Tetrahedron 64 (2008) 9574–9580

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Synthesis of five and six membered aminocyclitols: stereoselective Michael and Henry reaction approach with D-glucose derived α,β-unsaturated ester

Chaitali Chakraborty [a], Vinod P. Vyavahare [a], Vedavati G. Puranik [b], Dilip D. Dhavale [a,*]

[a] Department of Chemistry, Garware Research Centre, University of Pune, Pune 411 007, India
[b] Centre for Material Characterization, National Chemical Laboratory, Pune 411 008, India

ARTICLE INFO

Article history:
Received 21 April 2008
Received in revised form 14 July 2008
Accepted 15 July 2008
Available online 18 July 2008

Keywords:
Aminocyclitols
Carbohydrates
Henry reaction
Michael addition
Nitroinositol

ABSTRACT

The stereoselective intermolecular Michael addition of nitromethane to D-glucose derived α,β-unsaturated ester **7** afforded L-*ido*-configurated nitroester **8** as the only product that on reduction of the ester functionality, cleavage of 1,2-acetonide and the intramolecular Henry reaction afforded exclusively *muco*-nitroinositol **9**. While reduction of the ester functionality in **8**, deprotection of 1,2-acetonide, oxidative cleavage with $NaIO_4$ and the intramolecular Henry reaction afforded nitrocyclopentitol **13**. Nitrocyclitols **9** and **13** were converted to the hydroxyethyl substituted aminocyclohexitol **5** and aminocyclopentitol **6**, respectively.

1. Introduction

Among the C–C bond formation reactions, the Henry reaction of a carbonyl compound and a nitroalkane bearing α-hydrogen, leading to the formation of either β-nitroalcohol (with two newly generated stereocentres) or nitroolefin, is one of the well known classical named reactions.[1] The mild reaction conditions coupled with the new chiral catalyst or chiral substrate make both intra- and/or intermolecular Henry approaches more versatile in the synthesis of optically pure amino alcohols and natural products.[2] In particular, the nitrocyclitols obtained by an intramolecular Henry reaction constitute a key intermediate in the synthesis of aminocyclitols. This type of compounds, particularly five and six membered aminocyclitols, e.g., mannostatin A **1**,[3] allozamizoline **2**[4] and validamine **3**[5] (Fig. 1), are potent glycosidase inhibitors owing to their sugar-mimetic structures. In addition, aminocyclitol ring skeleton constitutes a structural subunit of complex natural products such as pancratistatin **4** and validamycins.[5,6] In the naturally occurring aminocyclitols, the presence of hydroxymethyl side chain is common and characteristic making them to be designated as C_7N-aminocyclitols.[7]

These C_7N-aminocyclitols containing natural products such as pyralomicins[8] and cetoniacytone A[9] are antibacterial and antitumour agents, respectively. As a part of our ongoing interest in the area of aminocyclitols, [10] we are now reporting the synthesis of hitherto unknown aminocyclohexitol **5** and aminocyclopentitol **6** with hydroxyethyl substituent.[11]

During the past two decades, the design of synthetic analogues of aminocyclitols with improved biological profile using asymmetric, enzymatic as well as chiron approaches has received

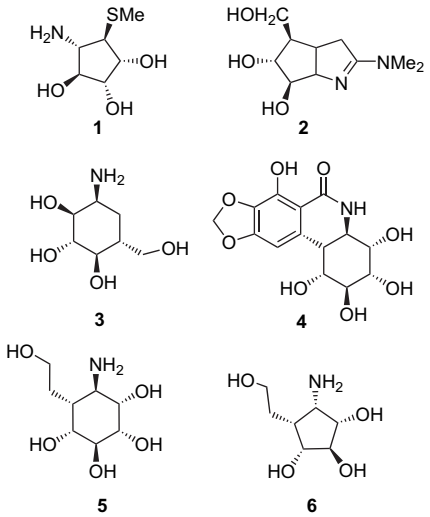


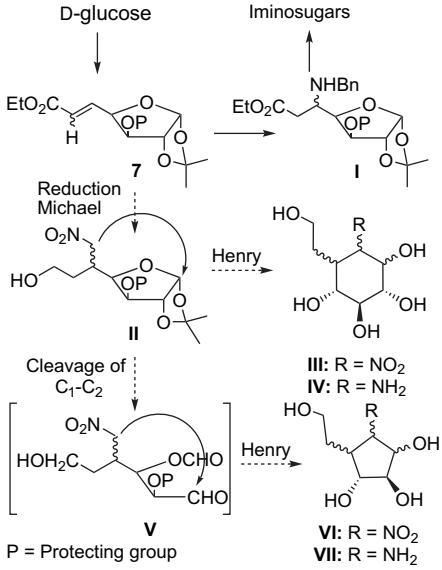
Figure 1. Structure of aminocyclitols.

* Corresponding author. Tel./fax: +91 20 25691728.
E-mail address: ddd@chem.unipune.ernet.in (D.D. Dhavale).

0040-4020/$ – see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2008.07.049

considerable attention.[7] In general, carbohydrates have been exploited as substrates utilizing aldol condensations,[12] rearrangement reactions (Ferrier and Claisen),[13] radical cyclizations,[14] cycloadditions,[15] ring closing metathesis and chemo enzymatic pathway.[7,16] However, the intramolecular Henry reaction approach to aminocyclitols using sugars is more appealing due to the easy access to introduce nitroalkane substituent in the polyhydroxylated carbon framework with aldehyde functionality. The literature survey indicates that the introduction of required nitroalkane moiety in the sugar substrate is achieved either by the intermolecular Henry reaction with other free aldehyde group[2,17] or by displacement of –OR (leaving group) in aldoses[18] in the synthesis of nitroinositol/aminocyclitols.

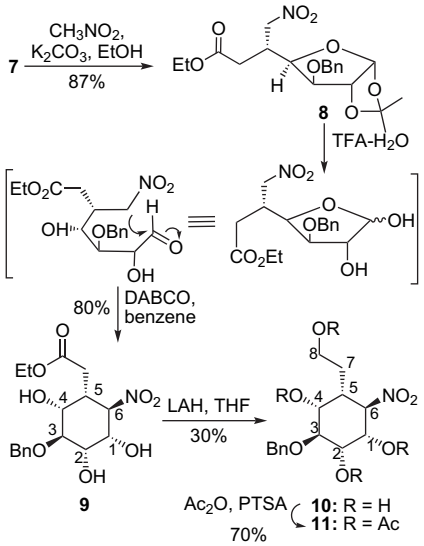
Recently, we reported the intermolecular Michael addition of benzyl amine to D-glucose derived α,β-unsaturated ester **7** to get C-5 epimeric β-aminoesters **I** that were exploited in the synthesis of mono- and bicyclic iminosuagars (Scheme 1).[19] Inspired with this observation, we thought of intermolecular Michael addition of nitromethane to α,β-unsaturated ester **7** to get the nitrosugar **II** with the required nitroalkane moiety suitably placed at C-5 of hexulose for the Henry reaction (Scheme 1). Thus, reduction of the ester and cleavage of 1,2-acetonide functionality in nitrosugar **II** followed by an intramolecular Henry reaction will afford nitrocyclohexitol ring skeleton **III** that could be elaborated to the hydroxyethyl substituted aminocyclohexitol **IV**. On the contrary, reduction and cleavage of 1,2-acetonide functionality in **II** followed by oxidative cleavage would lead to nitroaldose **V**, with one carbon atom less, that on intramolecular Henry reaction would lead to the formation of nitropentitol **VI**—an immediate precursor to aminocyclopentitol **VII**. Although the conjugate addition of nitroalkane with α,β-unsaturated carbonyl compounds has been widely studied,[20] the Michael addition of nitromethane with α,β-unsaturated ester **7** and subsequent Henry approach to aminocyclitols, to the best of our knowledge is not known. The Michael and the Henry reactions are expected to give eight stereoisomers of each **IV** and **VI**, however; our efforts in the exclusive and stereoselective synthesis of aminocyclitols **5** and **6** are discussed herein.



