layer was back-washed with dichloromethane (2 × 50 mL). The combined organic layer was dried ($MgSO_4$), and the solvent was removed under reduced pressure. The crude material was purified by a gravity column (SiO_2) eluted with hexane/ethyl acetate (3:1) to give 1.1 g (74%) of **11** as a red solid: mp 198–199 °C dec; IR 3230, 1590, 1555 cm^{-1}; NMR (500 MHz) δ 13.26 (s, 1 H, phenolic OH), 12.99 (s, 1 H, phenolic OH), 8.33–8.35 (m, 2 H, Ar H), 7.82–7.84 (m, 2 H, Ar H), 5.41 (s, 1 H, benzylic C*H*-OH), 4.00 (q, 1 H, J = 6.2 Hz, CH), 3.09 (s, 2 H, benzylic), 1.31 (d, 3 H, J = 6.2 Hz, CH_3), 0.88 (s, 9 H, *t*-Bu), 0.13 (s, 6 H, 2 $SiCH_3$).

Anal. Calcd for $C_{25}H_{30}O_7Si$: C, 63.81; H, 6.43. Found: C, 64.19; H, 6.44.

4-Demethoxy-13-dihydro-13-*O*-(*tert*-butyldimethylsilyl)-3′-*N*-(trifluoroacetyl)-8-nordaunomycin (12). To a solution of glycal **16** (190 mg, 0.51 mmol) in dry benzene (10 mL) were added aglycon **11** (200 mg, 0.43 mmol) and *p*-toluenesulfonic acid (5–7 mg). The solution was stirred at room temperature for 3 h, and another portion of **16** (100 mg, 0.27 mmol) was added. Stirring was continued for 18 h. The mixture was diluted with dichloromethane (30 mL) and washed with saturated aqueous sodium bicarbonate solution (2 × 30 mL). The aqueous layer was back-washed with dichloromethane (2 × 20 mL). The combined organic layer was dried ($MgSO_4$), and the solvent was removed under reduced pressure. The residue was redissolved in triethylamine/methanol (1:9, 15 mL) and stirred at room temperature for 1 h. The solvent was removed under reduced pressure, and the residue was dissolved in dichloromethane (20 mL). The organic solution was washed with saturated aqueous sodium bicarbonate solution (2 × 10 mL), and the aqueous layer was back-washed with dichloromethane (1 × 10 mL). The combined organic solution was dried ($MgSO_4$), and the solvent was removed under reduced pressure. The crude material was passed through a gravity column (SiO_2) eluted with hexane/ethyl acetate (3:1) to give 30 mg of starting material **11** (higher R_f fraction) and 140 mg (55% based on recovered starting material) of **12** (lower R_f fraction) as an inseparable mixture of 4 diasteromers: IR 3175, 1680, 1590, 1560 cm^{-1}.

Anal. Calcd for $C_{33}H_{40}O_{10}SiF_3N$: C, 56.96; H, 5.79; N, 2.01. Found: C, 57.00; H, 6.13; N, 2.01.

4-Demethoxy-13-dihydro-8-nordaunomycin (14). To a solution of glycoside **12** (140 mg, 0.2 mmol) in THF (10 mL) was added a solution of tetrabutylammonium fluoride (0.98 mmol, 1 M solution in THF). The solution was stirred at room temperature for 6 h, diluted with dichloromethane (20 mL), and washed with saturated aqueous sodium chloride solution (2 × 20 mL). The aqueous layer was back-washed with dichloromethane (2 × 10 mL) and the combined organic solution was dried ($MgSO_4$). The solvent was removed under reduced pressure and the crude material was purified by a gravity column (SiO_2) eluted with hexane/ethyl acetate (1:2) followed by ethyl acetate and 5% methanol in ethyl acetate to give 100 mg (85%) of **13** as a red solid.

To a solution of diol **13** (100 mg, 0.17 mmol) in THF (10 mL) was added a 0.05 N NaOH solution (19 mL, 0.95 mmol). The solution was stirred at room temperature for 18 h and solid CO_2 was added until the color of the solution changed from purple to red. The solvent was removed under reduced pressure. The residue was dissolved in methanol, and the white precipitate was filtered. The filtrate was concentrated and the residue was purified by a gravity column (SiO_2) eluted with methanol/dichloromethane (1:2) followed by methanol to give 41 mg (50%) of **14** as a dark red solid.

Anal. Calcd for $C_{25}H_{27}O_9N\cdot 2H_2O$: C, 57.57; H, 5.99; N, 2.68. Found: C, 57.70; H, 5.91; N, 2.70.

Acknowledgment. We thank Dr. J. Filppi of the Pioneering Life Sciences Department for biological evaluation. High-field NMR spectra were obtained at the Ohio State University Chemical Instrument Center funded in part by NIH Grant #1 S10 RR01458-01A1. Spectra were recorded by Dr. C. E. Cottrel.

Registry No. 1, 25060-18-8; **2**, 67122-24-1; **3**, 67122-25-2; **4**, 110798-14-6; **5**, 110798-15-7; **6**, 110798-16-8; **7**, 90269-82-2; **7a**, 110798-24-8; **8**, 110798-17-9; **9**, 110798-18-0; **10** (diastereomer 1), 110798-19-1; **10** (diastereomer 2), 110900-50-0; **11** (diastereomer 1), 110798-20-4; **11** (diastereomer 2), 110900-51-1; **12** (diastereomer 1), 110798-21-5; **12** (diastereomer 2), 110900-52-2; **12** (diastereomer 3), 111001-09-3; **12** (diastereomer 4), 110900-53-3; **13** (diastereomer 1), 110901-77-4; **13** (diastereomer 2), 110798-25-9; **13** (diastereomer 3), 110900-54-4; **13** (diastereomer 4), 110900-55-5; **14** (diastereomer 1), 110798-22-6; **14** diastereomer 2), 110900-56-6; **14** (diastereomer 3), 110900-57-7; **14** (diastereomer 4), 110900-58-8; **15**, 110798-23-7; **16**, 77398-05-1; ethyl acetoacetate lithium enolate, 33283-91-9.

