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Chain extension of acyclic sugar derivatives via the Baylis–Hillman reaction☆

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Abstract—Baylis–Hillman reactions on α,β-unsaturated sugar aldehydes with methyl vinyl ketone in the presence of Me_2S–$TiCl_4$ have been carried out to provide a convenient strategy for extending the sugar chain in its open form. The resulting Baylis–Hillman adducts have been further used as synthons for synthesising chain extended amino polyols.

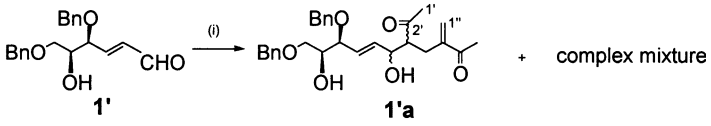
1. Introduction

Chain extended acyclic sugar derivatives with deoxy centres are an important class of compounds.[1] Among the several synthetic strategies available in the literature[2] for synthesising such compounds, Perlin hydrolysis of glycals[3] leading to the formation of α,β-unsaturated aldehydo sugar with deoxy centres of the type **1** or **2** may be considered to be a convenient route. To the best of our knowledge, only a few reports are available[4] where such aldehydo sugar derivatives have been used as synthons for syntheses of acyclic sugar derivatives of biological importance. From our group we have published[5] the syntheses of polyhydroxy deoxy amino and nitro sugar derivatives by Henry reaction of α,β-unsaturated aldehydo sugar with nitromethane. With the growing understanding of higher sugars, cyclic[6] or acyclic,[7] in biological processes, interest has grown towards syntheses of such sugar derivatives. In our ongoing programme on the syntheses of higher acyclic amino sugar derivatives, we wish to report another strategy of obtaining such sugar derived amino polyols from easily available **1** and **2** via a Baylis–Hillman reaction which has emerged as a useful carbon–carbon bond forming reaction[8] using different catalysts[9] during the last few years. In carbohydrates, this reaction has mainly been used to form a C-saccharide.[10] The present communication is, therefore, the first report of a Baylis–Hillman reaction on an α,β-unsaturated carbohydrate enal for extending the sugar chain where the unsaturation in the enal does not interfere with the electrophilicity of the aldehydic carbon.

2. Results and discussion

The Baylis–Hillman reaction was explored with the aldehydo sugar derivative **1′**, (2*E*)-4,6-di-*O*-benzyl-2,3-dideoxy-*aldehydo*-D-*threo*-hex-2-enose obtained by Perlin's reaction of easily available benzylated galactal.[4b] The attempt to couple **1′** with methyl vinyl ketone (MVK) in the presence of DABCO proved futile leading to the formation of a complex mixture. **1′a** was isolated from the mixture in 15% yield (Scheme 1).

However, treatment of **1**, (2*E*)-5-*O*-acetyl-4,6-di-*O*-benzyl-2,3-dideoxy-*aldehydo*-D-*threo*-hex-2-enose with MVK in the presence of Me_2S–$TiCl_4$ at 0°C till the complete disappearance of the starting material (TLC, 50 min) led to the formation of three products namely **3** (48%) as a major



Scheme 1. (i) MVK; DABCO; room temperature; 36 h; 15%.

☆ Part 2 in this series; for part 1, see Ref. 5. CDRI communication No. 6147.

Keywords: aldehyde; Baylis–Hillman reaction; carbanion; carbohydrate; polyol; zwitterion.

