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Concise and practical synthesis of (2*S*,3*R*,4*R*,5*R*) and (2*S*,3*R*,4*R*,5*S*)-1,6-dideoxy-1,6-iminosugars

Jayant N. Tilekar, Nitin T. Patil, Harishchandra S. Jadhav and Dilip D. Dhavale*

Department of Chemistry, Garware Research Center, University of Pune, Ganeshkhind Road, Pune 411 007, India

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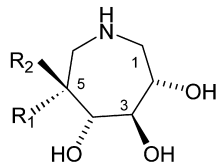
Abstract—The syntheses of (2*S*,3*R*,4*R*,5*R*) and (2*S*,3*R*,4*R*,5*S*)-1,6-dideoxy-1,6 iminosugars **1a** and **1b**, respectively, from D-glucose are described. The key transformations in this reaction sequence include regio-selective epoxide ring opening with *N*-benzylamine followed by intramolecular reductive amination of amino-aldehyde. © 2003 Published by Elsevier Science Ltd.

1. Introduction

In recent years, much attention has been focused on the preparation and evaluation of glycosidase inhibitory activities of various five- and six-member iminosugars namely polyhydroxy pyrrolidine and piperidine alkaloids.[1] However, only a few reports have appeared on the syntheses of seven-member iminosugars-azepanes **1** (Fig. 1), despite their promising glycosidase inhibitory activity.[2] Azepanes are also potentially useful as DNA minor groove binding ligands (MGBL).[3] The hydroxyl groups in azepanes adopt different conformations due to the flexibility of the seven-member ring (compared with five- or six-member rings), thereby increasing the probability of forming hydrogen bonds with the nitrogen bases thus rendering their ability to point into the minor groove of the DNA. The high water solubility, allowing them to circumvent the problem of poor bio-availability seen with many other MGBL's, is an additional advantage of these compounds. The designing of azepane molecules therefore is mainly concerned with the different positional and stereochemical orientation of the –OH functionality at C-2/C-3/C-4/C-5. In view of this, a variety of di-, tetra-hydroxylazepane analogues were synthesized and are being evaluated for their biological properties.[2c,4] In the continuation of our interest in the synthesis of polyhydroxylated piperidine and indolizidine alkaloids,[5] we are now describing a divergent synthetic route to (2*S*,3*R*,4*R*,5*R*)-1,6-dideoxy-1,6-imino-D-glucitol **1a**[6] and (2*S*,3*R*,4*R*,5*S*)-1,6-dideoxy-1,6-imino-L-iditol **1b**.



1a R_1= OH, R_2 = H
1b R_1= H, R_2 = OH

Figure 1.

2. Results and discussion

D-Glucose was converted to 5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-benzyl-α-D-xylo-hex-5-enofuranose (**2**) by the known method[7] (Scheme 1). Epoxidation of **2** with *m*CPBA in dichloromethane at room temperature afforded a diastereomeric mixture of 5,6-epoxides **3a** and **3b** in the ratio 55:45, respectively.[8]

The regio-selective nucleophilic attack of *N*-benzylamine, at the terminal carbon of the epoxy ring, in **3a** afforded 6-deoxy-6-*N*-benzylamino-1,2-*O*-isopropylidene-3-*O*-benzyl-α-D-gluco-furanose (**4a**).[9] Hydrogenolytic removal of the *N* and *O*-benzyl protecting groups in **4a**, with ammonium formate, 10% Pd–C in methanol under reflux gave an aminoalcohol, that was directly subjected to selective *N*-Cbz protection with benzylchloroformate, in the presence of sodium bicarbonate in methanol–water, to give **5a**. Removal of the 1,2-acetonide group in **5a** with triflouroacetic acid–water (3:2) followed by catalytic hydrogenation using 10% Pd–C in methanol afforded (2*S*,3*R*,4*R*,5*R*)-1,6-dideoxy-1,6-imino-D-glucitol **1a**.[10] Similar sequence of reactions was repeated with 5,6-anhydro-β-L-ido-furanose **3b**. Thus, epoxide ring opening

Keywords: carbohydrates; imino sugars; enzyme inhibitors; D-glucoazepane; L-idoazepane.

