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Stereoselective synthesis of *muco*-quercitol, (+)-*gala*-quercitol and 5-amino-5-deoxy-D-*vibo*-quercitol from D-mannitol

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Synthesis of *muco*-quercitol, (+)-*gala*-quercitol, and 5-amino-5-deoxy-D-*vibo*-quercitol is described from D-mannitol using ring closing metathesis and diastereoselective dihydroxylations as key steps.

1. Introduction

Polyhydroxylated cyclohexanes are called cyclitols, and cyclohexanepentols, a subclass of cyclitols, are called as quercitols. Quercitols are basically deoxyinositols having 16 diastereoisomers.[1] Among the various possible stereoisomers, three of them viz. (+)-*proto*,[2] (−)-*proto*,[3] and (−)-*vibo*[4] stereoisomers occur in nature.[5] Aminocyclitols are also a subclass of cyclitols and possess important biological activities such as glycosidase inhibitions, besides being the aglycon part of numerous aminoglycoside antibiotics, e.g., streptomycin and fortimycin.[6] Chiral cyclitols (including aminocyclitols) and chiral quercitols, being formally related to carbohydrates, are useful intermediates in organic chemistry and thus several synthesis toward them are known[5,7–9] in the literature. Notable among them are reports by Balci et al.[5,7] who have synthesized both racemic and optically active quercitols from 1,4-cyclohexadiene as a starting material.

In continuation with our ongoing research toward the synthesis of natural and unnatural azasugars, carbasugars, and hybrid sugars,[10] in this paper, we describe an approach toward *muco*-quercitol **1**, (+)-*gala*-quercitol **2**, and 5-amino-5-deoxy-D-*vibo*-quercitol **3** (Fig. 1) starting from commercially available D-mannitol using ring closing metathesis, diastereoselective dihydroxylation and regiospecific in situ opening of epoxide as key steps. Retrosynthetic analysis for our approach is shown in Scheme 1, which indicates the key starting material being aldehyde **4**, readily obtainable from D-mannitol.[11]

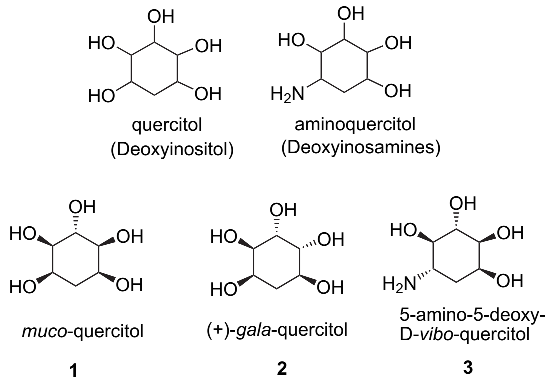

Figure 1.

2. Results and discussions

D-Mannitol derived aldehyde **4**[11] (Scheme 2) was initially reacted with allyl magnesium bromide to obtain homoallyl alcohol **5** (61%) as a diastereomeric mixture (70:30). On the other hand, allylation under the Barbier reaction conditions using zinc gave homoallyl alcohol **5** in an improved yield (82%) and with better anti-selectivity as a diastereomeric mixture (81:19). Deketalization of **5** with 10% HCl followed by acetylation of the resulting triol afforded a diastereomeric mixture (81:19) of triacetates **6** (66%) and

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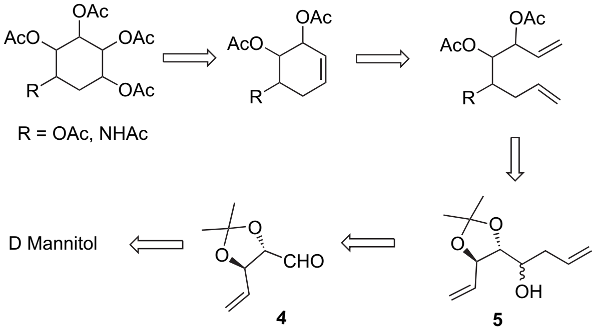


Scheme 1. Retrosynthetic analysis.

7 (15%), which were separated by column chromatography. The major isomeric diene **6** was subjected to ring closing metathesis with Grubbs' first generation ruthenium complex $[\mathrm{Ru}(=\mathrm{CHPh})\mathrm{Cl_2}(\mathrm{PCy_3})_2]$ (1 mol %)[12] at ambient temperature and the triacetate **8** was obtained in good yield (84%). Dihydroxylation of olefin **8** with OsO_4 yielded the diol **9**, which was characterized as its pentaacetate **11** whose spectral data and specific rotation were identical with those reported for the pentaacetate of *muco*-quercitol **1**.[13] For further confirmation of the structure, diol **9** was esterified with *p*-nitro-benzoyl chloride and pyridine to obtain di-(*p*-nitrobenzoate) **10** as a white crystalline solid. Its recrystallization with dichloromethane and hexane solvent system followed by X-ray crystallographic analysis (Fig. 2) confirmed that *cis*-dihydroxylation of the double bond *anti* to the allylic acetate group in **8** had occurred. This structure of diol **9** also confirmed the stereocentre that was generated during the formation of the homoallylic alcohol **5** with major *anti*-stereoselectivity. The formation of the major isomer of **5**, which was separated in the next step as its triacetate **6**, with *anti*-stereoselectivity can be explained through a Felkin-Anh non-chelation model[14] rather than by a chelation-Cram model[15] as the water solvates the metal ion and thereby competes with the chelate complex.

For the synthesis of (+)-*gala*-quercitol **2**, epoxidation of **8** with *m*-chloroperbenzoic acid in phosphate buffer (pH 8.0)[16] solution was performed, however, it gave a mixture of diastereomers of epoxide **12** (Scheme 3) and that too in low yield (36%).

We, therefore, decided to introduce the trans diol functionality using one pot *trans*-dihydroxylation with hydrogen peroxide in formic acid (presumably via the epoxide **12a**),[17] which gave a diol that was isolated and characterized as its pentaacetate **13** upon acetylation. The structure of **13** was assigned on the basis of comparison of its ^{1}H NMR spectral and specific rotation data with the reported value for the pentaacetate of (+)-*gala*-quercitol **2**.[8f] It is clear that the epoxidation would have taken place opposite to the allylic acetoxy group in **8**, i.e., from the β-direction followed by highly regioselective opening of this epoxide via preferred chair intermediate (path 'a') than a high energy twist-boat intermediate (path 'b') leading to the trans diol of similar configuration as that of (+)-*gala*-quercitol as shown in Figure 3.