Scheme 1. Synthetic strategy.

2. Results and discussion

Our synthetic route starts with α,β-unsaturated ester **7** obtained as a mixture of *E* and *Z*-isomers in the ratio 3:1 from D-glucose as reported earlier by us.[18] Having both the **7a** (*E*) and **7b** (*Z*) isomers in hand, the conjugate addition reaction with nitromethane was studied with different bases. The Michael addition of nitromethane (2.2 equiv) with **7a** at reflux for 5 h, using potassium carbonate as a base in ethanol, led to a reaction mixture from which the L-*ido* configured nitrosugar **8** was isolated in 87% yield (Scheme 2).[21] Our efforts to alter the stereochemistry at the prochiral C-5 centre under various reaction conditions (e.g., change of solvent, temperature, bases and stoichiometry) had no effect on the stereoselectivity. To understand the effect of the double bond geometry on the stereoselectivity, the reactions were also performed with **7b** (*Z*-isomer). Under identical reaction conditions as above, no change was observed in the stereoselectivity, but the reactions with *E*-isomer were found to be sluggish as compared to the *Z*-isomer. These findings led us to make use of the geometric mixture of α,β-unsaturated ester **7** for further studies.



Scheme 2. Synthesis of nitroinositol **10**.

The stereochemistry at the newly generated stereocentre C-5 could not be assigned from the ^{1}H NMR data. Fortunately, the nitrosugar **8** was obtained as a white crystalline solid and the single crystal X-ray analysis established the 5*R* absolute configuration (Fig. 2).[22,27]

In the next step, cleavage of 1,2-acetonide group in **8** with TFA/H_2O afforded a mixture of hemiacetals (as evident from the ^{1}H NMR spectrum of the column purified product), which was immediately subjected to the intramolecular Henry reaction. In general, the bases of choice for promoting nitroaldol reaction in sugars are alkoxides or hydroxides.[23] Therefore, the reaction of hemiacetal was performed using sodium ethoxide in ethanol, which under different reaction conditions (solvent and temperature) afforded a complex mixture of products. The use of triethylamine as well as diisopropylethyl amine in alcoholic solvents, at different reaction temperatures, also led to the complex mixture of products. However, the best results were obtained on treatment of hemiacetal with DABCO[24] (3.0 equiv) using benzene as a solvent at reflux for 1 h that afforded nitrocyclitol **9** as a single diastereomer in 80% yield.[25] The structure and the absolute configuration at the newly generated C-1 and C-6 stereocentres in **9** were assigned on the basis of ^{1}H NMR studies, wherein the assignment of the signals to the respective protons and the coupling constant information were obtained by COSY and decoupling experiments. In the formation of **9**, the hydroxylated carbons C2, C3 and C4 are derived from the D-glucose and the stereochemistry at C5 was established in the Michael addition product. Assuming that the same stereochemistry is

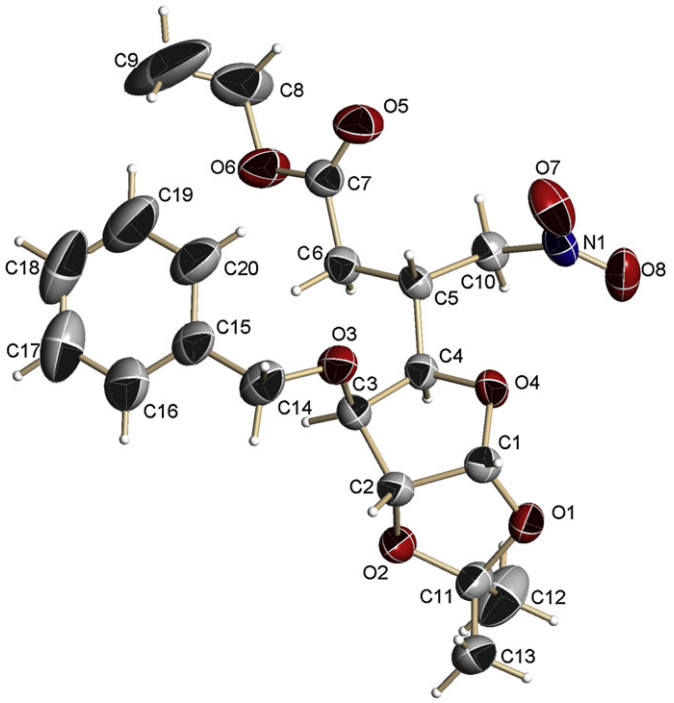


Figure 2. ORTEP drawing of compound **8**.

retained in the product **9**, the stereochemical outcome at C1 and C6 could be derived from the ^{1}H NMR splitting pattern of H-1 and H-6. Amongst the different cyclohexane ring protons, the most diagnostic and downfield proton was found to be the H-6 methine proton (deshielded due to strong −I effect of the nitro group), which appeared at δ 4.69 as a triplet. The large coupling constant ($J_{6,1}$=$J_{6,5}$=10.4 Hz) indicated that H-6/H-1 and H-6/H-5 are trans-diaxially oriented. While H-1 appeared at δ 4.35 as doublet of doublet, wherein the large coupling constant $J_{1,6}$=10.4 Hz is agreeing with trans-orientation of H-1/H-6, the small coupling constant $J_{1,2}$=3.3 Hz showed axial–equatorial relationship between H-1 and H-2. This established the absolute configurations at new stereocentres as 1*S* and 6*R*.

In the next step, reaction of **9** with LAH in THF at 0 °C led to the formation of primary alcohol **10** as a solid in only 30% yield with nitro-functionality intact.[26] Our attempts to increase the yield under various reaction conditions were unsuccessful. In order to confirm the absolute configurations, the nitroinositol **10** was first acetylated with acetic anhydride and pyridine in the presence of catalytic amount of DMAP, however; the reaction resulted into a complex mixture of products probably due to epimerization, at α-carbon to the nitro group, and elimination under basic condition. As an alternative, we thought of acetylation under mild acidic condition. Thus, the reaction of **10** with acetic anhydride in the presence of catalytic amount of PTSA afforded the corresponding tetra-acetylated derivative **11** as a white crystalline solid. The conformational and configurational assignments in **11** were made on the basis of coupling constant data, obtained by decoupling experiments. In the ^{1}H NMR spectrum, H-6 showed a triplet with large coupling constant ($J_{6,5}$=$J_{6,1}$=10.8 Hz) while H-1 appeared as a doublet of doublet ($J_{1,6}$=10.8; $J_{1,2}$=3.3 Hz). The large coupling constant between H-6 and H-1 indicated the trans-diaxial relationship of these protons, whereas the small coupling constant between H-1 and H-2 showed an axial-equatorial relationship. This observation was attributed to the conformational structure *muco*-nitroinositol **11** with absolute configurations as 1*S* and 6*R*. The structure **11** was further confirmed by single crystal X-ray analysis (Fig. 3).[27]

