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Stereoselective Synthesis of Olefinated Sugars[1]

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Abstract: The stereoselective synthesis of olefinated sugars at the anomeric center via Wittig reaction of α,β-glycosyl phosphonium tetrafluoroborates, easily prepared from α,β- methoxy glycosides, is described.

Until now various types of C-glycosides and C-nucleosides[2a,b] showing biological activities have been isolated. Therefore during the last years the chemistry of C-glycosides has attracted much attention and the synthesis of C-glycoside analogues of biologically active molecules became of interest.[2c] During the last years we became interested in the synthesis of C-glycosides, C-glycosylaminoacids[3] and especially of sugars which are olefinated at the anomeric center. This type of C-glycosides shows two specifical features. First Lehmann et al. could demonstrate that these C-glycosides are substrates for β-D-galactosidase[4] and α- and β-glucosidases.[5] Next the highly reactive 'enolether' function offers numerous possibilities for transformations and can therefore be regarded as a valuable synthon in the synthesis of various new C-glycosides. To date some syntheses especially for C-methyleneglycosides[2c,6a,b] have been worked out. Recently Chapleur[7] reported on the Wittig olefination of sugar lactones with methoxycarbonyl methyltriphenylphosphonium chloride.

Numerous glycosylphosphonates were prepared by Vasella et al..[8] But as far as we know they have never been used for the construction of C-glycosides. In the formation of spiro acetals Wittig type reactions using α-alkoxy phosphonium salts have been described.[9,10a-c]

Herewith we intend to report on the synthesis of C-glycosides olefinated at the anomeric center by the reaction of sugar phosphonium salts with aldehydes (Scheme 1).

We apply a method elaborated for the preparation of thioallyl-phosphonium-tetrafluoroborates,[11] to synthesize glycosylphosphonium salts starting from α,β-methoxy sugars which easily can be prepared. For example reaction

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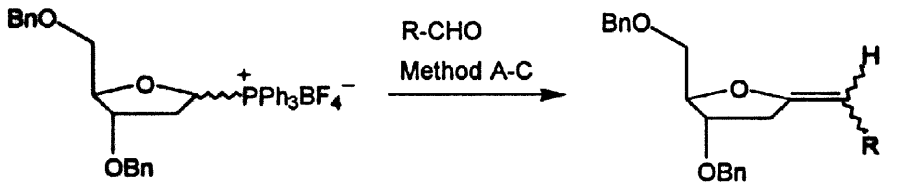
of methyl-3,5-di-*O*-benzyl-2-deoxy-D-ribofuranoside and hydrogentriphenylphosphonium tetrafluoroborate in acetonitrile at reflux for one hour gives the analytically pure phosphonium salt 1 in quantitative yield which can be stored in a freezer without decomposition. The pure β-isomer could be obtained after crystallization and an X-ray analysis was obtained.[12]

Scheme 1



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In Table 1 are summarized some results of the reaction of phosphonium salt 1 with various aromatic aldehydes.[13]

Table 1. Wittig reactions of phosphonium salt 1

Comp.	R	Method	Yield (%)	Ratio *E/Z*	mp (°C) *E*[a]	mp (°C) *Z*[a]
2a	Phenyl-	A	40	40/60	58	-
		B	38	8/92		
		C	58	65/35		
2b	p-Methoxyphenyl-	A	35	70/30	87	-
		B	36	55/45		
		C	56	60/40		
2c	2-Chloro-6-fluorophenyl-	A	25	56/44	-	-
		B	24	53/47		
		C	45	62/38		
2d	p-Methylthiophenyl-	A	29	50/50	100	-
		B	30	52/48		
		C	50	60/40		
2e	p-*N,N*-Dimethylaminophenyl-	A	26	57/43	116	
		B	35	60/40		
		C	50	75/25		
2f	p-Nitrophenyl-	A	30	35/65	-	92
		B	30	5/95		
		C	52	35/65		
2g	o-Nitrophenyl	A	29	41/59	-	-
		B	29	>99		
		C	45	46/54		
2h	p-Chlorophenyl-	A	33	37/63	69	57
		B	30	10/90		
		C	55	51/49		

a) The compounds were crystallized from ethanol.

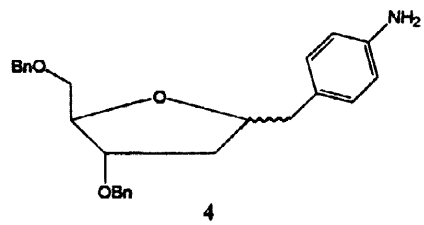
Method A: BuLi/THF -90°C to room temperature; Method B: BuLi/THF/HMPT (10%) -90°C to room temperature; Method C: t-BuOK/THF -90°C to room temperature

With n-BuLi as a base in THF (method A) or THF/HMPT (method B) yields are between 26% and 40%. Apart from cases **2b**, **2c** and **2e** formation of the *Z* isomers is slightly favored. In the cases **2a**, **2f**, **2g**, **2h** this effect can be improved when HMPT is added. Best yields up to 58% are obtained when the reaction is performed with K-*tert*-butylate in THF (method C). Here the *E* isomer is preferred apart from the cases **2f** and **2g**. Most isomers can be preparatively separated by MPLC.[13]

The pure *E* compounds can be completely converted into the *Z* isomers by irradiation at 254 nm in the presence of iodine in 10-15 min. Exception can be observed in the case **2c** and **2g** where the *E* isomer can not be transformed into the *Z* isomer. Also the reaction mixture can be directly irradiated in the presence of iodine to afford only the *Z* compound.[13]

The configuration was determined by the chemical shift of the vinyl proton in ^{1}H NMR spectra. Increment calculations done for olefinic compounds by Pascual, Meier and Simon[14] show that the vinylic protons of the *E* isomers (δ = 5.8-6.0 ppm) are shifted 0.5-0.8 ppm to a lower field than in the case of the *Z* isomers (δ = 5.15-5.3 ppm). Similar results were observed also by Chapleur[7]. A recently obtained X-ray analysis of compound *E*-**2b** gave further proof for the correct structure assignment[15] of the synthesized compounds.