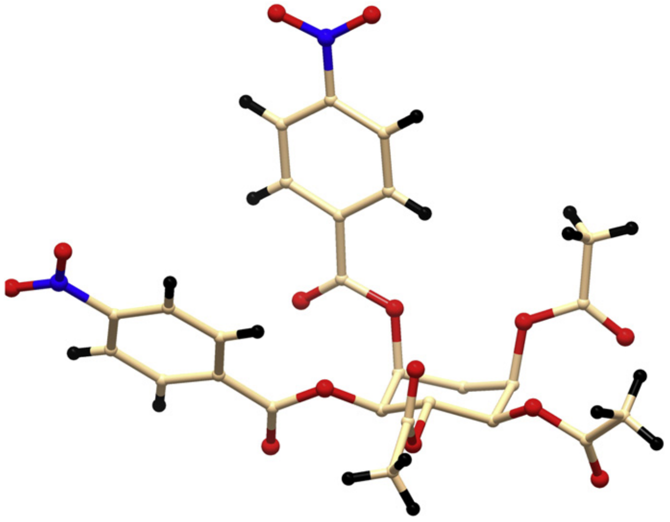
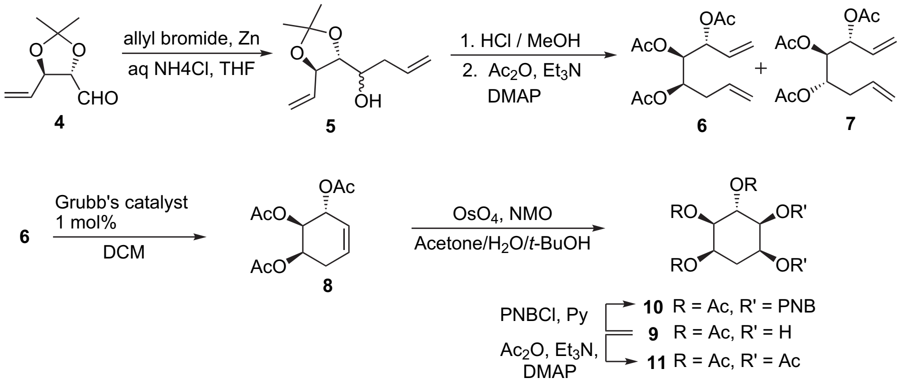
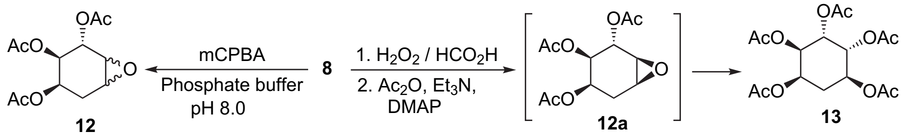


Figure 2. Molecular structure of compound **10**.

For the synthesis of aminoquercitol **3**, the isomeric mixture of alcohol **5** was converted to the corresponding tosylate **14** (Scheme 4) in good yield (90%) by using *p*-toluenesulfonyl chloride and pyridine. The isomeric mixture of the tosylate **14** was subjected to nucleophilic displacement with NaN_3 in DMF at 90 °C, which furnished the corresponding azide **15** in good yield (86%). However, surprisingly at this stage deprotection of the acetonide moiety of azide **15** with various reagents like 10% HCl in methanol, PTSA in ethanol, and acidic resin Amberlyst 15 in ethanol was unsuccessful and only decomposed products were obtained. The azide **15** was then reduced with PPh_3 and water and the crude primary amine was protected as the corresponding acetate. The two isomeric triacetates **16** (13%) and **17** (57%) were readily separated by column chromatography. At this stage, the acetonide deprotection of the major isomer **17** occurred smoothly in the presence of 10% HCl in methanol and the crude product upon acetylation resulted into the triacetate **18** (73%). The triacetate **18** was reacted with Grubbs' first generation catalyst (1 mol %) resulting into the cyclohexene derivative **19**, which was subjected to *cis*-dihydroxylation followed by acetylation to yield the pentaacetate **20** of aminoquercitol **3** as a single isomer. The absolute configuration of **20** was confirmed from its spectral and specific rotation data, which was identical with the literature data.[9d,18]



Scheme 2. Synthesis of *muco*-quercitol.



Scheme 3. Synthesis of (+)-*gala*-quercitol.

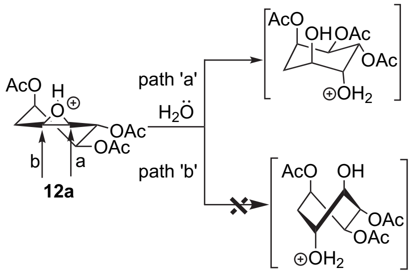
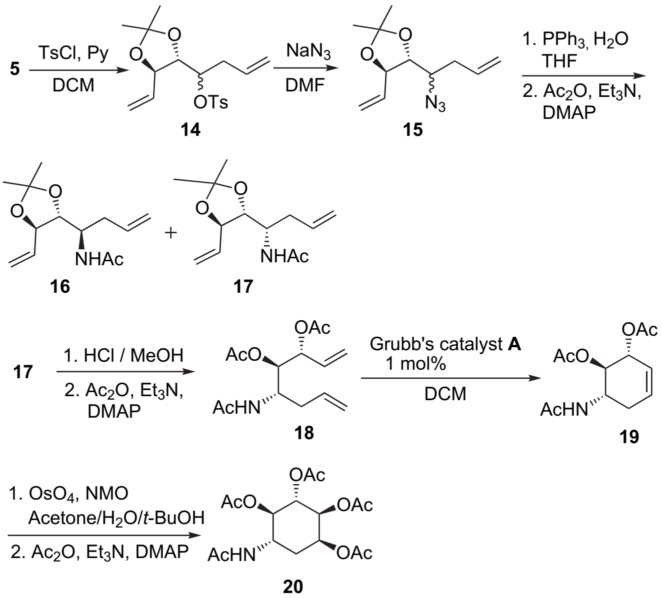


Figure 3.