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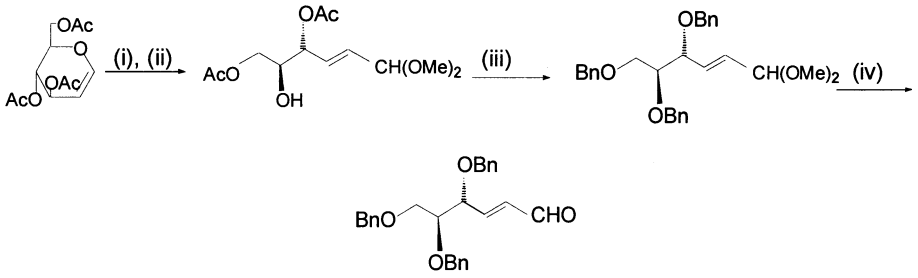
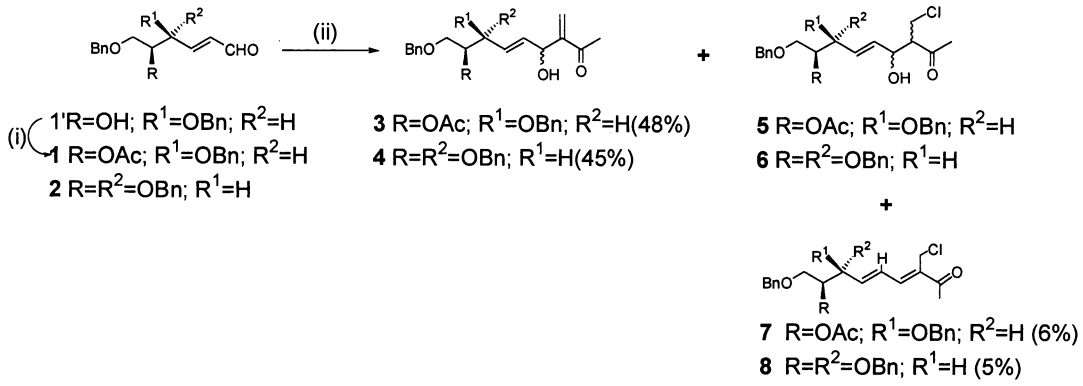
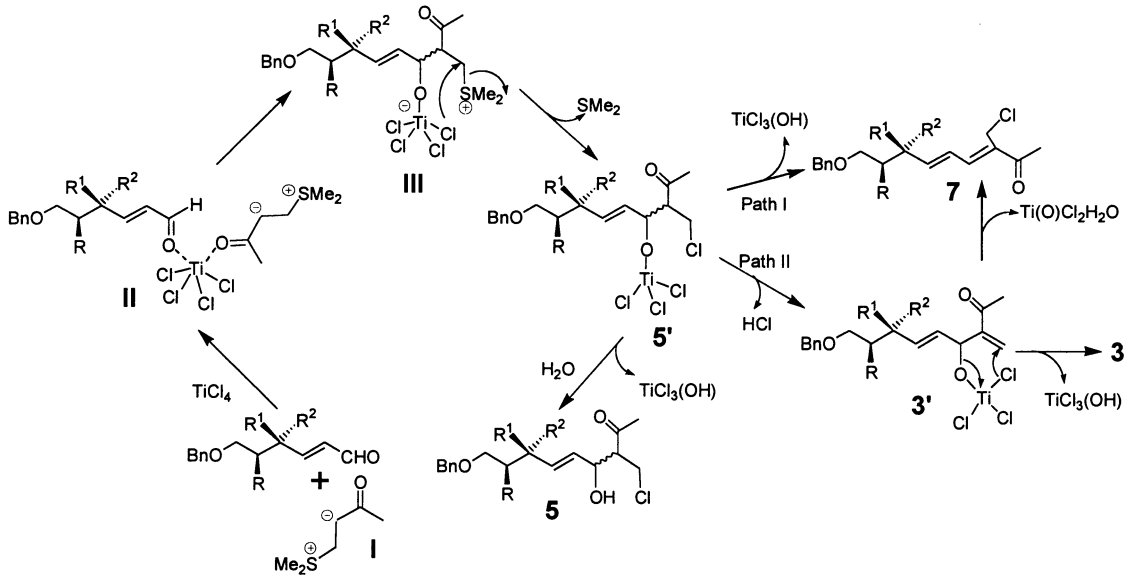


