) (e) DIBAL-H, DCM, 0 °C, 2 h, 78%; (f) BH_3.DMS, THF 0 °C to rt, 2 h, then NaOH, H_2O_2, 0 °C, 2 h, 65%; (g) pyridine, Ac_2O, DMAP, 24 h, 70%.

compounds **27** and **30** using 50% aqueous TFA afforded pseudo-α-D-mannopyranose **5** and pseudo-β-D-mannopyranose **6,** respectively. Compound **5** was converting to its acetate derivative **28** for further confirmation. The physical and spectral data of compounds **5**,[15c] **28**[15c,g] and **6**[15d] are in good agreement with the reported values.

For the synthesis of validamine analogue **15** and valiolamine analogue **16** (Scheme 4), compounds **24** and **25** were treated with Dess–Martin periodinate to furnish unstable keto compound, which on reaction with hydroxylamine hydrochloride salt in ethanol and pyridine (1:1) afforded oxime **31**. Stereoselective reduction of oxime **31** with $NaBH_4$ in presence of MoO_3 afforded amine.[18a] The crude amine was treated with di-*tert*-butyl dicarbonate to furnish Boc protected amine compound **32**, which on reduction with DIBAL-H afforded **33**. Regio- and stereoselective reduction of **33** in presence of BH_3.DMS followed by $NaOH/H_2O_2$ afforded alcohol **34** exclusively. Deprotection of **34** using 50% aqueous TFA gave validamine analogue **15**. For the sake of proper characterization, the crude product **15** was peracetylated with acetic anhydride to give **35** in 90% yields over 2 steps, whose spectral data was in accordance with the reported values.[13b] The compound **33** on reaction with OsO_4 afforded trihydroxy compound **36**, which on deprotection with 50% aqueous TFA gave valiolamine analogue **16**. The crude compound on acetylation afforded peractylated compound **37** in 90% yield over 2 steps, whose physical and spectral data are in accordance with reported values.[17c,d]

After successfully applying our strategy on mannose (Scheme 3), we designed an approach for the formal synthesis of Tamiflu from D-ribose (Scheme 5). Earlier synthesis for the Tamiflu reported with the use of Zn and In metal mediated reductive ring opening of 5-deoxy-5-halo-ribofuranoside followed by C–C bond formation using ethyl 2-(bromomethyl)acrylate **19**[18] to give **39** and **40** under ultrasonication. The above reaction also gave bi products[18a] posing problem in isolation of the product in pure form, and also ultrasonication condition is not practical for higher scale synthesis. To study the product formation in our condition, we carried the reductive elimination of **38** and allylation using substituted allyl halide **19**. 5-deoxy-5-iodo-ribosyl compound **38** obtained from D-ribose[18a] was treated with ethyl 2-(bromomethyl)acrylate **19** under standard $Mn/CrCl_3$ mediated domino NHK condition. The reaction completed in 5 h and yielded diastereomeric mixture of compounds **39** and **40** in 1:1 ratio without any visible impurities on the

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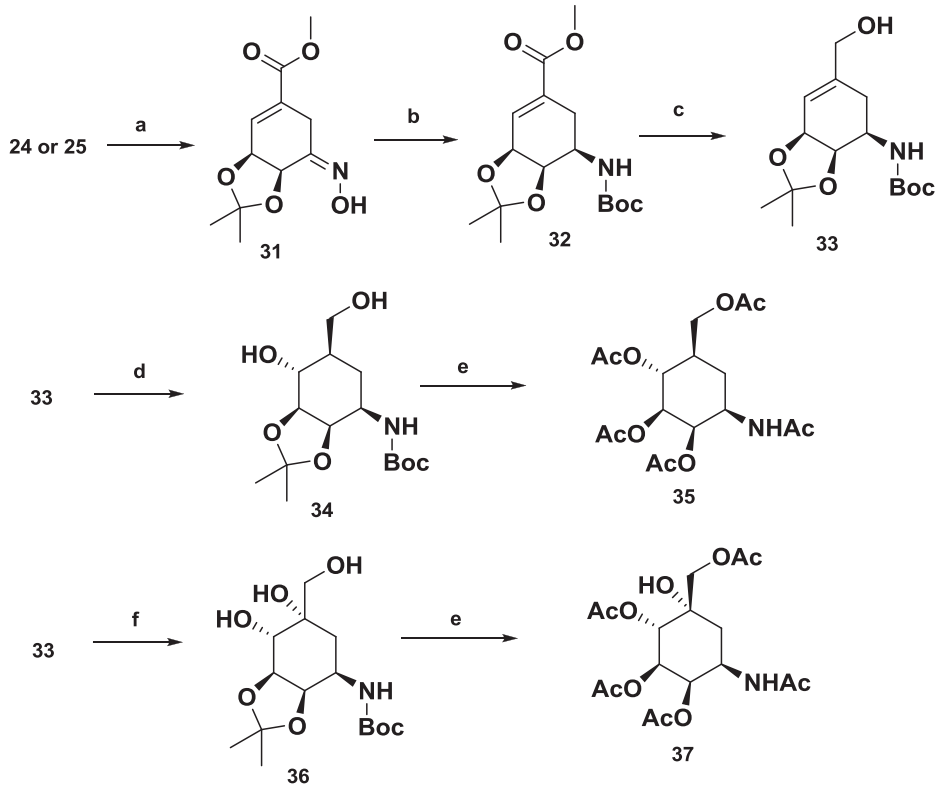
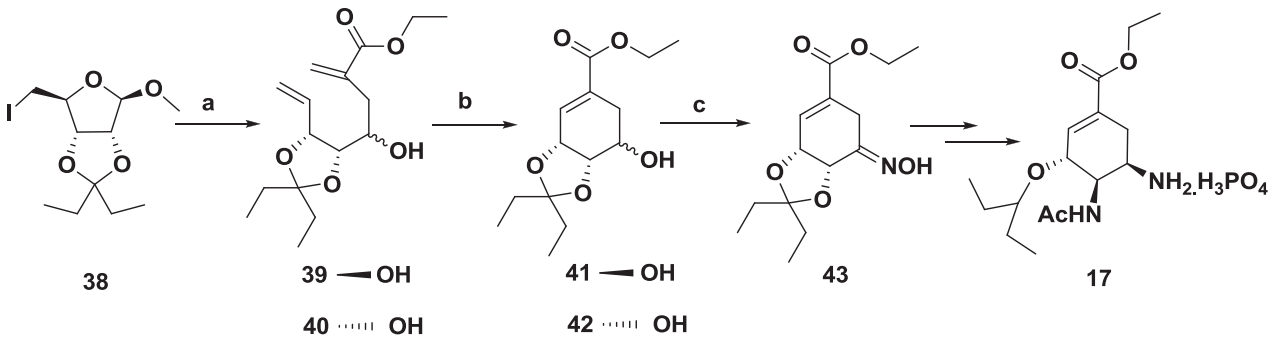


Scheme 4. Synthesis of validamine analogue 15 and valiolamine analouge 16. Reagents and conditions: (a) (i) Dess–Martin periodinane, DCM, rt, 1 h (ii) $NH_2OH{\cdot}HCl$, EtOH, Py, rt, 2 h, 70% (over 2 steps); (b) (i) MoO_3, $NaBH_4$, MeOH, 0 °C, 1 h, di-*tert*-butyl diocarbonate, 2 h, 70% (over 2 steps); (c) DIBAL-H in toluene, DCM, 0 °C, 2 h, 78%; (d) BH_3.DMS, THF 0 °C to rt, 2 h, then NaOH, H_2O_2, 0 °C, 2 h, 65% (e) (i) 50% aqueous CF_3COOH, rt, (ii) Ac_2O, Py, rt, 2 h, 90%; (f) OsO_4, NMO, acetone: water (4:1), 0 °C, 2 h, 90%.



Scheme 5. Formal synthesis of Tamiflu. Reagents and conditions: (a) $Mn/CrCl_3$ (20:1), THF:DMF (5:1), 8 h then $NiCl_2$ (cat), 19, TMSCl, 50 °C, 5 h, TBAF, rt, 2 h, 75%; (b) Hoveyda-Grubbs second generation catalyst, 1,2 dichloroethane, reflux, 3 h, 92%; (c) Dess–Martin periodinane, DCM, rt, 1 h, $NH_2OH{\cdot}HCl$, Py, rt, 2 h, 70%.

TLC, the products were well purified by simple column chromatographic technique. This method is useful for the scaling up of intermediate compounds **39** and **40** for the synthesis of Tamiflu **17**, which doesn't require any ultrasound assistance. Ring closing metathesis of diolefinic compounds **39** and **40** using Hoveyda-Grubbs catalyst second generation gave products **41** and **42,** respectively. Oxidation of secondary alcohol in **41** and **42** using Dess–Martin periodinane gave unstable ketone which on reaction with hydroxylamine hydrochloride salt in pyridine solvent afforded oxime **43** required for the synthesis of Tamiflu **17**.[18a]

Most of the carbasugars have pendant hydroxymethyl group in their structure. Generally in the carbasugar synthesis the hydroxymethyl group was introduced by reduction of corresponding ester. To avoid the reduction step and to get directly hydroxymethyl on carbasugar core structure, we prepared NHK precursor **20** as a nucleophile, and utilized this for the synthesis of pseudo-α-D-glucopyranose (**1**), pseudo-β-D-glucopyranose (**2**), 5a-carba-β-L-altropyranose (**7**) and 5a-carba-α-L-altropyranose (**8**) starting from D-xylose (Scheme 6). The 5-deoxy-5-iodo xylofuranose compound **44** was prepared from D-xylose in 3 steps.[30] The compound **44** on reaction with allyl nucleophile **20** under standard domino reductive ring opening, followed by allylation under $Mn/CrCl_3$ (NHK reaction) conditions afforded compounds **45** and **46** in 1:1 ratio. In the Fursntner's modified NHK condition[27] one has to use TBAF to deprotect the OTMS to get OH. Here in this case, TBAF will deprotect both the OTMS and OTBS groups. Therefore here we used 1N HCl for work up which could deprotect the OTMS group selectively giving rise to compounds **45** and **46**. The stereochemistry of the newly generated chiral centre in **45** and **46** were assigned after cyclisation in presence of Grubbs second generation catalyst which afforded compounds **47** and **48**. The stereochemistry of the newly created centre C-1 of **47** was ascertained by analyzing coupling constants for 6a-H (2.05, 1H, m, major couplings J=9.4 Hz, 17.0 Hz), 6e-H (2.40, dd, 1H, J=5.9 Hz, 17.0 Hz) and 1a-H (3.76, m, 1H, one of coupling