Scheme 4. Synthesis of 5-amino-5-deoxy-D-*vibo*-quercitol.

3. Conclusion

In summary, we have developed a new stereoselective entry to *muco*-quercitol **1**, (+)-*gala*-quercitol **2**, and 5-amino-5-deoxy-D-*vibo*-quercitol **3** as their peracetates from D-mannitol with full stereochemical control of the three-stereogenic centres using ring closing metathesis as a key step.

4. Experimental

4.1. General

The ^1H NMR and ^{13}C NMR spectra were recorded on JEOL-JNM 400 MHz and 100 MHz spectrometer, respectively. The chemical shift values are reported in parts per million using $CDCl_3$ as internal reference. All reactions were carried out using freshly distilled and dry solvents. Column chromatography was performed over silica gel (100–200 mesh) using hexane and ethyl acetate as eluents. Rotation values were recorded on Autopol II automatic polarimeter at the wavelength of sodium D-line (589 nm) at 25 °C. Elemental analyses were carried out on a Thermoquest CE-instruments EA-1110 C, H, N, S analyzer. Melting points were determined using a Fischer–John melting point apparatus. The mass spectra were recorded on a Micromass Quattro II Triple Quadrupole Mass Spectrometer.

*4.1.1. 1-((4R,5R)-2,2-Dimethyl-5-vinyl-1,3-dioxolan-4-yl)but-3-en-1-ol (**5**)*

To a cold (10 °C) and well stirred mixture of **4** (1 g, 6.41 mmol), Zn dust (0.838 g, 12.8 mmol) and allyl bromide (1.55 g, 12.8 mmol) in 20 mL THF, was added a saturated solution of NH_4Cl (3 mL). The mixture was stirred for 4 h at ambient temperature until the aldehyde was totally consumed (monitored by TLC). The mixture was filtered and the precipitate was thoroughly washed with $CHCl_3$ (4×5 mL). The aqueous layer was separated and treated with 5% HCl to dissolve the suspended turbid material. The clear solution was extracted with $CHCl_3$ (3×50 mL). The combined organic layer was washed successively with 10% $NaHCO_3$, water, and finally with brine solution. After removal of the solvent under reduced pressure a residue was obtained, which was purified by column chromatography (hexane/EtOAc, 9:1) to give compound **5** as a mixture of two diastereomers (81:19) (1.045 g, 82% yield). Colorless oil. R_f=0.45 (hexane/EtOAc, 9:1); ^1H NMR (400 MHz, $CDCl_3$): δ 5.91–5.78 (m, 2H, both isomers), 5.46–5.38 (m, 1H, both isomers), 5.29–5.25 (m, 1H, both isomers), 5.17–5.11 (m, 2H, both isomers), 4.46 (t, 1H, major, J=7.5 Hz), 4.37 (t, 1H, minor, J=7.6 Hz), 3.89–3.85 (m, 1H, major), 3.74 (dd, 1H, major, J=4.5, 3.4 Hz), 3.66 (dd, 1H, minor, J=3.1, 5.1 Hz), 3.48–3.47 (m, 1H, minor), 2.33–2.17 (m, 2H, both isomers), 1.47–1.42 (4×s, 6H, both isomers). ^{13}C NMR (100 MHz, $CDCl_3$): δ (major): 137.3, 135.0, 119.6, 119.3, 83.4, 79.1, 78.3, 71.2, 38.1; (minor): 136.1, 120.3, 109.9, 79.9, 69.8, 40.1. ν_{max} (neat film): 2986, 1633, 1454, 1373, 1228, 1065, 847 cm^{-1}. ESMS: m/z 221 [M+Na]$^+$. Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15; O, 24.21%. Found: C, 65.92; H, 9.12.

*4.1.2. Procedure for the deprotection of acetonide **5***

To a solution of **5** (500 mg, 2.52 mmol) in MeOH (2 mL) was added 2 mL of 10% HCl in methanol and the reaction mixture stirred for 5 h. The reaction mixture was concentrated under reduced pressure, diluted with water, and extracted with ethyl acetate (3×50 mL). The organic layer was dried over K_2CO_3 and the filtrate was concentrated under vacuum to obtain the corresponding triol, which was subjected to acetylation with excess of triethylamine, Ac_2O (1:1, 2 mL) and catalytic amount of DMAP at room temperature for 8 h. Removal of the solvent under reduced pressure gave a residue, which was purified by column chromatography (hexane/EtOAc, 9:1) to obtain a mixture of diastereomers as a colorless oil (**6**/**7**, 81:19 ratio) (581 mg, 81% yield).

*4.1.2.1. (3R,4R,5R)-Octa-1,7-diene-3,4,5-triyl triacetate (**6**).* Colorless oil (470 mg, 66% yield). $[\alpha]_D^{28}$ +19.23 (c 1.3, CH_2Cl_2). R_f=0.4 (hexane/EtOAc, 9:1); ^1H NMR (400 MHz, $CDCl_3$): δ 5.77–5.65 (m, 2H), 5.52–5.49 (m, 1H), 5.32–5.21 (m, 3H), 5.13–5.04 (m, 3H), 2.41–2.37 (m, 1H), 2.32–2.25 (m, 1H), 2.09 (s, 6H), 2.02 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.9, 169.8, 132.6, 132.0, 118.6, 118.3, 72.8, 71.6, 69.5, 35.0, 20.8, 20.8, 20.7. ν_{max} (neat film): 3080, 2923, 1746, 1372, 1219, 1023, 733 cm^{-1}. ESMS: m/z 307 [M+Na]$^+$. Anal. Calcd for $C_{14}H_{20}O_6$: C, 59.14; H, 7.09; O, 33.77. Found: C, 59.62; H, 7.11.

