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Vinylsulfone-modified carbohydrates: first general route to D-lividosamine (2-amino-2,3-dideoxy-D-glucose) and its new analogues

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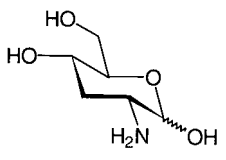
Abstract—A general route to D-lividosamine and its new analogues has been devised for the first time. The essence of the present synthetic route lies in the diastereoselective introduction of *N*-monoalkylated and *N*-dialkylated amines to C-2 carbons of methyl 2,3-dideoxy-3-C-phenylsulfonyl-α-D-hex-2-enopyranoside and methyl 2,3-dideoxy-3-C-phenylsulfonyl-β-D-hex-2-enopyranoside in equatorial configurations. The 2-amino-2,3-dideoxysugrs thus generated, are desulfonated reductively at C-3 sites to produce a known intermediate for the synthesis of D-lividosamine and several new 2-*N*-alkylamino- and 2-*N*,*N*-dialkylamino-2,3-dideoxy analogues.

1. Introduction

The most important mechanism of resistance to aminoglycoside antibiotics among resistant bacteria arises from enzymatic *N*-acetylation, *O*-phosphorylation, and *O*-nucleotidylation of specific sites in the antibiotics. To avoid such deactivation processes, several semisynthetic aminoglycoside antibiotics have been designed where either the hydroxyl groups undergoing enzymatic phosphorylation have been removed and/or the amino groups susceptible to acetylation have been masked by acylation or alkylation.[1] The interest in this class of compounds has been renewed with the discoveries that aminoglycoside antibiotics interact with a variety of RNA molecules.[2a–d] Other studies on aminoglycoside antibiotics have shown that: (a) the amines in these molecules play an important role in relation to their toxicities, either because of their basic characters or their interactions with phospholipid bilayers of the inner cortex tissue; and (b) regiochemical preferences of aminoglycosides are caused by steric reasons and/or the varying basicity of amino groups present in aminoglycosides.[2e] Interestingly, a study addressing the contribution of ring IV in the properties of neomycin B concluded that gross changes were tolerated in the structure of aminoglycoside antibiotics without significant effect on biological activity.[2f] It would, therefore, be appropriate to synthesize new antibiotics carrying various amino groups with varying basicities and steric bulks. However, the first step of such a synthesis will be the designing of methodologies for the generation of several new modified aminosugars having one or more deoxygenated centers and mono- or dialkylated amino groups at specific sites.

2. Results and discussion

D-Lividosamine (2-amino-2,3-dideoxy-D-glucose) (Fig. 1), isolated from *Streptomyces Lividus*,[3] is present in aminoglycoside antibiotics such as lividomycin-A, lividomycin–B and 3′-deoxykanamycin C.[4a] Several other aminosugars, structurally related to D-lividosamine are present in tobramycin, dibekacin and gentamicins.[4b–d] The essence of the synthetic strategy leading to the preparation of D-lividosamine and its alkylated analogues lies in the introduction of amino and *N*-alkyl amino groups. These must be introduced at the C-2 carbon of the pyranoses in equatorial configurations followed by (or prior to) deoxygenation at the C-3 site. Several methods of synthesis of D-lividosamine starting from D-glucose,[5] D-glucosamine,[6] ethyl 2,3-dideoxy-α-D-glycero-hex-2-enopyranoside-4-ulose,[7] tri-*O*-acetyl glucal,[8] 1,6-anhydro-β-D-glucose[9] and even from non-carbohydrate sources like 'naked sugars' have been



D-lividosamine

Figure 1.

Keywords: D-lividosamine; carbohydrates; vinyl sulfone; Michael addition.