The above mentioned highly reactive compounds **2** represent a group of valuable compounds for further synthetic reactions. For instance hydrogenation of *Z*-**2f** in the presence of palladium on charcoal gives compound **4** in 92 % yield and in a α,β-ratio of 1/1.[13] The hydrogenation step for all compounds will be examined in detail. In conclusion the whole pathway namely Wittig reaction of **1** followed by hydrogenation of **2** presents an effective method in the synthesis of an interesting class of C-nucleosides.



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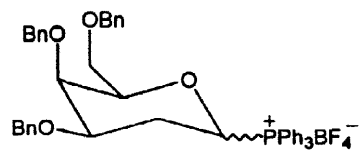
Under the above mentioned reaction conditions up to now we could not succeed in reacting aliphatic aldehydes with the five-membered phosphonium salt **1** in reasonable yields. The exception exists in the Wittig reaction with glyoxylic ester where yields of 34 % and *E/Z* ratios of 75:25 can be obtained.

Six-membered phosphonium salts like **3** can be successfully treated either with aliphatic aldehydes or with aromatic aldehydes. Preliminary results show *E/Z* ratios of 1/1 and yields in an average of 80%.



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Further applications of the above method will be presented in due course. Also various transformations of the highly reactive enolether function just are under investigation and first promising results have been obtained.

EXPERIMENTAL

General

The ^1H and the ^{13}C NMR spectra were taken with a Bruker AC 200 and a Bruker AC 500 spectrometer. The mass spectra including high resolution mass spectra were taken with a Finnigan Model MAT 95 mass spectrometer. The *E/Z* ratios were determined by ^1H NMR spectra. MPLC was performed using Silicagel Latek 60 (20μ), a Latek pump system (P-402, 10 bar) and a Latek variable UV detector VISI 6PRAP. Silica gel 60 (70-230 mesh, Merck) was used for column chromatography and silica gel F_{254} plates (Merck) were used for TLC.

Preparation of the phosphonium salt 1

A solution of 3,4-di-*O*-benzyl-2-deoxy-methyl-D-ribofuranoside (3.28 g, 10 mmol of a mixture α/β 1:1) in absol. acetonitrile (5mL) was treated with hydrogen triphenylphosphonium tetrafluoroborate (3.50 g, 10 mmol) in absol. acetonitrile (5 mL) at reflux. After 1 h, the mixture was concentrated in vacuo. The residue was treated with diethyl ether (10 mL) and the remaining oil was dried in vacuo to give the phosphonium salt **1** as a colourless foam (6.50 g, quant., mixture α/β 7:3). The solid was washed with tetrahydrofuran (25 mL) and crystallization of the insoluble residue (1.95 g) from dichloromethane/toluene gave the pure β-isomer; yield 1.60 g (25 %); mp 96 °C; ^1H NMR (500MHz, $CDCl_3$) δ 2.34 (dddd, 1H, J=5.8, J=11.0, J=13.2, J=17.6, 2-Ha), 2.73 (dddd, 1H, J=1.7, J=4.1, J=5.8, J=13.2, 2-Hb), 3.18 (dd, 1H, J=4.5, J=10.5, 5-Ha), 3.21 (dd, 1H, J=4.4, J=10.5, 5-Hb), 4.16 (ddd, 1H, J=1.7, J=2.3, J=5.8, 3-H), 4.29, 4.33 (2d, 2H, J=12.0, C$\underline{H_2}$Ph-), 4.37 (ddd, 1H, J=2.3, J=4.4, J=4.5, 4-H), 4.51, 4.58 (2d, 2H, J=11.9, C$\underline{H_2}$Ph-), 5.63 (ddd, 1H, J=5.8, J=9.1, J=11.0, 1-H), 7.14 (m, 2H, $\underline{Ph}$-CH_2), 7.25-7.35 (m, 8 H, $\underline{Ph}$-CH_2), 7.60-7.72 (m, 12 H, Ph-), 7.79 (m, 3 H, Ph-); ^{13}C NMR (125 MHz, $CDCl_3$) δ 34.5 (C-2), 69.1 (C-5), 71.6 (C$\underline{H_2}$Ph-), 73.2 (C$\underline{H_2}$Ph-), 73.5 (d, J=61.2, C-1), 79.2 (d, J=9.2, C-3), 86.5 (d, J=7.9, C-4), 115.6 (d, J=85.0, 3 C_αPPh), 127.7-130.6, 134.3, 135.6, 137.4 (Ph); HRMS found 559.23999 (M^+); calc. for $C_{37}H_{36}O_3P$ 559.24021. Further recrystallization from tetrachloromethane/dichloromethane gave satisfactory crystals for an X-ray analysis[12];); Anal. Calcd for $C_{237}H_{36}O_3PBF_4{\cdot}CCl_4$: C, 57.03; H, 4.53, Cl 17.72, Found: C, 57.09; H, 4.52, Cl 17.30.