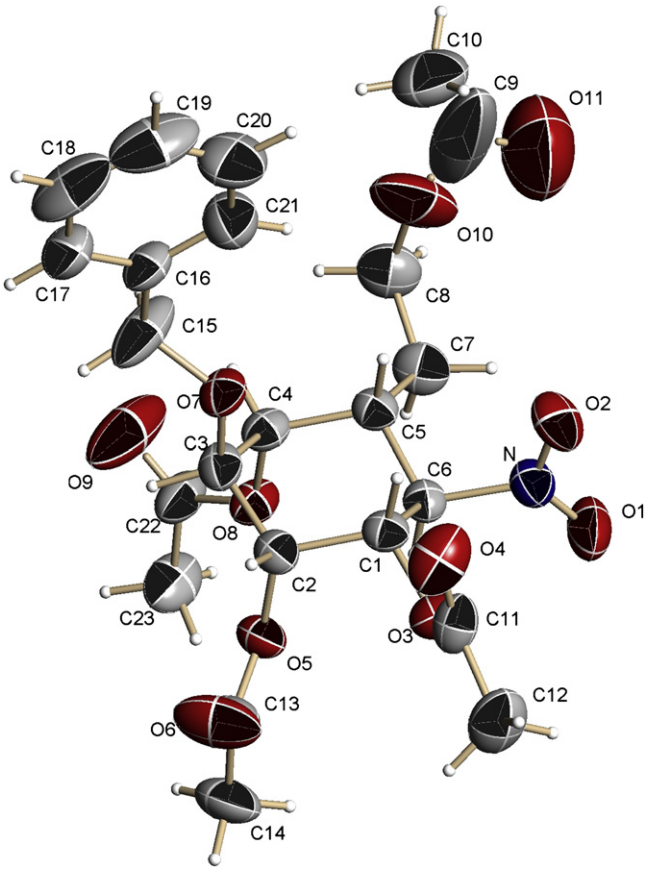
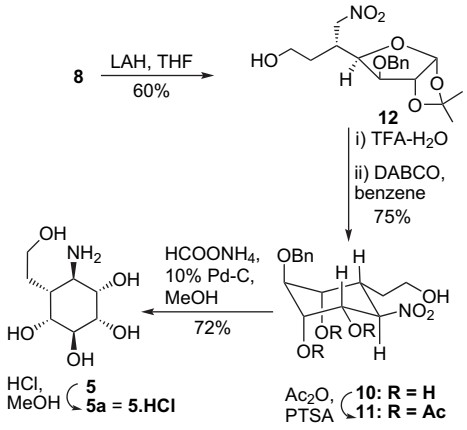


Figure 3. ORTEP drawing of compound **11**.

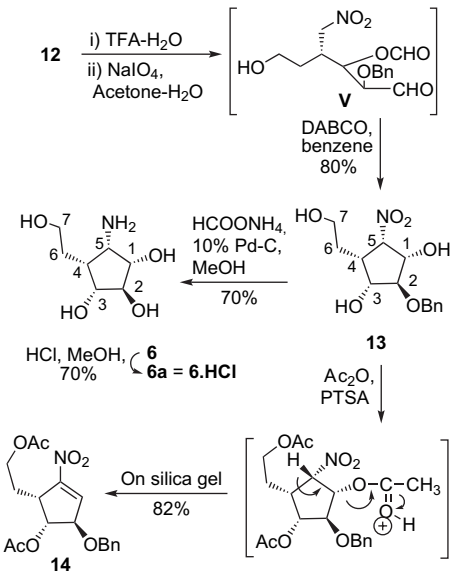
The low yield in the reduction of **9** to get alcohol **10** prompted us to find other method. Thus, as an alternative pathway (Scheme 3), the Michael adduct **8** was first subjected to reduction by LAH in THF at 0 °C to afford a primary alcohol **12** in 60% yield, with the nitro-functionality intact.[26] In the subsequent step, cleavage of 1,2-acetonide group in **12** with TFA/H_2O afforded a mixture of hemiacetals, which was directly subjected to the intramolecular Henry reaction with DABCO in benzene under reflux condition to get nitroalcohol **10** as the only product in 75% yield. The melting point, analytical and spectral data were found to be identical with the product obtained in the previous reaction sequence (**9** to **10**). The formation of the same inositol **10** in both the sequences indicated that the ester group in compound **9** is not having any significant role in the transition state for the stereoselective formation of the Henry product.



Scheme 3. Synthesis of aminocyclohexitol **5**.

In the final step, treatment of **10** with 10% Pd/C and ammonium formate in refluxing methanol afforded aminocyclohexitol **5** as a brown liquid, which was further converted to its hydrochloride salt **5a**. The spectral and analytical data were found to be in consonance with the assigned structure.

While targeting the synthesis of five membered aminocyclitol **6**, the nitroalcohol **12** was considered to be the key intermediate. Thus, as shown in Scheme 4, treatment of nitroalcohol **12** with TFA/H_2O followed by oxidative cleavage of C1–C2 bond with $NaIO_4$ in acetone/water (5:1) afforded nitroaldehyde **V** that on reaction with DABCO in benzene under reflux afforded nitrocyclopentitol **13** as the only stereoisomer in 80% yield. The assignment of the absolute configurations at the newly formed stereocentres was difficult on the basis of the ^{1}H NMR data of compound **13**. Therefore, compound **13** was acetylated using Ac_2O in the presence of PTSA (cat.) that afforded diacetylated nitroalkene **14**. The formation of **14** under mild acidic condition was surprising. This sequence probably involves first acetylation of **13** to give the tri-acetylated derivative that undergoes facile deacetylation to give di-acylated nitroolefin **14**. The efficient deacetylation in tri-acetylated derivative **13** indicated the cis-relative stereochemistry of H-1/H-5 in which the facile *anti*-elimination gives **14**. Based on this observation, the absolute configuration at the new stereocentres was tentatively assigned as 1*S* and 5*S*. It is worth to mention that in the six membered nitrocyclitol **10**, we have isolated the tetra-acetyl derivative in which trans-relative stereochemistry of protons at C6 and C1 precludes the *syn*-elimination leading to the formation of nitroolefin adduct.[25]



Scheme 4. Synthesis of aminocyclopentitol 6.

In the final step, treatment of **13** with 10% Pd/C and ammonium formate in refluxing methanol afforded aminocyclopentitol **6** as a semisolid, which was reacted with methanol/HCl to give the corresponding hydrochloride salt **6a**. The stereochemical assignment in **6** and **6a** was established from the ^{1}H NMR spectrum and decoupling experiments and the coupling constant values are given in Table 1. In compound **6a**, the absolute configurations at C2, C3 and C4 are derived from the substrate **12** and we presume that the same stereochemistry is retained in the product. In order to establish the configurations at C1 and C5, the splitting pattern of H-5 is decisive. In compounds **6** and **6a**, the H-5 appeared at δ 2.81 and 3.26 as a triplet with coupling constants $J_{5,1}$=9.1 and 9.0 Hz, respectively. The large coupling constant indicates cis-relative stereochemistry of H-5/H-1 and H-5/H-4, and established the absolute configurations as 1*S* and 5*S*.

Table 1
Coupling constant data for aminocyclopentitol **6** and its hydrochloride salt **6a**

Compound	$J_{1,2}$ (Hz)	$J_{2,3}$ (Hz)	$J_{3,4}$ (Hz)	$J_{4,5}$ (Hz)	$J_{6,1}$ (Hz)
6	9.1	—	4.2	7.2	9.1
6a	9.1	—	4.5	7.2	9.0

2.1. Explanation for the observed stereoselectivity in the Henry reaction

We believe that DABCO being a tertiary base abstracts the proton from the α-carbon to the nitro functionality in nitroalkane and the carbanion thus formed is more stabilized in the nitronate form under thermodynamically controlled condition. With this assumption, the observed stereoselectivity in the intramolecular Henry reaction to get **9**/**10** could be explained in terms of six membered cyclic transition states **TS 1** and **TS 2** in which the bulky $-CH_2CO_2Et$/$-CH_2CH_2OH$ and $-NO_2$ substituents are placed equatorially oriented (Fig. 4). Among the two transition states, the transition state **TS 1**, that assumes product-like geometry, is stabilized by the π-orbital overlap of C═O and C═N of the nitronate due to their parallel alignment, wherein the attack of the nitronate anion to the *Si*-face of the C═O group afforded **9**/**10**. However, the perpendicular orientation of C═O and C═N precludes the π-orbital overlap and disfavours the **TS 2** in which failure to attack from the *Re*-face of carbonyl group did not afford other stereomer.

The stereoselective formation of the nitrocyclopentitol **13** could also be explained on the basis of transition states for the intermediate **V**. We assumed, the two transition states **TS 3** and **TS 4**, in which C═O and C═N are parallelly oriented and allows overlap of π-orbitals. We believe that **TS 4** is stabilized due to the intramolecular hydrogen bonding between the carbonyl group and the quasi-axial C-3 hydroxyl group, wherein *Si*-face attack to the carbonyl group affords **13**, which is further stabilized by the intramolecular hydrogen bonding between the two quasi-axial hydroxyl groups.