* Corresponding author. Tel.: +91-20-560-1225; fax: +91-20-569-1728; e-mail: ddd@chem.unipune.ernet.in

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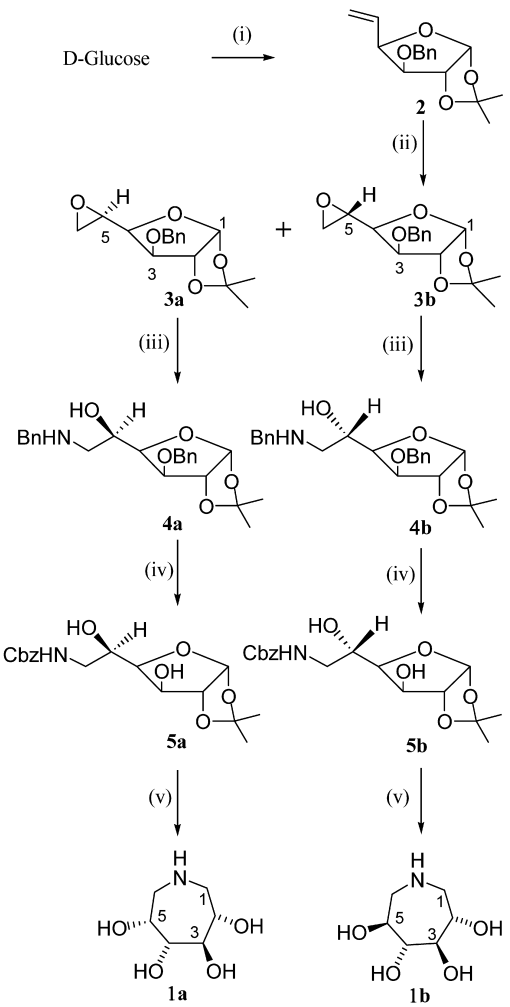

Scheme 1. *Reagents and conditions*: (i) Ref. 7; (ii) *m*CPBA, CH_2Cl_2, 25°C, 36 h; (iii) for **3a**, $BnNH_2$, neat, 25°C, 12 h; for **3b**, $BnNH_2$, 80°C, 12 h; (iv) (a) $HCOONH_4$, 10% Pd–C, MeOH, reflux, 40 min; (b) ClCOOBn, MeOH–H_2O, 0–25°C, 2 h; (v) (a) TFA–H_2O, 25°C, 2 h; (v) (a) TFA–H_2O, 25°C, 2 h; (b) 10% Pd–C, MeOH, H_2, 80 psi, 25°C, 24 h.

of **3b** with *N*-benzylamine at 80°C gave **4b**,[11] which on hydrogenolysis followed by *N*-Cbz protection afforded **5b**. Removal of the 1,2-acetonide group with TFA–water and catalytic hydrogenation with 10% Pd–C in methanol gave (2*S*,3*R*,4*R*,5*S*)-1,6-dideoxy-1,6-imino-L-iditol **1b**. The spectral and analytical data of **1b** were in consonance with that reported in the literature.

In conclusion, we have presented an efficient and straightforward chiron approach for the syntheses of tetrahydroxyazepane derivatives **1a** and **1b** that can be reproduced on multi-gram scale. The concept that we have shown herein clearly indicates a design strategy for the development of new analogues of this class of compounds.