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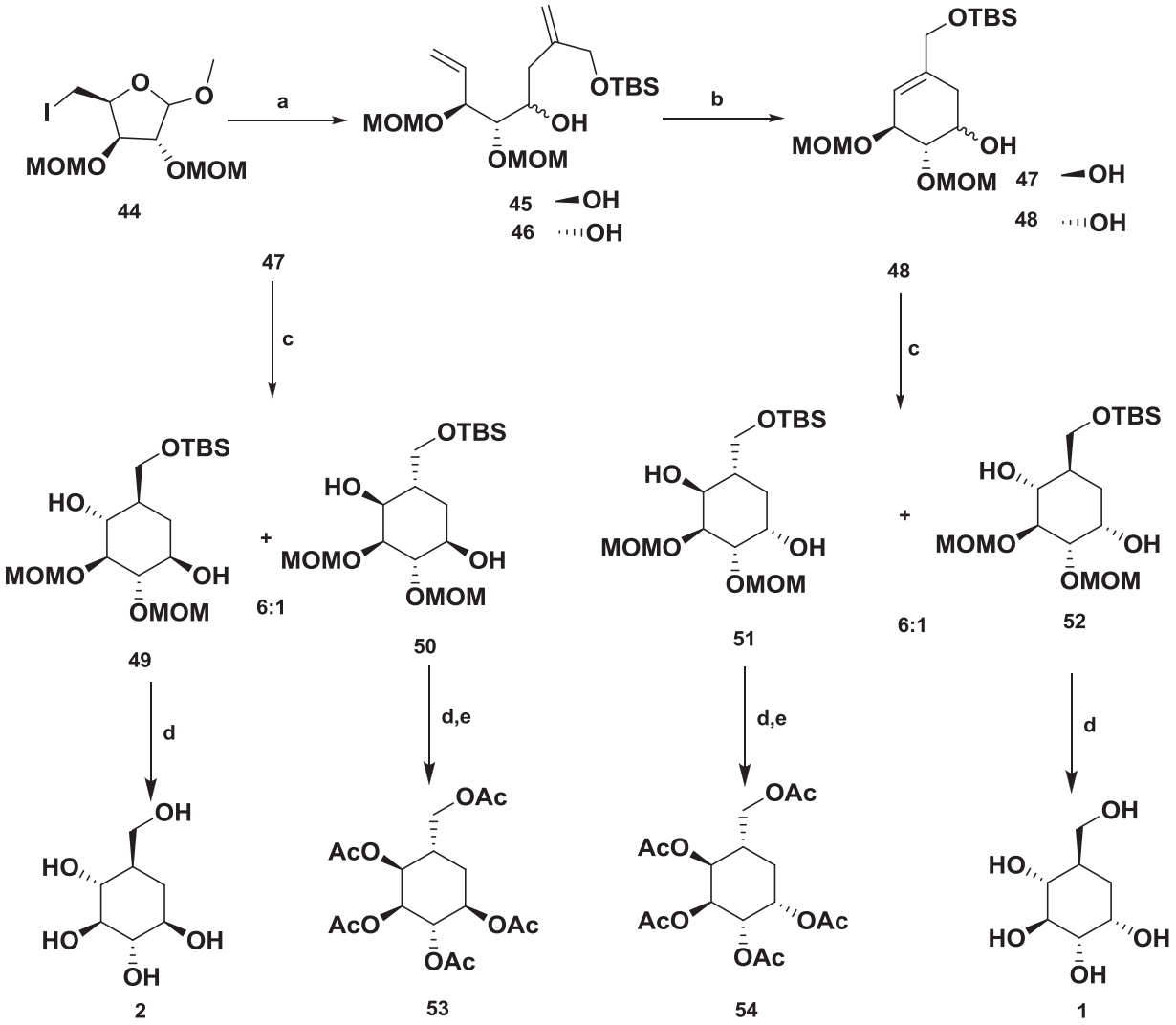

Scheme 6. Synthesis of 5a-carba-α-D-glucopyaranose 1, 5a-carba-β-D-glucopyaranose 2, 5a-carba-β-L-altropyranose 7 and 5a-carba-α-L-altropyranose 8. Reagents and conditions: (a) $Mn/CrCl_3$ (20:1), THF:DMF (5:1), 8 h then $NiCl_2$ (cat), 20, TMSCl, 50 °C, 5 h, 1N HCl, rt, 2 h, 75%; (b) Grubbs second generation catalyst, toluene, reflux, 3 h, 90%; (c) BH_3.DMS, THF 0 °C to rt, 2 h, then NaOH, H_2O_2, 0 °C, 2 h, 70%; (d) 6N MeOH (HCl), reflux, 1 h, 95% quantitative; (e) pyridine, Ac_2O, DMAP, 12 h, 95%.

J=9.4 Hz) suggesting the orientation of hydroxyl group in equitorial in six membered skeleton. Similarly the stereochemistry at C-1 of **48** was ascertained by analyzing the coupling constants for 6a-H (2.11, dd, 1H, *J*=7.1, 17.3), 6e-H (2.28, dd, 1H, *J*=4.8 Hz, 17.3 Hz) and 1e-H (3.77, dd, 1H, *J*=2.2 Hz, 4.8 Hz) suggesting the orientation of hydroxyl group is axial. Hydroboration-oxidation of olefin compound **47** using BH_3.DMS followed by NaOH/H_2O_2 afforded **49** and **50** in 6:1 ratio. Deprotection of **49** afforded pseudo-β-D-glucopyranose **2** whose data was in good accordance with the reported values.[9c] Deprotection of **50** afforded pseudo-α-L-altropyranose **8**, which was confirmed by converted to peracetyl derivative **53**, whose data was in good agreement with the literature values.[21a] Hydroboration-oxidation of olefin compound **48** using BH_3.DMS followed by NaOH/H_2O_2 treatment gave **51** and **52** in 6:1 ratio. Deprotection of **51** afforded pseudo-β-L-altropyranose **7** which was converted to peracetyl derivative **54**, whose data are also in good agreement with the reported values.[20b] Deprotection of **52** afforded pseudo-α-D-glucopyranose **1**, the physical and spectral data of **1** are in good accordance with the reported values.[15c] Here, noteworthy to mention is the facial selectivity of BH_3.DMS reduction of olefin, which was decided by the chirality at C-1 position. Major product being formed is *anti* to the existing C-1 hydroxy chiral centre.

3. Conclusions

We have developed an efficient method for the synthesis of various carbasugars and aminocarbasugars using domino reductive ring opening of 5-deoxy-5-halo furanosides followed by allylation for getting diolefinic species under NHK condition followed by RCM. This method is highly useful and convenient for the synthesis of different carbapyranoses and their analogues from cheaply available sugars in a short possible route in good overall yields.

4. Experimental

4.1. General information

All reactions are carried under nitrogen atmosphere in oven dried glassware equipped with magnetic stirrer and rubber septum unless otherwise indicated. All solvents are freshly distilled before use; THF over sodium and benzophenone; DCM over calcium hydride. All other commercial reagents were used without further purification, unless otherwise noted. Reactions were monitored by thin layer chromatography (TLC) of aliquots using glass sheets coated (0.25 mm layered thickness) with silica gel F_{254} (Merck

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Kiesel gel 60). TLC plates are viewed under UV light and charred with phosphomolybdic acid. Column chromatographies were carried out with silica gel 60–120 mesh or 100–200 mesh (Merck). NMR spectra were recorded in deuterated solvents on 300 MHz or 400 or 500 MHz or 600 MHz spectrometer at ambient temperature. Chemical shifts δ is given in ppm, coupling constant J are in Hz. The chemical shifts are reported in ppm on scale downfield from TMS as internal standard and signal patterns are indicated as follows: s, singlet; d, doublet; t, triplet; m, multiplet; br, broad peak. FTIR recorded as neat. Optical rotations were measured on polarimeter using a 1 mL cell with a one dm path length. For High (HRMS) resolution, *m/z* ratios are reported as values in atomic mass units.

*4.1.1. (S)-Methyl 4-((4R,5S)-2,2-dimethyl-5-vinyl-1,3-dioxolan-4-yl)-4-hydroxy-2-methylenebutanoate (**22**) and (R)-methyl 4-((4R,5S)-2,2-dimethyl-5-vinyl-1,3-dioxolan-4-yl)-4-hydroxy-2-methylenebutanoate (**23**).* To a flame dried two-necked round bottom flask, $CrCl_3$ (0.603 g, 3.81 mmol) and powdered activated Mn (4.19 g, 76.2 mmol) were taken in THF/DMF (21 mL/6 mL) and stirred for 2 h at rt under an inert atmosphere until the colour changed from violet to green. Compound **21** (0.8 g, 2.54 mmol) in THF (9 mL) was slowly added to it and stirred for 8 h. When TLC showed the absence of starting material, $NiCl_2$ (32 mg, 0.25 mmol) was added to the reaction mixture and stirred for 30 min. Then allyl bromo compound **18** (0.76 mL, 6.35 mmol) followed by TMSCl (0.48 mL, 3.18 mmol) were added. The reaction mixture was allowed to stir for an additional 5 h at 50 °C and diluted with diethyl ether (70 mL). Next, n-Bu_4NF (5 mL, 1M in THF, 5.08 mmol) was added and stirred at rt for 2 h. The reaction mixture was filtered through a pad of Celite using sintered funnel, concentrated and purified by column chromatography using ethyl acetate/hexane (2:8) to afford a mixture of **22** and **23** (489 mg, 75%) in a 1:1 ratio (by ^{1}H NMR) as a yellow oil, $[\alpha]_D^{20}$: +21° (*c* 1.1, $CHCl_3$); **IR** (Neat) ν_{max}: 3395, 2989, 2929, 1719, 1632, 1511, 1211, 750 cm^{-1}, **^{1}H NMR**, (400 MHz, $CDCl_3$): δ 1.37 (s, 3H), 1.40 (s, 3H), 1.50 (s, 3H), 1.53 (s, 3H), 2.34–2.46 (m, 2H), 2.55 (dd, 1H, *J*=3.2 Hz, 14.2 Hz), 2.87 (dd, 1H, *J*=2.9 Hz, 14.1 Hz), 3.76 (s, 3H), 3.78 (s, 3H), 3.75–3.81 (m, 2H), 3.97 (dd, 1H, *J*=6.2 Hz, 8.5 Hz), 4.07 (dd, 1H, *J*=4.2 Hz, 6.8 Hz), 4.62 (t, 1H, *J*=7.2 Hz), 4.68 (t, 1H, *J*=6.6 Hz) 5.26–5.44 (m, 4H), 5.71 (s, 1H), 5.75 (s, 1H), 5.99–6.11 (m, 2H), 6.27 (d, 1H, *J*=1.4 Hz), 6.28 (d, 1H, *J*=1.4 Hz); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 24.8, 25.3, 27.1, 27.6, 36.6, 36.9, 51.8, 52.1, 68.1, 69.1, 78.6, 79.0, 80.0, 80.0, 108.5, 108.6, 117.7, 119.5, 127.9, 128.4, 133.8, 134.0 136.4, 136.6, 167.5, 168.7; **HRMS** (ESI, Orbitrap) *m/z*: calcd for $C_{13}H_{20}O_5Na$ 279.1202, found 279.1199.