*4.1.2.2. (3R,4R,5S)-Octa-1,7-diene-3,4,5-triyl triacetate (**7**).* Colorless liquid (110 mg, 15% yield). $[\alpha]_D^{28}$ +3.61 (c 3.6, CH_2Cl_2). R_f=0.39

(hexane/EtOAc, 9:1); ^{1}H NMR (400Mz, $CDCl_3$): δ 5.77–5.69 (m, 2H), 5.42 (t, 1H, J=6.8 Hz), 5.33–5.29 (m, 2H), 5.28–5.18 (m, 1H), 5.17–5.08 (m, 3H), 2.33–2.30 (m, 2H), 2.11 (s, 3H), 2.08 (s, 3H), 2.07 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.9, 169.7, 132.0, 131.5, 119.9, 118.8, 72.9, 72.9, 70.6, 35.4, 20.9, 20.6. ν_{max} (neat film): 2943, 2854, 1731, 1644, 1434, 1372, 1024, 701 cm^{-1}. ESMS: *m*/*z* 307 $[M+Na]^+$. Anal. Calcd for $C_{14}H_{20}O_6$: C, 59.14; H, 7.09; O, 33.77. Found: C, 59.02; H, 7.06.

*4.1.3. (1R,2R,3R)-Cyclohex-4-ene-1,2,3-triyl triacetate (**8**)*

To a stirred solution of compound **6** (300 mg, 1.05 mmol) in dry CH_2Cl_2 (10 mL) at room temperature was added Grubbs' first generation catalyst (1 mol %, 8 mg). The mixture was stirred for 3 h and after completion of the reaction, the solvent was evaporated under reduced pressure and the crude product was purified by column chromatography (hexane/AcOEt, 9:1) to give compound **8** (228 mg, 84% yield) as a viscous liquid. $[\alpha]_D^{28}$ −83.76 (*c* 2.35, CH_2Cl_2). R_f=0.36 (hexane/EtOAc, 9:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.83–5.79 (m, 1H, H-1), 5.69–5.65 (m, 1H, H-2), 5.49 (dd, 1H, H-3, J=1.7 Hz), 5.35 (t, 1H, H-5, J=2.4 Hz), 5.15 (dd, 1H, H-4, J=6.8, 2.4 Hz), 2.54–2.49 (m, 1H), 2.37–2.32 (m, 1H), 2.09 (s, 3H), 2.08 (s, 3H), 2.07 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.4, 170.3, 170.2, 127.6, 124.0, 70.8, 69.3, 68.1, 28.9, 21.0, 20.8, 20.7. ν_{max} (neat film): 3043, 2930, 1743, 1654, 1432, 1371, 1229, 1047, 949, 705 cm^{-1}. ESMS: *m*/*z* 279 $[M+Na]^+$. Anal. Calcd for $C_{12}H_{16}O_6$: C, 56.24; H, 6.29; O, 37.46. Found: C, 56.93; H, 6.31.

*4.1.4. (1R,2R,3R,4S,5S)-Cyclohexane-1,2,3,4,5-pentayl pentaacetate (**11**)*

To a stirred solution of compound **8** (100 mg, 0.39 mmol) in a mixture of acetone, water, and *t*-butanol (1:1:0.4, 5 mL) at room temperature, were added NMO·H_2O (54 mg, 0.468 mmol) and catalytic amount of OsO_4 [4 μL of 2% *t*-BuOH solution]. The reaction mixture was stirred for 16 h and then it was treated with $Na_2S_2O_5$ (88 mg, 0.468 mmol). The reaction mixture was stirred for further 1 h and extracted with EtOAc (2×15 mL). The combined organic layer was washed with 1 N HCl (10 mL), water and finally with brine, and dried over Na_2SO_4. Removal of the solvent under reduced pressure gave a residue, which was purified by column chromatography (hexane/EtOAc, 3:7) to obtain the diol **9** (94 mg, 84% yield). To a solution of **9** (50 mg, 0.172 mmol) in 1 mL of dry CH_2Cl_2 were added excess of Ac_2O (2 mL), Et_3N (2 mL), and catalytic amount of DMAP and the reaction mixture was stirred for 6 h at ambient temperature. Removal of the solvent under reduced pressure gave a residue, which was purified by column chromatography (hexane/EtOAc, 3:2) to give pentaacetate of *muco*-quercitol **11** as a white solid (62 mg, 96% yield). Mp: 165–167 °C. $[\alpha]_D^{28}$ 0 (*c* 0.15, CH_2Cl_2). R_f=0.43 (hexane/EtOAc, 2:3); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.66 (t, 1H, J=9.4 Hz), 5.35 (dd, 2H, J=3.7, 3.4 Hz), 4.99 (dd, 2H, J=9.3, 3.4 Hz), 2.33 (dt, 1H, J=15.8, 4.1 Hz), 2.11 (s, 3H), 2.10 (s, 3H), 2.05 (s, 3H), 2.03 (s, 6H), 1.90 (dt, 1H, J=15.8, 3.4 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.0, 169.8, 169.6, 70.9, 67.5, 67.4, 28.6, 20.9, 20.6, 20.5. ν_{max} (neat film): 2991, 1719, 1159, 1071, 813, 663 cm^{-1}. ESMS: *m*/*z* 446 $[M+Na]^+$. Anal. Calcd for $C_{16}H_{22}O_{10}$: C, 51.34; H, 5.92; O, 42.74. Found: C, 52.42; H, 5.94.

*4.1.5. (1R,2R,3S,4S,5S)-4,5-Bis(4-nitrobenzoyloxy)cyclohexane-1,2,3-triyl triacetate (**10**)*

To a stirred solution of compound **9** (50 mg, 0.172 mmol) in 1 mL dry CH_2Cl_2 at room temperature, were added *p*-nitro-benzoyl chloride (141.18 mg, 0.78 mmol) and pyridine (1 mL) and the stirring continued for 16 h at room temperature. After removal of the solvent under reduced pressure a residue was obtained, which was purified by column chromatography (hexane/EtOAc, 9:1) to give compound **10** as a white solid (77 mg, 68% yield). Mp: 138–140 °C. $[\alpha]_D^{28}$ +48.4 (*c* 2.05, CH_2Cl_2). R_f=0.6 (hexane/EtOAc, 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.33 (d, 2H, J=7.0 Hz), 8.23 (m, 4H), 8.09 (d, 2H, J=8.0 Hz), 5.98 (br s, 1H), 5.80 (br s, 1H), 5.59 (br s, 1H), 5.32 (d, 1H, J=9.0 Hz), 5.19 (d, 1H, J=9.5 Hz), 2.54 (m, 1H), 2.19 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.6, 163.5, 163.4, 150.8, 134.6, 134.0, 130.8, 130.7, 123.7, 123.7, 69.2, 67.1, 67.0, 28.9, 20.9, 20.6. ν_{max} (neat film): 2987, 1715, 1434, 1160, 1071, 813, 662 cm^{-1}. ESMS: *m*/*z* 605 $[M+Na]^+$. Anal. Calcd for $C_{26}H_{24}N_2O_{14}$: C, 53.07; H, 4.11; N, 4.76; O, 38.06. Found: C, 54.59; H, 4.11; N, 4.75.