The tetrahydrofuran extract was concentrated in vacuo to afford the α-isomer as a colourless foam; yield 4.55 g (70 %); ^1H NMR (200MHz, $CDCl_3$) δ 2.16 (m, 2H, 2-H), 3.61 (d, 2H, J=4.9, 5-H), 4.07 (m, 1H, 3-H), 4.29, (s, 2H, C$\underline{H_2}$Ph-), 4.32 (m, J=4.5, 4-H), 4.52, (s, 2H, C$\underline{H_2}$Ph-), 6.06 (d, 1H, J=8.5, 1-H), 7.12 (m, 2H, $\underline{Ph}$-CH_2), 7.20-7.30 (m, 8 H, $\underline{Ph}$-CH_2), 7.60-7.70 (m, 12 H, Ph-), 7.75 (m, 3 H, Ph-); ^{13}C NMR (50 MHz, $CDCl_3$) δ 35.1 (C-2), 69.6 (C-5), 71.9 (C$\underline{H_2}$Ph-), 73.2 (d, J=67.2, C-1), 73.4 (C$\underline{H_2}$Ph-), 79.7 (d, J=6.0, C-3), 85.5 (d, J=7.2, C-4), 116.4 (d, J=84.2, 3 C_αPPh), 127.7-135.7 (Ph-).

Preparation of the enol ethers 2a - 2h

Method A:

To a solution of phosphonium salt **1** (650 mg, 1mmol) in absol. THF (5mL) at -90 °C n-BuLi (625 µL, 1.6 M in hexane, 1mmol)was added over a period of 5 min. The aldehyde (1mmol) in absol. THF (3 mL) was added over a period of 10 min, and the reaction mixture was kept for 1 h at -90 °C and then allowed to come to room temperature overnight. After concentration in vacuo the solution of the residue was washed with water, dried ($MgSO_4$), evaporated and filtrated on silica gel (eluent: cyclohexane/dichloromethane 1:1, containing 0.1 % triethylamine). E/Z ratios (see Table 1) were determined from the crude products. Separation and purification of the E/Z isomers could be afforded by MPLC on silica gel (eluent: cyclohexane/dichloromethane 9:1 - 8:2, containing 0.1 % triethylamine to afford the products **2a-2h**.

Method B:

The phosphonium salt **1** (650 mg, 1mmol) in absol. THF (5 mL) and HMPT (0.8 mL) at -90 °C was treated in the same manner as described above.

Method C:

To a solution of phosphonium salt **1** (650 mg, 1mmol) and the aldehyde (1 mmol) in absol. THF (7mL) at -90 °C *tert.*BuOK (112 mg, 1 mmol) in absol. THF (2 mL) was added. After stirring for 1h at -90 °C the mixture was allowed to come to room temperature overnight. Work up as described above gave the products **2a-2h**.

E-2,5-*Anhydro*-3-*deoxy*-4,6-*di*-*O*-*benzyl*-1-*phenyl*-D-*ribo*-*hex*-1-*enitol* (*E*-**2a**): mp 58 °C (ethanol); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.93 (ddd, 1H, J=1.8, J=3.0, J=16.6, 3-Ha), 3.08 (ddd, 1H, J=2.2, J=6.5, J=16.6, 3-Hb), 3.56 (dd, 1H, J=4.6, J=11.0, 6-Ha), 3.61 (dd, 1H, J=4.5, J=11.0, 6-Hb), 4.20 (m, 1H, 4-H), 4.45 (m, 1H, 5-H), 4.51 (s, 2H, $C\underline{H}_2$Ph-), 4.55 (s, 2H, $C\underline{H}_2$Ph-), 5.95 (s, 1H, 1-H), 7.14 (d, 2H, J=9.0, Ph-), 7.20-7.40 (m, 13 H, Ph-); ^{13}C NMR (50 MHz, $CDCl_3$) δ 35.0 (C-3), 70.1 (C-6), 71.3 ($\underline{C}H_2$Ph-), 73.7 ($\underline{C}H_2$Ph-), 78.6 (C-4), 83.7 (C-5), 100.6 (C-1), 124.7, 127.1-128.8, 137.3, 137.8 , 157.2 (C-2); MS (FAB) m/z (%) 386 (M^+, 100), 91 (96); HRMS found 386.18791 (M^+); calc. for $C_{26}H_{26}O_3$ 386.18820; Anal. Calcd for $C_{26}H_{26}O_3$: C, 80.80; H, 6.78. Found: C, 81.13; H, 7.29.

