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An Efficient Procedure for the Regioselective Monoprotection of 1,2-Diols

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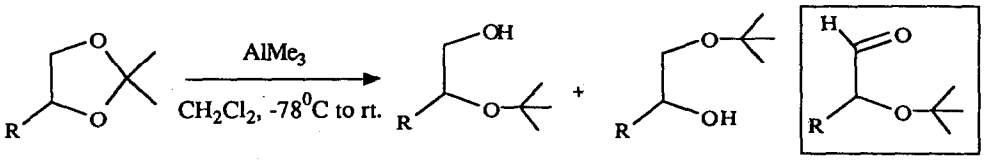
Abstract Nucleophilic ring opening of isopropylidene ketals by trimethylaluminum is described. This reagent offers a new method for selective monoprotection of 1,2-diols. The regioselectivity of this reaction was studied with simple diols and with carbohydrates.

Selective protection of a specific hydroxy group in a polyol is an important tool in organic synthesis [1]. One approach to the difficult problem of efficient monofunctionalization of diols containing similiar or equivalent hydroxy groups is the reductive [2] or oxidative [3] cleavage of acetals or ketals. A number of reagents have been developed, some of which have been routinely used in carbohydrate chemistry [4].

In connection with ongoing research, we had occasion to study the reaction between trimethylaluminum and ketals [5]. We disclose here an efficient method for the regioselective monoprotection of 1,2-diols (Scheme 1).



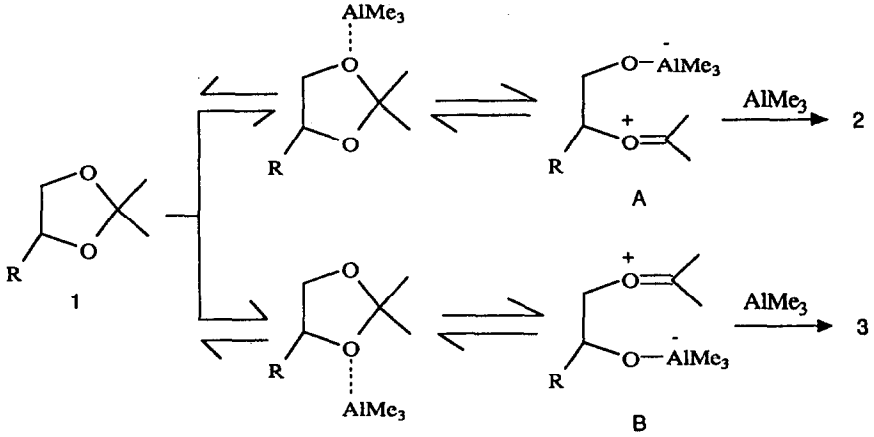
1 2 3 4

a R=Ph	yield:	2a R=Ph 74%	3a R=Ph 10%
b R=n-C_4H_9		2b R=n-C_4H_9 83%	—
c R=C_2H_5		2c R=C_2H_5 86%	—

Scheme 1

When isopropylidene ketals **1**, prepared easily from the corresponding diol, were treated with 3 eq of trimethylaluminum in dichloromethane, hydroxy tert.-butyl ethers **2** were obtained in good to excellent yield. The regiochemistry was determined by oxidation to the corrsponding aldehyde **4**. Only in the case of **1a**, was another regioisomer **3a** isolated. It is important to note that the more sterically demanding secondary alcohol was selectively protected as the tert.-butyl ether in this transformation.

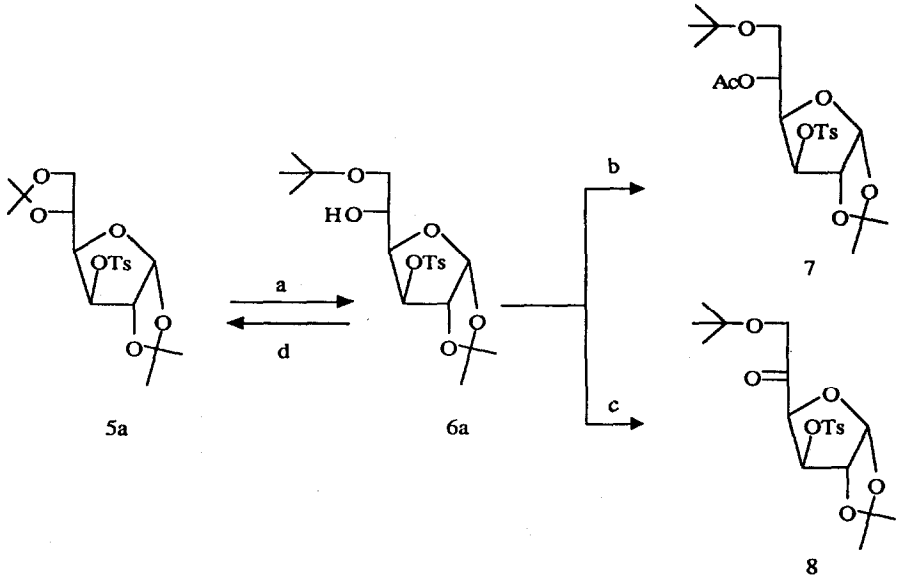
The mechanism of the reaction probably involves initial rapid and reversible association of the Lewis acid with the ketal oxygen, followed by the slow, rate-controlling cleavage of the ring to form the oxonium ion. Addition of a nucleophilic methyl to this intermediate gives the observed products on hydrolysis (Scheme 2). Intermediate **A** has the electron donating group R closer to the incipient oxonium ion than in **B**, hence it is more effective in stabilizing the positive charge. In addition, **A** was generated by the coordination of the trimethylaluminum to the less hindered oxygen atom [6], and its formation should be preferred due to steric and polar effects. Intermolecular delivery of methyl group was demonstrated as more than 2 eq of trimethylaluminum were needed to complete the reaction. The non-selective directing ability of a phenyl group has also been observed in a related system [7]. Solvent effects were also briefly studied; it was found that the reaction is more facile in dichloromethane than in other non-polar solvents, e.g. hexane and toluene. However, no change in regioselectivity was observed. The reaction did not occur in ether which is the solvent of choice in the reductive cleavage of ketals by LAH-$AlCl_3$.