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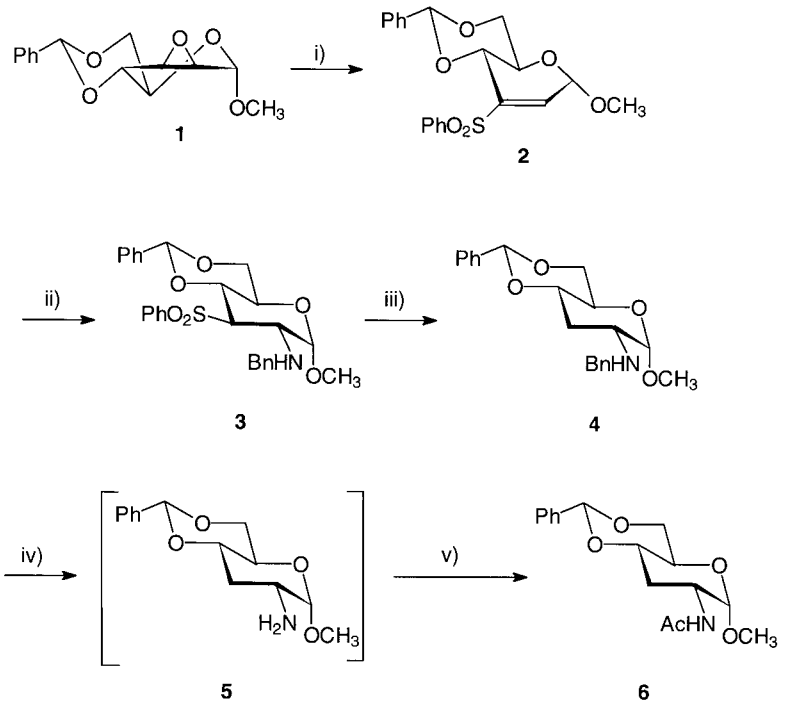
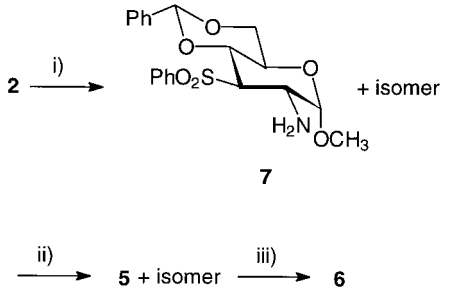


Scheme 1. *Reagents*: (i) Ref. 13, 88% (in 4 steps); (ii) $PhCH_2NH_2$, MeOH, reflux, 15 h, 90%; (iii) Mg, MeOH, reflux, 11 h, 90%; (iv) a. $Pd(OH)_2$, C, H_2, EtOH, rt, 22 h, b. Ac_2O, Py, rt, 4 h, 79%.

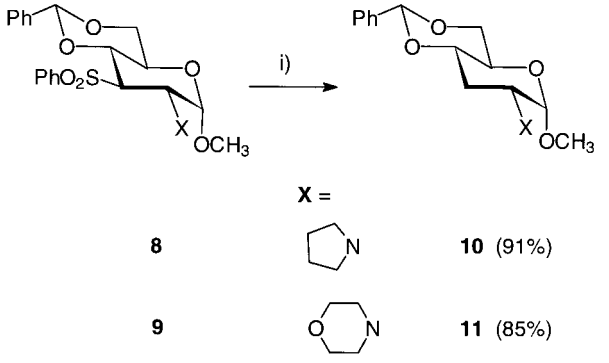
reported.[10] Nevertheless, no method[11,12] reported so far had the potential to be exploited as a general route for the synthesis of 2-amino-2,3-dideoxy-D-glucose and its analogues carrying various *N*-monoalkyl- and *N*-dialkylamino groups.

We have recently reported that amines, both primary and secondary, react in a diastereoselective fashion with methyl 2,3-dideoxy-3-*C*-phenylsulfonyl-α-D-hex-2-enopyranoside **2** and methyl 2,3-dideoxy-3-*C*-phenylsulfonyl-β-D-hex-2-enopyranoside **13**.[13] Such a C–N bond formation in Michael fashion at C-2 of the vinylsulfone-modified carbohydrates exclusively produced the thermodynamically more stable C–N equatorial aminosugars with primary amines. Secondary amines, on the other hand produced a mixture of *gluco*-(major) and *manno*-(minor) products with α-anomer **2**. The major isomers were separated by crystallization. Primary as well as secondary amines produced only the *gluco*-derivative with β-anomer **13**.[13] We envisaged that benzylamine would react with **2** and **13** to generate exclusively the *gluco*-isomer, from which the benzyl group could be removed reductively to generate the free amino function. In addition, the phenylsulfonyl group is very suitably located in all these products to generate methylene groups at C-3 via reductive desulfonation leading to the synthesis of a reported[5,6] intermediate **6** of D-lividosamine. Several partially and fully protected analogues of D-lividosamine could be synthesized using a similar approach.