3. Experimental

3.1. General

Melting points were recorded with Thomas Hoover melting point apparatus and are uncorrected. IR spectra (ν, cm^{-1}) were recorded on a Perkin–Elmer 1600 FTIR spectrophotometer as a thin film or in nujol mull. NMR spectra were recorded on a Varian Mercury instrument (300 MHz for ^1H and 75 MHz for ^{13}C) in $CDCl_3$ solvent, unless otherwise stated, with reference to TMS as an internal standard. Elemental analyses were carried out on a Hosli C, H-analyser. Optical rotations were measured using a Bellingham Stanley-ADP 220 digital polarimeter at 25°C. As and when required, the reactions were carried out in oven-dried glassware under dry N_2. Thin layer chromatography was performed on pre-coated plates (0.25 mm, silica gel 60 F_{254}). After work up, the organic rotavapor layer was washed with water, dried over anhydrous sodium sulphate and evaporated under reduced pressure using a rotavapor. Visualization was by absorption of UV light, or by thermal development after spraying with 2,4-dinitrophenylhydrazine solution and with basic aqueous potassium permanganate solution. Column chromatography was carried out on silica gel (100–200 mesh). Diethyl ether, dichloromethane, ethyl acetate and THF were purified and dried before use. Petroleum ether (PE) was the distillation fraction between 40 and 60°C. *N*-Benzylamine, benzyloxycarbonyl chloride and 10% Pd–C were purchased from Aldrich and/or Fluka.

3.1.1. 5,6-Anhydro-1,2-*O*-isopropylidene-3-*O*-phenylmethyl-α-D-gluco-1,4-furanose (3a) and 5,6-anhydro-1,2-*O*-isopropylidene-3-*O*-phenylmethyl-β-L-ido-1,4-furanose (3b). To a 0°C cooled solution of alkene **2** (2.0 g, 7.25 mmol) in CH_2Cl_2 (30 mL) was added *m*-chloroperbenzoic acid (3.75 g, 21.7 mmol) in two portions with an interval of 10 min. The stirred reaction mixture was warmed to room temperature and after 36 h diluted with CH_2Cl_2 (50 mL). The organic layer was washed with 1 M NaOH (20 mL×2), water (10 mL×2), was dried over anhydrous sodium sulphate and evaporated on rotovapor under reduced pressure. The crude oil thus obtained was purified by column chromatography, elution first with PE/ethyl acetate, 98/2 afforded **3a** (0.95 g, 45%) as a thick liquid: R_f (60% *n*-hexane/ethyl acetate) 0.52; $[\alpha]_D=-50.9$ (*c* 4.79, $CHCl_3$), lit.[8] $[\alpha]_D=-51.2$ (*c* 4.77, $CHCl_3$). Further elution with PE/ethyl acetate (95/5) afforded **3b** (0.85 g, 40%) as a thick liquid; R_f (60% *n*-hexane/ethyl acetate) 0.42; $[\alpha]_D=-79.5$ (*c* 6.45, $CHCl_3$), lit.[8] $[\alpha]_D=-78.7$ (*c* 6.50, $CHCl_3$). The spectral data of **3a** and **3b** were found to be in good agreement with that reported.

3.1.2. 6-Deoxy-6-*N*-phenylmethylamino-1,2-*O*-isopropylidene-3-*O*-phenylmethyl-α-D-gluco-1,4-furanose (4a). A solution of **3a** (1.4 g, 4.7 mmol) and *N*-benzylamine (0.56 g, 5.27 mmol) was stirred at room temperature under N_2 for 12 h and directly loaded on a silica gel column. Elution with PE/ethyl acetate, 4/1 afforded **4a** (1.2 g, 82%) as a thick liquid; (Found: C, 69.29; H, 7.49. $C_{23}H_{29}NO_5$ requires C, 69.16; H, 7.31%); R_f (40% ethyl acetate/*n*-hexane) 0.35; $[\alpha]_D=+15.32$ (*c* 0.19, $CHCl_3$); ν_{max} (neat) 3300–3000 (broad) cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.35 (3H, s, *Me*), 1.50 (3H, s, *Me*), 1.91 (1H, bs, exchanges with D_2O, O*H*/N*H*), 2.78 (1H, dd, *J*=12.3, 8.5 Hz, CH_2HBn), 2.99 (1H, dd, *J*=12.3, 3.0 Hz, CH_2HBn), 3.84 (2H, s, NCH_2Ph), 4.01 (1H, dd, *J*=8.5, 3.0 Hz, C_4–*H*), 4.08 (1H, d, *J*=3.0 Hz, C_3–*H*), 4.15 (1H, dt, *J*=8.5, 3.0 Hz, C_5–*H*), 4.57 (1H, d, *J*=3.5 Hz, C_2–*H*), 4.62 (2H, AB quartet *J*=11.8 Hz,

OCH_2Ph), 4.77 (1H, bs, exchanges with D_2O, O*H*/N*H*), 5.88 (1H, d, *J*=3.5 Hz, C_1–*H*), 7.3 (10H, bs, *Ph*); δ_C (75 MHz, $CDCl_3$) 26.1, 26.7, 51.4, 52.9, 65.8, 72.3, 81.6, 81.7, 82.2, 105.1, 111.6, 127.6, 127.7, 128.4, 128.5, 137.3, 137.4.