Stereoselective Access to α- and β-D-Fructofuranosyl C-Glycosides

Francesco Nicotra,* Luigi Panza, and Giovanni Russo

Dipartimento di Chimica Organica e Industriale dell'Università and Centro di Studio per le Sostanze Organiche Naturali del C.N.R., 20133 Milano, Italy

Received April 10, 1987

C-Glycosides have gained interest as potential inhibitors of metabolic processes[1] and as chiral intermediates in organic syntheses.[2] Although many examples of syntheses of these compounds have recently been described, in only few cases has the formation of a tri-C-substituted carbon center been reported.[3] In particular, in spite of the biological importance of D-fructose, the synthesis of C-fructosides has received little attention.[4,5]

In connection with a project directed toward the synthesis of potential inhibitors of carbohydrate metabolism, we were interested in developing an efficient method to obtain α- and/or β-C-D-fructofuranosides.

In principle both α- and β-C-D-fructofuranosides can be derived from a common precursor such as A (Scheme I) which, through differential manipulation of the groups C_x and C_y, leads to synthons such as B and C. B and C, besides being α- and β-C-D-fructofuranosides, contain an unprotected hydroxymethyl group that may be elaborated.

Results and Discussion

The Lewis acid catalyzed formation of an oxonium ion, and the subsequent addition of a proper C-nucleophile,[6] seemed the most suitable route to a C-fructoside. The stereochemistry of this reaction was not predictable. In fact whereas in glycopyranosides (in $^4C_1$ conformation) the anomeric effect leads the nucleophile to attack the oxonium ion from the α face,[6a] in glycofuranosides the anom-

(1) (a) Hanessian, S.; Pernet, A. G. *Adv. Carbohydr. Chem. Biochem.* **1976**, *33*, 111. (b) Nicotra, F.; Ronchetti, F.; Russo, G. *J. Org. Chem.* **1982**, *47*, 4459. (c) Reitz, A. B.; Nortey, S. O.; Marianoff, B. E. *Tetrahedron Lett.* **1985**, *26*, 3915. (d) Nicotra, F.; Perego, R.; Ronchetti, F.; Russo, G.; Toma, L. *Carbohydr. Res.* **1984**, *131*, 180. (e) Nicotra, F.; Panza, L.; Ronchetti, F.; Toma, L. *Tetrahedron Lett.* **1984**, *25*, 5937. (f) Chmielewsky, M.; BeMiller, J. N.; Cerretti, D. P. *Carbohydr. Res.* **1981**, *97*, C-1.

(2) See: Inch, T. D. *Tetrahedron* **1984**, *40*, 3161.

(3) (a) Dupuis, J.; Giese, B.; Hartung, J.; Leising, M. *J. Am. Chem. Soc.* **1985**, *107*, 4332. (b) Williams, D. R.; White, F. H. *Tetrahedron Lett.* **1985**, *26*, 2529. (c) Wilcox, C. S.; Long, G. W.; Suh, H. *Tetrahedron Lett.* **1984**, *25*, 395. (d) Fraser-Reid, B. *J. Org. Chem.* **1980**, *45*, 1344.

(4) Meuwly, R.; Vasella, A. *Helv. Chim. Acta* **1986**, *69*, 751.

(5) During the preparation of this manuscript, Bennek and Gary published the synthesis of 1-(D-fructofuranosyl)-2-propene as a mixture of anomers (Bennek, J. A.; Gary, R. G. *J. Org. Chem.* **1987**, *52*, 892).

(6) See: (a) Lewis, M. D.; Cha, J. K.; Kishi, Y. *J. Am. Chem. Soc.* **1982**, *104*, 4976. (b) Cupps, T. L.; Wise, D. S.; Townsend, L. B. *J. Org. Chem.* **1982**, *47*, 5115. (c) Kozikowski, A. P.; Sorgi, K. L. *Tetrahedron Lett.* **1982**, *23*, 2281. (d) Kozikowski, A. P.; Sorgi, K. L. *Tetrahedron Lett.* **1983**, *24*, 1563. (e) Wilcox, C. S.; Otoski, R. M. *Tetrahedron Lett.* **1986**, *27*, 1011.

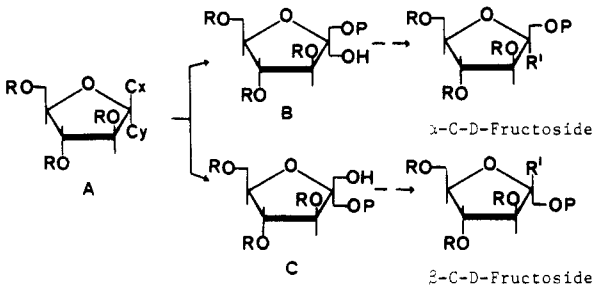
0022-3263/87/1952-5627$01.50/0

Table I. Reaction of D-Fructofuranosides 1 and 2 with Allyltrimethylsilane

compd	Lewis acid	solvent	temp, °C	time, h	α/β ratio[a]	yield, %
1	Me_3SiOTf	CH_3CN	0	1.5	80:20	92
1	Me_3SiOTf	CH_3CN	−20	12	75:25	94
1	Me_3SiOTf	CH_2Cl_2	20	36	75:25	93
2	BF_3OEt_2	CH_3CN	20	1.5	80:20	95
2	BF_3OEt_2	CH_3CN	0	1.5	80:20	98