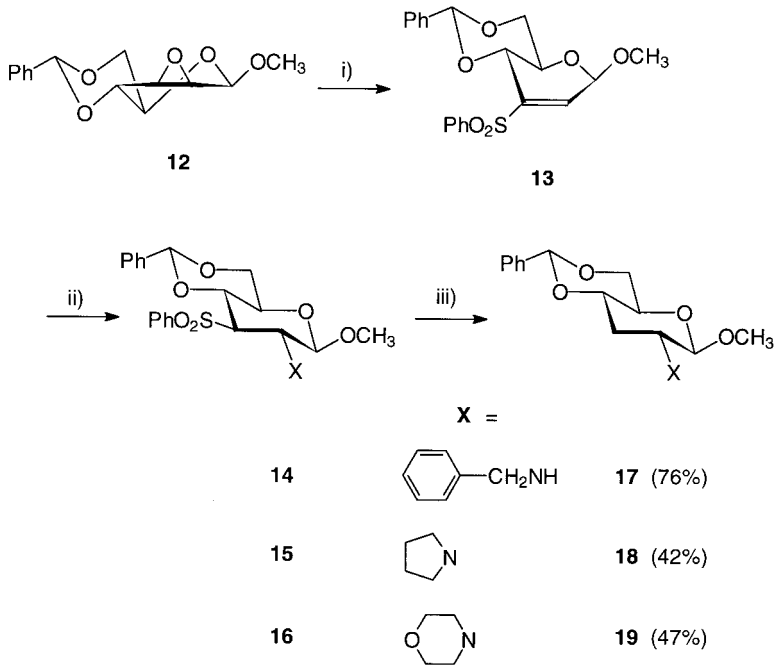
Compound **2**[13] was reacted with benzylamine in anhydrous methanol to produce **3**[14] exclusively in 90% yield. Compound **3** was desulfonated on treatment with magnesium in methanol in 90% yield to generate the 2-*N*-benzylamino-2,3-dideoxy product **4**. Compound **4** was debenzylated to **5** on treatment with palladium hydroxide on charcoal. Crude **5** was isolated as the acetyl derivative **6** (Scheme 1).[5,6] However, to reduce the number of steps involved in the synthesis of **6**, compound **2** was reacted directly with conc. aq. ammonia in dioxane. The reaction produced a mixture of products although the desired deoxyaminosugar **7** was present in a major amount (^{1}H-NMR). No attempt was made to establish the identity



Scheme 2. *Reagents*: (i) 30%, aq. NH_3, dioxane, rt, 24 h; (ii) MeOH, Mg, reflux, 3.5 h; (iii) Ac_2O, Py, rt, 16 h, 65% (in three steps).



Scheme 3. *Reagents*: (i) Mg/MeOH, reflux.



Scheme 4. *Reagents*: (i) Ref. 13, 75% (in 4 steps); (ii) for **13**: neat $PhCH_2NH_2$, 90–100°C, 3 h, 75%; for **14** and **15**: Ref. 13; (iii) MeOh, Mg, reflux.

of the impurity. The mixture was desulfonated as above and the free amino compound **5** was acylated. Pure **6** was crystallized out from benzene-pet. ether mixture in 65% overall yield (Scheme 2). Similarly, the pyrrolidino and morpholino derivatives **8**[13] and **9**[13] were desulfonated to **10** and **11** in 91 and 85% yields, respectively (Scheme 3).

In the β-series, compound **13**, which was obtained from epoxide **12**,[13] was reacted with neat benzylamine to produce exclusively the 2-*N*-benzylamino-2,3-dideoxy product **14**[14] in 90% yield. Compound **14** and previously synthesized **15**[13] and **16**[13] were desulfonated to **17**, **18** and **19** in 76, 42 and 47% yields, respectively (Scheme 4).