4.2. Experimental procedure for ring closing metathesis reaction

To the diastereomeric mixture of compounds **22** and **23** (470 mg, 1.83 mmol) in anhydrous 1,2 dichloro ethane (15 mL) under a nitrogen atmosphere, was added Hoveyda-Grubbs second generation catalyst (22 mg, 0.036 mmol) and the reaction mixture was refluxed for 2 h. After completion of the reaction, the reaction mixture was evaporated at reduced pressure to give a crude residue, which was purified by column chromatography using 100–200 silica gel mesh eluated by ethyl acetate/hexane (1.5:8.5: to 3:7) to give compounds **24** (200 mg, 47.8%) and **25** (200 mg, 47.8%) as yellow oils.

*4.2.1. (3aS,7S,7aR)-Methyl 7-hydroxy-2,2-dimethyl-3a,6,7,7a-tetrahydrobenzo[d][1,3]dioxole-5-carboxylate (**24**).* $[\alpha]_D^{20}$: +122.5° (*c* 1.0, $CHCl_3$); **IR** (Neat) ν_{max}: 3499, 2988, 2921, 2310, 1715, 1656, 1511, 1438, 1245, 1216, 1053, 770 cm^{-1}, **^{1}H NMR**, (300 MHz, $CDCl_3$): δ 1.33 (s, 3H), 1.38 (s, 3H), 2.18 (dd, 1H, *J*=7.9 Hz, 16.9 Hz), 2.73 (dd, 1H, *J*=4.5 Hz, 16.9 Hz), 3.7 (s, 3H), 3.84 (m, 1H), 4.03 (t, 1H, *J*=6.9 Hz), 4.68 (br s, 1H), 6.85 (s, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 25.7, 27.9, 29.3, 52.1, 68.7, 72.2, 77.8, 109.6, 130.5, 133.9, 166.5; **HRMS** (ESI, Orbitrap) *m/z*: calcd for $C_{11}H_{16}O_5Na$ 251.0889, found 251.0886.

*4.2.2. (3aS,7R,7aR)-Methyl 7-hydroxy-2,2-dimethyl-3a,6,7,7a-tetrahydrobenzo[d][1,3]dioxole-5-carboxylate (**25**).* $[\alpha]_D^{20}$: −21.2° (*c* 1.1, $CHCl_3$) {lit.[15d] $[\alpha]_D$: −23.93° (*c* 1.1, MeOH); **IR** (Neat) ν_{max}: 3434, 2987, 2952, 2851, 1712, 1651, 1438, 1376, 1297, 1238, 1094, 742 cm^{-1}, **^{1}H NMR**, (300 MHz, $CDCl_3$): δ 1.39 (s, 3H), 1.41 (s, 3H), 2.25 (br s, -OH), 2.51 (m, 1H), 2.65 (dd, 1H, *J*=4.5 Hz, 16.6 Hz), 3.78 (s, 3H), 3.95 (m, 1H), 4.42 (dd, 1H, *J*=2.2 Hz, 3.0 Hz), 4.73 (br s, 1H), 6.78 (s, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 25.9, 27.3, 27.7, 52.0, 66.8, 72.8, 75.4, 109.9, 129.1, 134.7, 166.7; **HRMS** (ESI, Orbitrap) *m/z*: calcd for $C_{11}H_{16}O_5Na$ 251.0889, found 251.0883.

*4.2.3. Conversion compound 24 to compound **25**.* To a solution of **24** (50 mg, 0.21 mmol) in DCM (5 mL) were added Dess–Martin periodinane (186 mg, 3.5 mmol) at rt for 1 h. After consumption of the starting material, the reaction was being quenched by adding saturated hypo solution (2 mL) followed by saturated $NaHCO_3$ (2 mL). The organic layer was extracted with DCM (3 mL×3), the combined fractions were collected and dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give crude product. The crude ketone was unstable and proceeded for next reaction without further purification. To the ketone dissolved in MeOH (2 mL) was added $NaBH_4$ (15.8 mg, 0.42 mmol) at 0 °C and stirred for 1 h. The reaction quenched by adding saturated NH_4Cl (2 mL) and the MeOH was removed using rotavapor followed by extraction of the aqueous layer with EtOAc (10×3 mL). The combined organic fractions were collected and dried over Na_2SO_4 to give crude **25**. Purification by column chromatography using ethyl acetate: hexane (1:5) as eluent gave **25** (35 mg, 70%) as an oil.

*4.2.4. (+)Methyl shikimate (**9**).* To the compound **24** (20 mg, 0.1 mmol) was added aqueous CF_3COOH (3 mL, 1:1 v/v) at ice-cold temperature and stirred at room temperature for 4 h. After completion of the reaction, the solvent was evaporated under reduced pressure to give crude compound **9** which was purified by column chromatography using MeOH:$CHCl_3$ (0.3:9.7) to afford pure compound **9** as a white solid (19 mg, 95%), mp 107–108 °C (lit.[16i,j] 113–115 °C). The physical and spectroscopic data of compound **9** were in exact agreement with the reported literature values.[16i,j] $[\alpha]_D^{20}$: +137° (*c* 0.84, MeOH) {lit.[16j] $[\alpha]_D$: +139° (*c* 0.4, MeOH); **IR** (Neat) ν_{max}: 3394, 2924, 2853, 1714, 1654, 1438, 1375, 1251, 1066 cm^{-1}, **^{1}H NMR**, (300 MHz, CD_3OD): δ 2.2 (dd, 1H, *J*=4.7 Hz, 17.9 Hz), 2.69 (dd, 1H, *J*=4.3 Hz, 17.9 Hz), 3.69 (m, 1H), 3.74 (s, 3H), 3.99 (dd, 1H, *J*=5.2 Hz, 11.7 Hz), 4.37 (br s, 1H), 6.8 (br s, 1H); **^{13}C NMR** (75 MHz, CD_3OD): δ 31.5, 52.4, 67.2, 68.4, 72.5, 130.2, 139.1, 168.7; **HRMS** (ESI, Orbitrap) *m/z*: calcd for $C_8H_{12}O_5Na$ 211.0576, found 211.0580.

*4.2.5. (+)Methyl 5-epi-shikimate (**10**).* Experimental procedure is similar to compound **9** synthesis. The crude product is purified by column chromatography eluated by using MeOH:$CHCl_3$ (0.3:9.7) to give pure **10** as a white solid (95%) mp 120–121 °C (lit.,[16h] 122–123 °C), $[\alpha]_D^{20}$: +51.5° (*c* 0.75, EtOH) {lit.[16h] $[\alpha]_D$: +53.7° (*c* 0.88, EtOH) the physical and spectral properties are in accordance with the literature values.;[16h] **IR** (Neat) ν_{max}: 3409, 2923, 2853, 1708, 1651, 1438, 1375, 1249, 1238, 1151, 1034 cm^{-1}, **^{1}H NMR**, (500 MHz, acetone-d_6): δ 2.38 (m, 1H), 2.49 (dd, 1H, *J*=5.4 Hz, 17.2 Hz), 3.7 (s, 3H), 3.86 (m, 1H), 3.94 (m, 1H), 4.30 (br s, 1H), 6.65 (br s, 1H); **^{13}C NMR** (125 MHz, CD_3COCD_3): δ 31.3, 52.9, 69.9, 70.2, 72.7, 130.2, 140.9, 168.3; **HRMS** (ESI, Orbitrap) *m/z*: calcd for $C_8H_{12}O_5Na$ 211.0576, found 251.0576.

*4.2.6. (3aR,4S,7aS)-6-(Hydroxymethyl)-2,2-dimethyl-3a,4,5,7a-tetrahydrobenzo[d][1,3]dioxol-4-ol (**26**).* To the compound **24** (100 mg,

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0.438 mmol) in DCM (5 mL) was added DIBAL-H (0.62 mL, 1.09 mmol) 25% w/v in toluene at −5 °C and stirred for 2 h. After completion of the reaction MeOH (1 mL) was added to quench the excess DIBAL-H followed by saturated potassium sodium tartarate (10 mL) and saturated NH_4Cl (5 mL). Mixture is extracted using ethylacetate (3×20 mL), all the organic fractions were collected and dried over Na_2SO_4, solvent was removed under reduced pressure using rotavapour. The crude product was purified by column chromatography using as ethylacetate: hexane (7.5:2.5) as eluent to give **26** as an oil, (67 mg, 78%). $[\alpha]_D^{20}$: +84.5° (*c* 1.42, $CHCl_3$); **IR** (Neat) ν_{max}: 3609, 3394, 2922, 2852, 1679, 1657, 1458, 1376, 1216, 1050, 772 cm^{-1}, **^{1}H NMR**, (600 MHz, $CDCl_3$): δ 1.40 (s, 3H), 1.48 (s, 3H), 2.05 (dd, *J*=6.0 Hz, 16.9 Hz), 2.35 (dd, 1H, *J*=4.1 Hz, 16.9 Hz), 3.84 (dd, 1H, *J*=8.6 Hz, 13.5 Hz), 4.01 (t, 1H, *J*=7.9 Hz), 4.07 (s, 2H), 4.66 (br s, 1H), 5.84 (s, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 25.8, 28.2, 31.2, 65.5, 69.3, 72.6, 79.1, 109.3, 118.1, 140.8; **HRMS** (ESI, Orbitrap) *m/z*: calcd for $C_{10}H_{16}O_4Na$ 223.0940, found 223.0936.

*4.2.7. (3aS,4R,7S,7aR)-5-(Hydroxymethyl)-2,2-dimethylhexa hydrobenzo[d][1,3]dioxole-4,7-diol (**27**).* To the compound **26** (60 mg, 0.3 mmol) in THF (5 mL), $BH_3{\cdot}Me_2S$ (0.08 mL, 0.9 mmol) was added drop wise at 0 °C, stirring continued for 2 h at rt. Then NaOH (3N, 0.5 mL) followed by H_2O_2 (30%, 0.5 mL) solution were added at 0 °C and stirring continued for 30 min at the same temperature. The reaction mixture was diluted with EtOAc, washed with water, brine, dried (Na_2SO_4), purified by column chromatography using MeOH: $CHCl_3$ (0.2: 9.8) as the eluent to give **27** as an oil (42 mg, 65%). $[\alpha]_D^{20}$: −16.2° (*c* 0.86, MeOH); **IR** (Neat) ν_{max}: 3668, 3439, 2922, 2852, 1377, 1166, 1066, 722 cm^{-1}, **^{1}H NMR**, (500 MHz, CD_3OD): δ 1.35 (s, 3H), 1.47 (s, 3H), 1.64 (m, 1H), 1.76 (m, 1H), 1.83 (m, 1H), 3.52 (dd, 1H, *J*=7.6 Hz, 10.5 Hz), 3.62 (dd, 1H, *J*=5.6 Hz, 10.8 Hz), 3.67 (dd, 1H, *J*=4.5 Hz, 10.8 Hz), 4.0 (dd, 1H, *J*=5.9 Hz, 7.6 Hz), 4.04 (dd, 1H, *J*=3.5 Hz, 8.0 Hz), 4.11 (dd, 1H, *J*=3.6 Hz, 5.0 Hz); **^{13}C NMR** (100 MHz, CD_3OD): δ 26.6, 28.4, 31.1, 38.8, 64.2, 67.7, 73.9, 80.2, 81.9, 109.9; **HRMS** (ESI, Orbitrap) *m/z*: calcd for $C_{10}H_{18}O_5Na$ 241.1046, found 241.1042.