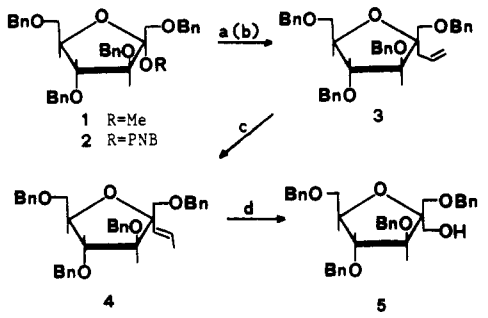
[a] Determined from ^{13}C NMR spectra.

Scheme I[a]



[a] P = protecting group.

Scheme II[a]



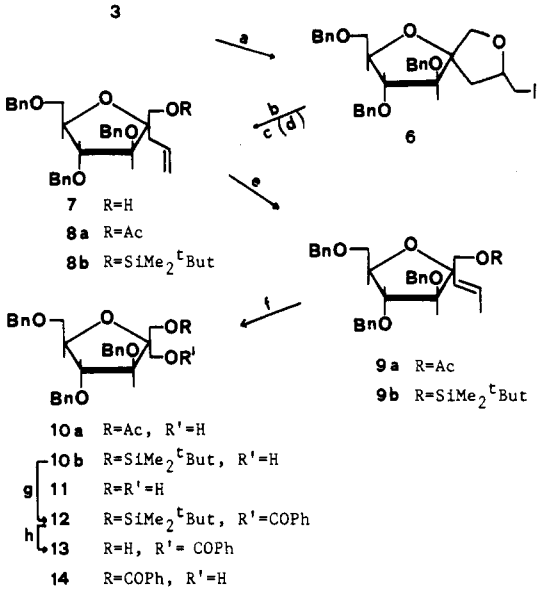
[a] Reagents and conditions: (a) $Me_3SiCH_2CH{=}CH_2$, Me_3SiOTf, CH_3CN, 0 °C (92%); (b) $Me_3SiCH_2CH{=}CH_2$, BF_3OEt_2, CH_3CN, 0 °C (98%); (c) $PdCl_2(CH_3CN)_2$, PhH, reflux (88%); (d) O_3, CH_2Cl_2, −78 °C; then $NaBH_4$, −78 °C → room temperature (71%).

eric effect has no influence in the stereochemistry of the reaction, which may depend on many other factors not yet clearly defined.[5,6b-e]

Methyl 1,3,4,6-tetra-*O*-benzyl-D-fructofuranoside (**1**) or 2-(*p*-nitrobenzoyl)-1,3,4,6-tetra-*O*-benzyl-D-fructofuranose (**2**), when treated with allyltrimethylsilane in the presence of a catalytic amount of a Lewis acid, afforded predominantly the α-*C*-D-fructofuranoside **3** (Scheme II). The results of different experimental conditions are given in Table I. The yields and the α/β ratios were independent on the nature of the leaving group, catalyst, temperature, and solvent employed. The anomeric configuration of **3** was deduced by the chemical shift value of C-1′ (38.65 ppm) compared to that of its epimer at C-2 (37.26 ppm). In fact it has been shown both in C-glycosides and C-nucleosides that the ^{13}C chemical shift of the carbon atom attached to the "anomeric" position is at higher field when this atom has a cis relationship with the C(2)-OR group than when there is a trans relationship.[7] Furthermore **3** showed a 4.5% NOE between H-1′ and H-3, which confirms the α orientation of the allylic substituent.

The allylic compound **3** was isomerized with $PdCl_2(CH_3CN)_2$ to the vinyl derivative **4**, which was in turn ozonized and the ozonide reduced with $NaBH_4$ to produce the alcohol **5** [B (P = Bn)].

Scheme III[a]



[a] Reagents and conditions: (a) I_2, THF–H_2O, pH 4, room temperature; (b) Zn, AcOH, Et_2O–MeOH, room temperature (70% from **3**); (c) Ac_2O, Py, room temperature, (quant.); (d) Me_2-*t*-Bu-SiCl, Et_3N, DMAP, CH_2Cl_2, room temperature (90%); (e) $PdCl_2(CH_3CN)_2$, PhH, reflux (98% and 92%); (f) O_3, CH_2Cl_2, −78 °C, then Ph_3P, evaporation and $Zn(BH_4)_2$, Et_2O, room temperature (75% from **10b**); (g) PhCOCl, Py, CH_2Cl_2, room temperature (84%); (h) AcOH, H_2O, THF, room temperature (95%).

The preparation of synthon C from **3** requires the selective deprotection of the hydroxymethyl group at C-1. In principle, D-fructofuranosides with the 1-hydroxyl group differently protected can be employed as a starting material, but their synthesis requires long and tedious work and reduces the overall yield. Consequently we considered a selective deprotection of the 1-hydroxyl group of **3**, taking advantage of the relative position of the double bond. Treatment of **3** with iodine results in iodocyclization and concomitant debenzylation[8] to afford the iodo derivative **6** (Scheme III). **6** was subjected to reductive elimination by treatment with zinc and acetic acid to afford the allyl derivative **7**.