3. Conclusion

In conclusion, intermolecular Michael addition of nitromethane to α,β-unsaturated ester **7** afforded **8** as the only isomer. Reduction of the ester and the cleavage of 1,2-acetonide functionality in **8** and intramolecular Henry reaction afforded nitrocyclitol **9** that was converted to the aminocyclohexitol **5**. While reduction, cleavage of 1,2-acetonide functionality in **8** and $NaIO_4$ mediated oxidative cleavage gave nitroaldose that on the intramolecular Henry reaction afforded nitropentitol **13**—an immediate precursor to aminocyclopentitol **6**. Both the Michael and the Henry reactions were highly stereoselective leading to the exclusive formation of thermodynamically stable products. It is worth to note that the structure and the stereochemistry of aminocyclohexitol **5** were found to be identical with that of the inositol ring **C** of the pancratistatin **4**. The readily available starting material, high yielding and stereoselective steps make our synthetic route more practicable and efficient for the synthesis of new analogues of aminocyclitols.

4. Experimental

4.1. General methods

Melting points were recorded with Thomas Hoover Capillary melting point apparatus and are uncorrected. IR spectra were recorded with an FTIR as a thin film or in Nujol mull or using KBr pellets and are expressed in cm^{-1}. ^{1}H (300 MHz) and ^{13}C (75 MHz)

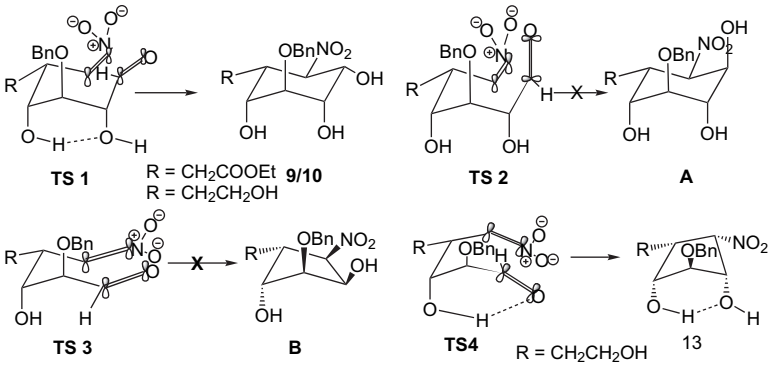


Figure 4. Explanation for observed stereoselectivity.

NMR spectra were recorded using $CDCl_3$ or D_2O as a solvent. Chemical shifts were reported in δ units (parts per million) with reference to TMS as an internal standard and J values are given in hertz. Elemental analyses were carried out with a Thermo electron corporation flash EA 1112 series CHNS-analyzer at the Department of Chemistry, University of Pune as well as at the analytical division, National Chemical Laboratory, Pune. Optical rotations were measured using a Jasco P-1020 polarimeter at 25 °C. Thin layer chromatography was performed on pre-coated plates (0.25 mm, silica gel 80 F_{254}). Column chromatography was carried out with silica gel (100–200 mesh). The reactions were carried out in oven-dried glassware under dry N_2. Methanol, benzene and THF were purified and dried before use. Distilled *n*-hexane and ethyl acetate were used for column chromatography. Pd/C (10%) and DABCO were purchased from Aldrich and/or Fluka and ammonium formate from Merck. After quenching of the reaction with water, the work-up involves washing of combined organic layers with water, brine, drying over anhydrous sodium sulfate and evaporation of the solvent at reduced pressure.

*4.1.1. Ethyl 1,2-O-isopropylidene-3-O-benzyl-5-nitromethyl-5,8-dideoxy-β-L-ido-heptofuranuronate (**8**)*

A solution of **7** (11.0 g, 31.81 mmol), nitromethane (3.78 mL, 89.54 mmol) and K_2CO_3 (9.28 g, 87.01 mmol) in ethanol (100 mL) was refluxed for 5 h. The solvent was evaporated under reduced pressure to get thick oil. Column chromatography and elution with *n*-hexane/ethyl acetate=9/1 afforded nitrosugar **8** (10.24 g, 87%) as a white crystalline solid: mp=82–84 °C; R_f 0.49 (*n*-hexane/ethyl acetate=4/1); $[\alpha]_D^{25}$ −58.1 (*c* 0.13, $CHCl_3$); IR (Nujol): 1728, 1558 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.23 (t, J=7.2 Hz, 3H), 1.31 (s, 3H), 1.48 (s, 3H), 2.27–2.30 (m, 2H), 3.05–3.07 (m, 1H), 3.89 (d, J=2.1 Hz, 1H), 4.10 (q, J=7.2 Hz, 2H), 4.19 (dd, J=7.8, 1.8 Hz, 1H), 4.44 (d, J=11.7 Hz, 1H), 4.80–4.87 (m, 3H), 4.79 (dd, J=13.2, 4.2 Hz, 1H), 5.87 (d, J=3.8 Hz, 1H), 7.24–7.31 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.8, 28.7, 27.1, 33.1, 33.3, 33.7, 72.1, 75.8, 79.2, 81.3, 82.0, 104.9, 112.1, 128.3, 128.5, 128.8, 138.9, 171.0. Anal. Calcd for $C_{20}H_{27}NO_8$: C, 58.87; H, 8.85. Found: C, 58.88; H, 8.50.

*4.1.2. (1S,2S,3S,4R,5R,6R)-3-(Benzyloxy)-5-(2-carbethoxymethyl)-6-nitrocyclohexane-1,2,4-triol (**9**)*

A solution of compound **8** (1.0 g, 2.44 mmol) in TFA/water (8:4, 10 mL) was stirred at 0 °C for 20 min and allowed to attain room temperature. The solution was stirred for 2 h and concentrated under reduced pressure. Column chromatography and elution with *n*-hexane/ethyl acetate (4/1) afforded a mixture of hemiacetal as a white solid (0.85 g, 94%). The ^1H NMR spectrum suggested a mixture of two anomers (α/β=7:3). To a well-stirred solution of the hemiacetal (0.78 g, 2.05 mmol) in benzene was added DABCO (0.89 g, 8.18 mmol) and the reaction mixture was refluxed for 1 h. On cooling, Amberlite IR-120 (acidic resin, 1.0 g) was added, stirred for 1 h and solvent was evaporated under reduced pressure. Column chromatography and elution with *n*-hexane/ethyl acetate (2/1) afforded compound **9** as a yellow liquid (0.81 g, 80%): R_f 0.53 (*n*-hexane/ethyl acetate=1/1); $[\alpha]_D^{25}$ −171.2 (*c* 0.12, $CHCl_3$); IR (neat): 3300–3450, 2929, 1728, 1554 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3/D_2O$) δ 1.19 (t, J=8.9 Hz, 3H), 2.23 (dd, J=16.2, 3.3 Hz, 1H), 2.70 (dd, J=16.2, 9.6 Hz, 1H), 2.83–2.98 (m, 1H), 3.83 (t, J=3.0 Hz, 1H), 3.98–4.18 (m, 4H), 4.35 (dd, J=10.4, 3.3 Hz, 1H), 4.48 (ABq, J=11.7 Hz, 2H), 4.69 (t, J=10.4 Hz, 1H), 7.21–7.32 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3/D_2O$) δ 14.1, 32.3, 37.2, 61.3, 69.8, 70.5, 72.1, 72.2, 75.3, 88.3, 127.5, 127.7, 127.9, 128.4, 128.5, 137.0, 171.7. Anal. Calcd for $C_{17}H_{23}NO_8$: C, 55.28; H, 8.28. Found: C, 55.44; H, 8.32.