Z-2,5-*Anhydro*-3-*deoxy*-4,6-*di*-*O*-*benzyl*-1-*phenyl*-D-*ribo*-*hex*-1-*enitol* (*Z*-**2a**): ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.83 (ddd, 1H, J=0.9, J=3.0, J=16.6, 3-Ha), 3.02 (ddd, 1H, J=1.5, J=6.4, J=16.6, 3-Hb), 3.61 (dd, 1H, J=4.8, J=10.6, 6-Ha), 3.65 (dd, 1H, J=4.4, J=10.6, 6-Hb), 4.17 (m, 1H, 4-H), 4.55 (s, 2H, $C\underline{H}_2$Ph-), 4.56 (s, 2H, $C\underline{H}_2$Ph-), 4.68 (m, 1H, 5-H), 5.22 (s, 1H, 1-H), 7.08 (t, 1H, J=7.3, Ph-), 7.20-7.40 (m, 12 H, Ph-), 7,57 (d, 2H J=9.0, Ph-); ^{13}C NMR (50 MHz, $CDCl_3$) δ 37.2 (C-3), 70.1 (C-6), 71.3 ($\underline{C}H_2$Ph), 73.6 ($\underline{C}H_2$Ph-), 77.5 (C-4), 86.7 (C-5), 98.5 (C-1), 124.8, 127.4-128.6, 136.8, 138.0, 155.7 (C-2); MS (70 eV) m/z (%) 386 (M^+, 36), 91 (100); HRMS found 386.18896 (M^+); calc. for $C_{26}H_{26}O_3$ 386.18820.

E-2,5-*Anhydro*-3-*deoxy*-4,6-*di*-*O*-*benzyl*-1-(4-*methoxyphenyl*)-D-*ribo*-*hex*-1-*enitol* (*E*-**2b**): mp 87 °C (ethanol); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.88 (ddd, 1H, J=1.8, J=3.4, J=16.4, 3-Ha), 3.03 (ddd, 1H, J=1.9, J=6.5, J=16.4, 3-Hb), 3.57 (dd, 1H, J=4.7, J=10.8, 6-Ha), 3.60 (dd, 1H, J=4.3, J=10.8, 6-Hb), 3.78 (s, 3H, $C\underline{H}_3OPh$-), 4.20 (m, 1H, 4-H), 4.44 (m, 1H, 5-H), 4.51 (s, 2H, $C\underline{H}_2Ph$-), 4.55 (s, 2H, $C\underline{H}_2Ph$-), 5.95 (s, 1H, 1-H), 6.82 (d, 2H, J=8.8, $CH_3O\underline{Ph}$-), 7.07 (d, 2H, J=8.8, $CH_3O\underline{Ph}$-), 7.20-7.40 (m, 10 H, Ph-); ^{13}C NMR (50 MHz, $CDCl_3$) δ 34.6 (C-3), 55.2 ($\underline{C}H_3OPh$-), 70.1 (C-6), 71.3 ($\underline{C}H_2Ph$-), 73.6 ($\underline{C}H_2Ph$-), 78.6 (C-4), 83.5 (C-5), 100.0 (C-1), 113,8 ($CH_3O\underline{Ph}$-), 127.4-130.0, 137.9, 138.2 , 155.6 (C-2), 157.1 ($CH_3O\underline{Ph}$-); MS (70 eV) m/z (%) 416 (M^+, 50), 308 (19), 202 (18), 187 (20), 121 (60);HRMS found 416.19857 (M^+); calc. for $C_{27}H_{28}O_4$ 416.19876.

Z-2,5-*Anhydro*-3-*deoxy*-4,6-*di*-*O*-*benzyl*-1-(4-*methoxyphenyl*)-D-*ribo*-*hex*-1-*enitol* (*Z*-**2b**): ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.78 (ddd, 1H, J=0.7, J=3.2, J=16.5, 3-Ha), 2.92 (ddd, 1H, J=1.8, J=6.4, J=16.5, 3-Hb), 3.60 (dd, 1H, J=4.7, J=10.6, 6-Ha), 3.64 (dd, 1H, J=4.3, J=10.6, 6-Hb), 3.78 (s, 3H, $C\underline{H}_3OPh$-), 4.13 (m, 1H, 4-H), 4.51 (s, 2H, $C\underline{H}_2Ph$-), 4.53 (s, 2H, $C\underline{H}_2Ph$-), 4.68 (m, 1H, 5-H), 5.17 (s, 1H, 1-H), 7.07 (d, 2H, J=8.8, $CH_3O\underline{Ph}$-), 7.20-7.40 (m, 10 H, Ph-), 7.48 (d, 2H, J=8.8, $CH_3O\underline{Ph}$-); ^{13}C NMR (50 MHz, $CDCl_3$) δ 36.8 (C-3), 55.1 ($\underline{C}H_3OPh$-), 70.1 (C-6), 71.1 ($\underline{C}H_2Ph$-), 73.4 ($\underline{C}H_2Ph$-), 77.5 (C-4), 86.2 (C-5), 97.8 (C-1), 113,5 ($CH_3O\underline{Ph}$-), 124.7-128.4, 137.7, 138.0, 153.8 (C-2), 156.9 ($CH_3O\underline{Ph}$-); HRMS found 416.19853 (M^+); calc. for $C_{27}H_{28}O_4$ 416.19876.