Scheme 2. (i) 0.01N H_2SO_4; $HgSO_4$; 1,4-Dioxan; room temperature; 4 h; 70%;[11] (ii) trimethylorthoformate; MeOH; PTSA; 4 Å mol. sieves;[11] 0°C; 4 h; (iii) pulverised NaOH; BnBr; TBAI; THF; 0°C; 24 h; 48% (iv) SiO_2; 10% oxalic acid; CH_2Cl_2; room temperature; 1.5 h; quant.[12]

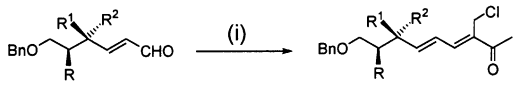


Scheme 3. (i) Ac_2O; Pyr.; 0°C; 10 h; quant.; (ii) MVK; Me_2S–$TiCl_4$; CH_2Cl_2; 0°C; 50 min.

product besides **7** (6%) and a small amount of a mixture of **3** and **5** (8%) Scheme 3. The identity of **5** was confirmed by comparing the PMR spectrum of pure compound **3** with the PMR spectrum of mixture of **3** and **5** which showed the presence of a signal at δ 5.67–5.71 for ethylenic protons for H-5 and H-6 and a multiplet at δ 3.57 for H-1′ of compound **5** along with signals characteristic for compound **3**. Both **3** and **5** were mixtures of their respective diastereoisomers. During the monitoring (on TLC) of the course of this reaction, it was noticed that the concentration of the starting material decreased considerably after 15 min along with the formation of **5** (major product) and **7** (trace amount) as evidenced from the NMR spectrum of the worked up product. A similar result was noticed when the reaction was performed under the same conditions with **2**, (2*E*)-4,5,6-tri-*O*-benzyl-2,3-dideoxy-*aldehydo*-D-*erythro*-



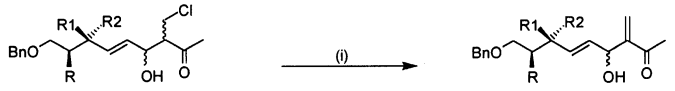
Scheme 4.



1 R=OAc; R^1=OBn; R^2=H
2 R=R^2=OBn; R^1=H

7 R=OAc; R^1=OBn; R^2=H (70%)
8 R=R^2=OBn; R^1=H (51%)

Scheme 5. MVK; Me_2S–$TiCl_4$; CH_2Cl_2; 0°C; 6–9 h.



5 R=OAc; R^1=OBn; R^2=H
6 R=R^2=OBn; R^1=H

3 R=OAc; R^1=OBn; R^2=H (55%)
4 R=R^2=OBn; R^1=H (52%)

Scheme 6. DBU; toluene; room temperature; 40 min.

hex-2-enose which was obtained by following the sequence as shown in Scheme 2 as Perlin hydrolysis of 3,4,6-tri-*O*-benzyl glucal was unsatisfactory.

The course of the reaction could, thus, be mechanistically rationalized as illustrated in Scheme 4.

β-Addition of dimethylsulfide to MVK resulted in the zwitterionic species **I** and subsequently its coordination to the titanium(IV) chloride coordinated sugar aldehyde **1** generated the complex **II** which involved 1,2-nucleophilic addition of the carbanion to the electrophilic aldehydic carbon providing the intermediate **III**. The intramolecular substitution of Me_2S^+ with Cl^- in **III** forms compound **5** via the intermediate **5′**. The formation of **3** or **7** could be explained on the basis of considering the involvement of intermediate **5′** which either follows path **I** to form **7** with the elimination of $TiCl_3(OH)$ or path **II** to form enone **3** (through the intermediate, **3′**) with the liberation of HCl and $TiCl_3(OH)$. Compound **7** could also be obtained from the intermediate **3′** by intramolecular Michael addition of Cl^- with concomitant β-elimination of $Ti(O)Cl_2{\cdot}H_2O$.