The conversion of the allylic substituent of **7** into the hydroxymethyl group was first attempted on the acetate **8a**. Isomerization to **9a**, ozonolysis, and direct reduction of the ozonide with $NaBH_4$, as reported for **3**, afforded mainly the diol **11** (60% yield) together with the expected product **10a** (only 26% yield). The reduction of the ozonide with Zn and acetic acid, and the subsequent reduction of the isolated aldehyde (in which the acetyl protecting group was still present) with $NaBH_4$ or with $Zn(BH_4)_2$, was very slow and afforded predominantly the diol **11**. We then turned to the *tert*-butyldimethylsilyl protecting group. **9b** was synthesized and submitted to ozonolysis.

(7) de las Eras, F. G.; Fernández-Resa, P. *J. Chem. Soc., Perkin Trans. 1* **1982**, 903 and references cited therein.

(8) (a) Rychnovsky, S. D.; Bartlett, P. A. *J. Am. Chem. Soc.* **1981**, *103*, 3963. (b) Nicotra, F.; Panza, L.; Ronchetti, G.; Russo, G.; Toma, L. *Carbohydr. res.*, in press.

The ozonide was reduced with triphenylphosphine and the recovered crude aldehyde was treated with $Zn(BH_4)_2$ ($LiAlH_4$ produced extensive desilylation) to afford the alcohol **10b** in good yield.

The synthetic scheme requires at last the protection of the free hydroxyl group of **10b** and the subsequent hydrolysis of the silyl ether to afford the synthon C. This conversion was not easily effected. In fact, treatment of **10b** with MEMCl resulted in extensive desilylation. Benzoylation afforded better results leading to **12** in 84% yield. The hydrolysis of the silyl protecting group of **12** with Bu_4NF afforded two monobenzoates (**13** and **14**) in 62% and 30% yield, which indicated a partial migration of the benzoyl group. Finally, treatment of **12** with acetic acid afforded only **13**, [C (P = COC_6H_5)] in 95% yield.

The utilization of synthons B and C for the synthesis of *C*-D-fructofuranosides of biological interest will be the subject of future reports.

Experimental Section

General. ^1H NMR spectra were recorded with a Varian XL200 spectrometer at 26 °C and ^{13}C NMR spectra with a Bruker WP80 spectrometer at 30 °C, unless otherwise indicated, for solutions in $CDCl_3$. The chemical shifts are reported in part per million downfield from $(CH_3)_4Si$ but with the deuteriochloroform resonance as internal standard. The signals of the aromatic carbons in the ^{13}C NMR spectra are not reported. $[\alpha]_D$ were measured on a Perkin-Elmer 241 polarimeter at 20 °C. All reactions were monitored by thin-layer chromatography on Merck silica gel precoated 60 F-254 plates. The spots were detected by UV light (245 nm) and with 50% sulfuric acid spray followed by heating at 110 °C for 5 min. Chromatography was performed by using 230–400-mesh Merck silica gel (silica gel/substance 40/1, unless otherwise indicated). Tetrahydrofuran (THF) was dried by distillation from sodium benzophenone ketyl, pyridine (Py) and CH_2Cl_2 by distillation from CaH_2, toluene by distillation from sodium, and CH_3CN by distillation from P_2O_5, shortly before use. Unless otherwise noted, commercial products were used without further purification. All air-sensitive reactions were run under nitrogen in glassware oven-dried overnight at 120 °C and assembled hot. Reagents were added via oven-dried syringes through septa. Usual workup refers to diluting with an organic solvent, washing with water to neutrality, drying over Na_2SO_4, and evaporating under reduced pressure.

2-(*p*-Nitrobenzoyl)-1,3,4,6-tetra-*O*-benzyl-D-fructofuranose (2). The procedure of Ness et al.[9] was modified as follows: to 1,3,4,6-tetra-*O*-benzyl-D-fructofuranose[9] (3.08 g, 5.7 mmol) in dry toluene (50 mL) were added freshly distilled Et_3N (2.5 mL, 17 mmol), *p*-nitrobenzoyl chloride (3.3 g, 17 mmol), and (dimethylamino)pyridine (40 mg). After 6 days the mixture was poured into water; usual workup and chromatography (hexane–ethyl acetate, 4/1 v/v) afforded **2** (3.47 g, mixture of anomers, 88% yield) which was crystallized from acetone–methanol (1:1): mp 65–67 °C (lit. mp 66–67 °C). Anal. Calcd for $C_{41}H_{39}NO_9$: C, 71.40; H, 5.70; N, 2.03. Found: C, 71.29; H, 5.67; N, 1.97.

1-(1,3,4,6-Tetra-*O*-benzyl-α-D-fructofuranosyl)-2-propene (3). In a typical procedure **1** (4.5 mmol) in dry CH_3CN or CH_2Cl_2 (15 mL) was stirred under an N_2 atmosphere with allyltrimethylsilane (13.5 mmol) and one drop of Me_3SiOTf. Alternatively **2** (4.5 mmol) in dry CH_3CN (15 mL) was stirred under an N_2 atmosphere with allyltrimethylsilane (13.5 mmol) and one drop of freshly distilled BF_3OEt_2. The reaction was monitored by TLC (hexane–ethyl acetate, 3/1 v/v) (1.5 h → 3 days, see Table I). The mixture was diluted with 5% $NaHCO_3$ and submitted to the usual workup and chromatography (hexane–ethyl acetate, 4/1 v/v) to afford a mixture of **3** and a minor amount of its epimer at C-2 (see Table I). **3**: ^1H NMR δ 2.54 (2 H, d, J = 7 Hz, H-1′a and b), 3.48–3.69 (4 H, m, H-1 and H-6), 4.00–4.23 (3 H, m, H-3, H-4, and H-5), 4.5–4.6 (8 H, m, OCH_2Ph), 5.08 (1 H, dd, J = 16 and 2 Hz, H-3′a), 5.10 (1 H, dd, J = 10 and 2 Hz, H-3′b), 5.9 (1 H, m, H-2′), 7.3 (20 H, m, Ar H); ^{13}C NMR (25.2 MHz) ppm 38.65 (t, C-1′), 70.98, 71.24, 72.01, 72.28, 73.20 and 73.37 (t, -OCH_2-), 80.52 (d, C-3), 85.17 (s, C-2), 85.17 and 86.52 (d, C-4 and C-5), 118.02 (t, C-3′), 133.49 (d, C-2′). Its β-anomer: ^{13}C NMR ppm 37.26 (t, C-1′), 117.46 (t, C-3′), 134 (d, C-2′). Anal. Calcd for $C_{37}H_{40}O_5$: C, 78.69; H, 7.14. Found: C, 78.61; H, 7.22.