Scheme 2

Since differential protection of the hydroxy group in a polyol is a more serious challenge, we turned our attention to carbohydrates. Treatment of 1,2:5,6-di-*O*-isopropylidene-3-*p*-toluenesulfonyl-*D*-glucofuranose **5a** with trimethylaluminum under the identical conditions as for **1** gave an essentially quantitative yield of the corresponding 6-*O*-tert.-butyl ether **6a** (Scheme 3). Elucidation of the structure in this case was made by a combination of chemical and spectroscopic evidence. First, the observation of the anomeric proton (δ=5.89ppm, d, J=3.70 Hz) in the ^1H NMR spectrum showed that the furanose ring was not opened. When the product **6a** was submitted to acidic conditions (TsOH, acetone, reflux), **5a** was regenerated via the deprotection of the-tert.-butyl ether and the isopropylidenation of the resulting diol. Thus, the basic structure of the molecule was unchanged. The ^{13}C and ^1H NMR spectra confirmed the presence of a furanose ring, one tert.-butyl group and

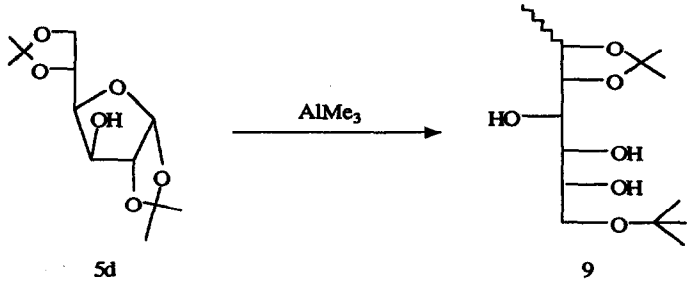
one isopropylidene ring. Four possible regioisomers should be taken into consideration as far as the regio- and chemo-selectivity are concerned. The location of the tert.-butyl group was determinated by careful examination of the 2D ^1H-^1H COSY spectra. The correlation found between the H-5 proton (δ=3.78ppm, m) and the hydroxyl proton (δ=2.43-2.45ppm br.s) indicated that the hydroxyl group was attached to C-5. In order to confirm this observation, the product **6a** was transformed into the acetyl derivative **7** under standard conditions (Ac_2O-Py.-DMAP). The low field shift of the H-5 proton in compound **7** (δ=4.92ppm), and the splitting pattern (ddd, J=9.52, 3.34 and 2.28 Hz) are in agreement with the deshielding effect of an acetyl group. Furthermore, when **6a** was submitted to a Swern oxidation[8], ketone **8** and not an aldehyde was obtained. We observed the low field shift of the H-6 protons which appeared now as an AB system (δ=4.05, 4.18ppm, J=18.5 Hz). The above mentioned structural information confirmed the proposed structure **6a**.



reagents and conditions: a) $AlMe_3$, CH_2Cl_2, -78°C, 4hrs, rt. 15hrs
b) PhCOCl, Py. DMAP, rt. c) Swern oxidation
d) Acetone, pTsOH, rt.