Therefore, in order to argue the formation of conjugated chloro derivative **7**, the reaction was continued even after 50 min and it was found that the conjugated chloro derivative was the sole product (70%) obtained after 6 h (Scheme 5). A similar observation was noted with the aldehyde **2**. Thus, this result suggested that the change in the length of reaction time led to a change in the nature of products.

In order to further authenticate the mechanism postulated, the same reaction was carried out strictly for 15 min. The crude adducts **5** and **6** thus obtained from their respective aldehydes, without chromatographic purification, were converted into the enones **3** and **4**, respectively, in 40 min by treating them with DBU in toluene[13] thus providing the yield of **3** and **4** as 55 and 52%, respectively (Scheme 6).[14]

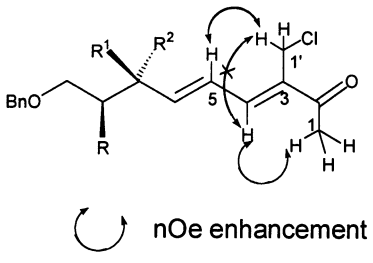
The configuration of the products **7** and **8** was established as [*Z*] at C-3 on the basis of nOe experiments. In the [*Z*] isomer, the distance between H-5 and H-1′; and H-4 and H-1 (methyl) was found to be well within the range for nOe to be observed. Thus, irradiation of the signal for H-5 enhanced the intensity of the signal for H-1′ by 7.5%. Conversely, irradiation of the signal for H-1′ enhanced the intensity of the signal for H-5 by 7.2%. In addition, irradiation of the signal for H-4 enhanced the intensity of the signal for H-1 (methyl) by 7.9%. Since no nOe was observed between H-4 and H-1′, the configuration was assigned as [*Z*] (Scheme 7).

The [*Z*] selectivity of the products **7** and **8** could be understood in terms of considering the *trans decalin like transition state* (TS A) of **3′** where as product with [*E*] geometry is possible when the intermediate attains *cis decalin like transition state* (TS B) which is energetically less favoured and thus the reaction proceeds predominantly through TS A leading to formation of [*Z*] selective product (Scheme 8).

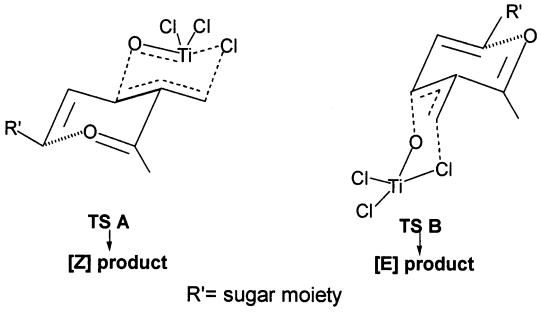
In order to show the synthetic utility of the Baylis–Hillman adducts **3** and **7** to form amino polyols and conjugated polyols, nucleophilic substitution reactions were performed on **7** with nitrogen nucleophiles and tri-*n*-butyltin hydride resulting in the formation of **9**–**11** whereas Michael reaction on **3** with a nitrogen nucleophile yielded **9**, the details of which are given in Table 1.

3. Conclusion

We have found that: (i) α,β-unsaturated aldehydes (carbohydrate enal) have been used for the first time as an electrophile in a Baylis–Hillman reaction where unsaturation does



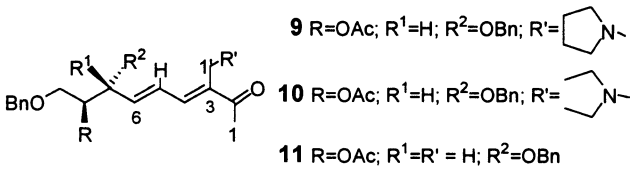
Scheme 7.



Scheme 8.

Table 1.

