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Baylis–Hillman Reaction: Convenient Ascending Syntheses and Biological Evaluation of Acyclic Deoxy Monosaccharides as Potential Antimycobacterial Agents†

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Abstract—A series of acyclic deoxy carbohydrate derivatives from easily available carbohydrate enals **1**, **2**, **3** or **5** were prepared involving the Baylis–Hillman reaction. These newly formed carbohydrate based Baylis–Hillman adducts and their amino derivatives were evaluated for their antimycobacterial activity against *Mycobacterium tuberculosis* $H_{37}R_v$. Among the compounds evaluated for their antimycobacterial activity, compound (**10**) showed the desired activity in the range of 3.125 μg/mL.

Introduction

With the resurgence of multidrug resistant (MDR) strains of *Mycobacterium tuberculosis,* tuberculosis has become directly responsible for more human deaths than any other single infectious agent.[1] An estimated one third of the world population currently is infected with the bacillus.[2] The mycobacterial cell wall[3] is the site of action of many of the first line antimycobacterial agents[4] and it contains numerous components that are presumed to be required for cell viability or survival in the host and are thus attractive drug targets.[5] Current frontline therapy consists of three drugs introduced in the 1950s: INH (Isonicotinic acid hydrazide), Rifampin and PZA (Pyrazinamide) for two months followed by four months of follow up therapy with INH and rifampin.[6] But the ineffectiveness of the present therapy is found to be responsible for both a very long duration of the therapy and the emergence of resistance to these drugs. Thus, the problem arising due to MDR-TB requires the development of new therapeutic agents that have unique mechanisms of action from presently used antitubercular drugs in order to treat drug resistant forms of the disease.[7] In our ongoing program on the search of new chemical entities based on easily available carbohydrates as antitubercular agents, our group is actively involved in the syntheses of acyclic, nitrogen containing deoxy sugar derivatives from α,β-unsaturated sugar aldehydes. We recently reported the syntheses[8] and antimycobacterial activity[9] of the acyclic amino alkanols from α,β-unsaturated sugar aldehydes via the Henry reaction. In continuation of this endeavour, we became interested in syntheses of acyclic deoxy sugar derivatives involving the Baylis–Hillman reaction between α,β-unsaturated sugar aldehydes of the type **1** and active olefins, namely methyl vinyl ketone (MVK) and acrylonitrile, which would generate new structural features in acyclic monosaccharides. The adducts derived from this reaction could be then evaluated for their antimycobacterial activity. In a previous paper,[10] we have described the subtleties involved in a Baylis–Hillman reaction of α,β-unsaturated sugar aldehydes with methyl vinyl ketone in the presence of Me_2S–$TiCl_4$. In this communication, we wish to report the antimycobacterial activity of compounds and their amino derivatives obtained via the Baylis–Hillman reaction of α,β-unsaturated sugar aldehydes with methyl vinyl ketone (MVK) and acrylonitrile.

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Chemistry

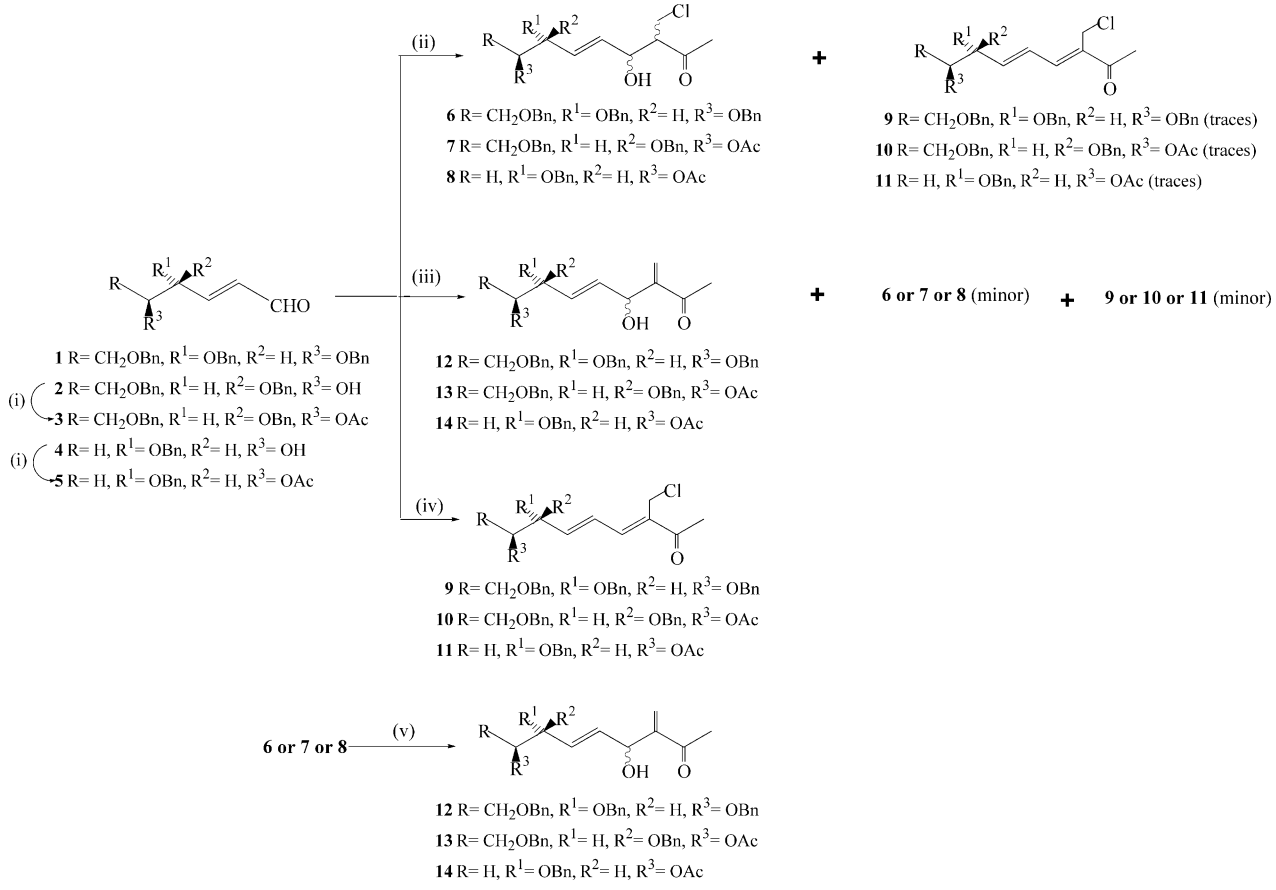
The syntheses were initiated with **1**,[10] 4,5,6-tri-*O*-benzyl-D-*erythro*-*aldehydo*-hex-2-enose, **3**,[11] 5-*O*-acetyl-4,6-di-*O*-benzyl-D-*threo*-*aldehydo*-hex-2-enose and **5,** 5-*O*-acetyl-4-*O*-benzyl-D-*glycero*-*aldehydo*-pent-2-enose. Treatment of aldehydes **1**, **3** and **5** with methyl vinyl ketone in presence of Me_2S–$TiCl_4$ led to the formation of adducts **6–14** depending on the reaction time as depicted in Scheme 1. Adducts **12–14** could be obtained when the reaction was run for 50 min–1 h or could also be obtained by treatment of adducts **6–8** with DBU in toluene. However, adducts **9–11** were obtained exclusively when the same reaction was continued for 6–9 h. Details of the course of the reaction and a plausible mechanism have been reported in the previous paper.[10]

Amino derivatives namely **15a–c**, **16a–e** and **17a–e** were obtained by nucleophilic substitution of Cl^- in compounds **9–11** (Scheme 2). During the reaction of diethylamine and *N*-benzyl-piperazine with compound **11**, acetyl group at C-8 was hydrolyzed and the compounds **17c** and **17e** were isolated with deprotected OH at C-8.

An attempt to react acrylonitrile with α,β-unsaturated sugar aldehydes in presence of Me_2S–$TiCl_4$ proved futile and the catalyst Me_2S–$TiCl_4$ was replaced with DABCO (1,4- diazabicyclo [2.2.2] octane). Reaction of **1** and **2**, 4,6-di-*O*-benzyl-D-*threo*-*aldehydo*-hex-2-enose with acrylonitrile in the presence of DABCO furnished the adducts **18** and **19**, respectively, as their diastereomeric mixtures. Michael addition of various amines was performed on the methylene double bond of the adducts **18** and **19** to furnish compounds **20a–b** and**21a–b** as their diastereomeric mixtures (Scheme 3). The IR spectra of the compounds **18–21** showed an absorption band in the range of 2227–2402 cm^{-1} characteristic of the nitrile group. The ^1H NMR, ^{13}C NMR and 2D NMR spectra were consistent with the assigned structures.

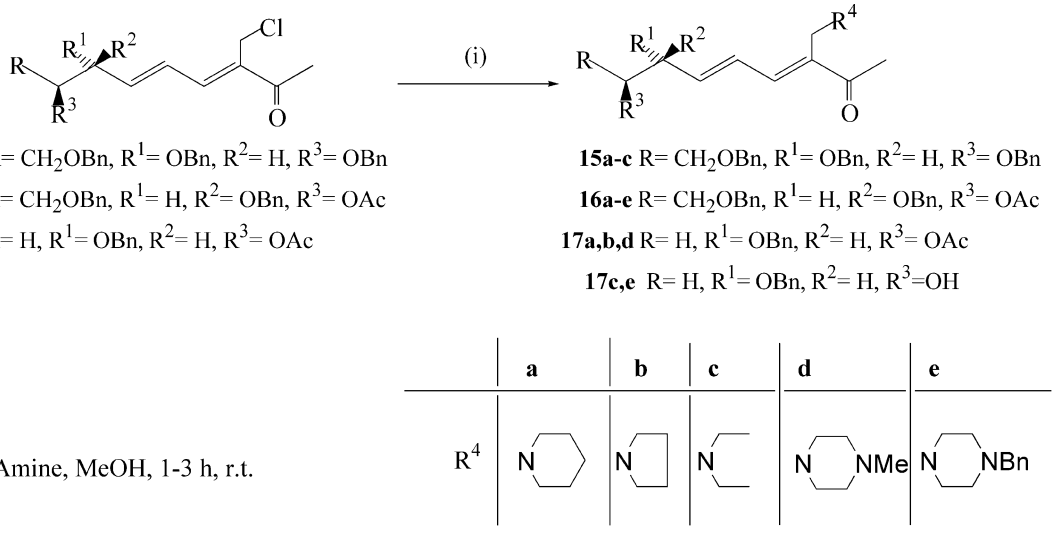
Results and Discussion

All the compounds were evaluated for their in vitro antimycobacterial activity in an Agar Dilution Assay system.[12] Ofloxacin was used as the standard drug (MIC = 1 μg/mL). The results of the antimycobacterial activity are summarized in Table 1. The results of the antimycobacterial assay clearly indicated that the conjugated derivative **10** containing chlorine derived from galactose having the *R*,*R* configuration at the chiral centers (C-7 and C-8) exhibited the maximum desired