*4.1.6. (2R,3R,4R)-7-Oxabicyclo[4.1.0]heptane-2,3,4-triyl triacetate (**12**)*

To a stirred mixture of **8** (100 mg, 0.35 mmol), 1,2-dichloroethane (3 mL), and phosphate buffer (3 mL, pH 8) was added *m*-chloroperbenzoic acid (274 mg, 1.05 mmol) in portions and the mixture was refluxed for 24 h. The reaction mixture was then diluted with 15 mL of 1,2-dichloroethane, and washed successively with aqueous 10% sodium thiosulfate (5 mL), aqueous sodium hydrogen carbonate (5 mL), and water (5 mL), and dried over Na_2SO_4. Concentration of the organic layer gave a residue that was purified by column chromatography (hexane/EtOAc, 5:1) to give epoxide **12** as a white solid. Mixture of two diastereomers (86:14) (36 mg, 36% yield). R_f=0.5 (hexane/EtOAc, 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.47 (dd, 1H, J=8.5, 2.2 Hz, major), 5.31 (d, 1H, J=8.2 Hz, minor), 5.22–5.20 (m, 1H, both isomers), 5.04 (dd, 1H, J=8.7, 2.2 Hz, major), 4.97 (dd, 1H, J=8.3, 2.6 Hz, minor), 3.52 (dd, 1H, J=3.6, 2.4 Hz, major), 3.29 (dd, 1H, J=4.1, 3.8 Hz, major), 3.22 (m, 1H, minor), 3.12 (d, 1H, J=3.4 Hz, minor), 2.35–2.18 (m, 2H, both isomers), 2.13 (s, 3H), 2.12 (s, 3H), 2.09 (s, 3H), 2.07 (s, 3H), 2.04 (s, 3H), 2.02 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.0, 167.4, 164.3, 69.6, 69.3, 68.7, 53.7, 51.8, 30.1, 29.6, 28.3, 21.6. ν_{max} (neat film): 3041, 2926, 1747, 1371, 1229, 1047, 949, 705 cm^{-1}. ESMS: *m*/*z* 295 $[M+Na]^+$. Anal. Calcd for $C_{12}H_{16}O_7$: C, 52.94; H, 5.92; O, 41.14. Found: C, 52.73; H, 5.94.

*4.1.7. (1R,2R,3R,4R,5S)-Cyclohexane-1,2,3,4,5-pentayl pentaacetate (**13**)*

A mixture of **8** (100 mg, 0.39 mmol) and 90% aqueous formic acid (1 mL) and 35% H_2O_2 (0.3 mL) was stirred for 2 h at 60 °C, and then concentrated under reduced pressure. The residue was treated with excess of Ac_2O (1 mL), Et_3N (1 mL), and catalytic amount of DMAP and the reaction mixture stirred for 4 h at ambient temperature. Removal of the solvent under reduced pressure gave a residue, which was purified by column chromatography (hexane/EtOAc, 8:2) to give pentaacetate **13** of (+)-*gala*-quercitol **2**. Colorless oil (113 mg, 77% yield). $[\alpha]_D^{28}$ −4.86 (*c* 1.85, CH_2Cl_2). R_f=0.6 (hexane/EtOAc, 2:3); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.42 (dd, 1H, J=5.3, 3.4 Hz), 5.24–5.34 (m, 3H), 5.15 (ddd, 1H, J=13.4, 8.8, 4.6 Hz), 2.19–2.29 (m, 1H), 2.13 (s, 3H), 2.11 (s, 3H), 2.06 (s, 3H), 2.03–2.19 (m, 1H), 2.03 (s, 3H), 2.02 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.7, 169.3, 169.3, 69.7, 68.1, 67.6, 66.6, 29.0, 20.9, 20.8, 20.7. ν_{max} (neat film): 3054, 2980, 1746, 1446, 1025 cm^{-1}. ESMS: *m*/*z* 446 $[M+Na]^+$. Anal. Calcd for $C_{16}H_{22}O_{10}$: C, 51.34; H, 5.92; O, 42.74. Found: C, 51.52; H, 5.94.

*4.1.8. 1-((4S,5R)-2,2-Dimethyl-5-vinyl-1,3-dioxolan-4-yl)but-3-enyl 4-methylbenzenesulfonate (**14**)*

To a stirred solution of compound **5** (1 g, 5.04 mmol) in dry CH_2Cl_2 (10 mL) at room temperature, were added *p*-toluenesulfonyl chloride (1.921 g, 10.08 mmol) and excess of pyridine (3 mL). The reaction mixture was stirred for 16 h. After removal of the solvent under reduced pressure a residue was obtained, which was purified by column chromatography (hexane/EtOAc, 9:1) to give compound **14** (1.614 g, 91%) as a thick liquid. R_f=0.5 (hexane/EtOAc, 9:1); ^{1}H NMR (400 MHz, $CDCl_3$) of the mixture of diastereomers (81:19): δ 7.79–7.75 (m, 2H, both isomers), 7.31–7.24 (m, 1H, both isomers), 5.76 (m, 1H, both isomers), 5.60 (m, 1H, both isomers), 5.39–5.35 (m, 1H, both isomers), 5.25–5.21 (m, 1H, both isomers), 5.05–4.98 (m, 2H, both isomers), 4.70 (dd, 1H, major, J=10.9, 5.8 Hz), 4.55