Substrate	Nucleophile	Time	Yield (%)	Product
7	Pyrrolidine	1 h	60	**9**
7	*N*,*N*-Diethyl amine	3 h	65	**10**
7	Tri-*n*-butyltin hydride	45 min	50.5	**11**
3	Pyrrolidine	10 h	45	**9**



not affect the electrophilicity of the electrophilic aldehydic carbon and the nature of product(s); (ii) the remarkable utility of the adduct **7** could be understood by nucleophilic substitution of Cl^- with various nucleophiles namely nitrogen and tri-*n*-butyltin hydride to form biologically important molecules and (iii) our observation presented in this communication describing how the nature of product(s) formed depends upon the reaction time given to react MVK and α,β-unsaturated aldehyde of type **1** in the presence of Me_2S–$TiCl_4$ is consistent with the findings published recently by Shi et al.[14c]

4. Experimental

4.1. General

All the reactions were monitored by warming the $CeSO_4$ (1% in 2N H_2SO_4) sprayed precoated silica gel TLC plates at 100°C or as stated otherwise. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker Avance DPX 200 FT Bruker Robotics Spectrometer. The subscript 'e' to the multiplicity in the assignment of PMR refers to merged signals. Mass spectra were recorded by JEOL SX 102/DA 6000 mass spectrometer using argon/xenon (6 kV, 10 mA) as the FAB gas. Organic solvents used were dried by standard methods. IR spectra were recorded on Perkin–Elmer 881 and FTIR-8210 PC Shimadzu Spectrophotometers. 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. Elemental analyses were carried out on Carlo-Erba-1108 instrument.

4.1.1. Diastereomeric mixture of (7*E*)-5-acetyl-9,11-di-*O*-benzyl-1,3,4,5,7,8-hexadeoxy-3-methylene-D-(*gulo*, *ido*, *galacto* and *talo*)-undec-7-ene-2-ulose (1′a). To a stirred solution of freshly distilled MVK (1.5 mL) and DABCO (321 mg, 2.86 mmol) was added a solution of aldehyde **1′** (1 g, 3.07 mmol) in MVK (2.5 mL). The solution was allowed to stir at room temperature for 36 h. On disappearance of the starting material on TLC, the reaction mixture was worked up by evaporating the excess MVK. The residue was extracted with dichloromethane and was washed successively with 1N HCl, $NaHCO_3$ and brine. The organic layer was then dried over Na_2SO_4 followed by evaporation to give crude product containing compound **1′a** which after column chromatographic purification over silica gel yielded pure **1′a** as pale yellow oil. Yield 15%; eluent for column chromatography: hexane–ethylacetate=3:1, v/v R_f 0.24 (hexane–ethylacetate=1:1, v/v); $[\alpha]_D=-24.5°$ (c=0.11, methanol); IR (neat, cm^{-1}) 3423 (OH), 1708 (C=O), 981 (C=C); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.12, 2.13 (2×s, 6H, 2×COCH_3), 2.32, 2.34 (2×s, 6H, 2×H-1), 2.52 (m, 2H, H-4), 2.85–2.92 (m, 1H, H-5), 3.51–3.59 (m, 2H, H-11a and H-11b), 3.76 (m, 1H, H-10), 3.96 (t, $J_{10,11}=J_{10,9}$=6.2 Hz, 1H, H-9), 4.17 (m, 1H, H-6), 4.33–4.64 (m, 4H, 2×CH_2Ph), 5.69–5.82 (m, 2H, H-7 and H-8), 5.82 (s, 1H, H_A-1″a), 5.85 (s, 1H, H_B-1″a), 6.04 (s, 1H, H_A-1″b), 6.09 (s, 1H, H_B-1″b), 7.31–7.35 (m, 10H, aromatic). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 25.69, 25.74 (COCH_3), 28.58, 30.21 (C-4), 31.74 (C-1), 55.65, 56.15, 56.27 (C-5), 70.53, 70.72, 70.79 (C-11 and CH_2Ph), 71.70, 72.38, 72.92, 79.51 (C-6, C-9 and C-10), 73.40 (CH_2Ph), 127.63, 127.69, 127.77, 127.86, 127.91, 129.01 (C-8 and aromatic), 128.37 (C-1″), 134.36, 135.37, 135.62 (C-7 and aromatic), 138.06, 145.64, 146.21 (C-3 and aromatic), 199.39, 199.58 (C-2), 212.33 (COCH$_3$). FAB MS m/z 489 $[M+Na]^+$, 449 $[M-OH]^+$, 359 $[M-OCH_2Ph]^+$, 341 $[M-(COCH_2+CH_2C(=CH_2)COCH_3)]^+$. Elemental analysis for $C_{28}H_{34}O_6$ (466.546) Calculated C: 72.07%, H: 7.34%. Found C: 71.78%, H: 7.81%.