A comparison of the efficiency of the present method for the synthesis of intermediate **6** over the earlier reported routes from carbohydrates would be pertinent here. The major difficulty encountered, in the synthesis of D-lividosamine from D-glucose[5] was the reduction of acetylimino-glycoside **20** (Fig. 2) to the corresponding amine which afforded a mixture of *ribo* and *arabino* isomers.[5c] The reduction of **20** with $LiAlH_4$, followed by acetylation, gave only 38% pure *ribo* isomer. In the case of synthesis from D-glucosamine, the deoxygenation of the secondary hydroxyl group, C-3, was problematic because of the stereoelectronic hindrance of an S_N2 process at this carbon. Moreover, the presence of the amino group, ironically, required an additional step for the protection of the amino group to get **21** (Fig. 2) as the starting material. These factors contributed to the lower overall yield of the final product;[6] in any case, this method could not have been used for the generation of analogues. The addition of NaN_3 to **22**[7](Fig. 2) always afforded a mixture at C-2 (*ribo:lyxo*). Further, the reduction of the carbonyl group again produced a mixture of isomers (*erythro* and *threo*). Thus, the overall yield was reduced to 7%.[7] Tri-*O*-acetyl glucal was converted to ethyl 2-acetamido-2,3-dideoxy-α-D-ribo-hexapyranoside via **23** (Fig. 2); the overall yield from glucal was less than 45%.[8] Synthesis of *N*-protected D-lividosamine starting from compound **24** (Fig. 2) had an overall yield of 29%.[9] Our methodology (Scheme 1) afforded **6** in overall 40% starting from methyl-α-D-glucopyranoside or in 56% from the *manno* epoxide **1**.

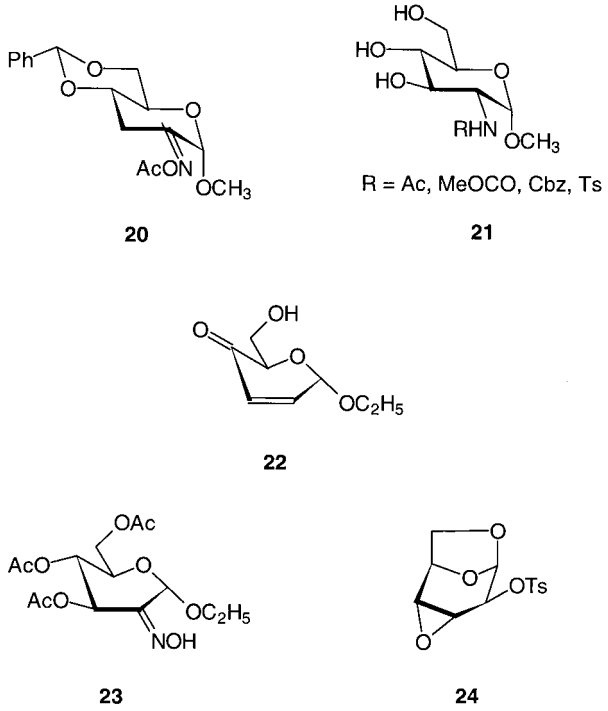


Figure 2.

3. Conclusion

Although the C–N bonds at the C-2 positions of naturally occurring aminosugars, D-glucosamine,[15] D-galactosamine,[15] D-lividosamine[3,15]are present in equatorial configurations, there are only a few reports on the synthesis of equatorially located *N*-alkyl and *N*,*N*-dialkyl-D-glucosamine derivatives via *N*-alkylation or *N*,*N*-dialkylation of glucosamine.[16] The other most commonly used methods for the synthesis of aminosugars, involved opening of epoxides **1** or **12** by amines that always produced the C-3 deoxy C-3 aminosugars and not the C-2 deoxy C-2 aminosugars.[17] Reactions of primary and secondary amines with methyl 2,3 anhydro-4,6-*O*-(phenylmethylene)-D-allopyranoside, on the other hand, produced exclusively the C-2 deoxy, C-2 amino products with the C–N bond in the axial configuration.[18] None of the above methods could have been used as a general route[11,12] for the synthesis of D-lividosamine and its analogues either because of the undesired configuration or position of the C–N bond and/or the additional functionalization of the C-3 hydroxyl groups required for the deoxygenation of the C-3 center. Our method circumvents both the problem of the introduction of *N*-monoalkylated and *N*-dialkylated amines to the C-2 carbon of pyranoses in equatorial configurations as well as the deoxygenation of the C-3 position. It also compares well with the reported[5–10] synthesis starting from D-glucosamine or D-glucose and could be used as a general route for the synthesis of D-lividosmaine and its analogues. Work is currently in progress to synthesize unnatural aminoglycoside antibiotics using some of these analogues of D-lividosamine.

4. Experimental

4.1. General

For general methods see Ref. 13.