(m, 1H, minor), 4.32 (m, 1H, both isomers), 3.81 (dd, 1H, J=8.0, 5.1 Hz), 3.75 (dd, 1H, minor, J=8.1, 3.1 Hz), 2.46–2.36 (m, 2H, both isomers), 2.42 (s, 3H), 1.34 (s, 3H, minor), 1.33 (s, 3H, major), 1.30 (s, 3H, minor), 1.27 (s, 3H, major). ^{13}C NMR (400 MHz, $CDCl_3$): δ 144.7, 135.3, 134.4, 134.2, 132.2, 131.5, 129.6, 127.9, 119.2, 109.6, 80.8, 79.6, 79.0, 78.6, 35.5, 26.8, 26.6, 21.6. ν_{max} (neat film): 2987, 2933, 1644, 1598, 1368, 1216, 1176, 1096, 815 cm^{-1}. ESMS: *m/z* 375 [M+Na]$^+$. Anal. Calcd for $C_{18}H_{24}O_5S$: C, 61.34; H, 6.86; O, 22.70; S, 9.10. Found: C, 61.46; H, 6.84.

4.1.9. (4R,5R)-4-(1-Azidobut-3-enyl)-2,2-dimethyl-5-vinyl-1,3-dioxolane (*15*)

To a stirred solution of tosylate **14** in dry DMF (4 mL) was added NaN_3 (1.106 g, 17.023 mmol). This heterogeneous mixture was stirred at 90 °C for 6 h, and then it was cooled to room temperature followed by addition of water (5 mL), and extraction with ether (3×10 mL). The combined organic layer was washed with brine solution and dried over Na_2SO_4. Removal of the solvent under reduced pressure gave a residue, which was purified by column chromatography (hexane/EtOAc, 95:5) to give azide **15** (819 mg, 86% overall yield for two steps) as a pale yellow liquid. R_f=0.7 (hexane/EtOAc, 9:1); ^{1}H NMR (400 MHz, $CDCl_3$) of the mixture of diastereomers (80:20): δ 6.34–6.27 (m, 2H, minor), 5.84–5.71 (m, 2H, both isomers), 5.43–5.09 (m, 5H, both isomers), 4.39 (dd, 1H, major, J=8.3, 7.6 Hz), 4.12–4.04 (m, 2H, minor), 3.77 (dd, 1H, minor, J=7.8, 5.1 Hz), 3.71 (dd, 1H, major, J=8.2, 2.9 Hz), 3.63–3.58 (m, 1H, minor), 3.10–3.05 (m, 1H, major), 2.54 (m, 1H, major), 2.42 (m, 1H, major), 2.29 (m, 1H, minor), 2.19 (m, 1H, minor), 1.46 (s, 3H, major), 1.44 (s, 3H, minor), 1.42 (s, 3H, major), 1.39 (s, 3H, minor). ^{13}C NMR (100 MHz, $CDCl_3$): δ 135.6, 135.6, 134.8, 134.7, 133.4, 133.3, 119.8, 119.1, 118.5, 118.4, 91.7, 82.2, 82.1, 81.7, 79.4, 79.3, 62.8, 59.2, 59.1, 35.3, 27.0, 26.5. ν_{max} (neat film): 3082, 2987, 2934, 2114, 1643, 1376, 1241, 1057, 927, 876, 510 cm^{-1}. ESMS: *m/z* 246 [M+Na]$^+$. Anal. Calcd for $C_{11}H_{17}N_3O_2$: C, 59.17; H, 7.67; N, 18.82; O, 14.33. Found: C, 59.38; H, 7.70; N, 18.78.

4.1.10. Procedure for the reduction of azide *15*

To a stirred solution of azide **15** (1 g, 4.478 mmol) in dry THF (3 mL) at room temperature, were added triphenylphosphine (1.408 g, 5.37 mmol) and water (0.32 ml, 17.952 mmol). The mixture was stirred for 10 h, diluted with ethyl acetate, and washed with brine. The organic layer was dried over Na_2SO_4 and then concentrated to give the crude amine. The crude amine was dissolved in CH_2Cl_2 (3 mL), treated with excess of Et_3N (2 mL) and Ac_2O (2 mL) at room temperature, and the mixture stirred for 4 h. The reaction mixture was extracted with CH_2Cl_2 (2×25 mL) and the organic layer washed with water, brine, and then dried over Na_2SO_4. Evaporation of the solvent followed by purification using SiO_2 column chromatography (hexane/EtOAc, 7:3) gave a mixture of diastereomers (**16**/**17**, 19:81 ratio) (749 mg, 70% yield).

*4.1.10.1. N-((S)-1-((4R,5R)-2,2-Dimethyl-5-vinyl-1,3-dioxolan-4-yl)-but-3-enyl)acetamide (**17**).* Viscous liquid (607 mg, 57% yield). $[\alpha]_D^{28}$ −20.64 (*c* 1.55, CH_2Cl_2). R_f=0.45 (hexane/EtOAc, 3:2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.83–5.67 (m, 3H), 5.42 (dd, 1H, J=17.0, 1.2 Hz), 5.27 (dd, 1H, J=10.2, 1.0 Hz), 5.12–5.06 (m, 2H), 4.16–4.10 (m, 1H), 4.04 (dd, 1H, J=8.5, 7.3 Hz), 3.74 (dd, 1H, J=8.5, 1.2 Hz), 2.35–2.31 (m, 2H), 2.02 (s, 3H), 1.42 (s, 3H), 1.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.0, 132.0, 131.5, 119.9, 118.9, 72.9, 70.6, 35.4, 20.9, 20.6. ν_{max} (neat film): 3436, 3282, 2981, 2929, 2854, 1646, 1556, 1443, 1375, 1296, 1236, 1175, 1097, 1065, 915, 741 cm^{-1}. [M+Na]$^+$. Anal. Calcd for $C_{13}H_{21}NO_3$: C, 65.25; H, 8.84; N, 5.85; O, 20.06. Found: C, 65.32; H, 8.83; N, 5.83.