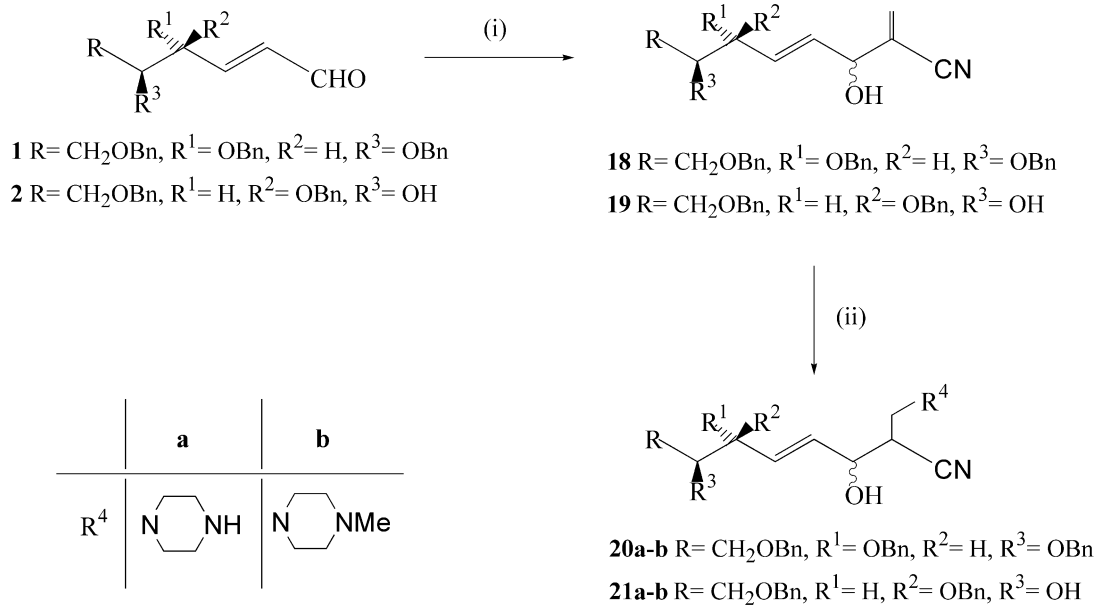


(i) Ac_2O, Pyr, 10 h, 0-4 ^0C; (ii) MVK, Me_2S-$TiCl_4$, CH_2Cl_2, 15 min., 0 ^0C; (iii) MVK, Me_2S-$TiCl_4$, CH_2Cl_2, 50 min.-1 h, 0 ^0C;
(iv) MVK, Me_2S-$TiCl_4$, CH_2Cl_2, 6 h-9 h, 0 ^0C; (v) DBU, Toluene, 40 min., r.t.

Scheme 1.



Scheme 2.



Scheme 3.

activity at 3.125 μg/mL. The analogous compound **9** obtained from glucose with the *S* configuration at C-7 and the *R* configuration at C-8 did not show any activity where as compound **11** carrying only one chiral center at C-7 with the *S* configuration obtained from arabinose showed activity at 25 μg/mL. This differential behaviour of the aforesaid compounds reveals the possible role(s) of either the configuration at the chiral centers or the bulky nature of the protecting group of the hydroxyl at C-8, which is benzyl ether in case of compound **9**, and acetyl group in case of compounds **10** and **11.** The role of protecting groups in carbohydrates for their antimycobacterial activity has also been emphasized by Reynolds' group in their recent publication.[13] Of the 12 compounds evaluated, compound **10** exhibited activity at 3.125 μg/mL, **20b** exhibited activity at 12.5 μg/mL, four compounds namely **11, 16b, 16d** and **21b** exhibited activity at 25 μg/mL and five compounds namely **16a, 16c, 17a, 18** and **19** exhibited activity at 50 μg/mL whereas compound **9** was completely inactive. Compound **10** was also found to be active in MABA (Microwell plate Alamar Blue Assay) at less than 25 μg/mL.

The high activity profile of compound **10** showed that extended conjugation in the molecule possibly mimics a substrate involved in the biosynthesis of mycobacterial cell wall components and thus, is recognized by an

Table 1. Results of in vitro antimycobacterial activity

Compd	Agar dilution method concentration in μg/mL				
	50	25	12.5	6.25	3.125
9	NA	NA	—	—	—
10	CI	CI	CI	CI	CI
11	CI	CI	—	—	—
16a	CI	NA	—	—	—
16b	CI	CI	—	—	—
16c	CI	NA	—	—	—
16d	CI	CI	—	—	—
17a	CI	NA	—	—	—
18	CI	NA	—	—	—
19	CI	NA	—	—	—
20b	CI	CI	CI	—	—
21b	CI	CI	NA	—	—

CI, complete inhibition; NA, not active; —not tested at particular concentration.

enzyme responsible for its assimilation in the mycobacterial cell wall thereby causing inhibition of biosynthesis. This compound was tested for its cytotoxicity and it was found non-cytotoxic. The compounds, namely **16a–d, 19** and **21b** that possessed the *R*,*R* configuration at the chiral centers showed activity which indicated the significant role of configuration of chiral centers in this type of molecules. Thus, the linear chain extended conjugated monosaccharides with defined chiral centers (*R*,*R*) could be exploited for development of new antimycobacterial drugs.

Conclusion

In conclusion, we have developed a convenient methodology for ascending syntheses of acyclic deoxy monosaccharides with various structural features as potential antimycobacterial agents from easily available α,β-unsaturated sugar aldehydes through Baylis–Hillman reaction. In this endeavour, the conjugated acyclic sugar derivative (**10**) with *R*,*R* configuration at the chiral centers was found to possess significant antimycobacterial activity at 3.125 μg/mL which could, therefore, be considered a potential molecule for further studies as an antimycobacterial agent. In vivo screening of this compound is in progress.

Experimental

All the reactions were monitored by thin-layer chromatography over silica gel coated TLC plates. The spots on TLC plates were visualized by warming the $CeSO_4$ (1% in 2 N H_2SO_4) sprayed plates in oven at 100 °C, or in iodine vapors. For column chromatography, silica gel (60–120 mesh) was used. IR spectra were recorded on Perkin-Elmer 881 and FTIR-8210 PC Shimadzu Spectrophotometers and the values are expressed in cm^{-1}. ^1H NMR, ^{13}C NMR, NOE spectra were recorded on Avance DPX 200 FT Bruker Robotics Spectrometer using TMS as an internal reference and $CDCl_3$ (77.0). FAB mass spectra were recorded on Jeol SX 102/DA 6000 mass spectrometer using Argon/Xenon (6 KV, 10 mA) as the FAB gas. Elemental analyses were carried out on Carlo-Erba-1108 instrument. Optical rotations were determined on Autopol III polarimeter using 1 dm cell at 28 °C in methanol as the solvent; concentrations mentioned are in g/100 mL.

General method for preparation of compounds 6–8 or 9–11

To the aldehyde (**1, 3** or **5**) (1.5 mmol) dissolved in dry CH_2Cl_2 (5 mL) was added MVK (3 mmol), Me_2S (0.15 mmol) and $TiCl_4$ (1.5 mmol) in succession at 0 °C. The reaction mixture was stirred at 0 °C for 15 min for obtaining compounds **6–8** or 6–9 h for obtaining compounds **9–11**. The reaction mixture was then quenched with sodium bicarbonate followed by filtration through Celite pad. The organic layer from the filtrate was separated and washed with brine solution and dried over Na_2SO_4. Evaporation of the solvent yielded crude reaction mixture which after chromatographic purification over silica gel yielded pure compound.

(3*Z*,5*E*)-7,8,9-Tri-*O*-benzyl-3-chloromethyl-1,3,4,5,6-pentadeoxy-D-*erythro*-non-3,5-diene-2-ulose (9). Oil (51%). Eluent for column chromatography: hexane/ethyl acetate = 9:1, v/v. R_f 0.62 (hexane/ethyl acetate = 4:1, v/v). $[\alpha]_D$ +11.3 (*c* 0.16, methanol). IR (neat, cm^{-1}) 1733 (C=O), 975 (C = C). ^1H NMR ($CDCl_3$, 200 MHz) δ 2.37 (s, 3H, H-1), 3.63 (dd_e, 2H, H-9a and H-9b), 3.77 (m, 1H, H-8), 4.24 (t, $J_{7,8} = J_{7,6} = 5.6$ Hz, 1H, H-7), 4.36 (s, 2H, H-1′), 4.41–4.75 (5×d, $J_{gem} = 11.8$ Hz, 6H, 3×CH_2Ph), 6.31 (dd, $J_{6,7} = 6.9$ Hz and $J_{6,5} = 15.1$ Hz, 1H, H-6), 6.72 (dd, $J_{5,4} = 11.3$ Hz and $J_{5,6} = 14.9$ Hz, 1H, H-5), 7.14 (d, $J_{4,5} = 11.2$ Hz, 1H, H-4), 7.25–7.31 (m, 15H, aromatic). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 25.48 (C-1), 35.41 (C-1′), 69.31 (C-9), 71.53, 72.96, 73.40 (3×CH_2Ph), 79.11, 80.07 (C-7 and C-8), 127.62, 127.66, 127.74, 127.81, 127.94, 128.26, 128.34, 128.39 (C-6 and aromatic), 135.92 (C-3), 137.82, 138.06, 138.23 (aromatic), 142.05, 143.49 (C-4 and C-5), 196.77 (C-2). FAB MS *m*/*z* 505 $[M]^+$. Elemental analysis calculated for $C_{31}H_{33}O_4Cl$ (505.05) C: 73.72%, H: 6.58%. Found C: 73.97%, H: 7.05%.