1-(1,3,4,6-Tetra-*O*-benzyl-α-D-fructofuranosyl)-1-propene (4). The mixture of **3** and its β-anomer (250 mg, 0.44 mmol) in benzene (15 mL) was refluxed overnight with a catalytic amount of $PdCl_2(CH_3CN)_2$. The mixture was filtered on a bed of silica gel, and the filtrate was evaporated to afford 250 mg of product in which **4** and **3** were present in a 95:5 ratio (measured by ^1H NMR). Pure **4** (220 mg, 88% yield) was obtained after chromatography (substrate/silica gel 1:100; hexane–ethyl acetate, 4/1 v/v): oil, $[\alpha]_D$ +6.3° (*c* 1, $CHCl_3$); ^1H NMR δ 1.72 (3 H, dd, J = 6 and 1.5 Hz, CH_3), 3.48–3.70 (4 H, m, H-1 and H-6), 3.97–4.22 (3 H, m, H-3, H-4, and H-5), 4.50–4.60 (8 H, m, OCH_2Ph), 5.60 (1 H, dd, J = 15.5 and 1.5 Hz, H-1′), 5.79 (1 H, dq, J = 15.5 and 6 Hz, H-2′), 7.3 (20 H, m, Ar H); ^{13}C NMR (25.2 MHz) ppm 17.81 (q, C-3′), 71.04, 71.78, 72.43, 72.92, 73.12 and 73.32 (t, -OCH_2-), 80.22 (d, C-3), 84.74 and 84.83 (d, C-4 and C-5), 88.41 (s, C-2), 125.11 and 131.77 (d, C-1′ and C-2′). Anal. Calcd for $C_{37}H_{40}O_5$: C, 78.69; H, 7.14. Found: C, 78.51; H, 7.16.

(1,3,4,6-Tetra-*O*-benzyl-α-D-fructofuranosyl)methanol (5). Ozone was bubbled through a stirred solution of **4** (100 mg, 0.18 mmol) in CH_2Cl_2–MeOH (5/3, 8 mL) at −78 °C for 10 min. The excess ozone was removed by bubbling with N_2, and $NaBH_4$ (8 mg, 0.2 mmol) was added. The mixture was stirred for 1 h at −78 °C and then allowed to warm to room temperature. $NaBH_4$ (8 mg) was added, after 1 h the solvent was evaporated, and the residue was submitted to the usual workup and chromatography (hexane–ethyl acetate, 5/2 v/v). **5** (71 mg, 71% yield) was obtained: oil; $[\alpha]_D$ +12.9° (*c* 1, $CHCl_3$); ^1H NMR δ 1.60 (1 H, OH), 3.40–3.80 (6 H, m, H-1, H-6, and H-1′), 3.94–4.48 (3 H, m, H-3, H-4, and H-5), 4.48–4.63 (8 H, m, OCH_2Ph), 7.3 (20 H, m, Ar H); ^{13}C NMR (25.2 MHz) ppm 64.19 (t, C-1), 70.79, 70.99, 72.00, 72.69, 73.33, and 73.72 (t, -OCH_2-), 81.03 (d, C-3), 84.59 and 84.59 (d, C-4 and C-5), 85.58 (s, C-2). Anal. Calcd for $C_{35}H_{38}O_6$: C, 75.79; H, 6.90. Found: C, 75.90; H, 6.72.

1-(3,4,6-Tri-*O*-benzyl-α-D-fructofuranosyl)-2-propene (7). To **3** (540 mg, 1 mmol) and potassium phthalate buffer (pH 4, 1 mL) in THF (2 mL) was added I_2 (700 mg, 3 mmol) in THF (0.5 mL) dropwise under stirring. After 30 min at room temperature aqueous $Na_2S_2O_3$ was added. Usual workup afforded **6** (555 mg, 96% yield) as a mixture of isomers. For the major isomer: ^1H NMR δ 1.62 (1 H, dd, J = 13 and 9.5 Hz, H-1′a), 2.34 (1 H, dd, J = 13 and 5.5 Hz, H-1′b), 3.24 (1 H, dd, J = 11 and 1.5 Hz, H-3′a), 3.28 (1 H, dd, J = 11 and 2 Hz, H-3′b); ^{13}C NMR (25.2 MHz) ppm 9.63 (t, CH_2I), 43.41 (t, C-1′), 70.50, 71.69, 71.69, 73.28 and 74.07 (t, -OCH_2-), 77.94, 81.61, 83.59 and 86.59 (d, C-3, C-4, C-5, and C-2′), 92.51 (s, C-2).