3.1.3. 6-Deoxy-6-*N*-phenylmethylamino-1,2-*O*-isopropylidene-3-*O*-phenylmethyl-β-L-ido-1,4-furanose (4b). A solution of **3b** (1.5 g, 1.53 mmol) and *N*-benzylamine (0.62 g, 1.67 mmol) was heated at 80°C for 5 h and the crude product on cooling was loaded on a silica gel column. Elution with PE/ethyl acetate (4/1) afforded **4b** (1.3 g, 85%) as a thick liquid; (Found: C, 69.01; H, 7.35. $C_{23}H_{29}NO_5$ requires C, 69.16; H, 7.31%); R_f (40% ethyl acetate/*n*-hexane) 0.39; $[\alpha]_D$=−50.07 (*c* 0.20, $CHCl_3$); ν_{max} (neat) 3300–3000 (broad) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 1.32 (3H, s, *Me*), 1.48 (3H, s, *Me*), 1.58–2.01 (1H, bs, exchanges with D_2O, O*H*/N*H*), 2.58–2.78 (2H, m, CH_2NHBn), 3.72 (2H, AB quartet, *J*=11.8 Hz, NHCH_2Ph), 3.95 (1H, d, *J*=3.5 Hz, C_3–*H*), 4.05–4.15 (2H, m, C_4–*H*, C_5–*H*), 4.37 (1H, d, *J*=11.5 Hz, OCH_2Ph), 4.53 (1H, d, *J*=3.5 Hz, C_2–*H*), 4.58 (1H, d, *J*=11.5 Hz, OCH_2Ph), 4.82 (1H, bs, exchanges with D_2O, O*H*/N*H*), 5.98 (1H, d, *J*=3.5 Hz, C_1–*H*), 7.25–7.35 (10H, m, *Ph*); ^{13}C NMR (75 MHz, $CDCl_3$), δ 26.2, 26.7, 50.9, 53.6, 67.1, 71.7, 81.0, 82.2, 104.7, 111.7, 126.9, 127.7, 128.2, 128.52, 128.5, 128.8, 128.9, 136.7, 136.9.

3.1.4. 6-Deoxy-6-*N*-benzyloxycarbonyl-1,2-*O*-isopropylidene-3-*O*-phenylmethyl-α-D-gluco-1,4-furanose (5a). A solution of **4a** (1.1 g, 2.75 mmol), ammonium formate (0.92 g, 15.1 mmol) and 10% Pd–C (0.2 g) in methanol (10 mL) was refluxed for 40 min. The catalyst was filtered through celite and washed with methanol (5 mL×2). To the filtrate, cooled to 0°C, was added sodium bicarbonate (0.725 g, 8.61 mmol) and benzyloxycarbonyl chloride (0.47 g, 2.70 mmol) and the stirred reaction mixture warmed to room temperature. After 2 h, methanol was removed under reduced pressure and the residue was extracted with ethyl acetate (5 mL×3). Combined extract was washed with brine, dried over anhydrous sodium sulphate and concentrated on rotovapor to afford a residue which was purified by column chromatography (chloroform/methanol, 9/1) to get **5a** (0.81 g, 84%) as a thick liquid; (Found: C, 58.02; H, 6.67. $C_{17}H_{23}NO_7$ requires C, 57.79; H, 6.55%); R_f (20% methanol/chloroform) 0.6; $[\alpha]_D$=+18.02 (*c* 0.20, $CHCl_3$); ν_{max} (neat) 3421, 1685 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.29 (3H, s, *Me*), 1.46 (3H, s, *Me*), 2.10–2.25 (1H, broad, exchanges with D_2O, O*H*/N*H*), 3.22–3.40 (1H, m, CH_2NHCbz), 3.50–3.65 (1H, m, CH_2NHCbz), 3.70–4.0 (1H, broad, exchanges with D_2O, O*H*/N*H*), 4.02 (2H, bs, C_3–*H* and C_5*H*), 4.33 (1H, bs, C_4–*H*), 4.50 (1H, d, *J*=3.6 Hz, C_2–*H*), 5.09 (2H, s, OCH_2Ph), 5.55 (1H, bs, exchanges with D_2O, O*H*/N*H*), 5.92 (1H, d, *J*=3.6 Hz, C_1–*H*), 7.30–7.45 (5H, m, *Ph*); δ_C (75 MHz, $CDCl_3$) 26.0, 26.7, 44.5, 67.1, 69.6, 74.8, 80.4, 85.0, 104.9, 111.7, 127.8, 128.0, 128.1, 128.5, 136.0, 158.0.