*4.2.8. Pseudo-α-D-mannopyranose (**5**).* To the compound **25** (30 mg, 0.13 mmol) was added aqueous CF_3COOH (3 mL, 1:1 v/v) at ice-cold temperature and stirred at room temperature for 4 h. After completion of the reaction, the solvent was evaporated under reduced pressure to give compound **5** as an oil (23 mg, 95%), The physical and spectroscopic data of compound **5** were in exact agreement with the reported literature values.[15c] $[\alpha]_D^{20}$: +2.5° (*c* 0.75, MeOH) {lit.[15c] $[\alpha]_D$: +1.9° (*c* 1.08, MeOH); **IR** (Neat) ν_{max}: 3389, 2922, 2853, 1461, 1219, 1120, 1048, 722 cm^{-1}, **^{1}H NMR**, (300 MHz, D_2O): δ 1.61–1.85 (m, 3H), 3.51 (t, 1H, *J*=9.8 Hz), 3.58–3.73 (m, 3H), 3.89 (br s, 1H), 3.96 (br s, 1H); **^{13}C NMR** (125 MHz, D_2O): δ 28.9, 39.3, 63.1, 69.6, 70.8, 72.9, 73.2; **HRMS** (ESI, Orbitrap) *m/z*: calcd for $C_7H_{14}O_5Na$ 201.0733, found 201.0729.

*4.2.9. (1S,2R,3S,4R,5R)-5-(Acetoxymethyl)cyclohexane-1,2,3,4-tetrayl tetraacetate (**28**).* To a solution of compound **5** (10 mg, 0.05 mmol) in pyridine (2 mL) were added acetic anhydride (0.05 mL, 0.56 mmol) and a few crystals of DMAP (cat) and the reaction mixture was stirred for 24 h at room temperature. After completion of the reaction 1 mL of aqueous NH_4Cl was added. The aqueous phase is extracted with DCM (3×5 mL). The combined organic layers were collected dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give a residue. The residue was purified on a column (ethyl acetate: hexane=1:4) to afford **28** as a white solid (15 mg, 70%) mp 77 °C (lit.,[15c] 80 °C). $[\alpha]_D^{20}$: +29° (*c* 1.0, $CHCl_3$) {lit.[15c] $[\alpha]_D$: +27.1° (*c* 3.95, $CHCl_3$). The physical and spectral properties are in accordance with the reported values.[15g]; **IR** (Neat) ν_{max}: 3610, 2956, 2925, 1738, 1514, 1369, 1217, 1042, 720 cm^{-1}, **^{1}H NMR**, (500 MHz, $CDCl_3$): δ 1.81–1.92 (m, 2H), 1.96 (s, 3H), 2.02 (s, 3H), 2.05 (s, 3H), 2.10 (s, 3H), 2.12 (s, 3H), 2.23 (m, 1H), 3.93 (dd, 1H, *J*=3.8 Hz, 11.4 Hz), 4.09 (dd, 1H, *J*=5.6 Hz, 11.4 Hz), 5.01 (dd, 1H, *J*=3.0 Hz, 6.4 Hz), 5.16–5.23 (m, 2H), 5.29 (m, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 20.9, 20.9, 21.0, 21.1, 21.2, 27.7, 35.8, 63.9, 68.5, 69.2, 69.5, 71.0, 169.5, 169.5, 170.2, 170.3, 171.0; **HRMS** (ESI, Orbitrap) *m/z*: calcd for $C_{17}H_{24}O_{10}Na$ 411.1261, found 411.1247.

*4.2.10. (3aR,4R,7aS)-6-(Hydroxymethyl)-2,2-dimethyl-3a,4,5,7a-tetrahydrobenzo[d][1,3]dioxol-4-ol (**29**).* Experimental procedure for the preparation of **29** is similar to compound **26** preparation. $[\alpha]_D^{20}$: −2.0° (*c* 1.38, $CHCl_3$); **IR** (Neat) ν_{max}: 3611, 3395, 2922, 2852, 1691, 1550, 1514, 1214, 1041, 749 cm^{-1}, **^{1}H NMR**, (500 MHz, $CDCl_3$): δ 1.39 (s, 3H), 1.42 (s, 3H), 2.18 (dd, *J*=4.4 Hz, 16.2 Hz), 2.32 (dd, 1H, *J*=8.2 Hz, 16.2 Hz), 2.82 (br s, -OH), 3.92–3.96 (m, 1H), 4.05 (s, 2H), 4.35 (dd, 1H, *J*=2.7 Hz, 6.1 Hz), 4.64 (s, 1H), 5.72 (s, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 25.8, 27.2, 29.2, 65.6, 66.7, 72.7, 75.5, 109.3, 119.5, 138.2; **HRMS** (ESI, Orbitrap) *m/z*: calcd for $C_{10}H_{16}O_4Na$ 223.0940, found 223.0936.

*4.2.11. (3aS,4R,5R,7R,7aR)-5-(Hydroxymethyl)-2,2-dimethylhexa hydrobenzo[d][1,3]dioxole-4,7-diol (**30**).* Experimental procedure for preparation of compound **30** is similar to compound **27** preparation $[\alpha]_D^{20}$: −6.8° (*c* 0.92, MeOH); **IR** (Neat) ν_{max}: 3419, 2924, 2854, 1463, 1379, 1264, 1220, 1072 cm^{-1}, **^{1}H NMR**, (500 MHz, CD_3OD): δ 1.36 (s, 3H), 1.46 (m, 1H), 1.51(s, 3H), 1.58 (q, 1H, *J*=12.0 Hz), 1.82 (m, 1H), 3.48–3.57 (m, 2H), 3.72 (dd, 1H, *J*=4.2 Hz, 10.6 Hz), 3.89 (dd, 1H, *J*=5.1 Hz, 7.4 Hz), 3.93 (m, 1H), 4.33 (t, 1H, *J*=4.5 Hz); **^{13}C NMR** (100 MHz, CD_3OD): δ 26.5, 28.5, 31.1, 42.0, 64.3, 68.9, 74.3, 78.5, 83.3, 110.5; **HRMS** (ESI, Orbitrap) *m/z*: calcd for $C_{10}H_{18}O_5Na$ 241.1046, found 241.1045.

*4.2.12. Pseudo-β-D-mannopyranose (**6**).* Experimental procedure for the preparation of compound **6** is similar to the compound **5** preparation to give solid compound **6** (95%), mp 218–219 °C, {lit.[15d] 223 °C} $[\alpha]_D^{20}$: +12.5 (*c* 0.42, MeOH), {lit.[15e] $[\alpha]_D$: +11.9° (*c* 0.65, MeOH) the physical and spectral data are in good agreement with the reported values.[15d]; **IR** (Neat) ν_{max}: 3362, 2922, 2855, 1461, 1376, 1219, 1220, 1048 cm^{-1}, **^{1}H NMR**, (500 MHz, D_2O): δ 1.52 (m, 2H), 1.75 (m, 1H), 3.41–3.50 (m, 2H), 3.59 (m, 1H), 3.73–3.79 (m, 2H), 4.0 (s, 1H); **^{13}C NMR** (125 MHz, D_2O): δ 29.3, 41.0, 63.2, 69.4, 70.6, 73.6, 74.8; **HRMS** (ESI, Orbitrap) *m/z*: calcd for $C_7H_{14}O_5Na$ 201.0733, found 201.0732.

*4.2.13. (3aS,7aR)-Methyl 7-(hydroxyimino)-2,2-dimethyl-3a,6,7,7a-tetrahydrobenzo[d][1,3]dioxole-5-carboxylate (**31**).* To a solution of **24** and **25** (400 mg, 1.7 mmol) in DCM (20 mL) were added Dess–Martin periodinane (1.48 g, 3.5 mmol) at rt for 1 h. After consumption of the starting material, the reaction is being quenched by adding saturated hypo solution (5 mL) followed by saturated $NaHCO_3$ (5 mL). The organic layer is extracted using DCM (10 mL×3) the combined fractions are collected and dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give the crude product. The crude ketone is unstable and proceeded for next reaction without further purification. To the crude ketone (1.7 mmol) in EtOH (2 mL) was added hydroxylamine hydrochloride (245 mg, 3.53 mmol) followed by pyridine (1 mL). The reaction mixture was stirred at room temperature for 2 h. The solution was poured into water and extracted with CH_2Cl_2 (3×50 mL). The combined organic fractions were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude oxime **31** was purified by ethyl acetate: hexane (1:9) to give **31** (295 mg, 70%, over two steps) as a yellow oil. **IR** (Neat) ν_{max}: 3588, 3543, 2988, 2928, 2853, 1716, 1660, 1438, 1339, 1226, 1046, 938, 772 cm^{-1}, **^{1}H NMR**, (500 MHz, $CDCl_3$): δ 1.39 (s, 3H), 1.42 (s, 3H), 3.02–3.08 (dt, 1H,

J=2.3 Hz), 3.75–3.81 (m, 4H), 4.66 (d, 1H, *J*=4.9 Hz), 4.83 (m, 1H), 6.8 (s, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 21.1, 26.6, 27.9, 52.2, 73.4, 73.8, 110.6, 126.7, 135.7, 152.5, 166.4 **HRMS** (ESI, Orbitrap) *m/z*: calcd for $C_{11}H_{16}O_5N$ 242.1023, found 241.1019.