4.1.1. Methyl 2-*N*-benzylamino–2,3-dideoxy-4,6-*O*-(phenylmethylene)-3-*C*-phenylsulfonyl-α-D-glucopyranoside (3). Benzylamine (1.01 mL, 9.29 mmol) was added to a solution of **2** (0.72 g, 1.86 mmol) in anhydrous methanol (25 mL). The solution was heated under reflux for 15 h. The product which crystallized out on cooling of the reaction mixture was filtered and washed with petroleum ether to yield **3** (0.83 g, 90%) as a white solid. It was recrystallized from methanol, m.p. 176–178°C; [Found: C, 65.51; H, 6.14; N, 2.87. $C_{27}H_{29}NO_6S$ requires C, 65.43; H, 5.90; N, 2.83%]; $[\alpha]_D^{28.5}$ + 27.9 (c=0.708, $CHCl_3$); ν_{max}(Nujol) 3463, 1645, 1380, 1363, 1284, 1112 cm^{-1}; δ_H 7.80 (2 H, m, aromatic), 7.39–7.05 (13 H, m, aromatic), 5.29 (1 H, s, PhC*H*), 4.60 (1 H, d, *J*=3.6 Hz, H-1), 4.19 (1 H, dd, *J*=3.5, 9.6 Hz), 3.92–3.68 (6 H, m), 3.53 (1 H, dd, *J*=3.6, 10.2 Hz), 3.36 (3 H, s, OMe); δ_C 141.8, 140.2, 136.5, 133.0, 129.0, 128.5, 128.2, 128.1, 127.9, 127.1, 126.2, 101.6, 98.2, 76.2, 69.2 (CH_2), 65.1, 62.2, 56.4, 55.3, 51.6 (CH_2); *m/z* (EI) 495 (2 M^+), 464 (10 M^+-OCH_3), 354 (67 M^+-SO_2Ph).

4.1.2. Methyl 2-*N*-benzylamino–2,3-dideoxy-4,6-*O*-(phenylmethylene)-3-*C*-phenylsulfonyl-β-D-glucopyranoside (14). A solution of **13** (0.24 g, 0.618 mmol) in neat benzylamine (2 mL) was heated for 3 h at 90–100°C. The reaction mixture was taken in EtOAc (40 mL), washed with water (3×15 mL), dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The resulting syrup was purified on silica gel (eluent 65% EtOAc–petroleum ether) to yield the title compound **14** (0.23 g, 75%) as a white solid, m.p. 143–144°C; [Found: C, 65.00; H, 6.70; N, 2.85. $C_{27}H_{29}NO_6S$ requires C, 65.43; H, 5.90; N, 2.83%]; $[\alpha]_D^{24}$ − 66.6 (c= 1.016, $CHCl_3$); ν_{max}($CHCl_3$) 3427, 1635, 1384, 1320, 1145, 1105 cm^{-1}; δ_H 7.76 (2 H, m, aromatic), 7.50–7.25 (11 H, m, aromatic), 7.03 (2 H, m, aromatic), 5.30 (1 H, s, PhC*H*), 4.49 (1 H, d, *J*=6.6 Hz, H-1), 4.29 (1 H, dd, *J*=4.8, 10.6 Hz), 4.13–3.91 (3 H, m), 3.73 (1 H, t, *J*=10.3 Hz), 3.62–3.36 (3 H, m), 3.58 (3 H, s, OMe). δ_C 140.3, 136.3, 133.4, 129.0, 128.8, 128.6, 128.4, 127.9, 127.0, 126.1, 106.5, 101.3, 75.8, 69.0 (CH_2), 66.9 (2 peaks), 57.2, 56.9, 53.0 (CH_2); *m/z* (EI) 355 (17, M^+-SO_2Ph^+H), 354 (7, M^+-SO_2Ph).

4.1.3. General procedure for the desulfonation of (3), (7), (8), (9), (14), (15) and (16). To a solution of substrate (1 mmol) in anhydrous methanol (35 mL), was added magnesium turnings (15 mmol). The reaction mixture was heated under reflux for 1–12 h. Solvent was evaporated to dryness under reduced pressure. The resulting residue was dissolved in EtOAc (50 mL), and filtered. The filtrate was washed with water (3×20 mL), dried over anhydrous Na_2SO_4, and evaporated to dryness under reduced pressure. The resulting syrup was purified by column chromatography on silica gel (eluents mentioned against each experimental procedure in brackets) to give pure desulfonated products.