E-2,5-*Anhydro*-3-*deoxy*-4,6-*di*-*O*-*benzyl*-1-(2-*chloro*-6-*fluoroxyphenyl*)-D-*ribo*-*hex*-1-*enitol*: *E/Z* mixture could not be separated by MPLC. Analytical data are determined from the mixture. (*E*-**2c**): ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.63 (dq, 1H, J=1.8, J=16.8, 3-Ha), 2.85 (dq, 1H, J=1.8, J=16.8, 3-Hb), 3.56 (dd, 1H, J=4.1, J=10.7, 6-Ha), 3.61 (dd, 1H, J=4.3, J=10.7, 6-Hb), 4.17 (m, 1H, 4-H), 4.54 (m, 5H, 5-H + 2 $C\underline{H}_2Ph$-), 5.81 (s, 1H, 1-H), 7.00-7.60 (m, 13 H, Ph-); ^{13}C NMR (50 MHz, $CDCl_3$) δ 34.7 (d, $J_{C\text{-}F}$=8.3, C-3), 69.9 (C-6), 71.1 ($\underline{C}H_2Ph$-), 73.5 ($\underline{C}H_2Ph$-), 78.2 (C-4), 85.1 (C-5), 90.6 (C-1), 113,9 (d, $J_{C\text{-}F}$=23.8), 124.9, 127.6 - 128.9, 137.7, 138.0, 159.7 (d, J=253), 160.3 (C-2);

Z-2,5-*Anhydro*-3-*deoxy*-4,6-*di*-*O*-*benzyl*-1-(2-*chloro*-6-*fluoroxyphenyl*)-D-*ribo*-*hex*-1-*enitol* (*Z*-**2c**): ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.86 (ddd, 1H, J=1.8, J=2.7, J=16.7, 3-Ha), 2.96 (ddd, 1H, J=1.5, J=6.5, J=16.7, 3-Hb), 3.62 (dd, 1H, J=5.0, J=10.7, 6-Ha), 3.67 (dd, 1H, J=5.0, J=10.7, 6-Hb), 4.20 (m, 1H, 4-H), 4.54 (m, 5H, 5-H + 2 $C\underline{H}_2Ph$-), 5.17 (s, 1H, 1-H), 7.00-7.60 (m, 13 H, Ph-); ^{13}C NMR (50 MHz, $CDCl_3$) δ 36.4 (C-3), 69.9 (C-6), 71.1 ($\underline{C}H_2Ph$-), 73.5 ($\underline{C}H_2Ph$-), 77.9(C-4), 86.3 (C-5), 87.7 (C-1), 113.8 (d $J_{C\text{-}F}$=23.3), 124.5, 127.6-128.9, 135.1, 137.5, 137.8, 158.0 (C-2), 159.7 (d, J=253); MS (70 eV) m/z (%) 438 (M^+, 1), 330 (16), 224 (39), 108 (20), 91 (57), 81 (100); Anal. Calcd for $C_{26}H_{24}ClFO_3$: C, 71.15; H, 5.51, Cl 8.08. Found: C, 70.77; H, 5.44, Cl 8.03.

E-2,5-*Anhydro*-3-*deoxy*-4,6-*di*-*O*-*benzyl*-1-(4-*methylthiophenyl*)-D-*ribo*-*hex*-1-*enitol* (*E*-**2d**): mp 100 °C (ethanol); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.46 (s, 3H, $C\underline{H}_3SPh$-), 2.90 (ddd, 1H, J=1.8, J=3.3, J=16.5, 3-Ha), 3.06 (ddd, 1H, J=2.1, J=6.5, J=16.5, 3-Hb), 3.57 (dd, 1H, J=4.6, J=10.8, 6-Ha), 3.60 (dd, 1H, J=4.3, J=10.8, 6-Hb), 4.21 (m, 1H, 4-H), 4.45 (m, 1H, 5-H), 4.52 (s, 2H, $C\underline{H}_2Ph$-), 4.55 (s, 2H, $C\underline{H}_2Ph$-), 5.95 (s, 1H, 1-H), 7.07 (d, 2H, J=8.4, $CH_3S\underline{Ph}$-), 7.19 (d, 2H, J=8.4, $CH_3S\underline{Ph}$-), 7.20-7.40 (m, 10 H, Ph-); ^{13}C NMR (50 MHz, $CDCl_3$) δ 16.3 ($\underline{C}H_3SPh$-), 34.9 (C-3), 69.9 (C-6), 71.2 ($\underline{C}H_2Ph$-), 73.5 ($\underline{C}H_2Ph$-), 78.5 (C-4), 83.6 (C-5), 99.9 (C-1), 127.1-129.8, 133.5, 134.0, 137.5, 137.8, 157.0 (C-2); MS (FAB) m/z (%) 432 (M^+, 1), 323 (28), 216 (17), 108 (100), 91 (60);HRMS found 432.17519 (M^+); calc. for $C_{27}H_{28}O_3S$ 432.17592; Anal. Calcd for $C_{27}H_{28}O_3S$: C, 74.97; H, 6.52. Found: C, 74.50; H, 6.49.