*4.2.14. (3aS,7R,7aR)-Methyl 7-(tert-butoxycarbonylamino)-2,2-dimethyl-3a,6,7,7a-tetrahydrobenzo[d][1,3]dioxole-5-carboxylate (**32**).* To a mixture of oxime **31** (280 mg, 1.16 mmol) and MoO_3 (250 mg, 1.74 mmol) in MeOH (8 mL) was added $NaBH_4$ (439 mg, 11.61 mmol) portionwise. An exothermic reaction occurred with vigorous gas evolution. The reaction mixture was stirred at room temperature for 50 min. To the reaction mixture was added brine and the precipitate was filtered off. The filtrate was extracted with EtOAc (3×10 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated under reduced pressure to give amine. To the crude amine taken MeOH (3 mL) was added Boc_2O (379 mg, 1.74 mmol) and stirred at room temperature for 3 h. The solvent was removed under reduced pressure. The crude product was purified by column chromatography using ethyl acetate: hexane (1:9) to afford **32**, 265 mg, 70% yield, as a syrup. $[\alpha]_D^{20}$: −38.5° (*c* 1.3, $CHCl_3$); **IR** (Neat) ν_{max}: 3744, 3610, 2981, 2926, 2853, 1783, 1715, 1659, 1514, 1368, 1246, 1168, 772 cm^{-1}, **^{1}H NMR**, (500 MHz, $CDCl_3$): δ 1.31 (s, 3H), 1.36 (s, 3H), 1.44 (s, 9H), 2.20 (m, 1H, major couplings *J*=16.8 Hz, 10.8 Hz), 2.67 (dd, 1H, *J*=5.2 Hz, 16.8 Hz), 3.75 (s, 3H), 3.95 (m, 1H, one of coupling *J*=10.8 Hz), 4.33 (d, 1H, *J*=4.3 Hz), 4.72 (m, 1H), 5.0 (d, 1H, *J*=9.2 Hz), 6.71 (m, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 25.5, 26.3, 27.6, 28.3, 47.5, 52.0, 73.0, 74.6, 79.7, 109.8, 129.8, 134.9, 155.1, 166.6 **HRMS** (ESI, Orbitrap) *m/z*: calcd for $C_{16}H_{25}O_6NNa$ 350.1574, found 350.1566.

*4.2.15. tert-Butyl (3aR,4R,7aS)-6-(hydroxymethyl)-2,2-dimethyl-3a,4,5,7a-tetrahydrobenzo[d][1,3]dioxol-4-ylcarbamate (**33**).* To the compound **32** (200 mg, 0.06 mmol) in DCM (10 mL) was added DIBAL-H (0.8 mL, 1.55 mmol) 25% w/v in toluene at −5 °C and stirred for 2 h. After completion of the reaction MeOH (1 mL) was added to quench excess DIBAL-H followed by saturated sodium, potassium tartarate (10 mL) and saturated NH_4Cl (5 mL). Compound is extracted using ethylacetate (3×20 mL), all the organic fractions were collected and dried over Na_2SO_4, solvent was removed under reduced pressure using rotavapour, the crude product is purified by column chromatography using ethylacetate: hexane (1:4) as eluent to give **33** as an oil (142 mg, 78% yield). $[\alpha]_D^{20}$: +3.5° (*c* 1.7, $CHCl_3$); **IR** (Neat) ν_{max}: 3395, 2980, 2929, 1639, 1513, 1367, 1219, 1168, 772 cm^{-1}; **^{1}H NMR**, (500 MHz, $CDCl_3$): δ 1.36 (s, 6H), 1.44 (s, 9H), 1.79 (br s, -OH), 2.06–2.21 (m, 2H), 3.91 (s, 1H), 4.03 (s, 2H), 4.31 (dd, 1H, *J*=2.3 Hz, 5.8 Hz), 4.65 (s, 1H), 5.02 (d, 1H, *J*=9.1 Hz), 5.65(s, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 26.4, 27.2, 27.5, 28.4, 47.9, 65.7, 73.8, 74.8, 79.6, 109.2, 119.8, 139.2, 155.3 **HRMS** (ESI, Orbitrap) *m/z*: calcd for $C_{15}H_{25}O_5NNa$ 322.1624, found 322.1616.

*4.2.16. tert-Butyl (3aR,4R,6R,7R,7aS)-7-hydroxy-6-(hydroxymethyl)-2,2-dimethylhexahydrobenzo[d][1,3]dioxol-4-ylcarbamate (**34**).* To the compound **33** (50 mg, 0.016 mmol) in THF (2 mL), $BH_3{\cdot}Me_2S$ (0.038 mL, 0.5 mmol) was added drop wise at 0 °C. Stirring continued for 2 h at rt. Then NaOH (3N, 0.5 mL) followed by H_2O_2 (30%, 0.7 mL) solution were added at 0 °C and stirring continued for 30 min at the same temperature. The reaction mixture was diluted with EtOAc, washed with water, brine, dried (Na_2SO_4) and purified by column chromatography using ethyl acetate: hexane (2:3) to give **22** as an oil (34 mg, 65%). $[\alpha]_D^{20}$: +5.0° (*c* 0.89, MeOH); **IR** (Neat) ν_{max}: 3367, 2921, 2852, 1697, 1661, 1504, 1368, 1219, 861 cm^{-1}; **^{1}H NMR**, (400 MHz, $CDCl_3$): (D_2O exchanged) δ 1.30 (m, H), 1.37 (s, 3H), 1.45 (s, 9H), 1.51 (s, 3H), 1.60 (m, 1H), 1.75 (m, 1H) 3.57–3.76 (m, 3H), 3.92–3.99 (m, 2H), 4.27 (t, 1H, *J*=4.4 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 26.4, 28.3, 39.9, 48.1, 66.2, 75.5, 79.7, 81.6, 109.6, 155.2; ESI (MS) *m/z*: [M+Na] 340.

*4.2.17. (1R,2S,3R,4R,6R)-4-Acetamido-6-(acetoxymethyl)cyclohexane-1,2,3-triyl triacetate (**35**).* Aqueous CF_3COOH {(1:1 v/v) 2 mL} was added to the compound **34** (15 mg, 0.004 mmol) at ice-cold temperature, the mixture was stirred at rt for 3 h. After completion of the reaction the solvent was removed under reduced pressure to give crude amine. To the crude amine were added pyridine (2 mL), Ac_2O (0.2 mL) and catalytic amount of DMAP at rt and stirred overnight. The solvent was removed under reduced pressure. The crude product was purified by column chromatography with 5% MeOH in $CHCl_3$ to afford pentaacetate **35** (16 mg, 90% from **34**) as a white solid. Mp 173–175 °C {lit.[13b] 175–178 °C}. The physical and spectral data are in accordance with the literature values.[13b] $[\alpha]_D^{20}$: +16.0° (*c* 0.52, $CHCl_3$); **IR** (Neat) ν_{max}: 3394, 2923, 2852, 1738, 1676, 1460, 1369, 1122, 1073, 772 cm^{-1}, **^{1}H NMR**, (500 MHz, $CDCl_3$): δ 1.56–163 (m, 1H), 1.97 (s, 6H), 1.97–2.1 (m, 2H), 2.04 (s, 3H), 2.06 (s, 3H), 2.21 (s, 3H), 3.97 (dd, 1H, *J*=3.6 Hz, 11.3 Hz), 4.05 (dd, 1H, *J*=6.1 Hz, 11.3 Hz), 4.27 (m, 1H), 4.94 (dd, 1H, *J*=2.8 Hz, 10.8 Hz), 5.17 (t, 1H, *J*=10.5 Hz), 5.45 (t, 1H, *J*=2.9 Hz), 5.49 (d, 1H, *J*=8.5 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 20.5, 20.7, 20.9, 23.2, 28.7, 37.9, 46.7, 63.7, 68.9, 71.5, 72.6, 169.2, 169.7, 170.1, 170.3, 170.7; **HRMS** (ESI, Orbitrap) *m/z*: calcd for $C_{17}H_{25}O_9NNa$ 410.1415, found 410.1410.

*4.2.18. tert-Butyl (3aR,4R,6S,7S,7aS)-6,7-dihydroxy-6-(hydroxymethyl)-2,2-dimethylhexahydrobenzo[d][1,3]dioxol-4-ylcarbamate (**36**).* To an ice cooled, stirred solution of compound **33** (50 mg, 0.016 mmol) in acetone/water (4:1) (1 mL) were added NMO (50 mg, 0.048 mmol) and OsO_4 (0.06 mL from 0.25 g in 20 mL toluene). The reaction was allowed to return to room temperature and stirred for another 2 h. The reaction mixture was quenched with solid $Na_2S_2O_3$. The solvent was removed under reduced pressure and extracted with ethyl acetate (2×15 mL). The combined organic extracts were washed with brine, separated, and dried over anhydrous Na_2SO_4. The solvent was removed on a rotary evaporator and the residue was purified by column chromatography on silica gel using ethyl acetate: hexane (3:2) as the eluent to give pure compound **30** (50 mg, 90%) as a colourless liquid. $[\alpha]_D^{20}$: −8.0° (*c* 1.1, MeOH); **IR** (Neat) ν_{max}: 3447, 3407, 3360, 2925, 1696, 1510, 1459, 1369, 1219, 1049 cm^{-1}, **^{1}H NMR**, (500 MHz, $CDCl_3$): δ 1.37 (s, 3H), 1.45 (s, 9H), 1.50 (s, 3H), 1.50–1.52 (m, 1H), 1.91 (m, 1H), 3.51 (d, 1H, *J*=11.2 Hz), 3.62 (d, 1H, *J*=6.7 Hz), 3.69 (d, 1H, *J*=11.1 Hz), 4.17 (m, 1H), 4.28–4.39 (m, 2H), 5.01 (d, 1H, *J*=8.9 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 26.2, 28.1, 28.3, 33.0, 44.6, 68.8, 73.2, 75.0, 75.1, 79.9, 80.0, 109.4, 155.4; **HRMS** (ESI, Orbitrap) *m/z*: calcd for $C_{15}H_{28}O_7N$ 334.1860, found 334.1858.

*4.2.19. (1R,2R,3S,4S,6R)-6-Acetamido-4-(acetoxymethyl)-4-hydroxycyclohexane-1,2,3-triyl triacetate (**37**).* An aqueous CF_3COOH (1:1 v/v) 2 mL was added to the compound **36** (20 mg, 0.06 mmol) at ice-cold temperature and the mixture was stirred at rt for 3 h. After completion of the reaction, the solvent was removed under reduced pressure to give crude amine. To the crude amine were added pyridine (2 mL), Ac_2O (0.2 mL), and catalytic amount of DMAP at rt and stirred for overnight. The solvent was removed under reduced pressure. The crude product was purified by column chromatography with 5% MeOH in $CHCl_3$ to afford pentaacetate **37** (24 mg, 90% from **36**) as a white solid mp 269 °C {lit[17c] 273 °C}.; $[\alpha]_D^{20}$: -17.0° (*c* 0.52, $CHCl_3$) {lit.[17c] $[\alpha]_D^{20}$: −15.6°} the physical and spectral data are in accordance with the literature values;[13b,17c] **IR** (Neat) ν_{max}: 2957, 2925, 2854, 1732, 1464, 1368, 1283, 1222, 1122, 1074 cm^{-1}, **^{1}H NMR**, (500 MHz, $CDCl_3$): δ 1.78 (t, 1H, *J*=12.9 Hz), 1.96 (s, 6H), 1.99–2.08 (m, 1H), 2.09 (s, 6H), 2.2 (s, 3H), 3.92 and 4.0 (ABq, 2H, *J*=11.4 Hz), 4.63–4.70 (m, 1H), 5.26 (d, 1H, *J*=10.2 Hz), 5.33 (dd,

1H, *J*=2.1 Hz, 10.2 Hz), 5.4 (d, 1H, *J*=8.3 Hz), 5.5 (s, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 20.5, 20.6, 20.7, 20.9, 23.3, 34.0, 43.7, 67.3, 69.8, 70.3, 71.5, 72.0, 169.2, 169.7, 169.8, 170.3, 170.5; **HRMS** (ESI, Orbitrap) *m/z*: calcd for $C_{17}H_{26}O_{10}N$ 404.1550, found 404.1537.