3.1.5. 6-Deoxy-6-*N*-benzyloxycarbonyl-1,2-*O*-isopropylidene-3-*O*-phenylmethyl-β-L-ido-furanose (5b). A reaction of **4b** (1.5 g, 3.75 mmol), ammonium formate (1.25 g, 19.1 mmol) and 10% Pd–C (0.3 g) in methanol (10 mL), followed by reaction with sodium bicarbonate (1.59 g, 18.9 mmol) and benzyloxycarbonyl chloride (1.01 g, 5.96 mmol), as stated in case of **4a**, afforded **5b** (0.78 g, 81%) as a thick liquid; (Found: C, 57.90; H, 6.77. $C_{17}H_{23}NO_7$ requires C, 57.79; H, 6.55%); R_f (20% methanol/chloroform) 0.55; $[\alpha]_D$=−9.75 (*c* 0.20, $CHCl_3$); ν_{max} (neat) 3350, 1699 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.32 (3H, s, *Me*), 1.48 (3H, s, *Me*), 1.60–1.85 (2H, bs, exchanges with D_2O, O*H*/N*H*), 3.29 (1H, dd, *J*=14.3, 6.1 Hz, H_2-CNHCbz), 3.48 (1H, dd, *J*=14.3, 3.3 Hz, H_2CNHCbz), 4.00–4.07 (1H, m, C_4–*H*), 4.10–4.17 (1H, m, C_5–*H*), 4.30 (1H, d, *J*=2.8 Hz, C_3–*H*), 4.50 (1H, d, *J*=3.3 Hz, C_2–*H*), 5.10 (2H, s, OCH_2Ph), 5.46–5.58 (1H bs, exchanges with D_2O, O*H*/N*H*), 5.95 (1H, d, *J*=3.3 Hz, C_1–*H*), 7.30–7.42 (5H, s, *Ph*); δ_C (75 MHz, $CDCl_3$) 26.2, 26.8, 44.9, 67.1, 70.3, 76.3, 79.9, 85.3, 104.8, 111.8, 128.0, 128.1, 128.4, 135.9, 157.2.

3.1.6. 1,6-Dideoxy-1,6-imino-(2*S*,3*R*,4*R*,5*R*)-D-glucitol (1a). A solution of **5a** (0.5 g, 1.41 mmol) in TFA–H_2O (5 mL, 3/2) was stirred at 25°C and after 2 h TFA was co-evaporated with benzene to furnish the hemiacetal as a thick liquid. A solution of hemiacetal in methanol and 10% Pd/C (0.1 g) was hydrogenated at 80 psi. After 18 h, the catalyst was filtered, washed with methanol (5 mL×2) and the filtrate concentrated to a sticky solid. The sticky solid was washed with chloroform and loaded on DOWEX-H^+ resin. Elution with 5% ammonia–methanol and evaporation of methanol afforded **1a** (0.17 g, 76%) as a sticky solid; (Found: C, 36.47; H, 8.90. $C_6H_{13}NO_4.2H_2O$ requires C, 36.18; H, 8.59%); R_f (20% methanol/chloroform) 0.11; ν_{max} (neat) 3555–3340, 1592, 1194 cm^{-1}; δ_H (300 MHz, D_2O) 2.65–2.87 (4H, m, H_2CNHCH_2), 3.40–3.52 (1H, m), 3.53–3.65 (2H, m), 3.78–3.88 (1H, m); δ_C (75 MHz, D_2O) 49.3, 49.6, 71.2, 73.3, 74.7, 75.2.