Z-2,5-*Anhydro*-3-*deoxy*-4,6-*di*-*O*-*benzyl*-1-(4-*methylthiophenyl*)-D-*ribo*-*hex*-1-*enitol* (*Z*-**2d**): ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.44 (s, 3H, $C\underline{H}_3SPh$-), 2.80 (ddd, 1H, J=0.7, J=3.2, J=16.5, 3-Ha), 3.00 (ddd, 1H, J=1.4, J=6.3, J=16.5, 3-Hb), 3.59 (dd, 1H, J=4.7, J=10.6, 6-Ha), 3.63 (dd, 1H, J=4.3, J=10.6, 6-Hb), 4.16 (m, 1H, 4-H), 4.53 (s, 2H, $C\underline{H}_2Ph$-), 4.54 (s, 2H, $C\underline{H}_2Ph$-), 4.66 (m, 1H, 5-H), 5.19 (s, 1H, 1-H), 7.17 (d, 2H, J=8.4, $CH_3S\underline{Ph}$-), 7.20-7.40 (m, 10 H, Ph-), 7.47 (d, 2H, J=8.4, $CH_3S\underline{Ph}$-); ^{13}C NMR (50 MHz, $CDCl_3$) δ 16.4 ($\underline{C}H_3SPh$-), 37.0 (C-3), 69.9 (C-6), 71.1 ($\underline{C}H_2Ph$-), 73.3 ($\underline{C}H_2Ph$-), 77.3 (C-4), 86.5 (C-5), 97.7 (C-1), 127.0-129.8, 133.6, 134.0, 137.5, 137.7, 155.6 (C-2); MS m/z (%) 432 (M^+, 2), 323 (20), 108 (70), 91 (100); HRMS found 432.17462 (M^+); calc. for $C_{27}H_{28}O_3S$ 432.17592;

E-2,5-*Anhydro*-3-*deoxy*-4,6-*di*-*O*-*benzyl*-1-(4-*N,N*-*dimethylaminophenyl*)-D-*ribo*-*hex*-1-*enitol* (*E*-**2e**): mp 116 °C (ethanol); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.89 (ddd, 1H, J=1.8, J=3.7, J=16.5, 3-Ha), 2.90 (s, 6H, $(C\underline{H}_3)_2NPh$-), 3.04 (ddd, 1H, J=2.1, J=6.6, J=16.5, 3-Hb), 3.55 (dd, 1H, J=4.7, J=10.6, 6-Ha), 3.58 (dd, 1H, J=4.6, J=10.6, 6-Hb), 4.17 (m, 1H, 4-H), 4.40 (m, 1H, 5-H), 4.48, 4.52 (AB, 2H, J=11.8, $C\underline{H}_2Ph$-), 4.54 (s, 2H, $C\underline{H}_2Ph$-), 5.93 (s, 1H, 1-H), 6.68 (d, 2H, J=8.8, $(CH_3)_2N\underline{Ph}$-), 7.04 (d, 2H, J=8.4, $(CH_3)_2N\underline{Ph}$-), 7.20-7.40 (m, 10 H, Ph-); ^{13}C NMR (50 MHz, $CDCl_3$) δ 34.4 (C-3), 40.6 ($\underline{C}H_3)_2NPh$-), 70.0 (C-6), 71.1 ($\underline{C}H_2Ph$-), 73.5 ($\underline{C}H_2Ph$-), 78.6 (C-4), 83.1 (C-5), 100.2 (C-1), 112.7 $(CH_3)_2N\underline{Ph}$-), 125.8, 127.5-128.9, 137.5, 137.8, 148.0 $(CH_3)_2N\underline{Ph}$-), 157.0 (C-2); MS (70 eV) m/z (%) 429 (M^+, 100), 200 (5), 134 (5), 91 (15); HRMS found 429.23027 (M^+); calc. for $C_{28}H_{31}NO_3$ 429.23039; Anal. Calcd for $C_{28}H_{31}NO_3$: C, 78.29; H, 7.27; N, 3.26. Found: C, 78.07; H, 7.29; N, 3.26.

Z-2,5-*Anhydro*-3-*deoxy*-4,6-*di*-*O*-*benzyl*-1-(4-*N,N*-*dimethylaminophenyl*)-D-*ribo*-*hex*-1-*enitol* *E/Z* mixture could not be separated by MPLC. Analytical data are determined from the mixture. (*Z*-**2e**): ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.78 (ddd, 1H, J=1.0, J=3.4, J=16.0, 3-Ha), 2.91 (s, 6H, $(C\underline{H}_3)_2NPh$-), 3.00 (ddd, 1H, J=2.1, J=6.3, J=16.0, 3-Hb), 3.58 (dd, 1H, J=5.1, J=10.8, 6-Ha), 3.63 (dd, 1H, J=4.6, J=10.8, 6-Hb), 4.13 (m, 1H, 4-H), 4.50, 4.54 (AB, 2H, J=11.8, $C\underline{H}_2Ph$-), 4.54 (s, 2H, $C\underline{H}_2Ph$-), 4.61 (m, 1H, 5-H), 5.17 (s, 1H, 1-H), 6.68 (d, 2H, J=8.8,

$(CH_3)_2N\underline{Ph}$-), 7.20-7.40 (m, 10 H, Ph-), 7.44 (d, 2H, J=8.4, $(CH_3)_2N\underline{Ph}$-); ^{13}C NMR (50 MHz, $CDCl_3$) δ 36.6 (C-3), 40.7 ($\underline{C}H_3)_2NPh$-), 70.0 (C-6), 71.0 ($\underline{C}H_2Ph$-), 73.3 ($\underline{C}H_2Ph$-), 77.4 (C-4), 85.8 (C-5), 98.1 (C-1), 112.7 $(CH_3)_2N\underline{Ph}$-), 125.8, 127.5-128.9, 137.5, 137.8, 148.0 $(CH_3)_2N\underline{Ph}$-), 152.5 (C-2); HRMS found 429.23038 (M^+); calc. for $C_{28}H_{31}NO_3$ 429.23039.