*4.1.10.2. N-((R)-1-((4R,5R)-2,2-Dimethyl-5-vinyl-1,3-dioxolan-4-yl)-but-3-enyl)acetamide (**16**).* Viscous liquid (142 mg, 13% yield). $[\alpha]_D^{28}$ +0.41 (*c* 3.85, CH_2Cl_2). R_f=0.44 (hexane/EtOAc, 3:2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.83–5.74 (m, 2H), 5.39–5.35 (m, 2H), 5.23 (d, 1H, J=10.2 Hz), 5.13 (d, 1H, J=3.8 Hz), 5.09 (s, 1H), 4.33 (dd, 1H, J=7.8, 7.5 Hz), 4.24–4.21 (m, 1H), 3.66 (dd, 1H, J=7.6, 7.0 Hz), 2.46–2.43 (m, 1H), 2.33–2.27 (m, 1H), 1.92 (s, 3H), 1.43 (s, 3H), 1.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.53, 135.44, 133.82, 118.95, 118.25, 109.18, 81.87, 80.36, 49.39, 35.27, 29.65. ν_{max} (neat film): 3283, 3079, 2986, 2931, 2856, 1650, 1553, 1438, 1372, 1244, 1215, 1063, 989, 924, 877, 695 cm^{-1}. ESMS: *m/z* 306 [M+Na]$^+$. Anal. Calcd for $C_{13}H_{21}NO_3$: C, 65.25; H, 8.84; N, 5.85; O, 20.06. Found: C, 65.28; H, 8.82; N, 5.83.

4.1.11. (3R,4R,5S)-5-Acetamidoocta-1,7-diene-3,4-diyl diacetate (*18*)

The same experimental procedure was followed for converting **17** (200 mg, 0.835 mmol) to **18** as was followed for the conversion of **5** to **6**. Purification was done by using SiO_2 column chromatography (hexane/EtOAc, 2:3). Colorless oil (174 mg, 73% yield over two steps). $[\alpha]_D^{28}$ −30.9 (*c* 1.1, CH_2Cl_2). R_f=0.5 (hexane/EtOAc, 2:3); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.84–5.64 (m, 3H), 5.39–5.31 (m, 3H), 5.10–5.05 (m, 3H), 4.35–4.30 (m, 1H), 2.12–2.02 (m, 2H), 2.11 (s, 3H), 2.06 (s, 3H), 2.03 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.8, 169.4, 132.8, 131.5, 120.2, 118.6, 74.1, 73.2, 48.0, 37.1, 23.3, 20.8, 20.6. ν_{max} (neat film): 3289, 3078, 2927, 2853, 1746, 1659, 1539, 1434, 1373, 1224, 1026, 938, 737 cm^{-1}. ESMS: *m/z* 306 [M+Na]$^+$. Anal. Calcd for $C_{14}H_{21}NO_5$: C, 59.35; H, 7.47; N, 4.94; O, 28.24. Found: C, 59.37; H, 7.50; N, 4.96.

4.1.12. (1R,2R,6S)-6-Acetamidocyclohex-3-ene-1,2-diyl diacetate (*19*)

The same experimental procedure was followed for converting **18** (150 mg, 0.529 mmol) to **19** as was followed for the conversion of **6** to **8**. Purification was done by using SiO_2 column chromatography (hexane/EtOAc, 1:4). Viscous liquid (110 mg, 81% yield). $[\alpha]_D^{28}$ −45.16 (*c* 1.55, CH_2Cl_2). R_f=0.5 (hexane/EtOAc, 1:4); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.81–5.71 (m, 1H, H-1), 5.72 (d, 1H, NH, J=8.7 Hz), 5.58–5.55 (m, 2H, H-2, H-3), 5.04 (dd, 1H, H-4, J=11.0, 7.3 Hz), 4.39–4.30 (m, 1H, H-5), 2.64–2.58 (m, 1H, H-6), 2.07–2.05 (m, 1H, H-6′), 2.08 (s, 3H, $COCH_3$), 2.06 (s, 3H, $COCH_3$), 1.94 (s, 3H, $COCH_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.1, 170.2, 169.7, 127.9, 124.9, 73.3, 72.0, 48.0, 31.6, 23.3, 21.0, 20.9. ν_{max} (neat film): 3463, 2963, 2926, 2853, 1744, 1649, 1412, 1370, 1241, 1048, 943, 890, 530 cm^{-1}. ESMS: *m/z* 278 [M+Na]$^+$. Anal. Calcd for $C_{12}H_{17}NO_5$: C, 56.46; H, 6.71; N, 5.49; O, 31.34. Found: C, 56.48; H, 6.70; N, 5.52.

4.1.13. (1S,2S,3S,4R,5S)-5-Acetamidocyclohexane-1,2,3,4-tetrayl tetraacetate (*20*)

The same experimental procedure was followed for converting **19** (100 mg, 0.39 mmol) to **20** as was followed for the conversion of **8** to **10**. Purification was done by using SiO_2 column chromatography (hexane/EtOAc, 1:9). Colorless oil (98 mg, 67% yield). $[\alpha]_D^{28}$ +9.66 (*c* 6.5, $CHCl_3$). R_f=0.5 (hexane/EtOAc, 1:9); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.66 (d, 1H, NH, J=8.8 Hz), 5.51 (t, 1H, H-3, J=10.0 Hz), 5.43 (dd, 1H, H-1, J=5.8, 3.2 Hz), 4.94–489 (m, 2H, H-2, H-4), 4.50–4.41 (m, 1H, H-5), 2.28–2.23 (m, 1H, H-6), 2.16 (s, 3H, $COCH_3$), 2.06 (s, 3H, $COCH_3$), 2.02 (s, 3H, $COCH_3$), 1.99 (s, 3H, $COCH_3$), 1.62–1.54 (ddd, 1H, H-6′, J=14.6, 12.7, 2.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.9, 169.7, 73.9, 71.6, 69.5, 66.8, 46.7, 31.9, 23.2, 20.9, 20.5. ν_{max} (neat film): 3288, 3074, 2925, 2853, 1745, 1665, 1605, 1555, 1433, 1371, 1232, 1160, 1046, 932, 736 cm^{-1}. ESMS: *m/z* 396 [M+Na]$^+$. Anal. Calcd for $C_{16}H_{23}NO_9$: C, 51.47; H, 6.21; N, 3.75; O, 38.57. Found: C, 51.83; H, 6.20; N, 3.73.