*4.1.3. (1S,2S,3S,4R,5R,6R)-3-(Benzyloxy)-5-(2-hydroxyethyl)-6-nitrocyclohexane-1,2,4-triol (**10**)*

To an ice cooled suspension of LAH (0.3 g, 7.59 mmol) in dry THF (5 mL) was added a solution of **9** (0.4 g, 1.08 mmol) in dry THF (5 mL) over a period of 10 min. The reaction mixture was warmed to room temperature and stirred for 1 h. On cooling to 0 °C, ethyl acetate (10 mL) was added, stirred for 10 min and quenched with saturated solution of Na_2SO_4 (2 mL). The solution was filtered, the residue washed with ethyl acetate (3×3 mL), and the organic layer evaporated and purified by column chromatography (*n*-hexane/ethyl acetate=4/8) to give **10** (0.27 g, 30%) as a white solid: mp=98–100 °C; R_f 0.53 (ethyl acetate); $[\alpha]_D^{25}$ −18.92 (*c* 0.22, CH_3OH); IR(Nujol): 2932–3383, 1554 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.24–1.41 (m, 1H), 1.75–1.80 (m, 1H), 2.45–2.53 (m, 1H), 3.25 (br s, 1H), 3.47–3.54 (m, 1H), 3.78 (t, J=3.3 Hz, 1H), 4.00 (br d, J=18.2 Hz, 2H), 4.20 (dd, J=10.8, 3.3 Hz, 1H), 4.57 (s, 2H), 4.84 (t, J=10.8 Hz, 1H), 7.23–7.32 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.0, 38.0, 58.2, 69.4, 70.7, 71.7, 71.9, 75.9, 89.2, 127.2 (s), 127.5, 128.1 (s), 137.3. Anal. Calcd for $C_{15}H_{21}NO_7$: C, 55.04; H, 8.47. Found: C, 55.23; H, 8.29. The ^1H NMR spectrum was not very clear due to poor solubility of the compound in $CDCl_3$. Addition of DMSO-d_6 to the solution leads to broadening of the signals.

*4.1.4. (1S,2S,3S,4R,5R,6R)-5-(2-Acetoxyethyl)-3-(benzyloxy)-nitrocyclohexane-1,2,4-triyl triacetate (**11**)*

To a solution of **10** (0.09 g, 0.27 mmol) in acetic anhydride (0.83 mL, 8.84 mmol) was added catalytic amount of PTSA (0.002 g, 0.01 mol) at 0 °C. The solution was warmed to room temperature and stirred for 18 h. The reaction mixture was concentrated under reduced pressure. Column chromatography and elution (*n*-hexane/ethyl acetate=4/1) afforded tetra-acetate **12** (0.09 g, 70%) as a white crystalline solid: mp=110–112 °C; R_f 0.89 (*n*-hexane/ethyl acetate=3/2); $[\alpha]_D^{25}$ +2.88 (*c* 1.8, $CHCl_3$); IR (Nujol): 1740 (br), 1558 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.45–1.82 (m, 1H), 1.75–1.92 (m, 1H), 1.97 (s, 3H), 1.98 (s, 3H), 2.08 (s, 3H), 2.07 (s, 3H), 2.73–

2.81 (m, 1H), 3.83 (br s, 1H), 3.97 (br m, 2H), 4.88 (ABq, J=11.7 Hz, 2H), 4.91 (t, J=11.4 Hz, 1H), 5.09 (br s, 1H), 5.52 (br s, 1H), 5.84 (dd, J=11.4, 3.3 Hz, 1H), 7.25–7.35 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.4, 20.7, 20.8, 25.8, 38.7, 60.8, 68.2, 69.1, 69.8, 72.7, 73.1, 85.5, 127.4, 127.8 (s), 128.1, 128.4, 138.4, 188.7, 189.0, 189.3, 170.4. Anal. Calcd for $C_{23}H_{29}NO_{11}$: C, 55.75; H, 5.90. Found: C, 55.80; H, 6.13.

4.1.5. 1,2-O-Isopropylidene-3-O-benzyl-5,6-dideoxy-5-nitromethyl-β-L-ido-hepto-1,4-furanose (**12**)

The reaction of **8** (2.0 g, 4.89 mmol) with LAH (0.37 g, 9.78 mmol) in dry THF (10 mL) followed by work-up as described for compound **10** and purification by column chromatography (n-hexane/ethyl acetate=4/1) afforded **12** as a pale yellow liquid (1.08 g, 60%): R_f 0.28 (n-hexane/ethyl acetate=3/2); $[\alpha]_D^{25}$ −52.04 (c 1.35, $CHCl_3$); IR (neat): 2932–3383, 1554 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.31(s, 3H), 1.47 (s, 3H), 1.51–1.58 (m, 2H), 2.39 (br s, exchanges with D_2O, 1H), 2.79–2.85 (m, 1H), 3.81 (t, J=8.3 Hz, 2H), 3.92 (d, J=3.3 Hz, 1H), 4.18 (dd, J=8.4, 3.3 Hz, 1H), 4.51 (d, J=11.7 Hz, 1H), 4.55 (dd, J=13.2, 8.8 Hz, 1H), 4.82 (d, J=3.9 Hz, 1H), 4.87 (d, J=11.7 Hz, 1H), 4.75 (dd, J=12.9, 4.2 Hz, 1H), 5.88 (d, J=3.9 Hz, 1H), 7.25–7.38 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.2, 28.8, 31.1, 33.8, 59.4, 71.8, 78.0, 78.8, 79.7, 81.3, 81.5, 104.3, 111.8, 127.8, 127.9, 128.2, 128.3, 138.8. Anal. Calcd for $C_{18}H_{25}NO_7$: C, 58.84; H, 5.88. Found: C, 58.99; H, 5.71.

4.1.6. (1S,2S,3S,4R,5R,6R)-3-(Benzyloxy)-5-(2-hydroxymethyl)-6-nitrocyclohexane-1,2,4-triol (**10**) from **12**

Compound **12** (1.0 g, 2.94 mmol) was dissolved in TFA/water (8:4, 10 mL), stirred at 0 °C for 20 min and allowed to warm up to room temperature. The solution was stirred for 2 h at room temperature and concentrated under reduced pressure. Column chromatography on silica gel (n-hexane/ethyl acetate=2/1) afforded the hemiacetal as a white solid (0.73 g, 82%).

To an ice cooled suspension of LAH (0.3 g, 7.59 mmol) in dry THF (5 mL) was added a solution of hemiacetal (0.20 g, 0.81 mmol) in dry THF (5 mL) over a period of 10 min. The reaction mixture was warmed to room temperature and stirred for 1 h. On cooling to 0 °C, ethyl acetate (10 mL) was added, stirred for 10 min and quenched with saturated solution of Na_2SO_4 (2 mL). The solution was filtered, the residue washed with ethyl acetate (3×5 mL), and the organic layer evaporated and purified by column chromatography (n-hexane/ethyl acetate=2/1) to give **10** (0.15 g, 75%) as a white solid. The spectral and analytical data of the compound match that of compound **10** synthesized earlier in Section 4.1.3.

4.1.7. (1S,2S,3S,4R,5R,6R)-6-Amino-5-(2-hydroxyethyl)-cyclohexane-1,2,3,4-tetraol (**5**)

To a well-stirred solution of compound **10** (0.11 g, 0.33 mmol) in dry methanol (10 mL) were added 5% Pd/C (0.1 g) and ammonium formate (0.15 g, 2.35 mmol). The reaction mixture was refluxed for 45 min and on cooling was filtered through Celite. Evaporation of solvent and purification by column chromatography (chloroform/methanol=1/9) afforded **5** (0.05 g, 72%) as a brown liquid: R_f 0.17 (CH_3OH); $[\alpha]_D^{25}$ +27.82 (c 0.34, CH_3OH); IR (neat): 2809–3381 cm^{-1}; ^{1}H NMR (300 MHz, D_2O) δ 1.72–1.87 (m, 2H), 2.10–2.22 (m, 1H), 3.38 (t, J=9.8 Hz, 1H), 3.58–3.88 (m, 1H), 3.70–3.82 (m, 1H), 3.84–3.94 (m, 2H), 3.98–4.04 (m, 1H), 4.07 (t, J=3.8 Hz, 1H); ^{13}C NMR (75 MHz, D_2O) δ 34.0, 40.9, 58.5, 63.8, 73.8, 75.2, 75.3, 77.3. Anal. Calcd for $C_8H_{17}NO_5$: C, 48.37; H, 8.27. Found: C, 48.49; H, 8.48.