Scheme 3

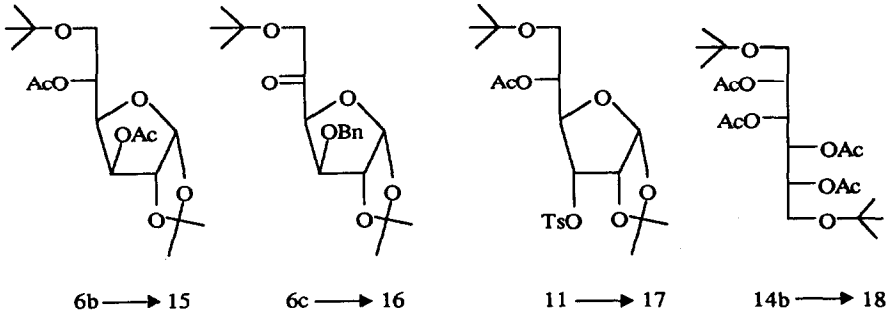
It is necessary to protect the 3-hydroxy group. The reaction of 1,2:5,6-di-*O*-isopropylidene-*D*-glucofuranose **5d** (R=H) with trimethylaluminum afforded a complex mixture. The disapperance of the anomeric proton in the ^1H NMR spectrum indicated that the furanose ring was opened in this case. One major compound isolated had physical data (^1H NMR, ^{13}C NMR, MS, IR and microanalysis) corresponding to the 6-*O*-tert.-butyl-1,2-*O*-isopropylidene-1-methyl-*D*-glucitol **9** (Scheme 4). No effort was made to determine the stereochemistry of the newly created chiral centre.



Scheme 4

The regioselectivity of the reaction is clearly determined by the directing effect of the 3-β-*p*-toluenesulfonyl group in **5a**. However, the acetate **5b** and the benzyl ether **5c** also opened in the same sense in satisfactory yields (Scheme 6). The epimer **10** of **5a**, which was prepared from 1,2:5,6-di-*O*-isopropylidene-D-glucofuranose by sequential oxidation and reduction, followed by tosylation, also opened in the same sense to give **11**. The reaction of the mannitol derivatives **12a**, **12b** and **12c** was then studied. The ditosylate **12a** and diacetate **12b** reacted slowly and gave only moderate yields of products with both ketal groups opened to furnish terminal t-tert-butyl groups. On the other hand, the dibenzyl derivative **12c** afforded the mono-ketal derivative **13c** with poor conversion but good yield.

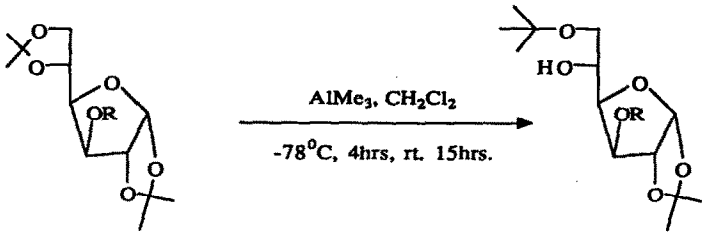
The structures assigned were confirmed by acetylation or oxidation and study of the physical data of the derivatives (Scheme 5). Thus, **6b** gave **15** on acetylation, **11** gave **17** and **14b** gave the tetra-acetate 18. The derivative **6c** afforded the ketone **16** on oxidation.



Scheme 5

One striking feature of this reaction is that the p-toluenesulfonyl group was intact even in the case of 1,2 : 5,6-di-*O*-isopropylidene-3-*p*-toluenesulfonyl-*D*-allo-furanose 10 where nucleophilic displacement of the *p*-toluenesulfonyl group was a sterically favored process. In contrast, we noticed in control experiments that the reaction of simple p-toluenesulfonyl derivatives, e.g., tosylated cyclododecanol, produced mixtures of methylated and elimination products (ratio 1/5).

The reversed regioselectivity between the simple ketals like **1** and the more complex carbohydrate derivatives may be the result of multiple binding sites for the trimethylaluminum. In any case, this new reaction should prove useful in the manipulation of complex carbohydrate structures.

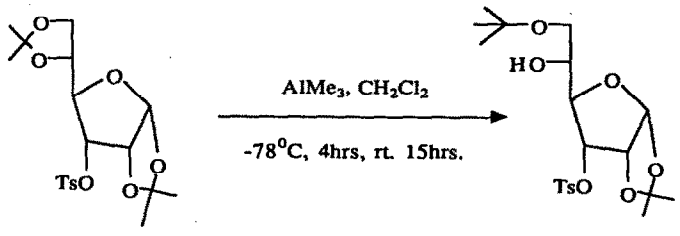


5

5a R=Ts
5b R=Ac
5c R=Bn

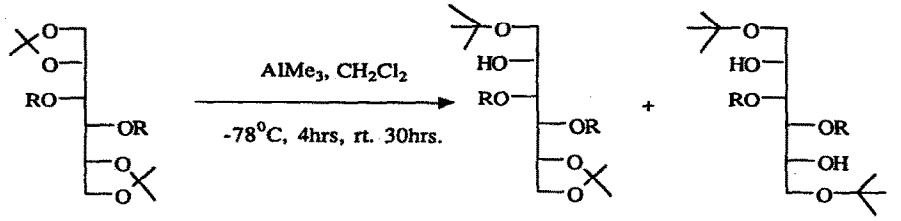
6

6a R=Ts 98%
6b R=H 86%
6c R=Bn 67% 81%[a]