4.1.2. (2*E*)-4,5,6-Tri-*O*-benzyl-2,3-dideoxy-*aldehydo*-D-*erythro*-hex-2-enose (2). The Perlin hydrolysis of 3,4,6-tri-*O*-acetyl-D-glucal followed by the protection of the aldehyde group with acetal group was done as per the literature procedure.[11] To a solution of acetal (12 g) in THF (127 mL), pulverised NaOH (8.6 g), benzyl bromide (13.8 mL) and TBAI (800 mg) were added in succession and stirred at 0°C for 6 h and later at room temperature for 18 h. On disappearance of starting material on TLC, the reaction mixture was worked up by diluting it with water, THF layer being lighter than alkali layer was separated followed by evaporation. The residue was dissolved in EtOAc. The alkali layer containing THF was evaporated followed by its extraction with 3×25 mL portions of EtOAc. The combined organic layers were washed with brine dried over anhydrous sodium sulphate and evaporated in vacuo to yield crude benzylated acetal which was chromatographed over silica gel. The pure acetal protected benzylated aldehyde was eluted in ethyl acetate–hexane (1:19) in 48% yield which was further treated with silica gel (70 g) acidified with 10% oxalic acid (~6 mL) in dichloromethane (50 mL) for 1 h at room temperature. The reaction mixture was neutralized with $NaHCO_3$ solution and filtered. The organic layer was separated from the filtrate, washed with brine solution and

dried over Na_2SO_4. Evaporation of the organic layer yielded pure **2** quantitatively as colourless syrup. R_f 0.8 (hexane–ethylacetate=7:3, v/v); $[\alpha]_D=+13.73°$ (c=0.31, methanol); IR (neat, cm^{-1}) 1691 (C=O); ^1H NMR ($CDCl_3$, 200 MHz) δ 3.62–3.64 (m, 2H, H-6a and H-6b), 3.74 (m, 1H, H-5), 4.33 (t, $J_{4,5}=J_{4,3}=5.6$ Hz, 1H, H-4), 4.39–4.72 (m, 6H, 3×CH_2Ph), 6.30 (dd, $J_{2,1}=7.8$ Hz and $J_{2,3}=15.8$ Hz, 1H, H-2), 6.83 (dd, $J_{3,4}=5.8$ Hz and $J_{3,2}=15.8$ Hz, 1H, H-3), 9.53 (d, $J_{1,2}=7.9$ Hz, 1H, H-1); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 68.80 (C-6), 71.99, 72.78, 73.37 (CH_2Ph), 78.04, 79.68 (C-4 and C-5), 125.75, 127.57, 127.68, 127.72, 127.81, 127.95, 128.31, 128.36, 137.45, 137.87, 138.27 (aromatic), 133.40 (C-2), 154.39 (C-3), 197.24 (C-1);.FAB MS m/z 415 $[M-1]^+$. Elemental analysis for $C_{27}H_{28}O_4$ (416. 49). Calculated C: 77.86%, H: 6.78%. Found C: 77.79%, H: 7.13%.

4.2. Typical reaction procedure for formation of compound 3/4, 5/6 and 7/8

To the aldehyde (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 min for **5/6**; 50 min to 1 h for **3/4** and 6–9 h for **7/8**. Sodium bicarbonate solution was added to quench the mixture followed by filtration through celite pad. The organic layer from the filtrate was separated and washed with brine solution. The water layer was again extracted with ethyl acetate and the organic layers were then combined to dry over sodium sulfate. On evaporation of the solvent crude product could be obtained which was further chromatographed to yield pure compound.