(3*Z*,5*E*)-8-*O*-Acetyl-7,9-di-*O*-benzyl-3-chloromethyl-1,3,4,5,6-pentadeoxy-D-*threo*-non-3,5-diene-2-ulose (10). Oil (70%). Eluent for column chromatography: hexane/ethyl acetate = 4:1, v/v. R_f 0.48 (hexane/ethyl acetate = 7:3, v/v). $[\alpha]_D$ +14.2 (*c* 0.23, methanol). IR (neat, cm^{-1}) 1733 (C=O), 974 (C = C), 765 (C–Cl). ^1H NMR ($CDCl_3$, 200 MHz) δ 2.08 (s, 3H, COCH_3), 2.38 (s, 3H, H-1), 3.58 (dd, $J_{9a,8} = 5.5$ Hz and $J_{9a,9b} = 10.2$ Hz, 1H, H-9a), 3.67 (dd, $J_{9b,8} = 4.7$ Hz and $J_{9b,9a} = 10.2$ Hz, 1H, H-9b), 4.29–4.79 (m, 5H, H-7 and 2×CH_2Ph), 4.37 (s, 2H, H-1′), 5.17 (q, $J_{8,9a} = J_{8,9b} = J_{8,7} = 5$ Hz, 1H, H-8), 6.16 (dd, $J_{6,7} = 6.2$ Hz and $J_{6,5} = 15$ Hz, 1H, H-6), 6.77 (dd, $J_{5,4} = 11.2$ Hz and $J_{5,6} = 14.7$ Hz, 1H, H-5), 7.12 (d, $J_{4,5} = 11.2$ Hz, 1H, H-4), 7.14–7.25 (m, 10H, aromatic). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 20.9 (COCH_3), 25.5 (C-1), 35.3 (C-1′), 68.1 (C-9), 73.2 (C-7), 71.7, 73.6 (2×CH_2Ph), 77.2 (C-8), 128.2, 128.3, 128.7, 128.8, 129.5 (C-6 and aromatic), 136.4 (C-3), 138.3, 139.7 (aromatic), 141.2, 141.03 (C-4 and C-5), 170.3 (COCH_3), 196.6 (C-2). FAB MS *m*/*z* 458 $[M+1]^+$, 422 $[M-Cl]^+$, 349 $[M-BnOH]^+$. Elemental analysis calculated for

$C_{26}H_{29}O_5Cl$ (456.99) C: 68.34%, H: 6.40%. Found C: 68.18%, H: 6.61%.

(3*Z*,5*E*)-8-*O*-Acetyl-7-*O*-benzyl-3-chloromethyl-1,3,4,5,6-pentadeoxy-D-glycero-octert-3,5-diene-2-ulose (11). Oil (51.7%). Eluent for column chromatography: hexane/ethyl acetate = 17:3, v/v. R_f 0.5 (hexane/ethyl acetate = 7:3, v/v). $[\alpha]_D$ +20.4 (*c* 0.14, methanol). IR (neat, cm^{-1}) 1712 (C=O), 879 (C = C), 756 (C–Cl). ^1H NMR ($CDCl_3$, 200 MHz) 2.07 (s, 3H, $COCH_3$), 2.40 (s, 3H, H-1), 4.17–4.26 (m_e, 3H, H-7, H-8a and H-8b), 4.30 (s, 2H, H-1′), 4.52 (d, J_{gem} = 12 Hz, 1H, CH_2Ph), 4.68 (d, J_{gem} = 12 Hz, 1H, CH_2Ph), 6.21 (dd, $J_{6,7}$ = 5.9 Hz and $J_{6,5}$ = 15.1 Hz, 1H, H-6), 6.80 (dd, $J_{5,4}$ = 11.3 Hz and $J_{5,6}$ = 15.2 Hz, 1H, H-5), 7.18 (d, $J_{4,5}$ = 11.3 Hz, 1H, H-4), 7.25–7.37 (m, 5H, aromatic). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 20.76 ($COCH_3$), 25.51 (C-1), 35.30 (C-1′), 65.35 (C-8), 71.36 (CH_2Ph), 76.50 (C-7), 127.82, 127.93, 128.48 (C-6 and aromatic), 136.73, 137.48 (C-3 and aromatic), 141.23, 141.38 (C-4 and C-5), 170.64 ($COCH_3$), 196.60 (C-2). FAB MS *m*/*z* 337 $[M]^+$, 301 $[M-Cl]^+$. Elemental analysis calculated for $C_{18}H_{21}O_4Cl$ (336.82) C: 64.19%, H: 6.29%. Found C: 63.61%, H: 6.45%.

General method for preparation of compounds 12–14

To the aldehyde (**1**, **3** or **5**) (1.5 mmol) dissolved in dry CH_2Cl_2 (5 mL) was added MVK (3 mmol), Me_2S (0.15 mmol) and $TiCl_4$ (1.5 mmol) in succession at 0 °C. The reaction mixture was stirred for 15–20 min and was quenched with sodium bicarbonate followed by filtration through Celite pad. The filtrate containing the organic layer was separated, washed with brine solution, and dried over sodium sulphate. The crude product containing **6**, **7** or **8** obtained on evaporation of the solvent was dissolved in dry toluene (5 mL) and DBU (2 mmol) was added to the solution and stirred for 40 min. On completion of the reaction, the organic layer was washed with 1 N HCl, $NaHCO_3$ and brine in succession and dried over Na_2SO_4. Evaporation of the solvent yielded crude **12**–**14**, which was further column chromatographed over silica gel to yield pure compound.

Mixture of (5*E*)-7,8,9-tri-*O*-benzyl-1,3,5,6-tetradeoxy-3-methylene-D-(*arabino* and *ribo*)-non-5-en-2-ulose (12). Oil (51%). Eluent for column chromatography: hexane/ethyl acetate = 41:9, v/v. R_f 0.52 (hexane/ethyl acetate = 7:3, v/v). IR (neat, cm^{-1}) 3420 (OH), 1632 (C=O), 972 (C = C). ^1H NMR ($CDCl_3$, 200 MHz) δ 2.31(s, 3H, H-1), 3.60–3.72 (m_e, 3H, H-8, H-9a and H-9b), 4.02 (t, $J_{7,8} = J_{7,6}$ = 6.3 Hz, 1H, H-7), 4.35 (d, J_{gem} = 11.8 Hz, 1H, CH_2Ph), 4.37 (d, J_{gem} = 11.8 Hz, 1H, CH_2Ph), 4.45–4.72 (m_e, 4H, CH_2Ph), 5.01 (brs, 1H, H-4), 5.76–5.80 (m_e, 2H, H-5 and H-6), 5.98 (d, $J_{1'a,1'b}$ = 1 Hz, 1H, H_A-1′a), 6.05 (s, 1H, H_A-1′b), 6.06 (s, 1H, H_B-1′a), 7.26–7.30 (m, 15H, aromatic). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 26.26 (C-1), 69.85 (C-9), 70.57 (CH_2Ph), 70.78, 71.0 (C-4), 72.76, 73.24 (CH_2Ph), 79.31, 80.22, 80.28 (C-7 and C-8), 126.17, 126.26 (C-1′), 127.35, 127.44, 127.56, 127.60, 127.77, 128.12, 128.19, 128.23 (C-6 and aromatic), 134.87 (C-5), 138.28, 138.38, 138.63 (aromatic), 148.92, 148.97 (C-3), 199.97, 200.12 (C-2). FAB MS *m*/*z* 469 $[M-OH]^+$. Elemental analysis calculated for $C_{31}H_{34}O_5$ (486.61) C: 76.52%, H: 7.04%. Found C: 76.23%, H: 7.60%.

Mixture of (5*E*)-8-*O*-Acetyl-7,9-di-*O*-benzyl-1,3,5,6-tetradeoxy-3-methylene-D-(*lyxo* and *xylo*)-non-5-en-2-ulose (13). Oil (55%). Eluent for column chromatography: hexane/ethyl acetate = 3:1, v/v. R_f 0.38 (hexane/ethyl acetate = 7:3, v/v). IR (neat, cm^{-1}) 3422 (OH), 1733 (C=O), 983 (C = C). ^1H NMR ($CDCl_3$, 200 MHz) δ 2.07 (s, 3H, $COCH_3$), 2.34 (s, 3H, H-1), 3.52 (dd, $J_{9a,8}$ = 5.9 Hz and $J_{9a,9b}$ = 10.5 Hz, 1H, H_A-9a), 3.55 (dd, $J_{9a,8}$ = 5.7 Hz and $J_{9a,9b}$ = 10.5 Hz, 1H, H_B-9a), 3.63 (dd, $J_{9b,8}$ = 4.4 Hz and $J_{9b,9a}$ = 10.5 Hz, 1H, H-9b), 4.11 (t, $J_{7,8} = J_{7,6}$ = 5.2 Hz, 1H, H-7), 4.33–4.63 (m_e, 4H, 2×CH_2Ph), 4.99 (brs, 1H, H-4), 5.11 (q, $J_{8,9a} = J_{8,9b} = J_{8,7}$ = 5.2 Hz, 1H, H-8), 5.60 (dd, $J_{5,4}$ = 5.6 Hz and $J_{5,6}$ = 15.6 Hz, 1H, H_A-5), 5.61 (dd, $J_{5,4}$ = 5.7 Hz and $J_{5,6}$ = 15.6 Hz, 1H, H_B-5), 5.85 (dd, $J_{6,7}$ = 5 Hz and $J_{6,5}$ = 15.6 Hz, 1H, H_A-6), 5.88 (dd, $J_{6,7}$ = 4.7 Hz and $J_{6,5}$ = 15.6 Hz, 1H, H_B-6), 5.99 (d, $J_{1'a,1'b}$ = 0.8 Hz, 1H, H-1′a), 6.10 (s, 1H, H-1′b), 7.19–7.29 (m, 10H, aromatic). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 21.5 ($COCH_3$), 26.7 (C-1), 68.9 (C-9), 71.3 (C-4), 71.4, 73.6 (2×CH_2Ph), 74.3, 77.9 (C-7 and C-8), 126.7 (C-1′), 128.0, 128.1, 128.8 (C-6 and aromatic), 135.5 (C-5), 138.4, 138.5 (aromatic), 149.3 (C-3), 170.9 ($COCH_3$), 200.4 (C-2). FAB MS *m*/*z* 421 $[M-OH]^+$. Elemental analysis calculated for $C_{26}H_{30}O_6$ (438.53) C: 71.21%, H: 6.90%. Found C: 70.90%, H: 6.54%.