10

11 77.7% 85.8%[a]



12

12a R=Ts
12b R=Ac
12c R=Bn

13

13a R=Ts —
13b R=Ac —
13c R=Bn 55% 92%[a]

14

14a R=Ts 56% 62.4%[a]
14b R=Ac 48%[b]
14c R=Bn 5%

a) Yield based on the reacted starting material b) Isolated as tetraacetate

Scheme 6

Experimental Section

All reactions were performed under an argon atmosphere. Melting points were determined with a Kofler apparatus and were uncorrected. Infrared (IR) spectra were recorded on a Perkin-Elmer spectrometer. ^{1}H NMR spectra were measured on a Varian-200 spectrometer in $CDCl_3$ with tetramethylsilane as internal standard (δ ppm). Splitting patterns were indicated as s (Singlet); d (doublet); t (triplet); q (quartet); m (multiplet); br.s (broad singlet). GC/MS were performed on a Hewlett 5890 Packard series II instruments with DB-5 capillary column. Microanalyses were accomplished at the Atlantic Microlab Inc. Products were purified by flash chromatography on silica gel 60 (230-400 mesh ASTM), Merck Art 9385. Solvents and reagents were purified acoording to standard laboratory techniques.

Ketals **1a-1c** were prepared from the corresponding 1,2-diols according to the literature[10]. Tosylation[11], benzylation [12] and acetylation [13] of 1,2:5,6-di-*O*-isopropylidene-*D*-glucofuranose, 1,2:5,6-di-*O*-isopropylidene-*D*-allofuranose and 1,2:5,6-di-*O*-isopropylidene-*D*-mannitol were carried out under standard conditions. 1,2:5,6-Di-*O*-isopropylidene-*D*-allofuranose was prepared from 1,2:5,6-di-*O*-isopropylidene-*D*-glucofuranose by sequential oxidation and reduction procedures [9].

General Procedure for the Nucleophilic Ring Opening of Isopropylidene Ketals with Trimethylaluminum: 1,2:5,6-Di-*O*-isopropylidene-3-*p*-toluenesulfonyl-*D*-glucofuranose **5a** (1mmol, 414mg) and freshly distilled dichloromethane were introduced under argon to a flame dried flask and cooled to -78°C. Trimethylaluminum (8eq. 2M solution in hexane) was then added dropwise. The reaction mixture was stirred at -78°c for 4hrs and at room temperature for 15hrs. It was then quenched by addition of aq. NH_4Cl. The precipitate was filtered off. The filtrate was extrated with dichloromethane repeatedly. The combined organic layers were washed with brine, dried over anhydrous sodium sulfate and concentrated in vaccuo. This gave the pure 6-*O*-tert-butyl ether **6a** as a colourless oil (422mg, 98%); IR: 3552, 3044, 2972, 1597, 1365, 1176, 1020 cm^{-1} ; ^{1}H NMR δ_H 7.84, 7.35 (4H, dd, J=8.32 Hz), 5.89 (1H, d, J=3.70 Hz), 4.90 (1H, d, J=2.7 Hz), 4.75 (1H, d, J=3.70 Hz), 4.16 (1H, dd, J=9.24, 2.70 Hz), 3.78 (1H, m), 3.56 (1H, dd, J=9.24, 2.82 Hz), 3.36 (1H, dd, J=9.24, 5.80 Hz), 2.43-2.45 (1H, br.s), 2.45 (3H, s), 1.46 (3H, s), 1.29 (3H, s), 1.16 (9H, s); ^{13}C NMR δ_{13C} 145.22, 132.46, 129.77, 128.19, 112.35, 104.82, 82.83, 82.00, 78.52, 73.29, 66.98, 62.67, 27.43, 26.49, 26.26, 21.64; m/z: 415 (M^+-15), 359 (M^+-71), 343 (M^+-87); Anal. Calcd. for $C_{20}H_{30}SO_8$: C, 55.80; H, 7.02. Found: C, 55.55; H, 6.99.

The following products were obtained by this procedure:

2a: Yield: 74%; m.p. 71-72°C (from ether-hexane); IR: 3579, 3028, 2970, 2933, 1601, 1450, 1389, 1189, 1083, 1036 cm^{-1}; ^{1}H NMR δ_H 7.2-7.4 (5H, m), 4.60 (1H, dd, J=7.26, 4.82 Hz), 3.46-3.54 (2H, m), 2.44 (1H, dd, J=8.38, 4.82 Hz), 1.17 (9H, s); ^{13}C NMR δ_{13C} 142.18, 128.12, 127.23, 126.27, 75.10, 74.79, 67.76, 28.71; m/z: 163 (M^+-31), 121 (M^+-73); Anal. Calcd. for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.16; H, 9.31.