A solution of **1a** (0.1 g) in methanol (5 mL) and two drops of concentrated hydrochloric acid was stirred at room temperature for 24 h. The solution was concentrated and the residue was dissolved in water (10 mL) and extracted with ether (2×10 mL). The aqueous layer was concentrated and residue washed with methanol-ether to give white gummy solid (0.085 g, 70%); $[\alpha]_D$=−19.5 (*c* 0.6, H_2O); lit.[10] $[\alpha]_D$=−15 (*c* 1, H_2O).

3.1.7. 1,6-Dideoxy-1,6-imino (2*S*,3*R*,4*R*,5*S*)-L-iditol (1b). Reaction of **5b** (0.2 g, 0.56 mmol) with TFA–H_2O, as in case of **5a**, followed by hydrogenation with 10% Pd–C in methanol gave **1b** (0.06 g 65%) as a thick liquid; (Found: C, 36.43; H, 8.77. $C_6H_{13}NO_4{\cdot}2H_2O$ requires C, 36.18; H, 8.59%); R_f (20% methanol/chloroform) 0.15; $[\alpha]_D$=+20.1 (*c* 0.2, H_2O); lit.[4e] $[\alpha]_D$=+19.9 (*c* 2, H_2O); ν_{max} (neat) 3560–3367, 1577, 1179 cm^{-1}; δ_H (300 MHz, D_2O) 2.95–3.07 (2H, dd, *J*=8.2, 13.8 Hz, H_2NHCH_2, 3.12–3.24 (2H, dd, *J*=1.9, 13.8 Hz, H_2CNHCH_2), 3.46–3.55 (2H, m, C_2–*H* and C_5–*H*), 3.84–3.96 (2H, m, C_3–*H* and C_4–*H*); δ_C (75 MHz, D_2O) 47.0, 67.8, 76.7.