Mixture of (5*E*)-8-*O*-acetyl-7-*O*-benzyl-1,3,5,6-tetradeoxy-3-methylene-D-(*erythro* and *threo*)-oct-5-en-2-ulose (14). Pale yellow oil (47%). Eluent for column chromatography: hexane/ethyl acetate = 3:1, v/v. R_f 0.49 (hexane/ethyl acetate = 1:1, v/v). IR (neat, cm^{-1}) 3450 (OH), 1739 (ester, C=O), 1674 (C=O), 975 (C = C). ^1H NMR ($CDCl_3$, 200 MHz) δ 2.05 (s, 3H, $COCH_3$), 2.37 (s, 3H, H-1), 4.06–4.16 (m_e, 3H, H-7, H-8a and H-8b), 4.42 (d, J_{gem} = 12.1 Hz, 1H, CH_2Ph_A), 4.43 (d, J_{gem} = 12.1 Hz, 1H, CH_2Ph_B), 4.62 (d, J_{gem} = 12.1 Hz, 1H, CH_2Ph_A), 4.64 (d, J_{gem} = 12.1 Hz, 1H, CH_2Ph_B), 5.03 (t, $J_{4,5} = J_{4,OH}$ = 4.3 Hz, 1H, H-4), 5.69 (dd, $J_{5,4}$ = 6.1 Hz and $J_{5,6}$ = 15.5 Hz, 1H, H-5), 5.91 (dd, $J_{6,7}$ = 5.2 Hz and $J_{6,5}$ = 15.8 Hz, 1H, H-6), 6.03 (s, 1H, H-1′a), 6.15 (s, 1H, H-1′b), 7.32–7.34 (m_e, 5H, Ph). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 20.83 ($COCH_3$), 26.33 (C-1), 66.15 (C-8), 70.57 (CH_2Ph), 70.74, 70.89, 76.68 (C-4 and C-7), 126.43 (C-1′), 127.63, 127.71, 127.79, 128.35 (C-6 and aromatic), 135.10 (C-5), 138.06 (aromatic), 148.87 (C-3), 170.78 ($COCH_3$), 200.04 (C-2). FAB MS *m*/*z* 319 $[M]^+$, 301 $[M-H_2O]^+$, 242 $[M-(OAc+H_2O)]^+$. Elemental analysis calculated for $C_{18}H_{23}O_5.\frac{1}{2}H_2O$ (328.39) C: 65.84%, H: 7.37%. Found C: 65.70%, H: 6.84%.

General method for preparation of compounds 15–17

To a stirred solution of the Baylis–Hillman adduct **9**–**11** (1 mmol) in dry methanol (10 mL), was added the required amine (2 mmol). The reaction was allowed to continue for 1–3 h at room temperature. On completion of reaction, excess of methanol was evaporated in vacuo

and the residue was chromatographed over basic alumina to yield amino alkanols **15a–c**, **16a–e** and **17a–e.**

(3*E*,5*E*)-7,8,9-Tri-*O*-benzyl-1,3,4,5,6-pentadeoxy-3-piperidinomethyl-D-*erythro*-non-3,5-diene-2-ulose(15a). Yellow oil (21.3%). Eluent for column chromatography/chloroform/methanol = 997:3, v/v. R_f 0.58 (on basic alumina TLC plate, chloroform/methanol = 39:1, v/v; iodine vapors used as developing agent). $[\alpha]_D$ + 10.9 (*c* 0.11, methanol). IR (neat, cm^{-1}) 1664 (C=O), 1216 (*tert*-amine), 985 (C = C). ^1H NMR ($CDCl_3$, 200 MHz) δ 1.50 (m, 10H, H-1″, H-2″ and H-3″), 2.38 (s, 3H, H-1), 3.28 (s, 2H, H-1′), 3.63 (dd_e, 2H, H-9a and H-9b), 3.74 (m, 1H, H-8), 4.18 (dd, $J_{7,8}$ = 5.5 Hz and $J_{7,6}$ = 6.9 Hz, 1H, H-7), 4.39–4.69 (m, 6H, 3×CH_2Ph), 6.15 (dd, $J_{6,7}$ = 7.3 Hz and $J_{6,5}$ = 15.1 Hz, 1H, H-6), 6.83 (dd, $J_{5,4}$ = 11.3 Hz and $J_{5,6}$ = 14.7 Hz, 1H, H-5), 7.15 (d, $J_{4,5}$ = 11.3 Hz, 1H, H-4), 7.20–7.40 (m, 15H, aromatic). FAB MS *m*/*z* 554 $[M+1]^+$, 462 $[M-CH_2Ph]^+$, 446 $[M-OCH_2Ph]^+$. Elemental analysis calculated for $C_{36}H_{43}O_4N$ (553.75) C: 78.09%, H: 7.83%, N: 2.53%. Found C: 78.32%, H: 7.54%, N: 2.14%.

(3*E*,5*E*)-7,8,9-Tri-*O*-benzyl-1,3,4,5,6-pentadeoxy-3-pyrrolidinomethyl-D-*erythro*-non-3,5-diene-2-ulose (15b). Yellow oil (22%). Eluent for column chromatography: chloroform/methanol = 997:3, v/v. R_f 0.58 (on basic alumina TLC plate, chloroform/methanol = 39:1, v/v; iodine vapors used as developing agent). $[\alpha]_D$ +17.2 (*c* 0.03, methanol). IR (neat, cm^{-1}) 1663 (C=O), 1216 (*tert*-amine), 758 (aromatic). ^1H NMR ($CDCl_3$, 200 MHz) δ 1.73 (brs, 8H, H-1″ and H-2″), 2.39 (s, 3H, H-1), 3.49 (s, 2H, H-1′), 3.64 (dd_e, 2H, H-9a and H-9b), 3.75 (m, 1H, H-8), 4.18 (dd, $J_{7,8}$ = 5.5 Hz and $J_{7,6}$ = 6.9 Hz, 1H, H-7), 4.45–4.70 (m, 6H, 3×CH_2Ph), 6.15 (dd, $J_{6,7}$ = 7.3 Hz and $J_{6,5}$ = 15.1 Hz, 1H, H-6), 6.85 (dd, $J_{5,4}$ = 11.3 Hz and $J_{5,6}$ = 14.7 Hz, 1H, H-5), 7.16 (d, $J_{4,5}$ = 11.3 Hz, 1H, H-4), 7.18–7.40 (m, 15H, aromatic). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 23.41 (C-2″), 26.09 (C-1), 48.96 (C-1′), 53.78 (C-1″), 69.63 (C-9), 71.18, 72.96, 73.37 (3×*C*H_2Ph), 79.27, 80.20 (C-7 and C-8), 127.59, 127.91, 128.32, 128.87, 138.17 (C-3, C-6 and aromatic), 140.8, 141.1 (C-4 and C-5), 199.8 (C-2). FAB MS *m*/*z* 540 $[M+1]^+$, 448 $[M-CH_2Ph]^+$. Elemental analysis calculated for $C_{35}H_{41}O_4N\,\frac{1}{2}H_2O$ (548.73) C: 76.61%, H: 7.71%, N: 2.55%. Found C: 76.47%, H: 6.88%, N: 1.51%.

(3*E*,5*E*)-7,8,9-Tri-*O*-benzyl-1,3,4,5,6-pentadeoxy-3-diethylaminomethyl-D-*erythro*-non-3,5-diene-2-ulose (15c). Yellow oil (28.5%). Eluent for column chromatography: chloroform/methanol = 997:3, v/v. R_f 0.58 (on basic alumina TLC plate, chloroform/methanol = 39:1, v/v; iodine vapors used as developing agent). IR (neat, cm^{-1}) 1663 (C=O), 1216 (*tert*-amine), 758 (aromatic). ^1H NMR ($CDCl_3$, 200 MHz) δ 0.99 (t, $J_{2'',1''}$ = 7 Hz, 6H, H-2″), 2.38 (s, 3H, H-1), 2.46 (q, $J_{1'',2''}$ = 7 Hz, 4H, H-1″), 3.36 (s, 2H, H-1′), 3.68 (dd_e, 2H, H-9a and H-9b), 3.73 (m, 1H, H-8), 4.17 (dd, $J_{7,8}$ = 5.4 Hz and $J_{7,6}$ = 6.9 Hz, 1H, H-7), 4.38–4.70 (m, 6H, 3×CH_2Ph), 6.13 (dd, $J_{6,7}$ = 7.3 Hz and $J_{6,5}$ = 15.1 Hz, 1H, H-6), 6.85 (dd, $J_{5,4}$ = 11.3 Hz and $J_{5,6}$ = 15.1 Hz, 1H, H-5), 7.11 (d, $J_{4,5}$ = 11.3 Hz, 1H, H-4), 7.20–7.40 (m, 15H, aromatic). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 11.46 (C-2″), 26.41 (C-1), 46.45 (C-1″), 47.89 (C-1′), 69.71 (C-9), 71.04, 72.94, 73.35 (3×*C*H_2Ph), 79.33, 80.22 (C-7 and C-8), 127.54, 127.64, 127.87, 128.20, 128.29, 129.04 (C-6 and aromatic), 138.12, 138.19, 138.41 (C-3 and aromatic), 139.76, 139.90 (C-4 and C-5), 200.06 (C-2). FAB MS *m*/*z* 542 $[M+1]^+$, 450 $[M-CH_2Ph]^+$, 434 $[M-OCH_2Ph]^+$. Elemental analysis calculated for $C_{35}H_{43}O_4N$ (541.74) C: 77.60%, H: 8.00%, N: 2.59%. Found C: 77.82%, H: 7.58%, N: 2.39%.