3a: Oil; Yield: 10%; IR: 3565, 2969, 2928, 1450, 1363, 1320, 1189, 1077 cm^{-1}; ^{1}H NMR δ_H 7.2-7.5 (5H, m), 4.79 (1H, dt, J=9.02, 2.26 Hz), 3.52 (1H, dd, J=9.02, 2.78 Hz), 3.32(1H, t, J=9.02 Hz), 3.08 (1H,

d, J=2 Hz), 1.21 (9H, s); ^{13}C NMR δ_{13C} 140.41, 128.20, 127.62, 126.09, 73.52, 73.06, 67.72, 27.48; m/z: 194 ($M^{+\cdot}$) 163 ($M^{+\cdot}$-31), 137 ($M^{+\cdot}$-57), 121 ($M^{+\cdot}$-73).

2b: Oil; Yield: 83%; IR: 3569, 3063, 2961, 2933, 1458, 1389, 1190, 1060 cm^{-1}; ^1H NMR δ_H 3.30-3.55 (3H, m), 2.3 (1H, br.s), 1.20-1.55 (6H, m), 1.17 (9H, s), 0.85 (3H, t, J=6.02 Hz); ^{13}C NMR δ_{13C} 73.73, 71.60, 65.13, 33.21, 28.62, 27.70, 22.86, 13.92; m/z: 174 ($M^{+\cdot}$), 159 ($M^{+\cdot}$-15), 143 ($M^{+\cdot}$-31); Anal. Calcd. for $C_{10}H_{22}O_2$: C, 68.92; H, 12.72. Found: C, 69.01; H, 12.70.

2c: Oil; Yield: 86%; IR: 3571, 3054, 2975, 2879, 1420, 1390, 1190, 1046, 1017 cm^{-1}; ^1H NMR δ_H 3.36-3.56 (3H, m), 2.29 (1H, br.s), 1.4-1.6 (2H, m), 1.18 (9H, s), 0.84 (3H, t, J=7.5 Hz); ^{13}C NMR δ_{13C} 73.71, 72.69, 64.67, 28.47, 25.98, 9.57; m/z: 146 ($M^{+\cdot}$), 115 ($M^{+\cdot}$-31).

6b: Yield: 86%; m.p. 84-85°C (from ether-hexane); IR: 3567, 3052, 2984, 1420, 1258, 1161, 1072, 1016 cm^{-1}; ^1H NMR δ_H 5.94 (1H, d, J=3.90 Hz), 4.51 (1H, d, J=3.66 Hz), 4.33 (1H, d, J=2.12 Hz), 4.00-4.15 (m, 2H), 3.40-3.65 (2H, m), 3.1-3.4 (2H, br.s), 1.47 (3H, s), 1.30 (3H, s), 1.21 (9H, s); ^{13}C NMR δ_{13C} 111.59, 104.92, 85.08, 80.20, 75.67, 73.69, 69.45, 62.64, 27.25, 26.62, 25.99; m/z: 277 ($M^{+\cdot}$+1), 261 ($M^{+\cdot}$-15), 247 ($M^{+\cdot}$+1-30), 189 ($M^{+\cdot}$-87). Anal. Calcd. for $C_{13}H_{24}O_6$: C, 56.51; H, 8.75. Found: C, 56.44; H, 8.69.

6c: Oil; Yield: 81%; IR: 3564, 3036, 2973, 2938, 1364, 1212, 1193, 1075 cm^{-1}; ^1H NMR δ_H 7.30-7.40 (5H, m), 5.90 (1H, d, J=3.76 Hz), 4.65, 4.66 (2H, dd, J=13 Hz), 4.57 (1H, d, J=3.76 Hz), 4.00-4.15 (3H, m), 3.61 (1H, dd, J=9.22, 3.06 Hz), 3.40 (1H, dd, J=9.22, 5.68 Hz), 1.47 (3H, s), 1.30 (3H, s). 1.18 (9H, s); ^{13}C NMR δ_{13C} 137.53, 128.42, 127.84, 127.72, 111.61, 105.06, 82.35, 81.89, 80.03, 73.20, 72.33, 67.86, 63.42, 27.51, 26.72, 26.26; m/z: 309 ($M^{+\cdot}$-57), 253 ($M^{+\cdot}$-113). Anal. Calcd. for $C_{20}H_{30}O_6$: C, 65.55; H, 8.25. Found: C, 65.69; H, 8.27.