Crude **6** (500 mg, 0.8 mmol) in Et_2O–MeOH (1/1, 2 mL) was stirred at room temperature with zinc powder (550 mg, 10 equiv) and two drops of glacial acetic acid. After 24 h, the mixture was filtered and the filtrate was evaporated. Usual workup and chromatography (substrate/silica gel, 1/100; hexane–ethyl acetate, 2/1 v/v) afforded **7** (318 mg, 70% yield from **3**): oil; $[\alpha]_D$ +27.0° (*c* 1.5, $CHCl_3$); ^1H NMR δ 2.17 (1 H, dd, J = 14.5 and 8 Hz, H-1′a), 2.26 (1 H, dd, J = 14.5 and 6.5 Hz, H-1′b), 3.17 (1 H, OH), 3.47 (1 H, dd, J = 10.5 and 3.5 Hz, H-6a), 3.48 (1 H, d, J = 10.5 Hz, H-1a), 3.67 (1 H, dd, J = 10.5 and 3.5 Hz, H-6b), 3.68 (1 H, d, J = 10.5 Hz, H-1b), 3.91 (1 H, dt, J = 7.5 and 3.5 Hz, H-5), 4.11 (1 H, d, J = 6.5 Hz, H-3), 4.40–4.76 (7 H, m, H-4 and OCH_2Ph), 7.3 (15 H, m, Ar H); ^{13}C NMR ppm 39.92 (t, C-1′), 65.80, 69.68, 72.73, 73.32 and 73.32 (t, -OCH_2-), 79.33 (d, C-3), 83.55 and 86.69 (d, C-4 and C-5), 84.09 (s, C-2), 118.65 (t, C-3′), 132.98 (d, C-2′). Anal. Calcd for $C_{30}H_{34}O_5$: C, 75.92; H, 7.22. Found: C, 75.78; H, 6.92.

1-(1-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-fructofuranosyl)-2-propene (8a). To **7** (200 mg, 0.42 mmol) in dry Py (1 mL) was added Ac_2O (0.1 mL). After 24 h at room temperature the mixture was poured into 10 mL of cold water. Usual workup afforded **8a** (224 mg, quantitative yield): oil; ^1H NMR δ 1.98 (3 H, s, OAc), 2.43 (2 H, br d, J = 7.5 Hz, H-1′a and b), 3.56 (2 H, br d, J = 4 Hz, H-6a and b), 4.00–4.12 (3 H, m, H-3, H-4, and H-5), 4.15 (2 H, s, H-1), 4.44–4.60 (6 H, m, OCH_2Ph), 5.02 (1 H, dd, J = 15

(9) Ness, R. K.; Diehl, H. W.; Fletcher, H. G., Jr. *Carbohydr. Res.* **1970**, *13*, 23.

and 2 Hz, H-3'a), 5.09 (1 H, dd, J = 10.5 and 2 Hz, H-3'b), 5.76 (1 H, ddt, J = 15, 10.5, and 7.5 Hz, H-2'), 7.3 (15 H, m, Ar H); ^{13}C NMR ppm 20.90 (q, CH_3), 39.26 (t, C-1'), 65.73, 70.80, 72.34, 72.48 and 73.43 (t, -OCH_2-), 80.70 (d, C-3), 83.78 and 86.46 (d, C-4 and C-5), 84.64 (s, C-2), 118.93 (t, C-3'), 132.92 (d, C-2'), 170.55 (s, C=O). Anal. Calcd for $C_{32}H_{36}O_6$: C, 74.39; H, 7.02. Found: C, 74.19; H, 6.83.

1-(1-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-fructofuranosyl)-1-propene (9a). **8a** (200 mg, 0.38 mmol) was treated with $PdCl_2(CH_3CN)_2$ as described for **3**. A 95/5 mixture of **9a** and **8a** was obtained (196 mg, 98% yield).

9a: ^{1}H NMR δ 1.70 (3 H, dd, J = 6.5 and 1.5 Hz, CH_3), 1.95 (3 H, s, OAc), 3.60 (2 H, d, J = 4.5 Hz, H-6), 4.01-4.28 (3 H, m, H-3, H-4, and H-5), 4.15 (1 H, d, J = 11.5 Hz, H-1a), 4.25 (1 H, d, J = 11.5 Hz, H-1b), 4.52-4.58 (6 H, m, OCH_2Ph), 5.45 (1 H, dq, J = 15.5 and 1.5 Hz, H-1'), 5.80 (1 H, dq, J = 15.5 and 6.5 Hz, H-2'), 7.3 (15 H, m, Ar H).

1-(1-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-fructofuranosyl)-methanol (10a) and (3,4,6-Tri-*O*-benzyl-D-fructofuranosyl)methanol (11). **9** (120 mg, 0.23 mmol) in EtOH (1 mL) was submitted to ozonolysis and reduction of the ozonide as reported for **4**. Workup and chromatography (hexane-ethyl acetate, 2:1) afforded **10a** (30 mg, 26% yield) and **11** (65 mg, 60% yield).

10a: ^{1}H NMR δ 2.00 (3 H, OAc), 3.54 (2 H, d, J = 5.5 Hz, H-6a and b), 3.59 (2 H, d, J = 3 Hz, H-1'a and b), 4.07 (1 H, dd, J = 5 and 4 Hz, H-4), 4.15 (1 H, q, J = 5 Hz, H-5), 4.16 (1 H, d, J = 4 Hz, H-3), 4.18 (1 H, d, J = 10 Hz, H-1a), 4.33 (1 H, d, J = 10 Hz, H-1b), 4.53 (6 H, m, OCH_2Ph), 7.3 (15 H, m, Ar H).