(3*E*,5*E*)-8-*O*-Acetyl-7,9,di-*O*-benzyl-1,3,4,5,6-pentadeoxy-3-piperidinomethyl-D-*threo*-non-3,5-diene-2-ulose (16a). Yellow oil (52.8%). Eluent for column chromatography: chloroform/methanol = 997:3, v/v. R_f 0.55 (on basic alumina TLC plate, chloroform/methanol = 39:1, v/v; iodine vapors used as developing agent). $[\alpha]_D$ +8.8 (*c* 0.11, methanol). IR (neat, cm^{-1}) 1664 (C=O), 1216 (*tert*-amine), 985 (C = C). ^1H NMR ($CDCl_3$, 200 MHz) δ 1.48 (m, 10H, H-1″, H-2″ and H-3″), 2.08 (s, 3H, COCH_3), 2.38 (s, 3H, H-1), 3.25 (s, 2H, H-1′), 3.57 (dd, $J_{9a,8}$ = 5.7 Hz and $J_{9a,9b}$ = 10.3 Hz, 1H, H-9a), 3.66 (dd, $J_{9b,8}$ = 4.4 Hz and $J_{9b,9a}$ = 10.4 Hz, 1H, H-9b), 4.25 (t, $J_{7,8} = J_{7,6}$ = 6.1 Hz, 1H, H-7), 4.46–4.62 (m_e, 4H, 2×CH_2Ph), 5.17 (m, 1H, H-8), 5.99 (dd, $J_{6,7}$ = 6.7 Hz and $J_{6,5}$ = 15.1 Hz, 1H, H-6), 6.86 (dd, $J_{5,4}$ = 11.1 Hz and $J_{5,6}$ = 14.4 Hz, 1H, H-5), 7.10 (d, $J_{4,5}$ = 11.0 Hz, 1H, H-4), 7.19–7.31 (m, 10H, aromatic). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 21.02 (CO*C*H_3), 24.23 (C-3″), 25.98 (C-2″), 26.34 (C-1), 53.19 (C-1′), 54.31 (C-1″), 68.26 (C-9), 71.25, 73.23 (2×*C*H_2Ph), 73.55, 77.36 (C-7 and C-8), 127.73, 128.16, 128.35, 128.98, 129.24, 137.47 (C-3, C-6 and aromatic), 137.78, 139.36 (C-4 and C-5), 170.33 (*C*OCH$_3$), 199.88 (C-2). FAB MS *m*/*z* 506 $[M+1]^+$. Elemental analysis calculated for $C_{31}H_{39}O_5N$ (505.66) C: 73.64%, H: 7.77%, N: 2.77%. Found C: 73.60%, H: 7.60%, N: 2.24%.

(3*E*,5*E*)-8-*O*-Acetyl-7,9,di-*O*-benzyl-1,3,4,5,6-pentadeoxy-3-pyrrolidinomethyl-D-*threo*-non-3,5-diene-2-ulose (16b). Yellow oil (60%). Eluent for column chromatography: chloroform/methanol = 997:3, v/v. R_f 0.55 (on basic alumina TLC plate, chloroform/methanol = 39:1, v/v; iodine vapors used as developing agent). $[\alpha]_D$ +5.3 (*c* 0.13, methanol). IR (neat, cm^{-1}) 1737 (C=O), 1217 (*tert*-amine), 981 (C = C). ^1H NMR ($CDCl_3$, 200 MHz) δ 1.69 (brs, 8H, H-1″ and H-2″), 2.08 (s, 3H, COCH_3), 2.38 (s, 3H, H-1), 3.43 (s, 2H, H-1′), 3.57 (dd, $J_{9a,8}$ = 5.5 Hz and $J_{9a,9b}$ = 12.7 Hz, 1H, H-9a), 3.67 (dd, $J_{9b,8}$ = 4.6 Hz and $J_{9b,9a}$ = 12.7 Hz, 1H, H-9b), 42.6 (t, $J_{7,8} = J_{7,6}$ = 5.5 Hz, 1H, H-7), 4.39–4.68 (m, 4H, 2xCH_2Ph), 5.17 (q, $J_{8,9a} = J_{8,9b} = J_{8,7}$ = 5.6 Hz, 1H, H-8), 6.16 (dd, $J_{6,7}$ = 6.2 Hz and $J_{6,5}$ = 15.1 Hz, 1H, H-6), 6.77 (dd, $J_{5,4}$ = 11.2 Hz and $J_{5,6}$ = 14.7 Hz, 1H, H-5), 7.08 (d, $J_{4,5}$ = 11.2 Hz, 1H, H-4), 7.26–7.40 (m, 10H, aromatic). ^{13}C NMR ($CDCl_3$, 50 MHz) 21.01 (CO*C*H_3), 23.47 (C-2″), 26.20 (C-1), 49.37 (C-1′), 53.89 (C-1″), 68.23 (C-9), 71.29, 73.23 (2×*C*H_2Ph), 73.55, 77.34 (C-7 and C-8), 127.76, 128.34, 138.35, 129.10, 137.88, 137.89 (C-3, C-6 and aromatic), 137.87, 139.25 (C-4 and C-5), 170.3 (*C*OCH$_3$), 196.2 (C-2). FAB MS *m*/*z* 492 $[M+1]^+$; 432 $[M-OAc]^+$. Elemental analysis calculated for $C_{30}H_{37}O_5N$ (491.63) C: 73.29%, H: 7.59%, N: 2.85%. Found C: 73.49%, H: 8.16%, N: 2.67%.

(3*E*,5*E*)-8-*O*-Acetyl-7,9,di-*O*-benzyl-1,3,4,5,6-pentadeoxy-3-diethylaminomethyl-D-*threo*-non-3,5-diene-2-ulose (16c). Yellow oil (65%). Eluent for column chromatography: chloroform/methanol = 997:3, v/v. R_f 0.58 (on basic alumina TLC plate, chloroform/methanol = 39:1, v/v; iodine vapors used as developing agent). $[\alpha]_D$ +2 (*c* 0.15, methanol). IR (neat, cm^{-1}) 1663 (C=O), 1216 (*tert*-amine), 756 (aromatic). ^1H NMR ($CDCl_3$, 200 MHz) δ 0.99 (t, $J_{2'',1''} = 7$ Hz, 6H, H-2″), 2.08 (s, 3H, $COCH_3$), 2.38 (s, 3H, H-1), 2.45 (q, $J_{1'',2''} = 7.1$ Hz, 4H, H-1″), 3.35 (s, 2H, H-1′), 3.57 (dd, $J_{9a,8} = 5.6$ Hz and $J_{9a,9b} = 12.7$ Hz, 1H, H-9a), 3.67 (dd, $J_{9b,8} = 4.6$ Hz and $J_{9b,9a} = 12.7$ Hz, 1H, H-9b), 4.24 (t, $J_{7,8} = J_{7,6} = 6.2$ Hz, 1H, H-7), 4.38–4.69 (m, 4H, 2×CH_2Ph), 5.17 (q, $J_{8,9a} = J_{8,9b} = J_{8,7} = 5.6$ Hz, 1H, H-8), 5.99 (dd, $J_{6,7} = 6.8$ Hz and $J_{6,5} = 15.1$ Hz, 1H, H-6), 6.88 (dd, $J_{5,4} = 11.2$ Hz and $J_{5,6} = 14.7$ Hz, 1H, H-5), 7.06 (d, $J_{4,5} = 11.2$ Hz, 1H, H-4), 7.20–7.40 (m, 10H, aromatic). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 11.52 (C-2″), 21.02 ($COCH_3$), 26.49 (C-1), 46.46 (C-1″), 48.02 (C-1′), 68.29 (C-9), 71.24, 73.24 (2×CH_2Ph), 73.59, 77.43 (C-7 and C-8), 127.64, 127.75, 128.35, 129.23 (C-6 and aromatic), 137.77, 138.71 (C-3 and aromatic), 137.63, 138.98 (C-4 and C-5), 170.35 ($COCH_3$), 200.12 (C-2). FAB MS *m*/*z* 494 $[M+1]^+$, 386 $[M-OBn]^+$. Elemental analysis calculated for $C_{30}H_{39}O_5N$ (493.65) C: 72.99%, H: 7.96%, N: 2.84%. Found C: 73.25%, H: 8.35%, N: 2.75%.

(3*E*,5*E*)-8-*O*-Acetyl-7,9,di-*O*-benzyl-1,3,4,5,6-pentadeoxy-3-(*N*-methyl) piperazinomethyl-D-*threo*-non-3,5-diene-2-ulose (16d). Yellow oil (55%). Eluent for column chromatography: chloroform/methanol = 199:1, v/v. R_f 0.55 (on basic alumina TLC plate, chloroform/methanol = 39:1, v/v; iodine vapors used as developing agent). $[\alpha]_D$ +4.5 (*c* 0.16, methanol). IR (neat, cm^{-1}) 1735 (C=O), 1217 (*tert*-amine), 983 (C=C). ^1H NMR ($CDCl_3$, 200 MHz) δ 2.08 (s, 3H, $COCH_3$), 2.24 (s, 3H, NCH_3), 2.37 (s, 3H, H-1), 2.37–2.47 (m, 8H, H-1″ and H-2″), 3.32 (s, 2H, H-1′), 3.56 (dd, $J_{9a,8} = 5.6$ Hz and $J_{9a,9b} = 12.7$ Hz, 1H, H-9a), 3.65 (dd, $J_{9b,8} = 4.7$ Hz and $J_{9b,9a} = 12.4$ Hz, 1H, H-9b), 4.25 (t, $J_{7,6} = J_{7,8} = 5.7$ Hz, 1H, H-7), 4.39–4.62 (m, 4H, 2×CH_2Ph), 5.19 (q, $J_{8,9a} = J_{8,9b} = J_{8,7} = 5$ Hz, 1H, H-8), 6.01 (dd, $J_{6,7} = 6.6$ Hz, $J_{6,5} = 15.1$ Hz, 1H, H-6), 6.83 (dd, $J_{5,4} = 11.3$ Hz and $J_{5,6} = 14.8$ Hz, 1H, H-5), 7.11 (d, $J_{4,5} = 11.3$ Hz, 1H, H-4), 7.24–7.38 (m, 10H, aromatic). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 21.04 ($COCH_3$), 26.28 (C-1), 45.94 (NCH_3), 52.26 (C-1′), 52.78, 55.14 (C-1″ and C-2″), 68.28 (C-9), 71.39, 73.29 (2×CH_2Ph), 73.57, 77.42 (C-7 and C-8), 127.66, 127.75, 127.81, 128.22, 128.39, 128.98 (C-6 and aromatic), 137.07, 137.76 (C-3 and aromatic), 138.27, 139.70 (C-4 and C-5), 170.31 ($COCH_3$), 199.60 (C-2). FAB MS *m*/*z* 521 $[M+1]^+$. Elemental analysis calculated for $C_{31}H_{40}O_5N_2$ $3H_2O$ (574.73) C: 64.79%, H: 8.07%, N: 4.87%. Found C: 64.97%, H: 7.51%, N: 4.84%.