9: Yield: 43%; m.p. 73-74°C (from hexane); IR: 3543, 3047, 2973, 2936, 1369, 1247, 1147, 1063 cm^{-1}; ^1H NMR δ_H 3.99-4.22 (3H, m), 3.89 (1H, dd, J=6.46, 3.50 Hz), 3.72 (1H, d, J=2.56 Hz), 3.56-3.68 (2H, m), 3.16 (1H, d, J=4.88 Hz), 3.11 (1H, d, J=5.94 Hz), 1.40 (3H, s), 1.35 (3H, s), 1.22 (9H, s), 1.18 (3H, d, J=6.48 Hz); ^{13}C NMR δ_{13C} 109.00, 75.78, 75.70, 74.98, 74.83, 70.67, 68.34, 66.75, 28.59, 26.74, 25.26, 19.20; m/z: 277 ($M^{+\cdot}$-15), 221 ($M^{+\cdot}$-71), 202 ($M^{+\cdot}$-89). Anal. Calcd. for $C_{14}H_{28}O_6$: C, 57.51; H, 9.65. Found: C, 57.45; H, 9.63.

11: Yield: 85.8%; m.p. 101-102°C (from ether-hexane); IR: 3571, 3059, 2970, 2934, 1596, 1452, 1366, 1177, 1121, 1018 cm^{-1}; ^1H NMR δ_H 7.83, 7.31 (4H, dd, J=8.34 Hz), 5.71 (1H, d, J=3.62 Hz), 4.80 (1H, dd, J=8.32, 4.78 Hz), 4.53 (1H, dd, J=4.78, 3.62 Hz), 4.10 (1H, dd, J=8.32, 3.56 Hz), 3.87 (1H, td, J=7.80, 3.56 Hz), 3.16-3.38 (2H, m), 2.42 (3H, s), 1.49 (3H, s), 1.26 (3H, s), 1.11 (3H, s); ^{13}C NMR δ_{13C} 145.08, 133.12, 129.63, 128.17, 113.33, 103.77, 77.87, 77.47, 75.78, 73.39, 69.92, 61.78, 27.35, 26.57, 26.51, 21.58; m/z: 415 ($M^{+\cdot}$-15), 359 ($M^{+\cdot}$-71); Anal. Calcd. for $C_{20}H_{30}SO_8$: C, 55.80; H, 7.02. Found: C, 55.68; H, 7.00.

13c: Oil; Yield: 92%; IR: 3559, 3060, 3030, 2971, 1603, 1451, 1365, 1193, 1066, 1026 cm^{-1}; ^1H NMR δ_H 7.2-7.4 (10H, m), 4.76 (2H, d, J=2.06 Hz), 4.65 (2H, d, J=1.96 Hz), 4.26 (1H, t, J=6.22 Hz), 3.90-4.05 (4H, m), 3.84 (1H, dd, J=8.16, 7.00 Hz), 3.66 (1H, dd, J=8.16, 2.48 Hz), 3.52 (1H, dd, J=9.0, 3.68 Hz), 3.38 (1H, dd, J=9.0, 5.66 Hz), 1.43 (3H, s), 1.34 (3H, s), 1.18 (9H, s); ^{13}C NMR δ_{13C} 138.55, 128.44, 128.34, 128.27, 127.82, 108.52, 79.36, 79.22, 75.94, 74.57, 73.85, 73.22, 69.53, 66.84, 62.50, 27.42, 26.50, 25.08; m/z: 458 ($M^{+\cdot}$), 401 ($M^{+\cdot}$-57); Anal. Calcd. for $C_{27}H_{38}O_6$: C, 70.72; H, 8.35. Found: C, 70.98; H, 8.39.

14a: Oil; Yield: 62%; IR: 3518, 3068, 3015, 2983, 1536, 1433, 1301, 1012 cm^{-1}; ^1H NMR δ_H 7.80, 7.31 (8H, J=8.32 Hz), 5.10 (2H, d, J=8.00 Hz), 3.22-3.40 (6H, m), 2.85 (2H, br.s), 2.41 (6H, s), 1.10 (18H, s); ^{13}C NMR δ_{13C} 144.82, 133.82, 129.56, 127.90, 78.60, 73.48, 68.11, 61.62, 27.35, 21.57; Anal. Calcd. for $C_{28}H_{42}S_2O_{10}$: C, 55.80; H, 7.02. Found: C, 55.79; H, 7.31.

Oxidation of Compound 2 Using Pyridinium Dichromate (PDC) as Oxidizing Agent: To the suspension of 5 eq. of PDC in dry dichloromethane, alcohol **2** was added dropwise under argon. The reaction was follow by TLC, once the reaction was completed, flash chromatography of the crude mixture yielded the pure carbonyl compound.

The following aldehydes were obtained by this procedure:

α-phenyl-α-tert-butyloxyacetaldehyde 4a: Oil; Yield: 82%; IR: 2968, 1727, 1448, 1365, 1287, 1186, 1091, 1066 cm^{-1}; ^1H NMR δ_H 9.55 (1H, d, J=2.48 Hz), 7.2-7.45 (5H, m), 4.88 (1H, d, J=2.48 Hz), 1.27 (9H, s); ^{13}C NMR δ_{13C} 200.62, 136.40, 128.63, 128.12, 126.70, 79.20, 75.77, 28.43; m/z: 192 ($M^{+\cdot}$), 177 ($M^{+\cdot}$-15, 10), 163 ($M^{+\cdot}$-29).