4.1.4. Methyl 2-*N*-benzylamino-2,3-dideoxy-4,6-*O*-(phenylmethylene)-α-D-ribo-hexopyranoside (4). Compound **3** (0.68 g, 1.37 mmol) was desulfonated (eluent 65% EtOAc–petroleum ether) in 11 h to yield a white solid **4** (0.41 g, 90%), m.p. 97–98°C; [Found: C, 70.62; H, 7.62; N, 3.67. $C_{21}H_{25}NO_4$ requires C, 70.96; H, 7.09; N, 3.94%]; $[\alpha]_D^{24}$ + 2.3 (c=0.103, $CHCl_3$); ν_{max}(Nujol) 3460, 1633, 1365, 1097 cm^{-1}; δ_H 7.35–7.20 (10 H, m, aromatic), 5.25 (1 H, s, PhC*H*), 4.69 (1 H, d, *J*=3.3 Hz, H-1), 4.26 (1 H, dd, *J*=3.3, 8.7 Hz), 3.80–3.47 (5 H, m), 3.42 (3 H, s, OMe), 2.92 (1 H, m), 2.33 (1 H, dt, *J*=4.2, 11.4 Hz), 1.74 (1 H, q, *J*=11.7 Hz); δ_C 140.1, 137.7, 128.9, 128.4, 128.2, 128.1, 127.1, 126.2, 101.6, 98.9, 77.2, 69.4 (CH_2), 64.3, 55.2, 55.0, 50.2 (CH_2), 31.0 (CH_2); *m/z* (EI) 355 (3 M^+), 324 (3, M^+-OCH_3).

4.1.5. Methyl 2-(acetylamino)-2,3-dideoxy-4,6-*O*-(phenylmethylene)-α-D-ribo-hexopyranoside (6). To a solution of **4** (0.44 g, 1.24 mmol) in ethanol (25 mL), was added palladium hydroxide on carbon (40 mg). The reaction mixture was shaken at ambient temperature for 22 h under hydrogen (35 lbs). The reaction mixture was then filtered through celite, washed with ethanol (3×15 mL), and the combined extract was concentrated under reduced pressure to a syrup. Ac_2O (1.17 mL, 1.26 mmol) was added to a solution of the crude syrup in anhyd. pyridine (20 mL). After 4 h at ambient temperature, the reaction mixture was poured into sat. aq. $NaHCO_3$ solution (50 mL) and extracted with chloroform (3×15 mL). The combined organic layer was dried over anhyd. Na_2SO_4, and concentrated under reduced pressure. The crude product was purified over silica

gel (eluent 40% EtOAc–petroleum ether) to afford a white solid **6** (0.30 g, 79% in 2 steps from **4**), m.p. 236°C (sublim); lit[5] 245°C (sublim) [Found: C, 62.62; H, 7.08; N, 4.37. $C_{16}H_{21}NO_5$ requires C, 62.52; H, 6.89; N, 4.56%]; $[\alpha]_D^{28}$ + 55.0 (c=2.208, $CHCl_3$); lit[5] + 55.5 (c=0.95); ν_{max}($CHCl_3$) 3333, 1733, 1650, 1550, 1358, 1116 cm^{-1}; δ_H 7.50–7.36 (5 H, m, aromatic), 5.74 (1 H, d, J=9.2 Hz), 5.55 (1 H, s, PhC*H*), 4.61 (1 H, d, J=3.5 Hz, H-1), 4.39–4.26 (2 H, m), 3.73 (3 H, m), 3.43 (3 H, s, OMe), 2.20 (1 H, dt, J=11.5 Hz), 2.01 (3 H, s, OCOMe), 1.82 (1 H, q, J=11.4 Hz); δ_C 169.5, 137.6, 129.2, 128.4, 126.3, 101.9, 98.0, 76.6, 69.4 (CH_2), 64.2, 55.1, 47.6, 30.9 (CH_2), 23.4. *m/z* (EI) 276 (3 M^+-OCH_3), 248 (28 M^+-$NHAcH^+$).