4.1.8. (1S,2S,3S,4R,5R,6R)-6-Amino-5-(2-hydroxyethyl)-cyclohexane-1,2,3,4-tetraol hydrochloride (**5a**)

A solution of **5** (0.05 g, 0.24 mmol) in methanol/HCl (10 mL, 0.5 M) was stirred at room temperature for 24 h. The solvent was evaporated under reduced pressure and the residue was washed with ethyl acetate, dry ether and dried in vacuum to get **5a** (0.05 g, 80% yield) as a semisolid: R_f 0.12 (CH_3OH) (elongated trail observed on TLC plate); $[\alpha]_D^{25}$ +1.29 (c 3.0, CH_3OH); IR (neat): 2888–3381 (br) cm^{-1}; ^{1}H NMR (300 MHz, D_2O) δ 1.52–1.75 (m, 2H), 1.93–2.74 (m, 1H), 3.22 (t, J=10.5 Hz, 1H), 3.55–3.85 (m, 2H), 3.87–3.80 (m, 2H), 3.87 (br s, 1H), 3.92 (br d, J=3.0 Hz, 1H); ^{13}C NMR (75 MHz, D_2O) δ 38.1, 51.7, 58.8, 82.7, 88.9, 70.3, 70.4, 72.4. Anal. Calcd for $C_8H_{18}ClNO_5$: C, 39.43; H, 7.45. Found: C, 39.73; H, 7.70.

4.1.9. (1S,2S,3R,4R,5S)-2-(Benzyloxy)-4-(2-hydroxymethyl)-5-nitrocyclopentane-1,3-diol (**13**)

To a cooled solution of hemiacetal (0.30 g, 0.92 mmol), obtained from **12**, in acetone/water (3:2, 10 mL) was added sodium metaperiodate (0.39 g, 1.83 mmol). After stirring for 1 h at 0 °C, the excess of sodium metaperiodate was decomposed using ethylene glycol (0.20 mL). The reaction mixture was filtered through Celite, residue washed with acetone and the combined solvent was evaporated under reduced pressure to afford a crude product. The crude product thus obtained was subjected to further reaction. To a well-stirred solution of aldehyde (0.25 g, 0.84 mmol) in benzene (10 mL), DABCO (0.34 g, 3.04 mmol) was added and the reaction mixture was refluxed for 1 h. On cooling, the acidic resin (Amberlite IR-120, 0.40 g) was added to the reaction mixture and stirred for 30 min. Filtration, removal of the solvent and purification by column chromatography with n-hexane/ethyl acetate (8/4) afforded a thick oil **13** (0.20 g, 80%): R_f 0.45 (n-hexane/ethyl acetate=1/1); $[\alpha]_D^{25}$ +7.70 (c 1.3, $CHCl_3$); IR (neat): 3338–3500 (br), 1580 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.82–1.72 (m, 1H), 1.78–1.95 (m, 1H), 2.80–2.80 (m, 1H), 3.00–3.40 (br, 1H, exchanges with D_2O), 3.42–3.80 (m, 1H), 3.80–3.70 (m, 1H), 3.73 (d, J=2.1 Hz, 1H), 4.17 (d, J=5.4 Hz, 1H), 4.00–4.35 (br, 2H, exchanges with D_2O), 4.40–4.85 (m, 4H), 7.21–7.28 (m, 5H); ^{13}C NMR (75 MHz, $CHCl_3$) δ 28.4, 45.0, 60.5, 71.8, 74.4, 79.7, 88.4, 94.1, 127.7, 127.8, 128.4, 137.2. Anal. Calcd for $C_{14}H_{19}NO_8$: C, 58.58; H, 8.44. Found: C, 58.39; H, 8.83.

4.1.10. (1R,2R,5R)-5-(2-Acetoxyethyl)-2-(benzyloxy)-4-nitrocyclopent-3-enyl acetate (**14**)

To a solution of **13** (0.10 g, 0.34 mmol) in acetic anhydride (0.80 mL, 8.4 mmol), catalytic amount of PTSA (0.005 g, 0.03 mmol) was added at 0 °C. The solution was warmed to room temperature and stirred for 18 h. Column chromatography (n-hexane/ethyl acetate=4/1) on silica gel afforded compound **14** (0.1 g, 82%) as a thick liquid: R_f 0.5 (n-hexane/ethyl acetate=4/1); $[\alpha]_D^{25}$ −114.45 (c 1.3, $CHCl_3$); IR (neat): 2872–3488 (br), 1743, 1525 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.72–1.81 (m, 1H), 1.95 (s, 3H), 2.00–2.09 (m, 1H), 2.13 (s, 3H), 3.71–3.72 (m, 1H), 3.92–3.99 (m, 1H), 4.04–4.12 (m, 1H), 4.85 (s, 2H), 4.78 (d, J=5.4 Hz, 1H), 5.38 (dd, J=7.8, 8.3 Hz, 1H), 6.84 (s, 1H), 7.25–7.35 (m, 5H); ^{13}C NMR (75 MHz, $CHCl_3$) δ 20.8, 20.9, 28.1, 40.9, 61.9, 72.8, 79.1, 83.4, 127.7, 128.1, 128.5, 132.9, 138.9, 153.4, 189.7, 170.8. Anal. Calcd for $C_{18}H_{21}NO_7$: C, 59.50; H, 5.83. Found: C, 59.87; H, 5.73.

4.1.11. (1S,2S,3R,4R,5S)-5-Amino-4-(2-hydroxyethyl)cyclopentane-1,2,3-triol (**6**)

To a well-stirred solution of compound **13** (0.12 g, 0.33 mmol) in dry methanol (10 mL) were added 5% Pd/C (0.1 g) and ammonium formate (0.1 g, 1.82 mmol). The reaction mixture was refluxed for 45 min and on cooling was filtered through Celite. Evaporation of solvent and purification by column chromatography (chloroform/methanol=1/9) afforded **6** (0.05 g, 70%) as a semisolid: R_f 0.12 (CH_3OH); $[\alpha]_D^{25}$ +27.45 (c 3.0, MeOH); IR (neat): 2800–3390 (br) cm^{-1}; ^{1}H NMR (300 MHz, D_2O) δ 1.80–1.72 (m, 1H), 1.74–1.98 (m, 2H), 2.81 (t, J=9.1 Hz, 1H), 3.52 (dd, J=8.1, 7.2 Hz, 1H), 3.55–3.72 (m, 3H), 3.94 (dd, J=7.2, 4.2 Hz, 1H); ^{13}C NMR (75 MHz, D_2O) δ 29.5, 43.1, 59.0, 60.5, 74.7, 81.8, 82.4. Anal. Calcd for $C_7H_{13}NO_8$: C, 40.58; H, 8.32. Found: C, 40.81; H, 8.87.

*4.1.12. (1S,2S,3R,4R,5S)-5-Amino-4-(2-hydroxyethyl)cyclopentane-1,2,3-triol hydrochloride (**6a**)*

Compound **6** (0.05 g, 0.28 mmol) was converted to its hydrochloride salt following the same procedure as **5a** to obtain a semisolid **6a** (0.05 g, 70%): R_f 0.20 (CH_3OH); $[\alpha]_D^{25}$ +7.41 (*c* 3.0, MeOH); IR (neat): 2878–3390 (br) cm^{-1}; ^1H NMR (300 MHz, D_2O) δ 1.81–1.78 (m, 1H), 1.84–2.02 (m, 1H), 2.20–2.40 (m, 1H), 3.28 (t, *J*=9.0 Hz, 1H), 3.58–3.72 (m, 1H), 3.75–3.98 (m, 3H), 4.05 (dd, *J*=7.2, 4.5 Hz, 1H); ^{13}C NMR (75 MHz, D_2O) δ 29.3, 40.8, 59.4, 60.3, 74.3, 78.0, 81.4. Anal. Calcd for $C_7H_{18}ClNO_4$: C, 39.35; H, 7.55. Found: 39.78, H, 8.00.