*4.2.20. Experimental procedure for the reductive elimination and NHK on **38**.* To a flame dried two-necked round bottom flask, $CrCl_3$ (347 mg, 2.19 mmol) and powdered activated Mn (2.41 g, 43.85 mmol) were taken in THF/DMF (12 mL/3 mL) and stirred for 2 h at rt under an inert atmosphere until the colour changed from violet to green. Compound **38** (500 mg, 1.46 mmol) in THF (3 mL) was slowly added to it and stirred for 8 h. When TLC showed the absence of starting material, $NiCl_2$ (19 mg, 0.14 mmol) was added to the reaction mixture and stirred for 30 min. Then allylbromo compound **19** (0.3 mL, 2.19 mmol) was added to it followed by the addition of TMSCl (0.27 mL, 2.19 mmol). The reaction mixture was allowed to stir for an additional 5 h at 50 °C, and diluted with diethyl ether (70 mL). Next, n-Bu_4NF (2.2 mL, 1M in THF, 2.19 mmol) was added and stirred at rt for 2 h. The reaction mixture was filtered through a pad of Celite using sintered funnel, concentrated and purified by column chromatography using ethyl acetate/hexane (0.5:9.5) to afford a mixture of **39** (163 mg, 37.5%) and **40** (163 mg, 37.5%) in a 1:1 ratio as oils.

*4.2.21. (S)-Ethyl 4-((4S,5R)-2,2-diethyl-5-vinyl-1,3-dioxolan-4-yl)-4-hydroxy-2-methylenebutanoate (**39**).* $[\alpha]_D^{20}$: −18.8° (*c* 0.95, $CHCl_3$); **IR** (Neat) ν_{max}: 2974, 2931, 2311, 1766, 1713, 1630, 1550, 1464, 1217, 1172, 1075, 932, cm^{-1}; **^{1}H NMR**, (300 MHz, $CDCl_3$): δ 0.84 (t, 3H, *J*=7.4 Hz), 0.9 (t, 3H, *J*=7.5 Hz), 1.23 (t, 3H, *J*=7.1 Hz), 1.59 (q, 2H, *J*=7.5 Hz), 1.69 (q, 2H, *J*=7.5 Hz), 2.34–2.5 (m, 1H), 3.72 (m, 1H), 4.0 (dd, 1H, *J*=4.3 Hz, 7.3 Hz), 4.14 (q, 2H, *J*=7.1 Hz), 4.54 (dd, 1H, *J*=7.3 Hz, 7.5 Hz), 5.23 (d, 1H, *J*=11.1 Hz), 5.28 (d, 1H, *J*=17.1 Hz), 5.62 (d, 1H, *J*=1.5 Hz), 6.0 (m, 1H), 6.2 (d, 1H, *J*=1.5 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 7.9, 8.6, 14.1, 28.2, 29.2, 37.1, 60.7, 68.3, 79.1, 79.9, 112.3, 119.4, 127.5, 134.4, 136.9, 167.1; **HRMS** (ESI, Orbitrap) *m/z*: calcd for $C_{13}H_{26}O_5Na$ 321.1672, found 321.1675.

*4.2.22. (R)-Ethyl 4-((4S,5R)-2,2-diethyl-5-vinyl-1,3-dioxolan-4-yl)-4-hydroxy-2-methylenebutanoate (**40**).* $[\alpha]_D^{20}$: +2.8° (*c* 0.48, $CHCl_3$) {lit.[18] $[\alpha]_D^{24}$: +3.75° (*c* 1.70, CH_2Cl_2)}; **IR** (Neat) ν_{max}: 2973, 2928, 1767, 1713, 1630, 1550, 1512, 1462, 1275, 1172, 932 cm^{-1}; **^{1}H NMR**, (500 MHz, $CDCl_3$): δ 0.89 (t, 3H, *J*=7.6 Hz), 0.95 (t, 3H, *J*=7.6 Hz), 1.3 (t, 3H, *J*=7.1 Hz), 1.63 (q, 2H, *J*=7.6 Hz), 1.70 (q, 2H, *J*=7.6 Hz), 2.44 (dd, 1H, *J*=9.1 Hz, 14.1 Hz), 2.87 (dd, 1H, *J*=3.9 Hz, 14.1 Hz), 3.76 (m, 1H), 3.96 (dd, 1H, *J*=6.7 Hz, 8.6 Hz), 4.22 (m, 2H), 4.69 (m, 1H), 5.27 (d, 1H, *J*=10.3 Hz), 5.41(d, 1H, *J*=17 Hz), 5.72 (s, 1H), 6.04 (m, 1H), 6.28 (s, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 8.0, 8.6, 14.1, 28.6, 29.7, 36.7, 61.2, 69.3, 78.7, 79.9, 112.5, 117.8, 128.3, 134.4, 137.0, 168.4; **HRMS** (ESI, Orbitrap) *m/z*: calcd for $C_{13}H_{26}O_5Na$ 321.1672, found 321.1670.

4.2.23. Experimental procedure for ring closing metathesis reaction. To a solutions of **39** or **40** (140 mg, 0.46 mmol) in anhydrous 1,2 dichloro ethane (8 mL) under a nitrogen atmosphere, was added Hoveyda-Grubbs second generation catalyst (6 mg, 0.009 mmol) and the reaction mixture was refluxed for 2 h. After completion of the reaction, the solvent was evaporated at reduced pressure to give a crude residue, which was purified by column chromatography using ethyl acetate: hexane (1.2:8.8) to give compound **41** or **42** (116 mg, 92%) as an oils.

*4.2.24. (3aR,7R,7aS)-Ethyl 2,2-diethyl-7-hydroxy-3a,6,7,7a-tetrahydrobenzo[d][1,3]dioxole-5-carboxylate (**41**).* $[\alpha]_D^{20}$: −67° (*c* 0.64, $CHCl_3$); **IR** (Neat) ν_{max}: 3670, 3396, 2975, 2934, 1712, 1655, 1464, 1366, 1245, 1172, 1070 cm^{-1}; **^{1}H NMR**, (500 MHz, $CDCl_3$): δ 0.89 (t, 3H, *J*=7.4 Hz), 0.92 (t, 3H, *J*=7.4 Hz), 1.30 (t, 3H, *J*=7.1 Hz), 1.65–1.70 (m, 4H), 2.24 (m, 1H), 2.78 (dd, 1H, *J*=4.5 Hz, 17.2 Hz), 3.92 (m, 1H), 4.12 (t, 1H, *J*=7.0 Hz), 4.23 (q, 2H, *J*=7.1 Hz), 4.77 (m, 1H), 6.94 (m, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 7.8, 8.5, 14.1, 29.1, 29.3, 29.6, 61.0, 68.9, 72.2, 77.8, 113.6, 130.4, 134.0, 166.1; **Mass** (ESI) *m/z* [M+Na]: 293.

*4.2.25. (3aR,7S,7aS)-Ethyl 2,2-diethyl-7-hydroxy-3a,6,7,7a-tetrahydrobenzo[d][1,3]dioxole-5-carboxylate (**42**).* $[\alpha]_D^{20}$: +45.2° (*c* 1.0, $CHCl_3$) {(lit.[18] +43.4)}; **IR** (Neat) ν_{max}: 3442, 2974, 2937, 1711, 1651, 1463, 1373, 1237, 1171, 1058, 1017, 925 cm^{-1}, **^{1}H NMR**, (500 MHz, $CDCl_3$): δ 0.85 (t, 3H, *J*=7.4 Hz), 0.92 (t, 3H, *J*=7.4 Hz), 1.30 (t, 3H, *J*=7.1 Hz), 1.57–1.71 (m, 4H), 2.42 (m, 1H), 2.68 (dd, 1H, *J*=5.0 Hz, 16.6 Hz), 3.92 (m, 1H), 4.21 (q, 2H, *J*=7.1 Hz), 4.43 (dd, 1H, *J*=2.7 Hz, 5.9 Hz), 4.75 (m, 1H), 6.78 (m, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 7.9, 8.4, 14.1, 27.6, 29.9, 60.9, 67.6, 72.9, 75.4, 113.7, 129.4, 134.7, 166.3; **Mass** (ESI) *m/z* [M+Na]: 293.

*4.2.26. (3aR,7aS)-Ethyl 2,2-diethyl-7-(hydroxyimino)-3a,6,7,7a-tetrahydrobenzo[d][1,3]dioxole-5-carboxylate (**43**).* To a solution of **41** or **42** (100 mg, 0.37 mmol) in DCM (6 mL) were added Dess–Martin periodinane (392 mg, 0.92 mmol) at rt for 1 h. After consumption of the starting material, the reaction is being quenched by adding saturated hypo solution (2 mL) followed by saturated $NaHCO_3$ (2 mL). The organic layer is extracted using DCM (5 mL×3), all the fractions are collected and dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give crude product. The crude ketone is unstable and proceeded for next reaction without further purification. To the crude ketone (0.37 mmol) in EtOH (1 mL) was added hydroxylamine hydrochloride (251 mg, 0.74 mmol) followed by pyridine (0.5 mL). The reaction mixture was stirred at room temperature for 2 h. The solution was poured into water and extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude oxime **43** was purified by ethylacetate: hexane (1:9) to give **43** (72 mg, 70%, over two steps) as yellow oil. 3395, 2976, 2934, 1713, 1645, 1498, 1464, 1240, 1216, 1172, 1071, 926 cm^{-1}, **^{1}H NMR**, (500 MHz, $CDCl_3$): δ 0.85 (t, 3H, *J*=7.5 Hz), 0.93 (t, 3H, *J*=7.5 Hz), 1.33 (t, 3H, *J*=7.5 Hz), 1.58–1.72 (m, 4H), 3.0 (d, 1H, *J*=21.9 Hz), 3.82 (d, 1H, *J*=21.9 Hz), 4.25 (q, 2H, *J*=6.8 Hz), 4.67 (d, 1H, *J*=5.2 Hz), 4.85 (m, 1H), 6.8 (s, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 8.1, 8.3, 14.1, 20.8, 29.6, 30.4, 61.1, 73.5, 73.6, 114.4, 126.8, 135.6, 152.7, 166.0; **HRMS** (ESI, Orbitrap) *m/z*: calcd for $C_{22}H_{14}O_5N$ 284.1492, found 284.1491.