11: ^{1}H NMR 3.43-3.76 (6 H, m, H-1, H-6, H-1'a and b), 4.02 (1 H, m, H-5), 4.26 (1 H, d, J = 6 Hz, H-3), 4.36 (1 H, dd, J = 7 and 6 Hz, H-4), 4.42-4.76 (6 H, m, OCH_2Ph), 7.3 (15 H, m, Ar H). Anal. Calcd for $C_{29}H_{32}O_6$: C, 73.09; H, 6.77. Found: C, 72.88; H, 6.92.

1-(1-*O*-(*tert*-Butyldimethylsilyl)-3,4,6-tri-*O*-benzyl-α-D-fructofuranosyl)-2-propene (8b). **7** (230 mg, 0.48 mmol) in dry CH_2Cl_2 (3 mL) was treated with freshly distilled Et_3N (0.1 mL, 0.72 mmol), ^{t}ButMe$_2$SiCl (88 mg, 0.58 mmol), and (dimethylamino)pyridine (6 mg). After 4 days at room temperature, usual workup and chromatography (hexane-ethyl acetate, 5/1 v/v) afforded **8b** (250 mg, 90% yield): oil; $[\alpha]_D$ +12.6° (c 1.3, $CHCl_3$); ^{1}H NMR δ 0.00 (3 H, s, SiMe), 0.03 (3 H, s, SiMe), 0.89 (9 H, s, Si-t-Bu), 2.47 (2 H, br d, H-1'a and b), 3.55-3.74 (3 H, m), 3.95 (1 H, d, J = 3 Hz, H-3), 4.02-4.25 (3 H, m), 4.50-4.64 (6 H, m, OCH_2Ph), 5.07 (1 H, dt, J = 15 and 1 Hz, H-3'a), 5.10 (1 H, dt, J = 7.5 and 1 Hz, H3'b), 5.88 (1 H, m, H-2'), 7.3 (15 H, m, Ar H); ^{13}C NMR ppm -5.51 (q, $SiCH_3$), 18.30 (s, $SiCMe_3$), 25.73 and 25.99 (q, t-Bu), 38.10 (t, C-1'), 64.04, 71.49, 72.09, 72.53 and 73.37 (t, -OCH_2-), 80.58 (d, C-3), 85.61 and 86.51 (d, C-4 and C-5), 85.97 (s, C-2), 118.02 (t, C-3'), 133.77 (d, C-2'). Anal. Calcd for $C_{36}H_{48}O_5Si$: C, 73.43; H, 8.22. Found: C, 73.58; H, 8.35.

1-(1-*O*-(*tert*-Butyldimethylsilyl)-3,4,6-tri-*O*-benzyl-α-D-fructofuranosyl)-1-propene (9b). **8b** (200 mg, 0.35 mmol) treated with $PdCl_2(CH_3CN)_2$ as reported for **3** afforded **9b** (184 mg, 92% yield): oil; $[\alpha]_D$ +10.9° (c 1, $CHCl_3$); ^{1}H NMR δ -0.03 (3 H, s, SiMe), -0.01 (3 H, s, SiMe), 0.86 (9 H, s, t-Bu), 1.70 (3 H, dd, J = 6.5 and 1.5 Hz, CH_3), 3.52-3.80 (4 H, m, H-1 and H-6), 3.99-4.14 (3 H, m, H-3, H-4, and H-5), 4.46-4.64 (6 H, m, OCH_2Ph), 5.54 (1 H, dd, J = 15.5 and 1.5 Hz, H-1'), 5.78 (1 H, dd, J = 15.5 and 6.5 Hz, H-2'), 7.3 (15 H, m, Ar H); ^{13}C NMR ppm -5.21 (q, $SiCH_3$), 18.07 (q, C-3'), 18.59 (s, $SiCMe_3$), 25.92 and 26.17 (q, t-Bu), 66.23, 71.73, 72.03, 72.94 and 73.49 (t, -OCH_2-), 80.45 (d, C-3), 85.54 and 88.14 (d, C-4 and C-5), 85.90 (s, C-2), 118.23 and 132.44 (d, C-1' and C-2'). Anal. Calcd for $C_{36}H_{48}O_5Si$: C, 73.43; H, 8.22. Found: C, 73.48; H, 8.37.

(1-*O*-(*tert*-Butyldimethylsilyl)-3,4,6-tri-*O*-benzyl-α-D-fructofuranosyl)methanol (10b). To **9b** (150 mg) were added 10 mL of a saturated solution of ozone in CH_2Cl_2 at -78 °C. After 5 min at -78 °C, PPh_3 (90 mg, 1.5 equiv) was added and the mixture was left to reach room temperature. The solvent was then removed under reduced pressure without warming, and the crude aldehyde was dissolved in Et_2O (5 mL) and reduced overnight with a solution of $Zn(BH_4)_2$[10] in Et_2O (10 mL, 0.18 M). Usual workup and chromatography (hexane-ethyl acetate, 4/1 v/v) afforded 110 mg (75% yield) of **10b**: oil; $[\alpha]_D$ +6.2° (c 1.5, $CHCl_3$); ^{1}H NMR δ 0.00 (3 H, s, SiMe), 0.04 (3 H, s, SiMe), 0.87 (9 H, s, t-Bu), 3.50 (1 H, dd, J = 16 and 5.5 Hz, H-6a), 3.58 (1 H, dd, J = 16 and 6 Hz, H-6b), 3.69 (1 H, d, J = 10 Hz, H-1a), 3.72 (2 H, s, H-1'a and b), 3.87 (1 H, d, J = 10 Hz, H-1b), 4.02 (1 H, dd, J = 5 and 3.5 Hz, H-4), 4.11 (1 H, d, J = 3.5 Hz, H-3), 4.13 (1 H, m, H-5), 4.41-4.65 (6 H, m, OCH_2Ph), 7.3 (15 H, m, Ar H); ^{13}C NMR ppm -5.61 (q, $SiCH_3$), 18.25 (s, $SiCMe_3$), 25.89 (q, t-Bu), 63.99, 64.08, 71.04, 71.89, 72.75 and 73.34 (t, -OCH_2-), 80.95 (d, C-3), 84.17 and 84.86 (d, C-4 and C-5), 86.13 (s, C-2). Anal. Calcd for $C_{34}H_{46}O_6Si$: C, 70.55; H, 8.01. Found: C, 70.32; H, 7.83.