(3*E*,5*E*)--8-*O*-Acetyl-7,9-di-*O*-benzyl-1,3,4,5,6-pentadeoxy-3-(*N*-benzyl) piperazinomethyl-D-*threo*-non-3,5-diene-2-ulose (16e). Yellow oil (51%). Eluent for column chromatography: chloroform. R_f 0.54 (on basic alumina TLC plate; hexane/ethyl acetate = 7:3, v/v; iodine vapors used as developing agent). $[\alpha]_D$ +9.1 (*c* 0.06, methanol). IR (neat, cm^{-1}) 1737 (ester, C=O), 1644 (C=O), 1216 (*tert*-amine), 759 (aromatic). ^1H NMR ($CDCl_3$, 200 MHz) δ 2.07 (s, 3H, $COCH_3$), 2.37 (s, 3H, H-1), 2.41 (brs, 8H, H-1″ and H-2″), 3.31 (s, 2H, H-1′), 3.46 (s, 2H, NCH_2Ph), 3.56 (dd, $J_{9a,8} = 5.4$ Hz and $J_{9a,9b} = 10.5$ Hz, 1H, H-9a), 3.65 (dd, $J_{9b,8} = 4.5$ Hz and $J_{9b,9a} = 10.4$ Hz, 1H, H-9b), 4.24 (t, $J_{7,8} = J_{7,6} = 6.2$ Hz, 1H, H-7), 4.41 (d, $J_{gem} = 12$ Hz, 1H, CH_2Ph), 4.43 (d, $J_{gem} = 12$ Hz, 1H, CH_2Ph), 4.51 (d, $J_{gem} = 12$ Hz, 1H, CH_2Ph), 4.64 (d, $J_{gem} = 12$ Hz, 1H, CH_2Ph), 5.16 (q, $J_{8,9a} = J_{8,9b} = J_{8,7} = 5.1$ Hz, 1H, H-8), 6.00 (dd, $J_{6,7} = 6.6$ Hz and $J_{6,5} = 15$ Hz, 1H, H-6), 6.82 (dd, $J_{5,4} = 11.3$ Hz and $J_{5,6} = 15.1$ Hz, 1H, H-5), 7.10 (d, $J_{4,5} = 11.1$ Hz, 1H, H-4), 7.26–7.36 (m, 10H, aromatic). ^{13}C NMR ($CDCl_3$, 50 MHz) 21.05 ($COCH_3$), 26.30 (C-1), 52.31 (C-1′), 52.86, 53.02 (C-1″ and C-2″), 62.87 (NCH_2Ph), 68.26 (C-9), 71.38, 73.28 (CH_2Ph), 73.55, 77.40 (C-7 and C-8), 127.01, 127.67, 127.75, 127.80, 128.16, 128.39, 128.98, 129.15 (C-6 and aromatic), 136.96, 137.74, 138.07 (C-3 and aromatic), 138.28, 139.74 (C-4 and C-5), 170.34 ($COCH_3$), 199.61 (C-2). FAB MS *m*/*z* 598 $[M+2]^+$, 489 $[M-OCH_2Ph]^+$. Elemental analysis calculated for $C_{37}H_{44}O_5N_2$ (596.77) C: 74.47%, H: 7.48%, N: 4.72%. Found C: 75.32%, H: 7.61%, N: 4.43%.

(3*E*,5*E*)-8-*O*-Acetyl-7-*O*-benzyl-1,3,4,5,6-pentadeoxy-3-piperidinomethyl-D-*glycero*-oct-3,5-diene-2-ulose (17a). Yellow oil (45.0%). Eluent for column chromatography: chloroform/methanol = 199:1, v/v. R_f 0.58 (on basic alumina TLC plate, chloroform/methanol = 39:1, v/v; iodine vapors used as developing agent). $[\alpha]_D$ +16.1 (*c* 0.12, methanol). IR (neat, cm^{-1}) 1664 (C=O), 1216 (*tert*-amine), 983 (C=C). ^1H NMR ($CDCl_3$, 200 MHz) δ 1.51 (m, 10H, H-1″, H-2″ and H-3″), 2.06 (s, 3H,$COCH_3$), 2.39 (s, 3H, H-1), 3.29 (s, 2H, H-1′), 4.12–4.22 (m, 3H, H-7, H-8a and H-8b), 4.49 (d, $J_{gem} = 12.1$ Hz, 1H, CH_2Ph), 4.67 (d, $J_{gem} = 12.1$ Hz, 1H, CH_2Ph), 6.03 (dd, $J_{6,7} = 6.2$ Hz and $J_{6,5} = 15.1$ Hz, 1H, H-6), 6.90 (dd, $J_{5,4} = 11.3$ Hz and $J_{5,6} = 15$ Hz, 1H, H-5), 7.14 (d, $J_{4,5} = 11.2$ Hz, 1H, H-4), 7.26–7.44 (m, 5H, aromatic). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 20.80 ($COCH_3$), 24.21 (C-3″), 25.92 (C-2″), 26.32 (C-1), 53.15 (C-1′), 54.30 (C-1″), 65.76 (C-8), 70.94 (CH_2Ph), 76.68 (C-7), 127.70, 127.80, 128.42, 129.37 (C-6 and aromatic), 137.60, 137.82 (C-3 and aromatic), 138.16, 139.36 (C-4 and C-5), 170.69 ($COCH_3$), 199.81 (C-2). FAB MS *m*/*z* 386 $[M+1]^+$, 326 $[M-OAc]^+$, 278 $[M-OCH_2Ph]^+$. Elemental analysis calculated for $C_{23}H_{31}O_4N$ $1/2H_2O$ (394.51) C: 70.02%, H: 8.17%, N: 3.55%. Found C: 69.27%, H: 7.80%, N: 2.41%.

(3*E*,5*E*)-8-*O*-Acetyl-7-*O*-benzyl-1,3,4,5,6-pentadeoxy-3-pyrrolidinomethyl-D-*glycero*-oct-3,5-diene-2-ulose (17b). Yellow oil (57.6%). Eluent for column chromatography: chloroform/methanol = 999:1, v/v. R_f 0.38 (on basic alumina TLC plate; hexane/ethyl acetate = 7:3, v/v; iodine vapors used as developing agent). $[\alpha]_D$ +21.1 (*c* 0.1, methanol). IR (neat, cm^{-1}) 1742 (C=O), 1232 (*tert*-amine), 981 (C=C). ^1H NMR ($CDCl_3$, 200 MHz) δ 1.71 (m, 8H, H-1″ and H-2″), 2.07 (s, 3H, $COCH_3$), 2.40 (s, 3H, H-1), 3.48 (s, 2H, H-1′), 4.20 (m, 3H, H-7, H-8a and H-8b), 4.48 (d, $J_{gem} = 12.1$ Hz, 1H, CH_2Ph), 4.67 (d, $J_{gem} = 12.1$ Hz, 1H, CH_2Ph), 6.06 (dd, $J_{6,7} = 6.3$ Hz and $J_{6,5} = 15.1$ Hz, 1H, H-6), 6.92 (dd, $J_{5,4} = 11.3$ Hz

and $J_{5,6}=15.1$ Hz, 1H, H-5), 7.14 (d, $J_{4,5}=11.4$ Hz, 1H, H-4), 7.25–7.34 (m, 5H, aromatic). ^{13}C NMR ($CDCl_3$, 50 Hz) 20.87 (CO*C*H$_3$), 23.49 (C-2″), 26.17 (C-1), 49.26 (C-1′), 53.89 (C-1″), 65.74 (C-8), 71.02 (*C*H$_2$Ph), 76.70 (C-7), 127.82 (C-3), 127.73, 128.43, 129.23, 137.82 (C-4, C-5, C-6 and aromatic), 170.73 (*C*OCH$_3$), 199.53 (C-2). FAB MS m/z 372 $[M+1]^+$. Elemental analysis calculated for $C_{22}H_{29}O_4N$ (371.48) C: 71.13%, H: 7.87%, N: 3.77%. Found C: 70.84%, H: 7.52%, N: 3.42%.

(3*E*,5*E*)-7-*O*-Benzyl-1,3,4,5,6-pentadeoxy-3-diethylaminomethyl-D-*glycero*-oct-3,5-diene-2-ulose (17c). Yellow oil (35.0%). Eluent for column chromatography: chloroform/methanol = 997:3, v/v. R_f 0.58 (on basic alumina TLC plate, chloroform/methanol = 39:1, v/v; iodine vapors used as developing agent). $[\alpha]_D$ +20.2 (*c* 0.18, methanol). IR (neat, cm^{-1}) 3415 (OH), 1663 (C=O), 1218 (*tert*-amine). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.02 (t, $J_{2'',1''}=7.1$ Hz, 6H, H-2″), 2.39 (s, 3H, H-1), 2.49 (q, $J_{1'',2''}=7.1$ Hz, 4H, H-1″), 3.40 (s, 2H, H-1′), 3.65 (m, 2H, H-8a and H-8b), 4.11 (q, $J_{7,8a}=J_{7,8b}=J_{7,6}=6.4$ Hz, 1H, H-7), 4.45 (d, $J_{gem}=11.6$ Hz, 1H, C*H*$_2$Ph), 4.67 (d, $J_{gem}=11.6$ Hz, 1H, C*H*$_2$Ph), 6.05 (dd, $J_{6,7}=7.1$ Hz and $J_{6,5}=15$ Hz, 1H, H-6), 6.93 (dd, $J_{5,4}=11.3$ Hz and $J_{5,6}=15$ Hz, 1H, H-5), 7.13 (d, $J_{4,5}=11.2$ Hz, 1H, H-4), 7.34 (m, 5H, aromatic). ^{13}C NMR ($CDCl_3$, 50 Hz) 11.34 (C-2″), 26.37 (C-1), 46.47 (C-1″), 47.57 (C-1′), 65.03 (C-8), 71.00 (*C*H$_2$Ph), 79.96 (C-7), 127.86, 128.48, 129.34 (C-6 and aromatic), 137.80, 138.35 (C-3 and aromatic), 138.81, 139.52 (C-4 and C-5), 200.00 (C-2). FAB MS m/z 332 $[M+1]^+$, 300 $[M-CH_2OH]^+$, 289 $[M-COCH_2]^+$. Elemental analysis calculated for $C_{20}H_{29}O_3N.\frac{1}{2}H_2O$ (340.47) C: 70.56, H: 8.88%, N: 4.11%. Found C: 70.30%, H: 8.65%, N: 3.29%.