4.3. Experimental procedure for reductive elimination and NHK on compound 44

To a flame dried two-necked round bottom flask, $CrCl_3$ (320 mg, 2.07 mmol) and powdered activated Mn (2.27 g, 41.1 mmol) were taken in THF/DMF (21 mL/6 mL) and stirred for 2 h at rt under an inert atmosphere until the colour changed from violet to green. Compound **44** (500 mg, 1.38 mmol) in THF (9 mL) was slowly added to it and stirred for 8 h. When TLC showed the absence of starting material, $NiCl_2$ (17 mg, 0.13 mmol) was added to the reaction mixture and stirred for 30 min. Then allylbromo compound **20** (910 mg, 3.42 mmol) in DMF (3 mL) was added to it followed by the addition of TMSCl (0.91 mg, 3.45 mmol). The reaction mixture was allowed to stir for an additional 5 h at 50 °C, and diluted with diethyl ether (30 mL). Next the reaction mixture was filtered through a pad of Celite using sintered funnel, to it 1N HCl (5 mL) was added and further stirred for 2 h at 0 °C and the reaction mixture was washed with water. The organic fraction was concentrated and dried over Na_2SO_4, purified by column chromatography using ethyl acetate: hexane (1:9) to afford **45** and **46** (404 mg, 75%) in a 1:1 ratio as oils.

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*4.3.1. (5S,6S,7R)-6-(Methoxymethoxy)-12,12,13,13-tetramethyl-9-methylene-5-vinyl-2,4,11-trioxa-12-silatetradecan-7-ol (**45**).* $[\alpha]_D^{20}$: +8.5° (*c* 1.0, $CHCl_3$); **IR** (Neat) ν_{max}: 3454, 2924, 2853, 1739, 1650, 1464, 1363, 1254, 1152, 1101, 1029 cm^{-1}, **^{1}H NMR**, (300 MHz, $CDCl_3$): δ 0.07 (s, 6H), 0.9 (s, 9H), 2.16 (dd, 1H, *J*=10.0 Hz, 14.3 Hz), 2.50 (d, 1H, *J*=14.3 Hz), 3.39 (s, 3H), 3.42 (s, 3H), 3.55 (t, 1H, *J*=4.9 Hz), 3.85 (m, 1H), 4.12 (s, 2H), 4.31 (dd, 1H, *J*=4.72 Hz, 7.3 Hz), 4.59–4.78 (m, 4H), 4.96 (s, 1H), 5.14 (s, 1H), 5.31 (d, 1H, *J*=10.3 Hz), 5.34 (d, 1H, *J*=17.3 Hz), 5.82 (m, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ −5.4, 18.3, 25.8, 36.7, 55.7, 56.1, 66.3, 69.8, 77.4, 84.3, 94.2, 98.3, 112.4, 118.9, 134.7, 145.7; **HRMS** (ESI, Orbitrap) *m/z*: calcd for $C_1H_{38}O_6NaSi$ 413.2329, found 413.2320.

*4.3.2. (5S,6S,7S)-6-(Methoxymethoxy)-12,12,13,13-tetramethyl-9-methylene-5-vinyl-2,4,11-trioxa-12-silatetradecan-7-ol (**46**).* $[\alpha]_D^{20}$: +21.5° (*c* 0.76, $CHCl_3$); **IR** (Neat) ν_{max}: 2924, 2853, 1465, 1254, 1217, 1152, 1102, 1029 cm^{-1}, **^{1}H NMR**, (500 MHz, $CDCl_3$): δ 0.08 (s, 6H), 0.9 (s, 9H), 2.28–2.43 (m, 2H), 3.38 (s, 3H), 3.45 (s, 3H), 3.47 (dd, 1H, *J*=3.39 Hz, 6.04 Hz), 3.9 (m, 1H), 4.13 (s, 2H), 4.32 (t, 1H, *J*=6.6 Hz), 4.58 (d, 1H, *J*=6.6 Hz), 4.71 (d, 1H, *J*=6.6 Hz), 4.78 (d, 1H, *J*=6.6 Hz), 4.89 (d, 1H, *J*=6.6 Hz), 4.97 (s, 1H), 5.14 (s, 1H), 5.29–5.40 (m, 2H), 5.58 (m, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ −5.4, -5.3, 18.3, 25.8, 38.1, 55.7, 56.3, 66.3, 69.3, 78.2, 82.5, 94.0, 98.4, 112.5, 119.3, 134.8, 145.5; **HRMS** (ESI, Orbitrap) *m/z*: calcd for $C_1H_{38}O_6NaSi$ 413.2329, found 413.2319.

4.4. Procedure for RCM

To the compound **45** or **46** (180 mg, 0.46 mmol) in anhydrous toluene (18 mL) under a nitrogen atmosphere, was added Grubbs second generation catalyst (39 mg, 0.0046 mmol) and the reaction mixture was refluxed for 2 h. After completion of the reaction, the solvent was evaporated at reduced pressure to give a crude residue, which was purified by column (ethyl acetate: hexane=1.5:8.5) to give compounds **47** or **48** (150 mg, 92%) as oils.

*4.4.1. (1R,5S,6S)-3-((tert-butyldimethylsilyloxy)methyl)-5,6-bis(methoxymethoxy)cyclohex-3-enol (**47**).* $[\alpha]_D^{20}$: −28° (*c* 1.0, $CHCl_3$); **IR** (Neat) ν_{max}: 3453, 2952, 2929, 2851, 2892, 2855, 1466, 1443, 1254, 1150, 1100, 838 cm^{-1}, **^{1}H NMR**, (500 MHz, $CDCl_3$): δ 0.06 (s, 6H), 0.9 (s, 9H), 2.05 (m, 1H, major couplings *J*=9.4 Hz and 17.0 Hz), 2.40 (dd, 1H, *J*=5.9 Hz, 17.0 Hz), 3.39 (s, 3H), 3.46 (s, 3H), 3.50 (dd, 1H, *J*=7.3 Hz, 9.6 Hz), 3.76 (m, 1H, one of coupling *J*=9.4 Hz), 3.90 (s, -OH), 4.02 (s, 2H), 4.00 and 4.04 (AB_q, 2H, *J*=14.4 Hz), 4.18(d, 1H *J*=7.3 Hz), 4.73 (d, 1H, *J*=6.8 Hz), 4.76 (d, 1H, *J*=6.8 Hz), 4.80 (d, 1H, *J*=6.5 Hz), 4.82 (d, 1H, *J*=6.5 Hz), 5.61 (s, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ −5.4, -5.4, 18.2, 25.8, 32.6, 55.4, 55.9, 65.3, 68.2, 77.5, 87.0, 96.4, 98.4, 119.8, 137.1; ESI (MS) *m/z*: [M+Na]: 385.

*4.4.2. (1S,5S,6S)-3-((tert-Butyldimethylsilyloxy)methyl)-5,6-bis(methoxymethoxy)cyclohex-3-enol (**48**).* $[\alpha]_D^{20}$: +44° (*c* 0.73, $CHCl_3$); **IR** (Neat) ν_{max}: 3424, 2924, 2898, 2851, 2827, 1687, 1465, 1444, 1213, 1148, 1099, 1029 cm^{-1}, **^{1}H NMR**, (500 MHz, $CDCl_3$): δ 0.05 (s, 6H), 0.88 (s, 9H), 2.11 (dd, 1H, *J*=7.1 Hz, 17.3 Hz), 2.28 (dd, 1H, *J*=4.8 Hz, 17.3 Hz), 3.38 (s, 3H), 3.41 (s, 3H), 3.77 (dd, 1H, *J*=2.2 Hz, 4.8 Hz), 4.03 (s, 2H), 4.08 (m, 1H), 4.24 (s, 1H), 4.70–4.78 (m, 4H), 5.68 (s, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ −5.4, -5.4, 18.2, 25.8, 31.3, 55.4, 55.7, 65.7, 66.5, 74.3, 80.9, 96.0, 97.1, 118.1, 139.0; [M+Na]: 385.

4.5. Experimental procedure for hydroboration/oxidation reaction

To the compounds **47** or **48** (100 mg, 0.27 mmol) in THF (5 mL), $BH_3{\cdot}Me_2S$ (0.08 mL, 0.85 mmol) was added drop wise at 0 °C. Stirring continued for 2 h at rt. To it NaOH (3N, 0.5 mL) followed by 30% H_2O_2 (0.7 mL) solution were added at 0 °C and stirring continued for 30 min at the same temperature. The reaction mixture was diluted with ethylacetate, washed with water, brine, dried Na_2SO_4, purified by column chromatography using ethyl acetate: hexane (1:4) as the eluent in case of **47** to give **49** (62 mg, 59.61%) and **50** (10 mg, 9.6%) in 6:1 ratio as oils. In case of **48** the solvent mixture was MeOH:$CHCl_3$ (0.2:9.8) for purification to give **51** (62 mg, 59.61%) and **52** (10 mg, 9.6%) in 6:1 ratio as oils.

*4.5.1. (1R,2S,3S,4R,5R)-5-((tert-Butyldimethylsilyloxy)methyl)-2,3-bis(methoxymethoxy)cyclohexane-1,4-diol (**49**).* $[\alpha]_D^{20}$: −25.5° (*c* 0.53, $CHCl_3$); **IR** (Neat) ν_{max}: 3440, 2925, 2854, 1466, 1377, 1253, 1212, 1095, 1025 cm^{-1}; **^{1}H NMR**, (500 MHz, $CDCl_3$): δ 0.06 (s, 6H), 0.88 (s, 9H), 1.55–1.68 (m, 2H), 1.98 (dt, 1H, *J*=4.15 Hz), 3.19 (t, 1H, *J*=8.9 Hz), 3.31 (t, 1H, *J*=8.9 Hz), 3.4 (dd, 1H, *J*=8.9 Hz, 11.8 Hz), 3.45 (s, 3H), 3.46 (s, 3H), 3.54 (m, 1H), 3.74 (d, 2H, *J*=4.8), 3.98 (s, -OH), 4.02 (s, -OH), (D_2O exchanged), 4.78–4.84 (m, 4H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ −5.3, 18.2, 25.8, 31.0, 40.1, 55.8 (2C), 64.4, 70.5, 72.9, 86.2, 88.1, 98.6, 98.7; **HRMS** (ESI, Orbitrap) *m/z*: calcd for $C_{17}H_{36}O_7NaSi$ 403.2122, found 403.2132.