4.3. Preparation of compound 3/4 from 5/6

To the reaction product **5/6**, obtained from the above reaction, dissolved in dry toluene (5 mL) was added DBU (1.5 equiv.) and the reaction mixture was stirred at room temperature for 40 min. On completion of the reaction as seen from TLC, reaction product was neutralized with 1N HCl followed by washing with $NaHCO_3$ and brine successively. The organic layer was dried over Na_2SO_4 and then evaporated to yield crude product containing **3/4** which was chromatographed to obtain pure compound **3/4**.

4.3.1. Diastereomeric 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 (3). Oil (55%). Eluent for column chromatography: hexane–ethylacetate=3:1, v/v. R_f 0.38 (hexane–ethylacetate=7:3, v/v). $[\alpha]_D=-19.2°$ (c=0.13, methanol). 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 (bs, 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 $C_{26}H_{30}O_6$ (438.494) C: 71.21%, H: 6.90%. Found C: 70.90%, H: 6.54%.

4.3.2. Diastereomeric 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 (4). Oil (52%). Eluent for column chromatography: hexane–ethylacetate=41:9, v/v. R_f 0.52 (hexane–ethylacetate=7:3, v/v). $[\alpha]_D=+19°$ (c=0.11, methanol). IR (neat, cm^{-1}) 3420 (OH), 1632 (C=O), 972 (C=C). ^1H NMR ($CDCl_3$, 200 MHz) δ 2.31 (s, 3H, H_A-1), 2.32 (s, 1H, H_B-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 (bs, 1H, H-4), 5.76–5.80 (m_e, 2H, H-5 and H-6), 5.98 (d, $J_{1a,1'b}=1$ 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 $C_{31}H_{34}O_5$ (486.577) C: 76.52%, H: 7.04%. Found C: 76.23%, H: 7.60%.

4.3.3. (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 (7). Oil (70%). Eluent for column chromatography: hexane–ethylacetate=4:1, v/v. R_f 0.48 (hexane–ethylacetate=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 $C_{26}H_{29}O_5Cl$ (456.987) C: 68.33%, H: 6.40%. Found C: 68.18%, H: 6.61%.

4.3.4. (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 (8). Oil (51%). Eluent for column chromatography: hexane–ethylacetate=9:1, v/v. R_f 0.62 (hexane–ethylacetate=4:1, v/v). $[\alpha]_D=+11.3°$ (c=0.16, methanol). IR (neat, cm^{-1}) 1733

[†] The diastereomers are arbitrarily named as A and B in the assignment of PMR spectrum of the diastereomeric mixture.

(C═O), 975 (C═C). ^{1}H 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×*C*H_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 $C_{31}H_{33}O_4Cl$ (505.023) C: 73.72%, H: 6.59%. Found C: 73.97%, H: 7.05%.

4.4. General procedure for formation of compounds 9 and 10

To a solution of **7** (1 mmol) in dry methanol (5 mL) was added the respective amine (2 mmol) and stirred for the time specified in Table 1. On completion of the reaction, volatiles were removed in vacuo and the crude reaction product was chromatographed over basic alumina to yield pure **9** and **10**.

4.4.1. (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 (9). 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 vapours 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). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.69 (bs, 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, 2×CH_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) δ 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 $C_{30}H_{37}O_5N$ (491.598) C: 73.29%, H: 7.59%, N: 2.85%. Found C: 73.49%, H: 8.16%, N: 2.67%.