(3*E*,5*E*)-8-*O*-Acetyl-7-*O*-benzyl-1,3,4,5,6-pentadeoxy-3-(*N*-methyl)-piperazinomethyl-D-*glycero*-oct-3,5-diene-2-ulose (17d). Yellow oil (31.2%). Eluent for column chromatography: chloroform/methanol = 999:1, v/v. R_f 0.11 (on basic alumina TLC plate; hexane/ethyl acetate = 7:3, v/v; iodine vapors used as developing agent). $[\alpha]_D$ +18.8 (*c* 0.14, methanol). IR (neat, cm^{-1}) 1738 (C=O), 1216 (*tert*-amine), 759 (aromatic). ^{1}H NMR ($CDCl_3$, 200 MHz) 2.06 (s, 3H, COC*H*$_3$), 2.25 (s, 3H, NC*H*$_3$), 2.38 (s, 3H, H-1), 2.42 (m, 8H, H-1″ and H-2″), 3.34 (s, 2H, H-1′), 4.17 (m, 3H, H-7, H-8a and H-8b), 4.47 (d, $J_{gem}=12$ Hz, 1H, C*H*$_2$Ph), 4.67 (d, $J_{gem}=12.1$ Hz, 1H, C*H*$_2$Ph), 6.04 (dd, $J_{6,7}=6.1$ Hz and $J_{6,5}=15.1$ Hz, 1H, H-6), 6.86 (dd, $J_{5,4}=11.2$ Hz and $J_{5,6}=15.1$ Hz, 1H, H-5), 7.15 (d, $J_{4,5}=11.2$ Hz, 1H, H-4), 7.27–7.37 ((m, 5H, aromatic). ^{13}C NMR ($CDCl_3$, 50 Hz) 20.79 CO*C*H$_3$), 26.26 (C-1), 45.85 (N*C*H$_3$), 52.30 (C-1′), 52.72, 55.06 (C-1″ and C-2″), 65.72 (C-8), 71.31 (*C*H$_2$Ph), 76.64 (C-7), 127.67, 127.82, 128.43, 129.06 (C-6 and aromatic), 137.25, 137.74 (C-3 and aromatic), 138.49, 139.53 (C-4 and C-5), 199.55 (C-2). FAB MS m/z 401 $[M+1]^+$, 293 $[M-OCH_2Ph]^+$. Elemental analysis calculated for $C_{23}H_{32}O_4N_2.1\frac{1}{2}H_2O$ (427.54) C: 64.61%, H: 8.25%, N: 6.55%. Found C: 64.11%, H: 7.56%, N: 5.85%.

(3*E*,5*E*)-7-*O*-Benzyl-1,3,4,5,6-pentadeoxy-3-(*N*-benzyl)-piperazinomethyl-D-*glycero*-oct-3,5-diene-2-ulose (17e). Yellow oil (37.4%). Eluent for column chromatography: chloroform/methanol = 997:3, v/v. R_f 0.18 (on basic alumina TLC plate; hexane/ethyl acetate = 7:3, v/v; iodine vapors used as developing agent). $[\alpha]_D$ +8.7 (*c* 0.02, methanol). IR (neat, cm^{-1}) 3405 (OH), 1216 (*tert*-amine), 760 (aromatic). ^{1}H NMR ($CDCl_3$, 200 MHz) 2.36 (s, 3H, H-1), 2.42 (brs, 8H, H-1″ and H-2″), 3.33 (s, 2H, H-1′), 3.46 (s, 2H, NC*H*$_2$Ph), 3.63 (m, 2H, H-8a and H-8b), 4.09 (m, 1H, H-7), 4.44 (d, $J_{gem}=11.6$ Hz, 1H, C*H*$_2$Ph), 4.65 (d, $J_{gem}=11.7$ Hz, 1H, C*H*$_2$Ph), 6.06 (dd, $J_{6,7}=7$ Hz and $J_{6,5}=15.2$ Hz, 1H, H-6), 6.85 (dd, $J_{5,4}=11.3$ Hz and $J_{5,6}=15.1$ Hz, 1H, H-5), 7.15 (d, $J_{4,5}=11.2$ Hz, 1H, H-4), 7.22–7.33 (m, 5H, aromatic). ^{13}C NMR ($CDCl_3$, 50 Hz) 26.20 (C-1), 52.29, 52.84, 52.96 (C-1′, C-1″ and C-2″), 62.85 (N*C*H$_2$Ph), 65.01 (C-8), 71.03 (O*C*H$_2$Ph), 79.92 (C-7), 126.97, 127.76, 127.87, 128.12, 128.47, 129.13 (C-6 and aromatic), 136.93, 137.74, 137.97 (C-3 and aromatic), 139.21, 139.82 (C-4 and C-5), 199.55 (C-2). FAB MS m/z 435 $[M+1]^+$, 327 $[M-OCH_2Ph]^+$. Elemental analysis calculated for $C_{27}H_{34}O_3N_2$ (434.58) C: 74.62%, H: 7.89%, N: 6.45%. Found C: 73.94%, H: 7.74%, N: 6.67%.

General method for preparation of compounds 18 and 19

Compounds **18** and **19** were prepared by the reaction of acrylonitrile with α, β- unsaturated sugar aldehydes **1** and **2**, respectively. A solution of the required aldehyde **1/2** (1 mmol) in acrylonitrile (1 mL) was added to a solution of DABCO (112 mg, 1 mmol) dissolved in acrylonitrile (0.5 mL) by stirring them together for 30 min. The reaction was allowed to continue for 48 h at room temperature. On completion of the reaction, the solvent was evaporated in vacuo and the residue obtained after evaporation of excess of acrylonitrile was dissolved in dichloromethane. The resulting solution was then washed with 1 N HCl, $NaHCO_3$ and brine. The organic layer was dried over Na_2SO_4. Evaporation of the solvent and column chromatography of the residue over silica gel yielded **18/19**.

Mixture of (4*E*)-6,7,8-tri-*O*-benzyl-1,2,4,5-tetradeoxy-2-methylene-D-(*arabino* and *ribo*)-octo-1-nitrile (18). Pale yellow oil (31.3%). Eluent for column chromatography: hexane/ethyl acetate = 41:9, v/v. R_f 0.38 (hexane/ethyl acetate = 7:3, v/v). IR (neat, cm^{-1}) 3413 (OH), 2229 (C≡N), 977 (C = C). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.45 (brs, O*H*, exchangeable with deuterium), 3.62 (dd$_e$, 2H, H-8a and H-8b), 3.73 (m, 1H, H-7), 4.07 (m, 1H, H-6), 4.40 (d, $J_{gem}=11.8$ Hz, 1H, C*H*$_2$Ph), 4.42 (d, $J_{gem}=11.7$ Hz, 1H, C*H*$_2$Ph), 4.51–4.69 (m$_e$, 5H, H-3 and 2×C*H*$_2$Ph), 5.70 (dd, $J_{4,3}=6$ Hz and $J_{4,5}=15.7$ Hz, 1H, H$_A$-4), 5.72 (dd, $J_{4,3}=6.1$ Hz and $J_{4,5}=15.9$ Hz, 1H, H$_B$-4), 5.89 (dd, $J_{5,6}=6.7$ Hz and $J_{5,4}=15.6$ Hz, 1H, H-5), 5.95 (s, 1H, H-1′a), 5.98 (s, 1H, H-1′b), 5.99 (s, 1H, H$_B$-1′a), 6.01 (d, $J_{1'b,1'a}=1.2$ Hz, 1H, H$_B$-1′b), 7.21–7.41 (m, 15H, aromatic). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 69.43 (C-8), 70.78, 70.87 (*C*H$_2$Ph), 71.83, 71.90 (C-3), 72.86, 73.21 (*C*H$_2$Ph), 78.85 (C-6), 80.00, 80.09 (C-7), 116.96 (C-1), 125.31 (C-2), 127.52, 127.63, 127.87, 128.22 (aromatic), 129.72, 129.82 (C-1′), 131.43, 131.70 (C-4), 131.96, 132.17 (C-5), 138.04, 138.11, 138.33 (aromatic). FAB MS m/z 470 $[M+1]^+$. Elemental analysis calculated for $C_{30}H_{31}NO_4$ (469.58) C: 76.74%, H:

6.65%, N: 2.98%. Found C: 76.60%, H: 6.67%, N: 1.90%.

Mixture of (4*E*)-6,8-di-*O*-benzyl-1,2,4,5-tetradeoxy-2-methylene-D-(*lyxo* and *xylo*)-octo-1-nitrile (19). Pale yellow oil (27.3%). Eluent for column chromatography: hexane/ethyl acetate = 39:11, v/v. R_f 0.52 (hexane/ethyl acetate = 1:1, v/v). IR (neat, cm^{-1}) 3759 (OH), 2227 (C≡N), 979 (C = C). ^1H NMR ($CDCl_3$, 200 MHz) δ 2.20 (brs, O*H*, exchangeable with deuterium), 3.58 (m, 2H, H-8a and H-8b), 3.77 (m, 1H, H-7), 4.00 (m, 1H, H-6), 4.38 (d, J_{gem} = 11.6 Hz, 1H, CH_2Ph), 4.40 (d, J_{gem} = 11.6 Hz, 1H, CH_2Ph), 4.50–4.69 (m_e, 3H, H-3 and CH_2Ph), 5.77–5.83 (m_e, 2H, H-4 and H-5), 5.98 (s, 1H, H-1′a), 6.03 (s, 1H, H-1′b), 7.26–7.38 (m_e, 10H, aromatic). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 70.41 (C-8), 70.87, 71.05 (*C*H_2Ph), 71.77 (C-3), 72.60, 72.72 (C-6), 73.34 (*C*H_2Ph), 78.76, 78.96 (C-7), 116.93 (C-1), 125.18 (C-2), 127.67, 127.75, 127.80, 127.93, 127.98, 128.34 (aromatic), 129.86 (C-1′), 130.98, 131.14 (C-5), 132.35, 132.67 (C-4), 137.68, 137.79 (aromatic). FAB MS *m*/*z* 380$[M+1]^+$, 402 $[M+Na]^+$. Elemental analysis calculated for $C_{23}H_{25}NO_4$ (379.46) C: 72.80%, H: 6.64%, N: 3.69%. Found C: 71.70%, H: 6.93%, N: 3.57%.