E-2,5-*Anhydro*-3-*deoxy*-4,6-*di*-*O*-*benzyl*-1-(4-*nitrophenyl*)-D-*ribo*-*hex*-1-*enitol* E/Z mixture could not be separated by MPLC. Analytical data are determined from the mixture. (*E*-**2f**): ^1H NMR (200 MHz, $CDCl_3$) δ 2.97 (ddd, 1H, J=2.2, J=3.2, J=16.8, 3-Ha), 3.15 (ddd, 1H, J=2.1, J=6.5, J=16.8, 3-Hb), 3.60 (dd, 1H, J=4.3, J=11.0, 6-Ha), 3.68 (dd, 1H, J=4.3, J=11.0, 6-Hb), 4.30 (m, 1H, 4-H), 4.52 (m, 1H, 5-H), 4.54 (s, 2H, $C\underline{H}_2Ph$-), 4.55 (s, 2H, $C\underline{H}_2Ph$-), 6.04 (s, 1H, 1-H), 7.22 (d, 2H, J=9.0, (p-$O_2N\underline{Ph}$-), 7.20-7.40 (m, 10 H, Ph-), 8.11 (d, 2H, J=9.0, (p-$O_2N\underline{Ph}$-); ^{13}C NMR (50 MHz, $CDCl_3$) δ 34.6 (C-3), 69.7 (C-6), 71.3 ($\underline{C}H_2Ph$-), 73.5 ($\underline{C}H_2Ph$-), 78.3 (C-4), 84.6 (C-5), 99.5 (C-1), 123.6 (p-$O_2N\underline{Ph}$-), 127.1-128.4, 137.2, 137.5, 144.3 and 144.6 (p-$O_2N\underline{Ph}$-), 161.9 (C-2).

Z-2,5-*Anhydro*-3-*deoxy*-4,6-*di*-*O*-*benzyl*-1-(4-*nitrophenyl*)-D-*ribo*-*hex*-1-*enitol* (*Z*-**2f**): mp 92 °C (ethanol); ^1H NMR (200 MHz, $CDCl_3$) δ 2.86 (dd, 1H, J=2.4,J=17.0, 3-Ha), 3.10 (ddd, 1H, J=1.1, J=6.3, J=17.0, 3-Hb), 3.63 (dd, 1H, J=4.0, J=10.2, 6-Ha), 3.68 (dd, 1H, J=4.0, J=10.2, 6-Hb), 4.23 (m, 1H, 4-H), 4.54 (s, 2H, $C\underline{H}_2Ph$-), 4.55 (s, 2H, $C\underline{H}_2Ph$-), 4.78 (m, 1H, 5-H), 5.32 (s, 1H, 1-H), 7.20-7.40 (m, 10 H, Ph-), 7.63 (d, 2H, J=9.0, (p-$O_2N\underline{Ph}$-), 8.11 (d, 2H, J=9.0, (p-$O_2N\underline{Ph}$-); ^{13}C NMR (50 MHz, $CDCl_3$) δ 36.8 (C-3), 69.7 (C-6), 71.1 ($\underline{C}H_2Ph$-), 73.3 ($\underline{C}H_2Ph$-), 77.1 (C-4), 87.8 (C-5), 97.0 (C-1), 123.7 (p-$O_2N\underline{Ph}$-), 127.1-128.3, 137.2, 137.5, 143.8 and 144.2 (p-$O_2N\underline{Ph}$-); 160.7 (C-2); MS (70 eV) m/z (%) 431 (M^+, 36), 217 (32), 108 (37), 91 (100); Anal. Calcd for $C_{26}H_{25}NO_5$: C, 72.37; H, 5.84; N, 3.25. Found: C, 71.87; H, 5.83; N, 3.20.

E-2,5-*Anhydro*-3-*deoxy*-4,6-*di*-*O*-*benzyl*-1-(2-*nitrophenyl*)-D-*ribo*-*hex*-1-*enitol* (*E*-**2g**): ^1H NMR (200 MHz, $CDCl_3$) δ 2.84 (ddd, 1H, J=1.8, J=3.2, J=16.5, 3-Ha), 3.03 (ddd, 1H, J=2.2, J=6.5, J=16.5, 3-Hb), 3.60 (dd, 1H, J=4.2, J=10.9, 6-Ha), 3.65 (dd, 1H, J=4.2, J=10.9, 6-Hb), 4.21 (m, 1H, 4-H), 4.50 (s, 2H, $C\underline{H}_2Ph$-), 4.52 (m, 1H, 5-H), 4.56 (s, 2H, $C\underline{H}_2Ph$-), 6.40 (s, 1H, 1-H), 7.20-7.40 (m, 12 H, Ph-), 7.46 (dt, 1H, J=1.2, J=8.0, (o-$O_2N\underline{Ph}$-), 7.85 (dt, 1H, J=1.2, J=8.0, (o-$O_2N\underline{Ph}$-); ^{13}C NMR (50 MHz, $CDCl_3$) δ 35.0 (C-3), 69.7 (C-6), 71.2 ($\underline{C}H_2Ph$-), 73.5 ($\underline{C}H_2Ph$-), 78.1 (C-4), 84.6 (C-5), 95.4 (C-1), 124.5, 125.4, 127.5-128.3, 129.4, 132.0, 137.3, 137.6, 146.9 (o-$O_2N\underline{Ph}$-); 160.7 (C-2); MS (70 eV) m/z (%) 431 (M^+, 0.4), 215 (7), 108 (19), 91 (100). HRMS found 432.18154 (M^+); calc. for $C_{26}H_{26}NO_5$ 432.18110.