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Supplementary data

X-ray crystallographic data for compound **10**.[19] Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.06.107.

References and notes

1. McCasland, G. E.; Furuta, S.; Johnson, L. F.; Shoolery, J. N. *J. Am. Chem. Soc.* **1961**, *83*, 2335.
2. McCasland, G. E.; Naumann, M. O.; Durham, L. J. *J. Org. Chem.* **1968**, *33*, 4220.
3. For recent synthesis of (+)-*proto*-quercitol and (−)-*proto*-quercitol, see: Gultekin, M. S.; Celik, M.; Turkut, E.; Tanyeli, C.; Balci, M. *Tetrahedron: Asymmetry* **2004**, *15*, 453.
4. For recent synthesis of (−)-*vibo*-quercitol, see: Ogawa, S.; Ohishi, Y.; Asada, M.; Tomoda, A.; Takahashi, A.; Ooki, Y.; Mori, M.; Itoh, M.; Korenaga, T. *Org. Biomol. Chem.* **2004**, *2*, 884.
5. Maras, A.; Seçen, H.; Sütbeyaz, Y.; Balci, M. *J. Org. Chem.* **1998**, *63*, 2039 and references cited therein.
6. Hooper, R. In *Aminoglycoside Antibiotics*; Umezawa, H., Hooper, I. R., Eds.; Springer: Berlin, 1981; p 7.
7. (a) Seçen, H.; Salamci, E.; Sütbeyaz, Y.; Balci, M. *Synlett* **1993**, 609; (b) Salamci, E.; Seçen, H.; Sütbeyaz, Y.; Balci, M. *J. Org. Chem.* **1997**, *62*, 2453; (c) Salamci, E.; Seçen, H.; Sütbeyaz, Y.; Balci, M. *Synth. Commun.* **1997**, *27*, 2223; (d) Balci, M. *Pure Appl. Chem.* **1997**, *69*, 97.
8. For recent approaches of quercitols (a) Hudlicky, T.; Cebulak, M. *Cyclitols and Derivatives*; VCH: New York, NY, 1993; 134; (b) Angelaud, R.; Landais, Y. *J. Org. Chem.* **1996**, *61*, 5202; (c) Maezaki, N.; Nagahashi, N.; Yoshigami, R.; Iwata, C.; Tanaka, T. *Tetrahedron Lett.* **1999**, *40*, 3781; (d) Yadav, J. S.; Maiti, A.; Sankar, A. R.; Kunwar, A. C. *J. Org. Chem.* **2001**, *66*, 8370; (e) Shih, T. L.; Kuow, S.; Lin, Y. L. *Tetrahedron Lett.* **2004**, *45*, 5751; (f) Shih, T. L.; Lin, Y. L.; Kuo, W. S. *Tetrahedron* **2005**, *61*, 1919; (g) Murugan, A.; Yadav, A. K.; Gurjar, M. K. *Tetrahedron Lett.* **2005**, *46*, 6235.
9. For recent approaches of aminoquercitols (a) Alegret, C.; Buchholz, J. B.; Riera, A. *Org. Lett.* **2006**, *8*, 3069; (b) Ogawa, S.; Asaada, M.; Ooki, Y.; Mori, M.; Itoh, M.; Korenaga, T. *Bioorg. Med. Chem.* **2005**, *13*, 4306; (c) Yu, J.; Spencer, J. B. *Tetrahedron Lett.* **2001**, *42*, 4219; (d) Contelles, J.; Pozuelo, C.; Jimeno, M. L.; Martinez, L.; Grau, A. M. *J. Org. Chem.* **1992**, *57*, 2625.
10. (a) Kumar, A.; Rawal, G. K.; Vankar, Y. D. *Tetrahedron* **2008**, *64*, 2379; (b) Ramana, D. V.; Vankar, Y. D. *Eur. J. Org. Chem.* **2007**, 5583; (c) Reddy, B. G.; Vankar, Y. D. *Angew. Chem., Int. Ed.* **2005**, *44*, 2001; (d) Jayakanthan, K.; Vankar, Y. D. *Org. Lett.* **2005**, *7*, 5441; (e) Jayakanthan, K.; Vankar, Y. D. *Tetrahedron Lett.* **2006**, *49*, 8667; (f) Rawal, G. K.; Rani, S.; Kumar, A.; Vankar, Y. D. *Tetrahedron Lett.* **2006**, *47*, 9117; (g) Rani, S.; Agarwal, A.; Vankar, Y. D. *Tetrahedron Lett.* **2003**, *44*, 5001.
11. Babjak, M.; Kapitan, P.; Gracza, T. *Tetrahedron* **2005**, *61*, 2471.
12. Grubbs, R. H. *Handbook of Metathesis*; Wiley–VCH: Weinheim, 2003; Vol. 2, Chapter 2.
13. Lee, Y. J.; Lee, K.; Jung, S. I.; Jeon, H. B.; Kim, K. S. *Tetrahedron* **2005**, *61*, 1987.
14. (a) Anh, N. T. *Top. Curr. Chem.* **1980**, *88*, 145; (b) Cherest, M.; Felkin, H. *Tetrahedron Lett.* **1968**, *9*, 2205.
15. (a) Cram, D. J.; Kopecky, K. R. *J. Am. Chem. Soc.* **1959**, *81*, 2748; (b) Cram, D. J.; Elhafez, F. A. A. *J. Am. Chem. Soc.* **1952**, *74*, 5828.
16. Ogawa, S.; Jikeda, N.; Takeda, H.; Nakagawa, Y. *Carbohydr. Res.* **1998**, *175*, 294.
17. Ogawa, S.; Aoki, Y.; Takagaki, T. *Carbohydr. Res.* **1987**, *164*, 499.
18. $[\alpha]_D^{28}$ +9.69 (c 6.5, $CHCl_3$), reported value is −9.6 for its enantiomer.
19. X-ray crystallographic data for compound **10** have been deposited at the Cambridge Crystallographic Data Centre and the deposition number is: CCDC 647945.