(1-*O*-(*tert*-Butyldimethylsilyl)-3,4,6-tri-*O*-benzyl-α-D-fructofuranosyl)methyl Benzoate (12). **10b** (100 mg) in dry CH_2Cl_2 (1 mL) was treated with dry Py (0.2 mL) and freshly distilled benzoyl chloride (24 μL). After 2 h at room temperature, usual workup and chromatography (hexane-ethyl acetate, 4/1 v/v) afforded **12** (99 mg, 84% yield): oil; $[\alpha]_D$ +13.8° (c 1.4, $CHCl_3$); ^{1}H NMR δ 0.00 (3 H, s, SiMe), 0.03 (3 H, s, SiMe), 0.87 (9 H, s, t-Bu), 3.54 (1 H, dd, J = 10 and 5.5 Hz, H-6a), 3.62 (1 H, dd, J = 10 and 5.5 Hz, H-6b), 3.82 (1 H, d, J = 10 Hz, H-1a), 3.91 (1 H, d, J = 10 Hz, H-1b), 4.05-4.12 (2 H, m, H-3 and H-4), 4.26 (1 H, dt, J = 6 and 5.5 Hz, H-5), 4.38 (1 H, d, J = 11.5 Hz, H-1'a), 4.51-4.58 (6 H, m, OCH_2Ph), 4.63 (1 H, d, J = 11.5 Hz, H-1'b), 7.20-8.20 (20 H, m, Ar H); ^{13}C NMR ppm -5.51 (q, $SiCH_3$), 18.30 (s, $SiCMe_3$), 25.92 (q, t-Bu), 62.42, 64.09, 70.76, 71.97, 72.70 and 73.31 (t, -OCH_2-), 81.12 (d, C-3), 84.76 and 85.54 (d, C-4 and C-5), 84.87 (s, C-2), 165.18 (s, C=O). Anal. Calcd for $C_{41}H_{50}O_7Si$: C, 72.11; H, 7.38. Found: C, 72.33; H, 7.18.

(1-*O*-Benzoyl-3,4,6-tri-*O*-benzyl-β-D-fructofuranosyl)-methanol (13). **12** (63 mg) was treated with AcOH, H_2O, and THF (3/1/1, 10 mL). After 36 h at room temperature, usual workup (extraction with ethyl acetate) and chromatography (hexane-ethyl acetate, 4/1 v/v) afforded **13** (50 mg, 95% yield): $[\alpha]_D$ +37.3° (c 1, $CHCl_3$); ^{1}H NMR δ 3.52 (1 H, dd, J = 10.5 and 3.5 Hz, H-6a), 3.66 (1 H, d, J = 12 Hz, H-1'a), 3.68 (1 H, dd, J = 10.5 and 3.5 Hz, H-6b), 3.83 (1 H, d, J = 12 Hz, H-1'b), 4.24 (1 H, d, J = 12 Hz, H-1a), 4.30 (1 H, d, J = 6 Hz, H-3), 4.32 (1 H, d, J = 12 Hz, H-1b), 4.44 (1 H, dd, J = 7 and 6 Hz, H-4), 4.46-4.75 (6 H, m, OCH_2Ph), 7.20-8.00 (20 H, m, Ar H); ^{13}C NMR ppm 63.13, 65.25, 69.54, 72.57, 72.92 and 73.31 (t, -OCH_2-), 80.03 (d, C-3), 83.17 and 85.42 (d, C-4 and C-5), 83.60 (s, C-2), 166.06 (s, C=O). Anal. Calcd for $C_{35}H_{36}O_7$: C, 73.92; H, 6.38. Found: C, 73.76; H, 6.52.

(10) Gensler, W. J.; Johnson, F.; Sloan, A. D. B. *J. Am. Chem. Soc.* **1960**, *82*, 6074.

Synthetic Elaboration of Diosphenols. 2.† Manifold Pathways in the Reaction of Cyclotene Dimethylthiocarbamate with Halide Ion

Anthony A. Ponaras* and Ömer Zaim

Department of Chemistry, The Catholic University of America, Washington, D.C. 20064

Received April 29, 1987

We recently reported[1] that treatment of 1,2-cyclopentanedione dimethylthiocarbamate (**1**) with lithium chloride in acetonitrile/acetic acid gave 2-chloro-2-cyclopenten-1-one (**2a**) in 96% yield and that high yields of simple substitution were also obtained with other *3-unsubstituted* 1,2-cycloalkanediones by using lithium bromide and chloride (Figure 1).

We now report that the simple structural alteration of replacing the vinyl hydrogen of **1** by methyl causes the course of our reaction to be more complex. Thus, when cyclotene dimethylthiocarbamate (**3**) is treated with lithium chloride in boiling acetic acid, chlorine is attached not only to C-2 but also to C-5. This "abnormal" initial

† Part 1: see ref 1.

0022-3263/87/1952-5630$01.50/0