4.1.6. Compound 6 via ammonia addition route. To a mixture of 30% aqueous ammonia (10 mL) in dioxane (15 mL), **2** (0.39 g, 1 mmol) was added and the solution was stirred at rt for 24 h. The reaction mixture was evaporated to dryness and the residual dioxane was co-evaporated with anhyd. methanol. The crude reaction mixture was desulfonated using Mg in MeOH (see general procedure). Methanol was evaporated to dryness. The resulting residue was taken in EtOAc (50 mL) and the insoluble matters were filtered. The filtrate was washed with water (3×20 mL), dried over Na_2SO_4, filtered and the filtrate was evaporated under reduced pressure. The residue was dried further by coevaporating with dry pyridine and dissolved in dry pyridine (10 mL). Acetic anhydride (5 eq.) was added to this solution and the reaction mixture was stirred at rt for 16 h. The reaction mixture was partitioned between $NaHCO_3$ solution (30 mL) and dichloromethane (25 mL×3). The organic layer was dried over Na_2SO_4, filtered and the filtrate was evaporated to dryness. Residual pyridine was co-evaporated with toluene. Flash silica column afforded a mixture of products (eluent 55% EtOAc–petroleum ether) from which the desired product was obtained in pure form by crystallization from benzene–petroleum ether (0.2 g, 65%).

4.1.7. Methyl 2,3-dideoxy-4,6-*O*-(phenylmethylene)-2-*N*-pyrrolidino-α-D-ribo-hexopyranoside (10). Compound **8** (0.30 g, 0.65 mmol) was desulfonated (eluent 60% EtOAc–petroleum ether) in 4 h to yield a pale brown solid **10** (0.14 g, 91%); m.p. 141–142°C; [Found: C, 67.55; H, 7.36; N, 4.18. $C_{18}H_{25}NO_4$ requires C, 67.68; H, 7.89; N, 4.38%]; $[\alpha]_D^{24}$ + 66.9 (c=0.539, $CHCl_3$); ν_{max}($CHCl_3$) 2933, 2400, 1450, 1383, 1133, 1100 cm^{-1}; δ_H 7.55–7.25 (5 H, m, aromatic); 5.56 (1 H, s, PhC*H*), 4.73 (1 H, d, J=3.1 Hz, H-1), 4.28 (1 H, dd, J=3.5, 9.0 Hz), 3.83–3.56 (3 H, m), 3.45 (3 H, s, OMe), 2.65–2.41 (5 H, m), 2.23 (1 H, dt, J= 4.0, 11.5 Hz), 2.00 (1 H, q, J=11.6 Hz), 1.81 (m, 4 H); δ_C 137.5, 129.0, 128.2, 126.2, 101.8, 99.0, 77.2, 69.4 (CH_2), 64.1, 63.7, 54.9, 51.6 (CH_2), 29.8 (CH_2), 23.0 (CH_2); *m/z* (EI) 319 (20 M^+), 304 (40 M^+-CH_3), 288 (30 M^+-OCH_3).

4.1.8. Methyl 2,3-dideoxy-2-*N*-morpholino-4,6-*O*-(phenylmethylene)-α-D-ribo-hexopyranoside (11). Compound **9** (0.35 g, 0.74 mmol) was desulfonated (eluent 35% EtOAc–petroleum ether) in 7 h to yield a white solid **11** (0.21 g, 85%), m.p. 118–120°C; [Found: C, 64.85; H, 6.93; N, 4.03. $C_{18}H_{25}NO_5$ requires C, 64.46; H, 7.51; N, 4.18%]; $[\alpha]_D^{28}$ + 99.3 (c=0.141, $CHCl_3$); ν_{max}(Nujol) 3444, 2358, 1633, 1377, 1108 cm^{-1}; δ_H 7.53–7.27 (5 H, m, aromatic), 5.55 (1 H, s, PhC*H*), 4.80 (1 H, d, J=3.1 Hz, H-1), 4.27 (1 H, dd, J=3.3, 8.8 Hz), 3.80–3.54 (7 H, m), 3.43 (3 H, s, OMe), 2.85–2.65 (3 H, m), 2.45 (2 H, m), 2.10 (1 H, dt, J=11.3, 4.0 Hz), 2.00 (1 H, q, J=11.2 Hz); δ_C 137.4, 128.8, 128.0, 126.0, 101.5, 99.0, 77.4, 69.2 (CH_2), 66.9 (CH_2), 64.2, 63.2, 54.4, 50.4 (CH_2), 26.3 (CH_2); *m/z* (EI) 335 (5 M^+), 320 (12 M^+-CH_3), 304 (10 M^+-OCH_3).