General method for preparation of compounds 20 and 21

To a stirred solution of the Baylis–Hillman adduct **18/19** (1 mmol) in dry methanol (10 mL), was added the required amine (2 mmol). The reaction was allowed to continue for 24 h at room temperature. On completion of reaction, excess of methanol was evaporated in vacuo and the residue was chromatographed over basic alumina to yield amino alkanols **20a–b** and **21a–b.**

Mixture of (4*E*)-6,7,8-tri-*O*-benzyl-1,2,4,5-tetradeoxy-2-piperazinomethyl-D-(*allo*, *altro*, *gluco* and *manno*)-octo-1-nitrile (20a). Yellow oil (60.3%). Eluent for column chromatography: chloroform/methanol = 99:1, v/v. R_f 0.50 (on basic alumina TLC plate; chloroform/methanol = 39:1, v/v; iodine vapors were used as developing agent). IR (neat, cm^{-1}) 3449 (OH), 2402 (C≡N), 1217 (*tert*-amine), 929 (C = C). ^1H NMR ($CDCl_3$, 200 MHz)δ 1.67 (brs, O*H*, exchangeable with deuterium), 2.16–2.82 (m_e, 11H, H-1″, H-2″, H-1′ and H-2), 3.62 (m_e, 2H, H-8a and H-8b), 3.77 (m, 1H, H-7), 4.11 (m_e, 1H, H-6), 4.41–4.70 (m_e, 7H, H-3 and 3×CH_2Ph), 5.85 (dd_e, $J_{4,3}$ = 5.4 Hz, 1H, H-4), 5.95 (dd, $J_{5,6}$ = 6.3 Hz and $J_{5,4}$ = 15.7 Hz, 1H, H-5), 7.25–7.30 (m_e, 15H, aromatic). ^{13}C NMR ($CDCl_3$, 50 MHz) 35.07, 35.40 (C-2), 44.67 (C-2″), 52.79, 57.11, 57.86 (C-1′ and C-1″), 69.62 (C-8), 70.89 (*C*H_2Ph), 71.07 (C-3), 72.90, 73.31 (*C*H_2Ph), 79.20, 80.29 (C-6 and C-7), 118.58 (C-1), 127.48, 127.65, 127.80, 128.22, 128.30 (aromatic), 130.92, 132.38 (C-4 and C-5), 138.28, 138.59 (aromatic). FAB MS *m*/*z* 556 $[M+1]^+$, 464 $[M-C_7H_7]^+$. Elemental analysis calculated for $C_{34}H_{41}N_3O_4$ (555.71) C: 73.49%, H: 7.44%, N: 7.56%. Found C: 72.96%, H: 7.02%, N: 7.42%.

Mixture of (4*E*)-6,7,8-tri-*O*-benzyl-1,2,4,5-tetradeoxy-2-(*N*-methyl)piperazinomethyl-D-(*allo*, *altro*, *gluco* and *manno*)-octo-1-nitrile (20b). Yellow oil (81.9%). Eluent for column chromatography: chloroform/methanol = 199:1, v/v. R_f 0.5 (on basic alumina TLC plate; chloroform/methanol = 39:1, v/v; iodine vapors were used as developing agent). IR (neat, cm^{-1}) 3679 (OH), 2245 (C≡N), 1365 (*tert*-amine), 981 (C = C). ^1H NMR ($CDCl_3$, 200 MHz) δ 2.23 (s, 3H, NCH_3), 2.30–2.70 (m_e, 9H, H-2, H-1″ and H-2″), 2.80–2.87 (m, 2H, H-1′), 3.63 (dd_e, 2H, H-8a and H-8b), 3.77 (q, $J_{7,8a} = J_{7,8b} = J_{7,6}$ = 4.4 Hz, 1H, H-7), 4.12 (m, 1H, H-6), 4.37–4.70 (m_e, 7H, H-3 and 3×CH_2Ph), 5.79 (dd, $J_{4,3}$ = 5.4 Hz and $J_{4,5}$ = 15.6 Hz, 1H, H-4), 5.97 (dd, $J_{5,6}$ = 6.4 Hz and $J_{5,4}$ = 16 Hz, 1H, H-5), 7.26–7.36 (m_e, 15H, aromatic). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 33.85, 34.35 (C-2), 45.78 (N*C*H_3), 53.22, 53.36, 54.71, 54.84, 56.79, 57.02 (C-1′, C-1″ and C-2″), 69.71 (C-8), 70.83 (*C*H_2Ph), 71.85, 71.95 (C-3), 72.79, 72.92 (*C*H_2Ph), 77.21, 79.26, 79.34, 80.26, 80.40 (C-6 and C-7), 118.54 (C-1), 127.43, 127.59, 127.66, 127.81, 128.20, 128.30 (aromatic), 130.67, 130.91, 132.30, 132.68 (C-4 and C-5), 138.32, 138.66 (aromatic). FAB MS *m*/*z* 570 $[M+1]^+$, 478 $[M-CH_2Ph]^+$. Elemental analysis calculated for $C_{35}H_{43}N_3O_4$ (569.75) C: 73.79%, H: 7.61%, N: 7.38%. Found C: 74.93%, H: 7.82%, N: 6.76%.

Mixture of (4*E*)-6,8-di-*O*-benzyl-1,2,4,5-tetradeoxy-2-piperazinomethyl-D-(*gulo*, *ido*, *galacto* and *talo*)-octo-1-nitrile (21a). Yellow oil (32%). Eluent for column chromatography: chloroform/methanol = 99:1, v/v. R_f 0.35 (on basic alumina TLC plate; chloroform/methanol = 39:1, v/v; iodine vapors used as developing agent). IR(neat, cm^{-1}) 3685 (OH), 2245 (C≡N), 1384 (*tert*-amine), 927 (C = C). ^1H NMR ($CDCl_3$, 200 MHz) 2.00 (brs, O*H*, exchangeable with deuterium), 2.55–2.92 (m_e, 11H, H-1″, H-2″, H-1′ and H-2), 3.58 (m, 2H, H-8a and H-8b), 3.79 (m, 1H, H-7), 4.05 (m, 1H, H-6), 4.36–4.59 (m_e, 3H, H-3 and CH_2Ph), 4.65 (d, J_{gem} = 11.4 Hz, 1H, CH_2Ph), 4.68 (d, J_{gem} = 11.6 Hz, 1H, CH_2Ph), 5.82–5.94 (m_e, 2H, H-4 and H-5), 7.26–7.32 (m_e, 10H, aromatic). ^{13}C NMR ($CDCl_3$, 50 MHz) 34.34 (C-2), 45.85, 45.98 (C-2″), 54.70, 57.86 (C-1′ and C-1″), 70.55, 70.68 (C-8), 70.98 (*C*H_2Ph), 71.68, 72.86, 73.07 (C-3 and C-6), 73.44 (*C*H_2Ph), 79.36, 79.46 (C-7), 118.60 (C-1), 127.64, 127.82, 127.91, 128.35 (aromatic), 130.15, 130.34, 132.97 (C-4 and C-5), 137.88, 138.05 (aromatic). FAB MS *m*/*z* 466 $[M+1]^+$. Elemental analysis calculated for $C_{27}H_{35}N_3O_4$ (465.60) C: 69.65%, H: 7.58%, N: 9.03%. Found C: 69.42%, H: 7.01%, N: 8.89%.

Mixture of (4*E*)-6,8-di-*O*-benzyl-1,2,4,5-tetradeoxy-2-(*N*-methyl) piperazinomethyl-D-(*gulo*, *ido*, *galacto* and *talo*)-octo-1-nitrile (21b). Yellow oil (33%). Eluent for column chromatography: chloroform/methanol = 199:1, v/v. R_f 0.33 (on basic alumina TLC plate; chloroform/methanol: 39:1, v/v; iodine vapors used as developing agent). IR (neat, cm^{-1}) 3679 (OH), 2245 (C≡N), 1365 (*tert*-amine), 981 (C = C). ^1H NMR ($CDCl_3$, 200 MHz) 2.29 (s, 3H, NCH_3), 2.50–2.80 (m_e, 9H, H-2, H-1″ and H-2″), 2.92 (m, 2H, H-1′), 3.58 (m, 2H, H-8a and H-8b), 3.79 (m, 1H, H-7), 4.05 (m, 1H, H-6), 4.37–4.60 (m_e, 3H, H-3 and CH_2Ph), 4.65 (d, J_{gem} = 11.7 Hz, 1H, CH_2 Ph), 4.68 (d, J_{gem} = 11.7 Hz, 1H, CH_2Ph), 5.82–5.93 (m, 2H, H-4 and H-5), 7.26–7.32 (m_e, 10H, aromatic). ^{13}C NMR ($CDCl_3$, 50 MHz) 34.49 (C-2), 45.69 (N*C*H_3), 53.05, 53.33, 54.65, 54.79, 57.03, 58.81 (C-1′, C-1″ and

C-2″), 70.50, 70.64, 70.90 (C-8 and CH_2Ph), 71.39, 71.57, 72.81, 73.00, 77.33, 79.37 (C-3, C-6 and C-7), 73.39 (CH_2Ph), 127.62, 127.79, 127.89, 128.37 (aromatic), 130.06, 130.24, 130.92, 132.95, 133.15, 133.47 (C-4 and C-5), 137.81, 137.98 (aromatic). FAB MS m/z 480 $[M+1]^+$, 460 $[M-(H_2O+1)]^+$, 442 $[M-(2H_2O+1)]^+$. Elemental analysis calculated for $C_{28}H_{37}N_3O_4 \frac{1}{2}H_2O$(488.63) C: 68.83%, H: 7.84%, N: 8.60%. Found C: 68.91%, H: 7.88%, N: 8.38%.

Biological Activity

Agar dilution method[12]

Briefly, 2-fold serial dilutions of each test compound/drug were incorporated into 7H10 agar. Inoculum of *M. tuberculosis* $H_{37}Rv$ was prepared from fresh Lowenstein–Jensen slants adjusted to 1 mg/mL (wet weight) in Tween 80 (0.05%) saline and diluted to 10^{-2} to give a concentration of approximately 10^7 cfu/mL. The 5 μL of bacterial suspension was spotted into 7H10 agar tubes containing 2-fold serial dilution of drugs per mL. The tubes were incubated at 37 °C and final readings were recorded on 30 days. The MICs were read as the minimum concentration of drugs/compounds that completely inhibited the growth of *M. tuberculosis* per spot. Ofloxacin was used as the standard drug.

Microwell plate alamar blue assay[14] (MABA)

Antimycobcaterial activity was determined by Microwell plate-based Alamar blue assay (MABA) using *M. tuberculosis* $H_{37}Ra$ as a surrogate for the virulent $H_{37}Rv$ strain. The results of MABA have been found comparable to the standard BACTEC 460 system based assay. The standard antitubercular drugs Rifamycin, Isoniazid, *p*-Amino salicylic acid, Ethambutol and Ethionamide (MIC range $3 < 0.3$ μg/mL) were taken as positive controls. A compound showing MIC < 12.5 μg/mL was considered active.

Cytotoxicity studies

The most active compound **(10)** was tested for its cytotoxicty. In short, mouse macrophage cell line J 744A.1 which is the important cell line for *M. tuberculosis* infection has been used for the assay. The assay is based on the MTT [3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyl-2H-tetrazolium bromide] reduction. The drug concentrations used for the assay were 50, 25 and 12.5 μg/mL in parallel with known toxic compounds and standard antimycobacterial drugs like Rifampicin and Sparfloxacin. The cell death was significantly lower (8–10-fold) than the toxic compound and very similar to standard drugs.

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