α-tert-butyloxyhexanal 4b: Oil; Yield: 92%; IR: 3048, 2963, 2937, 2873, 2802, 1726, 1464, 1390, 1189, 1083 cm^{-1}; ^1H NMR δ_H 9.59 (1H, d, J=2.94 Hz), 3.75 (1H, td, J=7.05, 2.94 Hz), 1.20-1.55 (6H, m), 1.18 (9H, s), 0.88 (3H, t, J=6.8 Hz); ^{13}C NMR δ_{13C} 206.62, 77.08, 74.60, 30.99, 28.19, 26.90, 22.36, 13.66; m/z: 157 ($M^{+\cdot}$-15), 143 ($M^{+\cdot}$-29).

Swern Oxidation: 3 eq. of DMSO was added dropwise to a solution of oxalyl chloride (1.5 eq.) in dichloromethane at -78°c. Stirring was continued for about 15minutes followed by addition of the alcohol in dichloromethane. The reaction mixture was stirred for 1hr and triethylamine (5 eq.) was added dropwise at the same temperature. The cooling bath was then removed and aq. $NaHCO_3$ solution was added at room temperature. The aqueous phase was extracted with dichloromethane, the combined organic phase was dried and evaporated to give the slight yellow crude mixture which was purified by the flash chromatography.

The following carbonyl compounds were obtained by this procedure:

8: Oil; Yield: 81%; IR: 3185, 3050, 2973, 2935, 1740, 1654, 1597, 1374, 1213, 1190, 1177, 1092 cm^{-1}; ^1H NMR δ_H 7.68, 7.32 (4H, dd, J=8.36 Hz), 6.03 (1H, d, J=3.68 Hz), 5.11(1H, d, J=3.24 Hz), 4.86 (1H, d, J=3.24 Hz), 4.82 (1H, d, J= 3.68 Hz), 4.18, 4.05 (2H, dd, J=18.5 Hz), 2.42 (3H, s), 1.44 (3H, s),

1.29 (3H, s), 1.50 (9H, s); ^{13}C NMR δ_{13C} 201.96, 145.57, 132.00, 129.93, 128.05, 112.92, 105.07, 82.66, 82.44, 74.23, 67.11, 27.12, 26.57, 26.22, 21.64; m/z: 413 (M^{+}-15), 371 (M^{+}-57), 341 (M^{+}-87), 313 (M^{+}-115)

16: Oil; Yield: 89%; IR: 3063, 2972, 2937, 1734, 1452, 1374, 1212, 1190, 1161, 1106, 1075, 1025 cm^{-1}; ^{1}H NMR δ_H 7.15-7.35 (5H, m), 6.03 (1H, d, J=3.62 Hz), 4.81 (1H, d, J=3.54 Hz), 4.57 (1H, d, J=3.54 Hz), 4.50, 4.60 (2H, dd, J=11.54 Hz), 4.35 (1H, d, J=3.62 Hz), 4.20, 4.30 (2H, dd, J=18.66 Hz), 1.45 (3H, s), 1.30 (3H, s), 1.15 (9H, s); ^{13}C NMR δ_{13C} 204.58, 136.78, 128.38, 127.95, 127.66, 112.32, 105.65, 84.80, 83.53, 81.73, 73.99, 72.47, 67.64, 27.22, 26.85, 26.27; m/z: 349 (M^{+}-15), 307 (M^{+}-57), 289 (M^{+}-75), 249 (M^{+}-115). Anal. Calcd. for $C_{20}H_{28}O_6$: C, 65.92; H, 7.74. Found: C, 65.75; H, 7.78.

Acetylation of 11: To a solution of 6-*O*-tert.-butyl-1,2-*O*-isopropylidene-3-*p*-toluenesulfonyl-*D*-allofuranose (110 mg, 0.26 mmol) in dry pyridine, 3eq of acetic anhydride (0.78 mmol, 78 µl and catalytic amount of DMAP was added at 0°c. The reaction mixture was stirred at room temperature for 20h. After evaporation of the solvent, flash chromatography (eluent: ether/hexane=2/3) gave the desired compound 17 (116 mg, yield 96%). m.p. 107-108°C (hexane-ether); IR: 3050, 2971, 1741, 1597, 1367, 1217, 1189, 1177, 1019 cm^{-1}; ^{1}H NMR δ_H 7.34, 7.86 (4H, dd, J=8.5 Hz), 5.70 (1H, d, J=3.72 Hz), 5.03 (1H, td, J=6.22 Hz), 4.85 (1H, dd, J=8.70, 4.70 Hz), 4.52 (1H, dd, J=4.70, 3.72 Hz), 4.30 (1H, dd, J=8.70, 3.70 Hz), 3.43 (1H, dd, J=9.38, 6.40 Hz), 3.35 (1H, dd, J=9.38, 6.00 Hz), 2.44 (3H, s), 2.02 (3H, s), 1.49 (3H, s), 1.26 (3H, s), 1.10 (9H, s); ^{13}C NMR δ_{13C} 170.14, 145.29, 133.49, 129.78, 128.33, 113.60, 104.01, 77.49, 76.90, 76.26, 73.36, 70.99, 59.42, 28.18, 27.14, 26.44, 21.43, 20.72; m/z: 457 (M^{+}-15), 399 (M^{+}-73), 357 (M^{+}-115). Anal. Calcd. for $C_{22}H_{32}SO_9$: C, 55.92; H, 6.83. Found: C, 56.02; H, 6.83.