4.4.2. (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 (10). 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 vapours used as developing agent). $[\alpha]_D$=+2° (*c*=0.15, methanol). IR (neat, cm^{-1}) 1663 (C═0), 1216 (tert. amine), 756 (aromatic). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.99 (t, $J_{2'',1''}$=7 Hz, 6H, H-2″), 2.08 (s, 3H, CO*C*H_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 (CO*C*H_3), 26.49 (C-1), 46.46 (C-1″), 48.02 (C-1′), 68.29 (C-9), 71.24, 73.24 (2×*C*H_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 (*C*OCH$_3$), 200.12 (C-2). FAB MS *m*/*z* 494 $[M+1]^+$, 386 $[M-OBn]^+$. Elemental analysis calculated for $C_{30}H_{39}O_5N$ (493.614) C: 72.99%, H: 7.96%, N: 2.84%. Found C: 73.25%, H: 8.35%, N: 2.75%.

4.4.3. (3*E*,5*E*)-8-*O*-Acetyl-7,9-di-*O*-benzyl-1,3,4,5,6-pentadeoxy-3-methyl-D-*threo*-non-3,5-diene-2-ulose (11). To a stirred solution of compound **7** (300 mg, 0.66 mmol) in dry toluene (10 mL) was added tri-*n*-butyltin hydride (0.25 mL, 0.93 mmol) and 1,1′-azobis (cyclohexane carbonitrile) (25 mg, 0.11 mmol) at 110°C. The reaction was continued at the same temperature for 45 min. On completion of reaction, the reaction vessel was cooled and saturated solution of KF (25 mL) was added and the reaction mixture was stirred for 18 h. The insoluble matter was filtered off and the organic layer was separated from the filtrate, washed with brine and dried over Na_2SO_4. Evaporation of the solvent in vacuo yielded crude reaction product which was chromatographed over silica gel (hexane–ethylacetate=17:3, v/v) to furnish compound **11** as colourless oil (50.5%). R_f 0.58 (hexane–ethylacetate=7:3, v/v). $[\alpha]_D$=−2.6° (*c*=0.16, methanol). IR (neat, cm^{-1}) 1737 (ester, C═O), 1661 (C═O). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.87 (s, 3H, H-1′), 2.09 (s, 3H, COCH_3), 2.35 (s, 3H, H-1), 3.58 (dd, $J_{9a,8}$=5.5 Hz and $J_{9a,9b}$=10.4 Hz, 1H, H-9a), 3.67 (dd, $J_{9b,8}$=4.7, 10.4 Hz, 1H, H-9b), 4.26 (t, $J_{7,6}$=$J_{7,8}$=5.9 Hz, 1H, H-7), 4.43 (d, J_{gem}=12.1 Hz, 2H, CH_2Ph), 4.53 (d, J_{gem}=12.1 Hz, 1H, CH_2Ph), 4.64 (d, J_{gem}=11.9 Hz, 1H, CH_2Ph), 5.17 (q, $J_{8,9a}$=$J_{8,9b}$= $J_{8,7}$= 5.2 Hz, 1H, H-8), 5.98 (dd, $J_{6,7}$=6.8 Hz and $J_{6,5}$=15.1 Hz, 1H, H-6), 6.67 (dd, $J_{5,4}$=10.9 Hz and $J_{5,6}$=15.1 Hz, 1H, H-5), 6.98 (d, $J_{4,5}$=10.6 Hz, 1H, H-4), 7.26–7.30 (m, 10H, aromatic). ^{13}C NMR ($CDCl_3$, 50 Hz) δ 11.57 (C-1′), 21.04 (CO*C*H_3), 25.59 (C-1), 68.29 (C-9), 71.45, 73.00 (2×*C*H_2Ph), 73.64, 77.64 (C-7 and C-8), 127.69, 127.76, 128.39, 129.36 (C-6 and aromatic), 136.91, 137.35, 137.48, 137.76, 137.79 (C-3, C-4, C-5 and aromatic), 170.38 (*C*OCH$_3$), 199.69 (C-2). FAB MS *m*/*z* 423 $[M+1]^+$, 315 $[M-OCH_2Ph]^+$. Elemental analysis calculated for $C_{26}H_{30}O_5.H_2O$ (440.51) C: 70.88%, H: 7.32%. Found C: 71.20%, H: 7.00%.

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