Acknowledgements

We are grateful to Prof. M. S. Wadia for helpful discussions and to Department of Science and Technology, New Delhi for the financial support (SR/S1/OC-21/2005). C. C. is thankful to the University of Pune for the stipend.

Supplementary data

Supplementary data of the NMR spectra associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.07.049.

References and notes

1. For review on the Henry reaction, see: Luzzio, F. A. *Tetrahedron* **2001**, *57*, 915–945.
2. (a) Sato, K.; Akai, S.; Shoji, H.; Sugita, N.; Yoshida, S.; Nagai, Y.; Suzuki, K.; Nakamura, Y.; Kajihara, Y.; Funabashi, M.; Yoshimura, J. *J. Org. Chem.* **2008**, *73*, 1234–1242; (b) Boruwa, J.; Barua, N. C. *Tetrahedron* **2006**, *62*, 1193–1198; (c) Gogoi, N.; Boruwa, J.; Barua, N. C. *Tetrahedron Lett.* **2005**, *46*, 7581–7582; (d) Allmendinger, L.; Bauschke, G.; Paintner, F. F. *Synlett* **2005**, 2615–2618; (e) Zhang, H. L.; Oniciu, D. C.; Mueller, R.; McCosar, B. H.; Popa, E. *ARKIVOC* **2005**, *10*, 285–291; (f) Soengas, R. G.; Estévez, J. C.; Estévez, R. J. *Tetrahedron: Asymmetry* **2003**, *14*, 3955–3963; (g) Ishikawa, T.; Shimizu, Y.; Kudoh, T.; Saito, S. *Org. Lett.* **2003**, *5*, 3879–3882; (h) Trost, B. M.; Yeh, V. S. C.; Ito, H.; Bremeyer, N. *Org. Lett.* **2002**, *4*, 2621–2623; (i) Andersch, J.; Bols, M. *Chem.—Eur. J.* **2001**, *7*, 3744–3747.
3. Aoyagi, T.; Yamamoto, T.; Kojiri, K.; Morishima, H.; Nagai, M.; Hamada, M.; Takeuchi, T.; Umezawa, H. *J. Antibiot.* **1989**, *42*, 883–889.
4. (a) Sakuda, S.; Isogai, A.; Matsumoto, S.; Suzuki, A.; Koseki, K. *Tetrahedron Lett.* **1986**, *27*, 2475–2478; (b) Sakuda, S.; Isogai, A.; Matsumoto, S.; Suzuki, A. *J. Antibiot.* **1987**, *40*, 296–300.
5. (a) El Ashry, E. S.; Rashed, N.; Shobier, A. H. *Pharmazie* **2000**, *55*, 251–262; (b) El Ashry, E. S.; Rashed, N.; Shobier, A. H. *Pharmazie* **2000**, *55*, 331–348; (c) El Ashry, E. S.; Rashed, N.; Shobier, A. H. *Pharmazie* **2000**, *55*, 403–415; (d) Dwek, R. A.; Butters, T. D.; Platt, F. M.; Zitzmann. *Nat. Rev. Drug Discov.* **2002**, *1*, 65–75; (e) Horii, S.; Iwasa, T.; Mizuta, E.; Kameda, Y. *J. Antibiot.* **1971**, *24*, 59–63.
6. (a) Chen, X.; Fan, Y.; Zheng, Y.; Shen, Y. *Chem. Rev.* **2003**, *103*, 1955–1978; (b) Donohoe, T. Y.; Johnson, P. D.; Keenan, M. *Org. Lett.* **2005**, *7*, 1275–1277; (c) Trost, B. M.; Crawley, M. L. *Chem. Rev.* **2003**, *103*, 2921–2943; (d) Kobayashi, Y.; Miyazaki, H.; Shiozaki, M. *J. Org. Chem.* **1994**, *59*, 813–822; (e) Knapp, S.; Sebastian, M. J.; Ramanathan, H. *J. Org. Chem.* **1983**, *48*, 4786–4788; (f) Sakuda, S.; Sujiyama, Y.; Zhou, Z.-Y.; Takao, H.; Ikeda, H.; Hakinuma, K.; Yamada, Y.; Nagasawa, H. *J. Org. Chem.* **2001**, *66*, 3356–3361; (g) Ho, J. H.; Mohareb, R. M.; Ahn, J. H.; Sim, T. B.; Rapoport, H. *J. Org. Chem.* **2003**, *68*, 109–114; (h) Hudlicky, T.; Rinner, U.; Finn, K. J.; Ghiviriga, I. *J. Org. Chem.* **2005**, *70*, 3490–3499; (i) Serrano, P.; Llebaria, A.; Delgado, A. *J. Org. Chem.* **2005**, *70*, 7829–7840; (j) Marco-Contelles, J.; Khiar, N.; Destabel, C.; Bernabe, M.; Martinez-Grau, A.; Chiara, J. L. *J. Org. Chem.* **1997**, *62*, 7397–7412; (k) Mahmud, T.; Flatt, P. M.; Wu, X. *J. Nat. Prod.* **2007**, *70*, 1384–1391; (l) Alegret, C.; Benet-Buchholz, J.; Riera, A. *Org. Lett.* **2006**, *8*, 3069–3072; (m) Chiara, J.; Garcia, A.; Sesmilo, E.; Vacas, T. *Org. Lett.* **2006**, *8*, 3935–3938.
7. (a) Sureshan, K. M.; Ikeda, K.; Asano, N.; Watanabe, Y. *Tetrahedron* **2008**, *64*, 4072–4080; (b) El Blidi, L.; Ahbala, M.; Bolte, J.; Lemaire, M. *Tetrahedron: Asymmetry* **2006**, *17*, 2684–2688; (c) Kelebekli, L.; Çelik, M.; Şahin, E.; Kara, Y.; Balci, M. *Tetrahedron Lett.* **2006**, *47*, 7031–7035; (d) Palaniappan, N.; Ayers, S.; Gupta, S.; Habib, E.-S.; Reynolds, K. A. *Chem. Biol.* **2006**, *13*, 753–764; (e) Chênevert, R.; Jacques, F. *Tetrahedron: Asymmetry* **2006**, *17*, 1017–1021; (f) Huang, Z.; Kakinuma, K.; Eguchi, T. *Bioorg. Chem.* **2005**, *33*, 82–89; (g) El Blidi, L.; Crestia, D.; Gallienne, E.; Demuynck, C.; Bolte, J.; Lemaire, M. *Tetrahedron: Asymmetry* **2004**, *15*, 2951–2954; (h) Akiyama, M.; Awamura, T.; Kimura, K.; Hosomi, Y.; Kobayashi, A.; Tsuji, K.; Kuboki, A.; Ohira, S. *Tetrahedron Lett.* **2004**, *45*, 7133–7136; (i) Arakawa, K.; Bowers, S. G.; Michels, B.; Trin, V.; Mahmud, T. *Carbohydr. Res.* **2003**, *338*, 2075–2082; (j) Mahmud, T. *Nat. Prod. Rep.* **2003**, *20*, 137–166; (k) Ogawa, S.; Fujieda, S.; Sakata, Y.; Ishizaki, S.; Hisamatsu, S.; Okazaki, K. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 3461–3463; (l) Tanaka, K. S.; Winters, G. C.; Batchelor, R. J.; Einstein, F. W.; Bennet, A. J. *J. Am. Chem. Soc.* **2001**, *123*, 998–999; (m) Gravier-Pelletier, C.; Maton, W.; Dintinger, T.; Tellier, C.; Le Merrer, Y. *Tetrahedron* **2003**, *59*, 8705–8720 and references cited therein.
8. Kawasaki, T.; Kuzuyama, T.; Furihata, K.; Itoh, N.; Seto, H.; Dairi, T. *J. Antibiot.* **2003**, *56*, 957–966.
9. Wu, X.; Flatt, P. M.; Schlorke, O.; Zeeck, A.; Dairi, T.; Mahmud, T. *ChemBioChem* **2007**, *8*, 239–248.
10. (a) Jachak, S. M.; Karche, N. P.; Dhavale, D. D. *Tetrahedron Lett.* **2001**, *42*, 4925–4928; (b) Chakraborty, C.; Vyavahare, V.; Dhavale, D. D. *Tetrahedron* **2007**, *63*, 11984–11990.