Z-2,5-*Anhydro*-3-*deoxy*-4,6-*di*-*O*-*benzyl*-1-(2-*nitrophenyl*)-D-*ribo*-*hex*-1-*enitol* (*Z*-**2g**): ^1H NMR (200 MHz, $CDCl_3$) δ 2.87 (ddd, 1H, J=1.0, J=2.9, J=17.0, 3-Ha), 3.07 (ddd, 1H, J=1.6, J=6.4, J=17.0, 3-Hb), 3.60 (dd, 1H, J=4.7, J=10.6, 6-Ha), 3.65 (dd, 1H, J=4.3, J=10.6, 6-Hb), 4.18 (m, 1H, 4-H), 4.53 (s, 4H, 2 $C\underline{H}_2Ph$-), 4.69 (m,

1H, 5-H), 5.76 (s, 1H, 1-H), 7.15 (dt, 1H, J=1.2, J=7.7, (o-O_2NPh-), 7.20-7.40 (m, 10 H, Ph-), 7.44 (dt, 1H, J=1.2, J=7.7, (o-O_2NPh-), 7.76 (dt, 1H, J=1.2, J=8.1, (o-O_2NPh-), 8.16 (dt, 1H, J=1.2, J=8.1, (o-O_2NPh-); ^{13}C NMR (50 MHz, $CDCl_3$) δ 37.7 (C-3), 69.7 (C-6), 71.2 (CH_2Ph-), 73.4 (CH_2Ph-), 77.2 (C-4), 87.5 (C-5), 91.9 (C-1), 124.0, 124.8, 127.1-128.3, 130.2, 130.38, 131.7, 137.3, 137.5, 146.9 (o-O_2NPh-); 159.9 (C-2); MS (70 eV) m/z (%) 431 (M^+, 0.2), 215 (9), 108 (37), 91 (100); Anal. Calcd for $C_{26}H_{25}NO_5$: C, 72.37; H, 5.84; N, 3.25. Found: C, 72.29; H, 5.83; N, 3.17.

E-2,5-*Anhydro*-3-*deoxy*-4,6-*di*-*O*-*benzyl*-1-(4-*chlorophenyl*)-D-*ribo*-*hex*-1-*enitol* (*E*-**2h**): mp 69 °C (ethanol); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.87 (ddd, 1H, J=1.9, J=3.2, J=16.5, 3-Ha), 3.04 (ddd, 1H, J=2.2, J=6.4, J=16.5, 3-Hb), 3.56 (dd, 1H, J=4.6, J=11.0, 6-Ha), 3.60 (dd, 1H, J=4.4, J=11.0, 6-Hb), 4.21 (m, 1H, 4-H), 4.46 (m, 1H, 5-H), 4.51 (s, 2H, CH_2Ph-), 4.54 (s, 2H, CH_2Ph-), 5.93 (s, 1H, 1-H), 7.05 (d, 2H, J=8.6, (p-ClPh-), 7.22 (d, 2H, J=8.6, (p-ClPh-), 7.20-7.40 (m, 10 H, Ph-); ^{13}C NMR (50 MHz, $CDCl_3$) δ 35.0 (C-3), 69.9 (C-6), 71.3 (CH_2Ph-), 73.6 (CH_2Ph-), 78.5 (C-4), 83.8 (C-5), 99.5 (C-1), 127.5-128.3, 129.4, 135.3, 137.6, 137.8, 157.8 (C-2). MS (70 eV) m/z (%) 420 (M^+, 17), 312 (16), 206 (34), 108 (33), 91 (100); Anal. Calcd for $C_{26}H_{25}ClO_3$: C, 74.19; H, 5.99; Cl, 8.42. Found: C, 73.65; H, 5.99; N, 8.45.

Z-2,5-*Anhydro*-3-*deoxy*-4,6-*di*-*O*-*benzyl*-1-(4-*chlorophenyl*)-D-*ribo*-*hex*-1-*enitol* (*Z*-**2h**): mp 57 °C (ethanol); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.84 (ddd, 1H, J=0.9, J=3.0, J=17.5, 3-Ha), 2.98 (ddd, 1H, J=1.6, J=6.4, J=17.5, 3-Hb), 3.60 (dd, 1H, J=4.7, J=10.6, 6-Ha), 3.64 (dd, 1H, J=4.3, J=10.6, 6-Hb), 4.17 (m, 1H, 4-H), 4.54 (s, 4H, 2 CH_2Ph-), 4.68 (m, 1H, 5-H), 5.17 (s, 1H, 1-H), 7.21 (d, 2H, J=8.6, (p-ClPh-), 7.20-7.40 (m, 10 H, Ph-), 7.47 (d, 2H, J=8.6, (p-ClPh-),; ^{13}C NMR (50 MHz, $CDCl_3$) δ 37.2 (C-3), 70.0 (C-6), 71.2 (CH_2Ph-), 73.4 (CH_2Ph-), 77.5 (C-4), 86.8 (C-5), 97.3 (C-1), 127.6-128.4, 129.9, 135.3, 137.7, 137.9, 156.4 (C-2). MS (20 eV) m/z (%) 420 (M^+, 100), 312 (25), 206 (59), 108 (59), 91 (46); HRMS found 420.14903 (M^+); calc. for $C_{26}H_{25}ClO_3$ 420.14922.

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