4.1.9. Methyl 2-*N*-benzylamino-2,3-dideoxy-4,6-*O*-(phenylmethylene)-β-D-ribo-hexopyranoside (17). Compound **14** (0.51 g, 1.03 mmol) was desulfonated (eluent 70% EtOAc–petroleum ether) in 2 h to yield a white solid **17** (0.28 g, 76%), m.p. 123–124°C; [Found: C, 70.51; H, 6.98; N, 3.85. $C_{21}H_{25}NO_4$ requires: C, 70.96; H, 7.09; N, 3.94%]; $[\alpha]_D^{24}$ − 97.0 (c=0.470, $CHCl_3$); ν_{max}($CHCl_3$) 3416, 1508, 1475, 1316, 1150 cm^{-1}; δ_H 7.57–7.21 (5 H, m, aromatic), 5.54 (1 H, s, PhC*H*), 4.34 (2 H, m), 3.95–3.42 (5 H, m), 3.55 (3 H, s, OMe), 2.78 (1 H, m), 2.44 (1 H, dt, J=4.3, 11.9 Hz), 1.64 (1 H, q, J=11.6 Hz); δ_C 139.8, 137.5, 129.0, 128.5, 128.3, 128.1, 127.1, 126.2, 106.4, 101.7, 76.6, 70.4, 69.1 (CH_2), 57.0, 56.8, 50.7 (CH_2), 33.5 (CH_2); *m/z* (EI) 355 (6 M^+), 340 (11, M^+-OCH_3).

4.1.10. Methyl 2,3-dideoxy-4,6-*O*-(phenylmethylene)-2-*N*-pyrrolidino-β-D-ribo-hexopyranoside (18). Compound **15** (0.61 g, 1.33 mmol) was desulfonated (eluent 60% EtOAc–petroleum ether) in 3 h to yield a pale brown solid **18** (0.18 g, 42%), m.p. 141–142°C; [Found: C, 67.47; H, 8.07; N, 4.26. $C_{18}H_{25}NO_4$ requires C, 67.68; H, 7.89; N, 4.38%]; $[\alpha]_D^{24}$ − 69.6 (c=0.376, $CHCl_3$); ν_{max}(Nujol) 3450, 1379, 1103 cm^{-1}; δ_H 7.52–7.27 (5 H, m, aromatic), 5.55 (1 H, s, PhC*H*), 4.45 (1 H, d, J=7.8 Hz, H-1), 4.33 (1 H, dd, J=4.9, 10.5 Hz), 3.78 (1 H, t, J=9.5 Hz), 3.67–3.40 (2 H, m), 3.55 (3 H, s, OMe), 2.79–2.56 (m, 5 H), 2.40 (1 H, m), 1.78 (5 H, m); δ_C 137.4, 128.9, 128.1, 126.0, 105.2, 101.5, 76.5, 69.8, 69.0 (CH_2), 61.9, 56.4, 51.1 (CH_2), 31.5 (CH_2), 23.1 (CH_2); *m/z* (EI) 319 (5 M^+), 304 (12 M^+-CH_3).

4.1.11. Methyl 2,3-dideoxy-2-*N*-morpholino-4,6-*O*-(phenylmethylene)-β-D-ribo-hexopyransoide (19). Compound **16** (0.27 g, 0.57 mmol) was desulfonated (eluent 65% EtOAc– petroleum ether) in 1 h to yield a pale brown solid **19** (0.09 g, 47%); m.p. 138–139°C; [Found: C, 64.59; H, 8.26; N, 3.71. $C_{18}H_{25}NO_5$ requires C, 64.46; H, 7.51; N, 4.18%]; $[\alpha]_D^{28.5}$ − 36.9 (c=0.188, $CHCl_3$); ν_{max}(Nujol) 3475, 1643, 1382, 1190, 1095 cm^{-1}; δ_H 7.52–7.27 (5 H, m, aromatic), 5.54 (1 H, s, PhC*H*), 4.48 (1 H, d, J=8.2 Hz, H-1), 4.32 (1 H, dd, J=4.8, 10.5 Hz) 3.82–3.61 (6 H, m), 3.56 (3 H, s, OMe), 3.38 (1 H, m), 2.87 (2 H, m), 2.65 (3 H, m), 2.26 (1 H, dt, J=4.3, 11.9 Hz), 1.70 (q, 1 H, J=11.5 Hz); δ_C 137.4, 129.1, 128.3, 126.2, 103.8, 101.6, 77.0, 70.2, 69.0 (CH_2), 66.9 (CH_2), 63.6, 56.5, 50.4 (CH_2), 30.2 (CH_2); *m/z* (EI) 335 (11 M^+), 320 (21 M^+-OCH_3).

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