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References

1. (a) Wong, C. H.; Halcomb, R. L.; Ichikawa, Y.; Kajimato, T. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 521. (b) Winchester, B.; Fleet, G. W. J. *Glycobiology* **1992**, *2*, 199. (c) Horita, K.; Yoshioka, T.; Tanaka, T.; Oikawa, Y.; Yonemitsu, O. *Tetrahedron* **1986**, *42*, 3021. (d) Look, G. C.; Fotsch, C. H.; Wong, C. H. *Acc. Chem. Res.* **1993**, *26*, 182.
2. (a) Stutz, A. E. *Iminosugars as Glycosidase Inhibitors. Nojirimycin and Beyond*; Wiley/VCH: Weinheim, 1999. (b) Fairbank, A. J.; Carpenter, N. C.; Fleet, G. W. J.; Ramsden, N. G.; Censi de Bello, I.; Winchester, B. G.; Al-Daher, S. S.; Nagahashi, G. *Tetrahedron* **1992**, *48*, 3365 and references cited therein. (c) Merrer, Y. L.; Poitout, L.; Depazy, J.; Dosbaa, I.; Geoffroy, S.; Foglietti, M. *Bioorg. Med. Chem.* **1997**, *5*, 519. (d) Kajimoto, T.; Liu, K. K.-C.; Pederson, R. L.; Zhong, Z.; Ichikawa, Jr. Y.; Porco, J. A.; Wong, C.-H. *J. Am. Chem. Soc.* **1991**, *113*, 6187 and references cited therein.
3. Johnson, H. A.; Thomas, N. R. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 237 and references cited therein.
4. (a) Lohray, B. B.; Jayamma, Y.; Chatterjee, M. *J. Org. Chem.* **1995**, *60*, 5958. (b) Painter, G. F.; Falshaw, A. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1157. (c) Moris-Varas, F.; Qian, X.; Wong, C. H. *J. Am. Chem. Soc.* **1996**, *118*, 7647. (d) Qian, X.; Moris-Varas, F.; Fitzgerald, M. C.; Wong, C. H. *Bioorg. Med. Chem.* **1996**, *4*, 2055. (e) Merrer, Y. L.; Poitout, L.; Depazy, J.; Dosbaa, I.; Geoffroy, S.; Foglietti, M. *Bioorg. Med. Chem.* **1997**, *5*, 519. (f) Poitout, L.; Merrer, Y. L.; Depazy, J. *Tetrahedron Lett.* **1994**, *35*, 3293. (g) Poitout, L.; Merrer, Y. L.; Depazy, J. *Tetrahedron Lett.* **1996**, *37*, 1613. (h) Armbruster, J.; Stelzer, F.; Landenberger, P.; Wieber, C.; Hunkler, D.; Keller, M.; Prinzbach, H. *Tetrahedron Lett.* **2000**, *41*, 5483. (i) Herdeis, C.; Mohareb, R. M.; Neder, R. B.; Schwabenlander, F.; Tesler, J. *Tetrahedron: Asymmetry* **1999**, *10*, 4521.
5. (a) Dhavale, D. D.; Desai, V. N.; Sindkhedkar, M. D.; Mali, R. S.; Castellari, C.; Trombini, C. *Tetrahedron: Asymmetry* **1997**, *9*, 1475. (b) Dhavale, D. D.; Saha, N. N.; Desai, V. N. *J. Org. Chem.* **1997**, *62*, 7482. (c) Dhavale, D. D.; Desai, V. N.; Saha, N. N. *J. Chem. Soc., Chem. Commun.* **1999**, 1719. (d) Patil, N. T.; Tilekar, J. N.; Dhavale, D. D. *J. Org. Chem.* **2001**, *66*, 1065. (e) Saha, N. N.; Desai, V. N.; Dhavale, D. D. *Tetrahedron* **2001**, *57*, 39. (f) Patil, N. T.; Tilekar, J. N.; Dhavale, D. D. *Tetrahedron Lett.* **2001**, *42*, 747. (g) Patil, N. T.; John, S.; Sabharwal, S. G.; Dhavale, D. D. *Bioorg. Med. Chem.* **2002**, *10*, 2155.
6. For the first synthesis of per-acetylated derivative of **1a** see: Paulsen, H.; Todt, K. *Chem. Ber.* **1967**, *100*, 512.
7. Josan, J. S.; Eastwood, F. W. *Carbohydr. Res.* **1968**, *7*, 161.
8. Although compounds 5,6-anhydro-1,2-*O*-isopropylidene-3-*O*-benzyl-α-D-gluco-furanose **3a** and 5,6-anhydro-1,2-*O*-isopropylidene-3-*O*-benzyl-β-L-ido-furanose **3b** are known in the literature, we have synthesized them by an independent route which gives direct access to both the C-5 epimers. The spectral and analytical data of **3a**,**b** were found to be in consonance with that reported. For **3a** see: Jarosz, S. *Carbohydr. Res.* **1988**, *183*, 217 and references cited therein.
9. Yamashita, M.; Takahashi, C.; Seo, K. *Hetrocycles* **1993**, *36*, 651.
10. We have characterized **1a** independently by spectral and analytical methods. However, during the preparation of our manuscript we came to know the recent report for the hydrochloride salt of **1a** see: Joseph, C. C.; Regeling, H.; Zwanenburg, B.; Chittenden, G. J. F. *Tetrahedron* **2002**, *58*, 6907. We have converted **1a** to its hydrochloride salt and our analytical data was found to be identical with that reported.
11. The reaction of **3b** with *N*-benzylamine or with *N*-benzyllithiumamide at room temperature was found to be sluggish and ~85% of starting compound was recovered even after 72 h in both the cases. The use of *N*-benzyllithiumamide at high temperature however, led to mixture of products.