*4.5.2. (1R,2S,3S,4S,5S)-5-((tert-Butyldimethylsilyloxy)methyl)-2,3-bis(methoxymethoxy)cyclohexane-1,4-diol (**50**).* $[\alpha]_D^{20}$: +38.4 (*c* 0.19, $CHCl_3$); **IR** (Neat) ν_{max}: 3461, 2928, 2855, 1467, 1254, 1215, 1148, 1103, 1033 cm^{-1}, **^{1}H NMR**, (400 MHz, $CDCl_3$): δ 0.08 (s, 6H), 0.9 (s, 9H), 1.64 (m, 1H), 1.79 (m, 1H), 2.14 (m, 1H), 3.40 (s, 3H), 3.43 (s, 3H), 3.62–3.81 (m, 4H), 3.80–3.97 (m, 2H), 4.67–4.80 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ −5.5, -5.5, 18.1, 25.8, 36.7, 55.7, 55.9, 65.9, 68.9, 71.1, 77.1, 78.7, 97.2, 97.5; **HRMS** (ESI, Orbitrap) *m/z*: calcd for $C_{17}H_{36}O_7NaSi$ 403.2122, found 403.2136.

*4.5.3. Pseudo-β-D-glucopyranose (**2**).* To the compound **49** (30 mg, 0.078 mmol) in methanol (1 mL) was added HCl (6N, 1 mL) and the reaction mixture was refluxed for 30 min. After completion of the reaction, solvent was removed under reduced pressure to give crude compound which on purification with column chromatography using MeOH:$CHCl_3$ (1:4) as eluent gave pure compound **2** (13 mg, 95%) as an oil. The physical and spectroscopic data of compound **9** were in exact agreement with the reported literature values.[9c] $[\alpha]_D^{20}$: +8.1° (*c* 0.16, MeOH) {lit.[9c] $[\alpha]_D^{20}$: +6.7° (*c* 0.15, MeOH); **IR** (Neat) ν_{max}: 3389, 2922, 2853, 1461, 1219 cm^{-1}; **^{1}H NMR**, (400 MHz, CD_3OD): δ 1.18 (q, 1H, *J*=12.9 Hz), 1.52 (m, 1H), 1.96 (ddd, 1H, *J*=3.6 Hz, 4.6 Hz, 12.9 Hz), 3.08–3.23 (m, 3H), 3.42 (ddd, 1H, *J*=4.7 Hz, 8.6 Hz, 12.9 Hz), 3.58 (dd, 1H, *J*=6.1 Hz, 10.7 Hz), 3.74 (dd, 1H, *J*=4.0 Hz, 10.7 Hz); **^{13}C NMR** (100 MHz, CD_3OD): δ 33.7, 42.2, 64.2, 72.9, 74.8, 78.9, 79.0; **HRMS** (ESI, Orbitrap) *m/z*: calcd for $C_{17}H_{14}O_5Na$ 201.0733, found 201.0730.

*4.5.4. (1R,2S,3S,4S,5S)-5-(Acetoxymethyl)cyclohexane-1,2,3,4-tetrayl tetraacetate (**53**).* To the compound **50** (8 mg, 0.021 mmol) in methanol (1 mL) was added HCl (6N, 1 mL) and the reaction mixture was refluxed for 30 min. After completion of the reaction, solvent was removed under reduced pressure to give crude compound. To the crude compound dissolved pyridine(1 mL), acetic anhydride (0.3 mL) and few crystal of DMAP were added and stirred for overnight at rt. Aqueous NH_4Cl was added to the reaction mixture and the organic fraction was extracted with ethylacetate (2×10 mL). The collected organic fractions were combined and solvent was removed under reduced pressure to give oily compound, which on column chromatography with ethyl acetate: hexane (1:4) afforded pure **53** (7 mg**, 95%** from **50**). The physical and spectroscopic data of compound **53** were in exact agreement with the reported literature values.[21a] $[\alpha]_D^{20}$: −15.1° (*c* 0.3, $CHCl_3$); **IR** (Neat) ν_{max}: 2919, 2851, 1737, 1715, 1462, 1374, 1242, 1184, 1079 cm^{-1}, **^{1}H NMR**, (400 MHz, $CDCl_3$): δ 1.93–1.99 (m, 2H), 2.01 (s,

3H), 2.03 (s, 3H), 2.04 (s, 3H), 2.06 (s, 3H), 2.08 (s, 3H), 2.40 (q, 1H, *J*=5.7), 4.10 (dd, 1H, *J*=6.2 Hz, 11.4 Hz), 4.14 (dd, 1H, *J*=6.2 Hz, 11.4 Hz), 4.99 (m, 1H), 5.13 (dd, 1H, *J*=3.0 Hz, 7.5 Hz), 5.23–5.28 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 20.6, 20.7, 20.8, 20.8, 20.9, 27.6, 34.2, 63.5, 69.0, 69.1, 69.3, 70.2, 169.5, 169.7, 169.8, 169.8, 170.6; **HRMS** (ESI, Orbitrap) *m/z*: calcd for $C_{17}H_{28}O_{10}N$ $[M+NH_4]^+$ 406.1707, found 406.1721.

*4.5.5. (1S,2S,3S,4S,5S)-5-((tert-Butyldimethylsilyloxy)methyl)-2,3-bis(methoxymethoxy)cyclohexane-1,4-diol (**51**).* $[\alpha]_D^{20}$: +22.3 (*c* 0.65, $CHCl_3$); **IR** (Neat) ν_{max}: 3440, 2950, 2928, 2890, 2856, 1467, 1391, 1253, 1148, 1102, 1029, 916, 834, 776 cm^{-1}; **^{1}H NMR**, (400 MHz, $CDCl_3$): δ 0.07 (s, 6H), 0.9 (s, 9H), 1.37 (q, 1H, *J*=12 Hz), 1.75 (m, 1H), 1.89 (m, 1H), 3.42 (s, 3H), 3.43 (s, 3H), 3.7 (d, 2H, *J*=5.7 Hz), 3.76 (m, 1H), 3.88 (m, 1H), 3.93 (m, 1H), 4.70–4.78 (m, 4H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ −5.5, -5.5, 18.2, 25.8, 30.3, 38.8, 55.8, 55.9, 66.0, 67.0, 70.1, 80.2, 81.3, 98.0, 98.05; **HRMS** (ESI, Orbitrap) *m/z*: calcd for $C_{17}H_{36}O_7NaSi$ 403.2122, found 403.2133.

*4.5.6. (1S,2S,3S,4R,5R)-5-((tert-Butyldimethylsilyloxy)methyl)-2,3-bis(methoxymethoxy)cyclohexane-1,4-diol (**52**).* $[\alpha]_D^{20}$: −17.8 (*c* 0.75, $CHCl_3$); **IR** (Neat) ν_{max}: 3741, 2923, 2852, 1513, 1454, 1219, 1029 cm^{-1}, **^{1}H NMR**, (400 MHz, $CDCl_3$): δ 0.06 (s, 6H), 0.89 (s, 9H), 1.40 (t, 1H, *J*=12.7 Hz), 1.86 (ddd, 1H, *J*=3.6 Hz, 7.3 Hz, 14.5 Hz), 2.01 (m, 1H), 3.37–3.49 (m, 8H), 3.60–3.67 (m, 2H), 3.84 (dd, 1H, *J*=4.4 Hz, 9.9 Hz), 4.12 (m, 1H), 4.7–4.9 (m, 4H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ −5.5, 18.2, 25.9, 29.3, 37.8, 55.6, 55.8, 63.9, 68.0, 72.7, 79.7, 84.4, 96.5, 98.6; **HRMS** (ESI, Orbitrap) *m/z*: calcd for $C_{17}H_{36}O_7NaSi$ 403.2122, found 403.2135.

*4.5.7. (1S,2S,3S,4S,5S)-5-(Acetoxymethyl)cyclohexane-1,2,3,4-tetrayl tetraacetate (**54**).* Experimental procedure is similar to compound **53** preparation, to give **54** as a solid mp 103–104 °C, {lit.[20d] 105–106.5 °C }, $[\alpha]_D^{20}$: +8° (*c* 0.5, $CHCl_3$), {lit.[20b] $[\alpha]_D^{20}$: +7° (*c* 0.75, $CHCl_3$); **IR** (Neat) ν_{max}: 2924, 2853, 1738, 1433, 1367, 1214, 1032 cm^{-1}, **^{1}H NMR**, (500 MHz, $CDCl_3$): δ 1.75 (q, 1H, *J*=11.5 Hz), 1.94 (m, 1H), 1.96 (s, 6H), 2.01 (s, 3H), 2.06 (s, 3H), 2.09 (s, 3H), 2.30 (m, 1H), 4.01 and 4.03 (ABq, 2H, *J*=11.4 Hz), 5.03 (dd, 1H, *J*=2.9 Hz, 10.5 Hz), 5.14 (m, 1H), 5.22 (m, 1H), 5.28 (dd, 1H, *J*=3.0 Hz, 4.8 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 20.7, 20.8, 20.9, 27.0, 34.35, 63.9, 67.9, 68.3, 68.6, 68.7, 169.2, 169.3, 170.0 (2C), 170.8; **HRMS** (ESI, Orbitrap) *m/z*: calcd for calcd for $C_{17}H_{28}O_{10}N$ 406.1707, found 406.1720.

*4.5.8. Pseudo-α-D-glucopyranose (**1**).* Experimental procedure is similar to the preparation of compound **2**. Compound **1** obtained as a white solid mp 144–145 °C, {lit.[15c] 146–147 °C}, $[\alpha]_D^{20}$: +61° (*c* 0.3, MeOH), {lit.[15c] $[\alpha]_D^{20}$: +63° (*c* 0.6, MeOH); **IR** (Neat) ν_{max}: 3610, 2926, 2850, 1368, 1220, 1032, 772 cm^{-1}, **^{1}H NMR**, (300 MHz, D_2O): δ 1.40 (td, 1H, *J*=15.0 Hz, 18.0 Hz), 1.78–1.90 (m, 2H), 3.23 (t, 1H, *J*=9.8 Hz), 3.38 (dd, 1H, *J*=3.0 Hz, 9.8 Hz), 3.53 (t, 1H, *J*=9.8 Hz), 3.60–3.70 (m, 2H), 4.03 (m, 1H); **^{13}C NMR** (125 MHz, D_2O): δ 30.7, 38.6, 62.9, 69.4, 73.6, 74.4, 75.0; **HRMS** (ESI, Orbitrap) *m/z*: calcd for $C_{17}H_{14}O_5Na$ 201.0733, found 201.0730.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2016.02.044.

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