The following compounds were obtained by this procedure:

3,5-Di-acetyl-6-*O*-tert.-butyl-1,2-*O*-isopropylidene-*D*-glucofuranose 15: Yield 91%; IR: 2971, 2928, 2852, 1744, 1370, 1216, 1160, 1071, 1021, 854 cm^{-1}; ^{1}H NMR δ_H 5.88 (1H, d, J=3.72 Hz), 5.30 (1H, d, J=2.88 Hz), 5.07 (1H, ddd, J=9.60, 4.90, 2.34 Hz), 4.47 (1H, dd, J=9.60, 2.88 Hz), 4.42 (1H, d, J=3.72 Hz), 3.62 (1H, dd, J=10.80, 2.34 Hz), 3.49 (1H, dd, J=10.80, 4.90 Hz), 2.00 (3H, s), 1.97 (3H, s), 1.48 (3H, s), 1.27 (3H, s), 1.13 (9H, s); ^{13}C NMR δ_{13C} 169.81, 169.57, 112.27, 105.00, 83.19, 76.32, 74.84, 73.08, 69.28, 61.18, 27.31, 26.62, 26.25, 20.87, 20.64; m/z: 345 (M^{+}-15), 289 (M^{+}-71), 287 (M^{+}-73), 245 (M^{+}-115). Anal. Calcd. for $C_{17}H_{28}O_8$: C, 56.66; H, 7.83. Found: C, 56.75; H, 7.86.

2,3,4,5-Tetraacetyl-1,6-di-*O*-tert-butyl-*D*-mannitol 18: Yield 48% (two steps from 12b); IR: 3051, 2971, 1741, 1365, 1214, 1089, 1036 cm^{-1}; ^{1}H NMR δ_H 5.45 (2H, d, J=7.6 Hz), 5.01 (2H, br.q, J=5.60 Hz), 3.45 (2H, dd, J=10.1, 4.68 Hz), 3.30 (2H, dd, J=10.1, 5.68 Hz), 2.03 (6H, s), 2.00 (6H, s), 1.09 (18H, s); ^{13}C NMR δ_{13C} 170.02, 169.74, 73.29, 69.83, 68.84, 60.38, 27.26, 21.02, 20.89; m/z: 389 (M^{+}-73), 303 (M^{+}-159), 231 (M^{+}/2); Anal. Calcd. for $C_{22}H_{38}O_{10}$: C, 57.13; H, 8.28. Found: C, 57.30; H, 8.22.

5-Acetyl-6-*O*-tert-butyl-1,2-*O*-isopropylidene-*D*-glucofuranose 7: Yield: 94%; IR: 2971, 2936, 1741, 1596, 1465, 1365, 1217, 1177, 1093; ^{1}H NMR δ_H 7.34, 7.77 (4H, dd, J=8.38 Hz), 5.85 (1H,

d, J=3.66 Hz), 5.02 (1H, d, J=2.72 Hz), 4.92 (1H, ddd, J=9.52, 3.34, 2.28 Hz), 4.68 (1H, d, J=3.66 Hz), 4.62 (1H, dd, J= 9.52, 2.72 Hz), 3.65 (1H, dd, J=10.94, 2.28 Hz), 3.50 (1H, dd, J=10.94, 2.28 Hz), 3.50 (1H, dd, J=10.94, 3.34 Hz), 2.44 (3H, s), 1.98 (3H, s), 1.49 (3H, s), 1.29 (3H, s), 1.13 (9H, s); ^{13}C NMR δ_{13C} 170.15, 145.51, 133.03, 130.07, 128.20, 112.75, 104.87, 82.66, 80.55, 75.73, 69.51, 60.00, 27.21, 26.47, 26.32, 21.48, 20.87; m/z: 457 (M^{+}-15), 399 (M^{+}-73); Anal. Calcd. for $C_{22}H_{32}SO_9$: C, 55.92; H, 6.83. Found: C, 55.86; H, 6.78.

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