11. For hydroxyethyl substituted aminocyclopentitols, see: (a) Bojstrup, M.; Lundt, I. *Org. Biomol. Chem.* **2005**, *3*, 1738–1745; (b) Bojstrup, M.; Fanefjord, M.; Lundt, I. *Org. Biomol. Chem.* **2007**, *5*, 3164–3171.
12. (a) Grosheintz, J. M.; Fischer, H. O. L. *J. Am. Chem. Soc.* **1948**, *70*, 1476–1479; (b) Grosheintz, J. M.; Fischer, H. O. L. *J. Am. Chem. Soc.* **1948**, *70*, 1479–1484.
13. (a) Ferrier, R. J.; Middleton, S. *Chem. Rev.* **1993**, *93*, 2779–2831; (b) Rassu, G.; Auzzas, L.; Battistini, L.; Casiraghi, G. *Mini-Rev. Org. Chem.* **2004**, *1*, 343–357.
14. (a) Marco-Contelles, J.; Alhambra, C.; Martinez-Grau, A. *Synlett* **1998**, 693–699; (b) Marco-Contelles, J.; Pozuelo, C.; de Opazo, E. *Carbohydr. Res.* **2001**, *332*, 342–349; (c) Gomez, A. M.; Moreno, E.; Uriel, C.; Jarosz, S.; Valverde, S.; Lopez, J. C. *Tetrahedron: Asymmetry* **2005**, *16*, 2401–2407.
15. Denmark, S. E.; Juhl, M. *Helv. Chim. Acta* **2002**, *85*, 3712–3736.
16. Madsen, R. *Eur. J. Org. Chem.* **2007**, 399–415 and references within.
17. (a) Magerlein, B. J. *Tetrahedron Lett.* **1970**, *1*, 33–36; (b) Moorman, A. R.; Martin, T.; Borchardt, R. T. *Carbohydr. Res.* **1983**, *113*, 233–239; (c) Suami, T.; Sasai, H.; Matsuno, K. *Chem. Lett.* **1983**, 819–822; (d) Suami, T.; Sasai, H.; Matsuno, K.; Suzuki, N. *Tetrahedron Lett.* **1984**, *25*, 4533–4536; (e) Corey, E. J.; Samuelsson, B.; Luzzio, F. A. *J. Am. Chem. Soc.* **1984**, *106*, 3682–3683; (f) Luzzio, F. A.; Moore, W.J. *Abstracts of Papers*, 207th National Meeting of the American Chemical Society, San Diego, CA; March 13–17; American Chemical Society: Washington, DC, 1994; Div. Org. Chem. No. 330; (g) Knapp, S. *Chem. Rev.* **1995**, *95*, 1859–1876; (h) Borrachero, P.; Dianez, M. J.; Estrada, M. D.; Gomez-Guillen, M.; Gomez-Sanchez, A.; Lopez-Castro, A.; Perez-Garrido, S. *Carbohydr. Res.* **1993**, *247*, 239–248; (i) Hossain, N.; Garg, N.; Chattopadhyay, J. *Tetrahedron* **1993**, *49*, 10061–10068; (j) Koll, P.; Stenns-Seelhorst, W.; Brandenburg, H. *Liebigs Ann. Chem.* **1991**, 201–206.
18. (a) Rosini, G.; Ballini, R. *Synthesis* **1988**, 833–847; (b) *Nitro Compounds Recent Advances in Synthesis and Chemistry*; Feuer, H., Nielsen, A. T., Eds.; VCH: Weinheim, 1990; (c) Ono, N. *The Nitro Group in Organic Synthesis*; Wiley-VCH: New York, NY, 2001; (d) *The Chemistry of Amino, Nitroso, Nitro and Related Groups*; Patai, S., Ed.; Wiley: Chichester, UK, 1996; (e) Adams, J. P. *J. Chem. Soc., Perkin Trans. 1* **2002**, 2586–2597.
19. Patil, N. T.; Tilekar, J. N.; Dhavale, D. D. *J. Org. Chem.* **2001**, *66*, 1065–1074.
20. (a) Hayashi, Y.; Okano, T.; Aratake, S.; Hazelard, D. *Angew. Chem.* **2007**, *46*, 4922–4925; (b) Van Neck, T.; Van Mierloo, S.; Dehaen, W. *Molecules* **2007**, *12*, 395–405; (c) Zou, W.; Wu, A.-T.; Bhasin, M.; Sandbhor, M.; Wu, S.-H. *J. Org. Chem.* **2007**, *72*, 2686–2689; (d) Barco, A.; Baricordi, N.; Benetti, S.; De Risi, C.; Pollini, G. P. *Tetrahedron Lett.* **2006**, *47*, 8087–8090; (e) Ji, X.-M.; Mo, J.; Liu, H.-M.; Sun, H.-P. *Carbohydr. Res.* **2006**, *341*, 2312–2320; (f) Ballini, R.; Bosica, G.; Fiorini, D.; Palmieri, A.; Petrini, M. *Chem. Rev.* **2005**, *105*, 933–971.
21. The ^1H and ^{13}C NMR spectra of crude mixture showed additional signals <10%, probably due to the other diastereomer. Assuming that the additional signals are due to the other isomer, the ratio of two diastereomers is L-*ido*/D-*gluco*=92:08.
22. The observed stereoselectivity was in accordance with that reported previously by us in the conjugate addition of substituted amines with α,β-unsaturated esters **7** and was rationalized in terms of Felkin–Anh transition states see Refs. 19,20f.
23. (a) Tronchet, J. M. J.; Pallie, K. D.; Barbalat- Rey, F. *J. Carbohydr. Chem.* **1985**, *4*, 29–52; (b) Saeki, H.; Iwashige, T. *Chem. Pharm. Bull.* **1968**, *16*, 2410–2415; (c) Kovar, J.; Baer, H. H. *Can. J. Chem.* **1973**, *51*, 1801–1811; (d) Kovar, J.; Baer, H. H. *Carbohydr. Res.* **1975**, *39*, 19–32; (e) Kovar, J.; Baer, H. H. *Carbohydr. Res.* **1975**, *45*, 161–180; (f) Soengas, R. G.; Estevez, J. C.; Estevez, R. J. *Org. Lett.* **2003**, *15*, 4457–4459; (g) Otero, J. M.; Fernandez, F.; Estevez, J. C.; Estevez, R. J. *Tetrahedron: Asymmetry* **2005**, *16*, 4045–4049.
24. The use of DABCO as a most efficient base in the Henry reaction, under microwave reaction condition, is reported by Gan, C.; Chen, X.; Lai, G.; Wang, Z. *Synlett* **2006**, 387–390.
25. The reaction mixture was heated for a prolonged period of 8 h. Compound **9** was the only product, which could be isolated while no formation of nitroalkene or any other stereoisomer was detected in the reaction mixture. The ^1H and ^{13}C NMR spectra of crude reaction mixture showed additional signals <05% probably due to the side product.
26. Our observation was found to be analogous to that reported wherein $-NO_2$ functionality is compatible under LAH condition see Ref. 1.
27. The crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as deposition nos. CCDC-685631 (**8**) and CCDC-685632 (**11**). Copies of the data can be obtained, free of charge, on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk].