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Wittig chain extension of unprotected carbohydrates: formation of carbohydrate-derived α,β-unsaturated esters

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Abstract

Unprotected carbohydrates react with Wittig reagents **6** and **7** to give unsaturated esters. This homologation has been used to prepare an intermediate (**18**) previously employed in a synthesis of Kdo (**19**).

Keywords: Sugars, unprotected; Wittig reaction; Michael reaction; Chain extension

1. Introduction

In connection with other work, we needed to homologate several carbohydrates into α,β-unsaturated esters, as summarized in Scheme 1. Treatment of D-glucose with the Wittig reagent, $Ph_3P = CHCOOMe$ (**2**) [1], gave, after workup, material that appeared to be a mixture of *C*-glycosyl compounds [1]; evidently, the initial—and desired—unsaturated ester **3** underwent intramolecular Michael addition (Scheme 2). This type of behavior has often been observed before [2], and the extent to which the Michael process occurs depends not only on the reaction conditions [2], but also on the nature of the substrate. Although it is likely that conformationally restricting features of the substrate

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[1] The crude product was not separated into its components; the assignment rests on the following: IR carbonyl absorption at 1732 cm^{-1}; CIMS 254 [M + 18]; very weak olefinic signals in the ^1H NMR spectrum; and on analogy with observations reported in ref. [2].

[2] In a conformationally restricted example, a special experimental procedure (an acid wash of the ylide) suppressed Michael addition (see ref. [3]).

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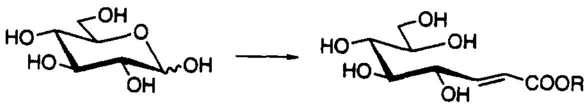
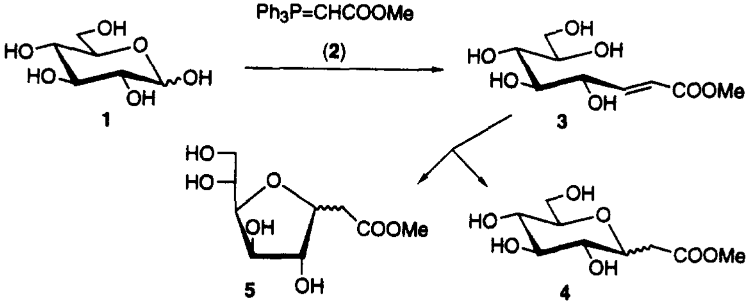


Scheme 1.



Scheme 2.

(such as *O*-isopropylidene groups) could inhibit the Michael closure, it is difficult to identify all the structural characteristics that determine the rate of such cyclizations [4].

$Ph_3P{=}CHCOOBu\text{-}t$
6

$Ph_3P{=}CHCOOCHPh_2$
7

2. Results and discussion

We have found that use of a bulky *O*-alkyl group in the Wittig reagent largely, if not completely, suppresses the Michael reaction and allows the resulting unsaturated ester to be easily isolated [3]. We have used the ylides **6** [6] and **7**, both of which are generated from the corresponding phosphonium bromides by brief treatment with aq sodium hydroxide.

Reagent **6** reacts with glucose in hot dioxane to give the desired unsaturated ester **8** in 66% yield (see Scheme 3, entry 1). The isolated material has exclusively the *E* geometry, as judged by analysis of the ^1H NMR spectrum (300 MHz). The choice of solvent is important; dioxane is very suitable but, in DMF alone, olefination is unacceptably slow. Where necessary, some DMF can be added to solubilize the starting material. The reaction is general, and our results are summarized in Scheme 3, which also lists the experiments with ylide **7**. This ylide was prepared by the straightforward route summarized in Scheme 4.

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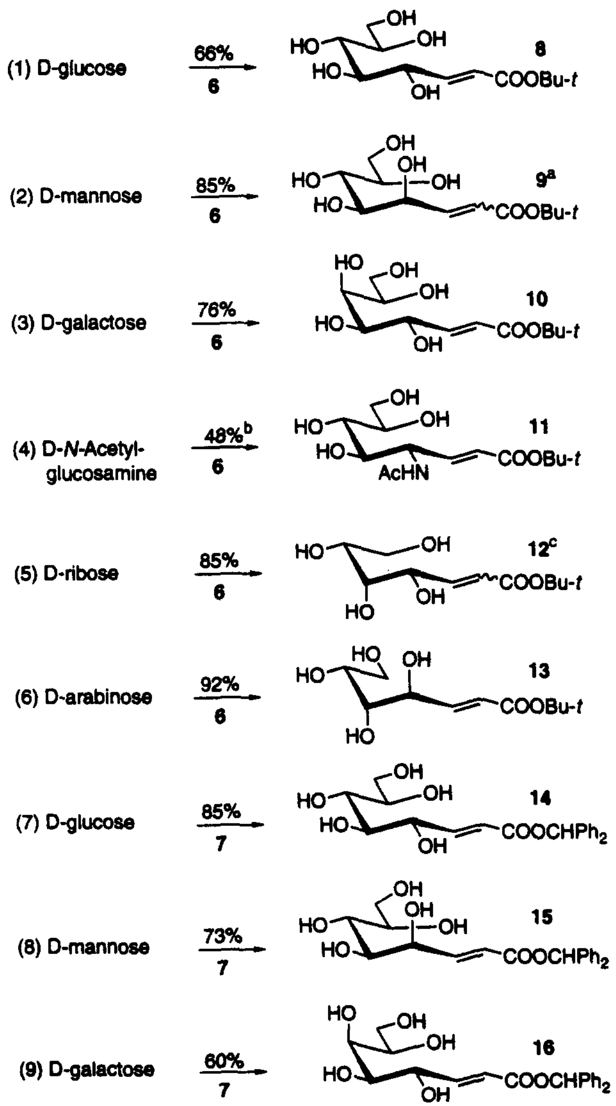
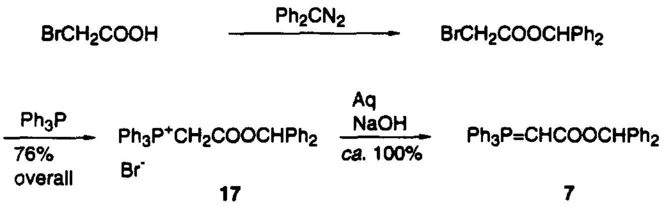
[3] Premature Michael addition also occurs with arsenic-based ylides: see ref. [5].



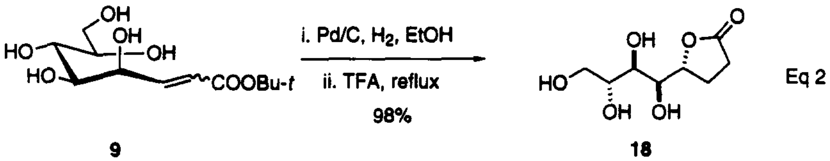
[a] *E*:*Z* = 2:1. [b] After correction for recovered starting material. [c] *E*:*Z*=3:1

Scheme 3.

When the diphenylmethyl reagent **7** is used, then the double bond in the product esters, as well as the carboxyl protecting group, should be removable in the same operation (i.e., exposure to Pd/C–hydrogen), while the *tert*-butyl esters would require hydrogenation and then acid treatment. We have used the two-step sequence, followed by spontaneous lactonization, to prepare **18** (Scheme 5), which is an intermediate in a

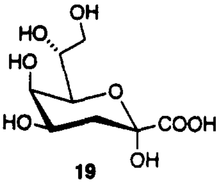


Scheme 4.



Scheme 5.

reported [7] synthesis of Kdo (**19**) [4]. The present route to **18** is more efficient than that used [7] earlier (83% versus 46%, from D-mannose).



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3. Experimental

General methods.—The same general experimental procedures as previously reported [9] were followed.

Diphenylmethyl 2-(triphenylphosphonium)acetate bromide (**7**).—Anhydrous Et_2O (200 mL) was added to a stirred mixture of benzophenone hydrazone (13.0 g, 66.4 mmol), Na_2SO_4 (15.51 g, 119 mmol), and yellow HgO (35.20 g, 162 mmol) under Ar. Satd anhyd ethanolic KOH (5.0 mL) was added, and stirring was continued for 75 min [10]. The wine-colored solution was then added dropwise to a stirred and cooled (0 °C) solution of 2-bromoacetic acid (11.00 g, 79.16 mmol) in acetone (100 mL). Stirring was continued overnight, the solution was diluted to 300 mL with Et_2O, and then washed with aq NaOH (2 N, 1 × 200 mL), and with brine (1 × 200 mL). The organic phase was dried ($MgSO_4$) and evaporated. The residue was dissolved in Et_2O (200 mL), and Ph_3P (19.00 g, 72.4 mmol) was added. The mixture was stirred for 24 h, and the precipitate

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[4] For a very recent approach, see ref. [8].

was filtered off to afford the phosphonium bromide salt (24.92 g, 60%). The mother liquor was stirred for an additional 24 h, affording another batch (6.93 g, 16%; total 76%) of the product (**17**). The salt did not melt, but decomposed at 170 °C; FTIR (Nujol mull) 1734, 1494, 1161 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.73 (d, J_{PH} 14 Hz, 2 H, H-2), 6.69 (s, 1 H, OC*H*Ph$_2$), 7.14–7.34 (m, 11 H, ArH), 7.50–7.57 (m, 6 H, ArH), 7.66–7.84 (m, 8 H, ArH); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 33.33 (dt′, $^1J_{PC}$ 55 Hz, C-2), 79.85 (d′, O*C*HPh), 117.77 (ds′, $^1J_{PC}$ 88 Hz, quaternary aromatic carbon attached to phosphorus), 127.24 (d′), 128.18 (d′), 128.45 (d′), 130.19 (dd′, $^2J_{PC}$ 13 Hz, aromatic carbon *ortho* to phosphorus), 133.77 (dd′, $^3J_{PC}$ 11 Hz, aromatic carbon *meta* to phosphorus), 135.07 (dd′, $^4J_{PC}$ 3 Hz, aromatic carbon *para* to phosphorus), 138.64 (s′, quaternary aromatic carbon of diphenylmethyl), 163.73 (ds′, $^2J_{PC}$ 4 Hz, C-1); HRMS: m/z calcd for $C_{33}H_{27}O_2P$ [M − HBr] 486.1749; found 486.1743. Anal. Calcd for $C_{33}H_{28}BrO_2P$: C, 69.85; H, 4.97; Br, 14.08. Found: C, 70.11; H, 4.86; Br, 13.71.

tert-*Butyl 2,3-dideoxy-*D-gluco-*oct-2-enonate* (**8**).—Aq NaOH (2 N, 25 mL) was added to a solution of *tert*-butyl 2-(triphenylphosphonium)acetate bromide [6] (4.70 g, 10.3 mmol) in $CHCl_3$ (25 mL) in a separatory funnel, and the mixture was shaken gently for 5 min. The organic phase was dried ($MgSO_4$) and evaporated. The residue was dissolved in dry dioxane (25 mL), and D-glucose (1.81 g, 10.1 mmol) was added. The mixture was then heated at 95 °C for 3 h, care being taken not to exceed this temperature. The mixture was cooled to room temperature and then evaporated. The residue was partitioned between water (100 mL) and CH_2Cl_2 (2 × 50 mL). Evaporation of the aq phase and recrystallization of the residue from MeOH, gave **8** (1.84 g, 66%): mp 157–158 °C; $[\alpha]_D$ −16° (*c* 0.82, H_2O); FTIR (Nujol mull) 1689, 1654 cm^{-1}; ^{1}H NMR (D_2O, 300 MHz): δ 1.51 [s, 9 H, C(C*H*$_3$)$_3$], 3.54–3.66 (m, 2 H), 3.72–3.88 (m, 3 H), 4.41–4.47 (m, 1 H, H-4), 6.08 (dd, *J* 16, *J* 2 Hz, 1 H, H-2), 6.86 (dd, *J* 16, *J* 6 Hz, 1 H, H-3); ^{13}C NMR (Me$_2$SO-d_6, 75.5 MHz): δ 27.79 [q′, C(*C*H$_3$)], 63.31 (t′, C-8), 70.76 (d′), 71.19 (d′), 71.99 (d′), 72.30 (d′), 79.54 (s′, O*C*Me$_3$), 121.54 (d′, C-2), 148.47 (d′, C-3), 165.21 (s′, C-1); CIMS: m/z calcd for $C_{12}H_{22}O_7$ 278, found 296 [M + 18]. Anal. Calcd for $C_{12}H_{22}O_7$: C, 51.79; H, 7.97. Found: C, 51.55; H, 7.94.

tert-*Butyl 2,3-dideoxy-*D-manno-*oct-2-enonate* (**9**).—Reagent **6**, prepared as described for the preparation of **8**, and on the same scale, was dissolved in dry dioxane (50 mL), and D-mannose (1.82 g, 10.0 mmol) was added. The mixture was then heated at 70 °C for 2 h. (In this experiment temperature control was not determined to be critical, but the proportion of *E*-isomer was shown to fall at higher temperature.) The mixture was cooled to room temperature and then evaporated. The residue was partitioned between water (100 mL) and CH_2Cl_2 (2 × 50 mL). The aq phase was evaporated, and the residue was recrystallized from MeOH–$CHCl_3$ (by dissolution in MeOH, followed by addition of $CHCl_3$) to give **9** (2.38 g, 85%) as a 2:1 *E*:*Z* mixture of isomers. The crystallization was done by dissolving the material in MeOH and then adding $CHCl_3$ until the solution became turbid. The solution was then left to stand for several hours to give crystalline **9**: mp 153–158 °C; FTIR (MeOH cast) 1686, 1640 cm^{-1}; ^{1}H NMR (Me$_2$SO-d_6, 300 MHz): δ 1.42 (apparent s), 3.33–3.77 (m), 3.98 (d, *J* 8 Hz, H-4), 4.08–4.17 (m), 4.25–4.47 (m), 4.95–5.13 (m), 5.72 (dd, *J* 12, *J* 2 Hz, H-2$_{Z\ \text{isomer}}$), 5.89 (dd, *J* 17, 3 Hz, H-2$_{E\ \text{isomer}}$), 6.13 (dd, *J* 12, *J* 8 Hz, H-2$_{Z\ \text{isomer}}$), 7.08 (dd, *J* 17, *J* 4 Hz, H-2$_{E\ \text{isomer}}$); ^{13}C NMR (Me$_2$SO-d_6, 100.6 MHz): (signals for *Z* isomer are marked with an asterisk) δ 27.81 [q′, C(CH_3)$_3$], 63.76 (t′), 67.07* (d′), 69.64 (d′), 69.80 (d′), 70.70* (d′), 71.15 (d′), 71.31* (d′), 72.07 (d′), 79.42 (s′, OCMe$_3$), 79.95* (s′, OCMe$_3$), 120.97 (d′, C-2), 121.36* (d′, C-2), 150.04* (d′, C-3), 151.03 (d′, C-3), 165.33 (s′, C-1); CIMS: m/z calcd for $C_{12}H_{22}O_7$ 278, found 296 [M + 18]. Anal. Calcd for $C_{12}H_{22}O_7$: C, 51.79; H, 7.97. Found: C, 51.28; H, 7.87.

Fractional crystallization from EtOH gave a mixture rich in the *Z* isomer, and evaporation of the mother liquor affords the *E* isomer (42% recovery): mp 161–162 °C; $[\alpha]_D$ +33 (*c* 0.92, H_2O); FTIR (Nujol mull) 1686, 1640 cm^{-1}; ^1H NMR (D_2O, 300 MHz): δ 1.49 [s, 9 H, C(CH_3)$_3$], 3.61–3.88 (m, 5 H), 4.35–4.41 (m, 1 H, H-4), 6.08 (dd, *J* 16, *J* 2 Hz, 1 H, H-2), 7.05 (dd, *J* 16, *J* 6 Hz, 1 H, H-3); ^{13}C NMR (Me_2SO-d_6, 100.6 MHz): δ 27.86 [q′, C(CH_3)$_3$], 63.81 (t′, C-8), 69.67 (d′), 69.84 (d′), 71.19 (d′), 72.12 (d′), 79.47 (s′, OCMe$_3$), 121.00 (d′, C-2), 151.09 (d′, C-3), 165.37 (s′, C-1); CIMS: m/z calcd for $C_{12}H_{22}O_7$ 278, found 296 [M + 18]. Anal. Calcd for $C_{12}H_{22}O_7$: C, 51.79; H, 7.97. Found: C, 51.34; H, 7.90.

tert-*Butyl 2,3-dideoxy*-D-galacto-*oct-2-enonate* (**10**).—Reagent **6**, prepared as described for the preparation of **8**, and on the same scale, was dissolved in dry dioxane (50 mL), and D-galactose (1.82 g, 10.0 mmol) was added. The mixture was then heated at 95 °C for 10 h, care being taken not to exceed this temperature. The mixture was cooled to room temperature and then evaporated. The residue was partitioned between water (100 mL) and CH_2Cl_2 (2 × 50 mL). The aq phase was evaporated, and the residue was recrystallized from MeOH–$CHCl_3$ (by dissolution in hot MeOH, followed by addition of $CHCl_3$ until the mixture became cloudy), to give **10** (2.13 g, 76%), which contained < 5 mol% water (^1H NMR) even after storage under high vacuum for 5 days. The material had mp 143–145 °C; $[\alpha]_D$ −5.10° (*c* 1.8, H_2O); FTIR (Nujol mull) 1694, 1646 cm^{-1}; ^1H NMR (D_2O, 300 MHz): δ 1.52 [s, 9 H, C(CH_3)$_3$], 3.50–3.78 (m, 4 H), 3.92–3.99 (m, 1 H), 4.61–4.67 (m, 1 H, H-4), 6.08 (dd, *J* 17, *J* 2 Hz, 1 H, H-2), 6.99 (dd, *J* 17, *J* 4 Hz, 1 H, H-3); ^{13}C NMR (D_2O, 100.6 MHz): δ 28.02 [q′, C(CH_3)$_3$], 63.91 (t′, C-8), 70.18 (d′), 70.54 (d′), 70.88 (d′), 72.24 (d′), 83.46 (s′, OCMe$_3$), 123.49 (d′, C-2), 149.27 (d′, C-3), 168.78 (s′, C-1); HRMS: m/z calcd for $C_{11}H_{19}O_7$ 263.1131 [M − CH_3], found 263.1123. We were unable to remove all water from the sample, and a combustion analysis was not obtained.

tert-*Butyl 4-acetamido-2,3,4-trideoxy*-D-gluco-*oct-2-enonate* (**11**).—Reagent **6**, prepared as described for the preparation of **8**, and on the same scale, was dissolved in dry 1:1 dioxane–DMF (50 mL), and 2-acetamido-2-deoxy-α-D-glucopyranose (2.22 g, 10.0 mmol) was added. The mixture was then heated at 90 °C for 4 h, cooled to room temperature, and evaporated. The residue was partitioned between water (100 mL) and CH_2Cl_2 (1 × 50 mL; 2 × 25 mL). The aq phase was evaporated, and the residue was warmed with 1:1 EtOH–$CHCl_3$ (75 mL) (swirling). Insoluble material [2-acetamido-2-deoxy-α-D-glucopyranose (0.153 g)] was filtered off, and the filtrate was evaporated. The new residue was dissolved in hot $CHCl_3$ (50 mL), the solution was cooled to room temperature, and hexane was added to precipitate a further crop (215 mg) of starting material. Evaporation of the mother liquor gave material (2.61 g) that was crystallized from EtOH–$CHCl_3$ (by dissolution in EtOH, followed by addition of $CHCl_3$), to give **11** (1.29 g, 41%, 48%, corrected for recovered 2-acetamido-2-deoxy-α-D-glucopyranose): mp 171–172 °C; $[\alpha]_D$ +30° (*c* 2.0, H_2O); FTIR (KBr disk) 1690 cm^{-1}; ^1H NMR (1% Me_2SO-d_6 in D_2O, 300 MHz): δ 1.48 [s, 9 H, OC(CH_3)$_3$], 2.06 (s, 3 H, N-COCH_3), 3.54 (dd, *J* 8, *J* 3 Hz, 1 H), 3.57–3.78 (m, 2 H), 3.83 (dd, *J* 12, *J* 3 Hz, 1 H), 3.96 (dd, *J* 8, *J* 3 Hz, 1 H), 4.68 (dd, *J* 7, *J* 7 Hz, 1 H, H-4), 5.99 (d, *J* 16 Hz, 1 H, H-2), 6.82 (dd, *J* 16, *J* 6 Hz, 1 H, H-3); ^{13}C NMR (D_2O, 75.5 MHz): δ 22.81 (q′, $COCH_3$), 28.12 [q′, $C(CH_3)_3$], 54.34 (d′, C-4), 63.68 (t′, C-8), 71.24 (d′, two coincident peaks), 71.80 (d′), 83.71 (s′, $OCMe_3$), 125.14 (d′, C-2), 144.54 (d′, C-3), 168.40 (s′, C-1), 174.83 (s′, N-*C*OMe); HRMS: m/z calcd for $C_{14}H_{26}NO_7$ [M + H] 320.1709, found 320.1707. Anal. Calcd for $C_{14}H_{25}NO_7$: C, 52.65; H, 7.89; N, 4.39. Found: C, 52.58; H, 7.81; N, 4.33.

tert-*Butyl 2,3-dideoxy*-D-ribo-*hept-2-enonate* (**12**) .—Reagent **6**, prepared as described for the preparation of **8**, and on the same scale, was dissolved in dry 1:1 dioxane–DMF (25 mL), and D-ribose (1.51 g, 10.1 mmol) was added. The mixture was then heated at 75 °C for 4.5 h, cooled to room temperature, and evaporated. The residue was shaken with a mixture of water (100 mL) and CH_2Cl_2 (50 mL). The layers were separated, and the water was extracted with CH_2Cl_2 (2 × 50 mL). The aq phase was evaporated by freeze-drying. The resulting solid **12** (2.11 g, 85%) was a 3:1 *E*:*Z* mixture of isomers (^1H NMR): mp 80–93 °C; FTIR (MeOH cast) 1694, 1654 cm^{-1}; ^1H NMR (D_2O, 300 MHz) δ 1.57 [s, $C(CH_3)_3$]; 3.65–3.75 (m), 3.76–3.92 (m), 4.60 (ddd, *J* 5, *J* 4, 1.5 Hz, H-$4_{E\text{-isomer}}$), 5.29–5.35 (m, H-$4_{Z\text{-isomer}}$), 6.02 (dd, *J* 11, *J* 1 Hz, H-$2_{Z\text{-isomer}}$), 6.14 (dd, *J* 16, 1.5 Hz, H-$2_{E\text{-isomer}}$), 6.29 (dd, *J* 12, *J* 9 Hz, H-$3_{Z\text{-isomer}}$), 7.03 (dd, *J* 16, *J* 5 Hz, H-$3_{E\text{-isomer}}$). ^{13}C NMR (D_2O, 75 MHz) [peaks marked with an asterisk correspond to (minor) *Z*-isomer] δ 27.46 [q′, $C(CH_3)_3$], 62.78 (t′, C-7), 62.83 (t′)*, 67.94 (d′)*, 71.17 (d′), 71.70 (d′)*, 71.87 (d′), 73.87 (d′)*, 82.87 [s′ $C(CH_3)_3$], 83.31 [s, $C(CH_3)_3$]*, 123.98 (d′, C-2), 143.49 (d′, C-3)*, 145.63 (d′, C-3), 167.46 (s′, C-1)*, 167.88 (s, C-l); CIMS: m/z calcd for $C_{11}H_{20}O_6$ 248, found 266 [M + 18]. Anal. Calcd for $C_{11}H_{20}O_6$: C, 53.22; H, 8.12. Found: C, 53.38; H, 8.26.

tert-*Butyl 2,3-dideoxy*-D-arabino-*hept-2-enonate* (**13**).—Reagent **6**, prepared as described for the preparation of **8**, and on the same scale, was dissolved in dry 1:1 dioxane–DMF (25 mL), and D-arabinose (1.50 g, 10.0 mmol) was added. The mixture was then heated at 75 °C for 4 h, cooled to room temperature, and then evaporated. The residue was shaken with a mixture of water (100 mL) and CH_2Cl_2 (50 mL). The layers were separated and the water was extracted with CH_2Cl_2 (2 × 50 mL). The aq phase was evaporated, the residue was dissolved in MeOH (50 mL), and the solvent was evaporated again. This procedure of evaporation from MeOH was repeated once more. The residue was dissolved in Et_2O (300 mL), and the solution was set aside for 24 h. The resulting solid was filtered off and recrystallized from $CHCl_3$–hexane (by dissolution in $CHCl_3$, followed by addition of hexane), affording **13** (2.29 g, 92%): mp 148–149 °C; $[\alpha]_D$ 7.1° (*c* 1.7, H_2O); FTIR (MeOH cast) 1702 cm^{-1}; ^1H NMR (D_2O, 500 MHz): δ 1.36 [s, 9 H, $C(CH_3)_3$], 3.46–3.53 (m, 2 H), 3.58–3.63 (m, 1 H), 3.67 (dd, *J* 12, *J* 3 Hz, 1 H), 4.42–4.46 (m, 1 H, H-4), 5.92 (ddd, *J* 15, 2, *J* 1 Hz, 1 H, H-2), 6.81 (ddd, *J* 15, 4.5, 1 Hz, 1 H, H-3); ^{13}C NMR (D_2O–1% Me_2SO-d_6, 75.5 MHz): δ 28.29 [q′, $C(CH_3)_3$], 63.76 (t′, C-7), 70.75 (d′), 71.82 (d′), 73.52 (d′), 83.47 (s′, $OCMe_3$), 123.78 (d′, C-2), 149.14 (d′, C-3), 168.66 (s′, C-1); CIMS: m/z calcd for $C_{11}H_{20}O_6$ 248, found 266 [M + 18]. Anal. Calcd for $C_{11}H_{20}O_6$: C, 53.22; H, 8.12. Found: C, 53.35; H, 8.13.

Diphenylmethyl 2,3-dideoxy-D-gluco-*oct-2-enonate* (**14**) .—Aq NaOH (2 N, 75 mL) was added to a solution of **17** (6.15 g, 10.8 mmol) in $CHCl_3$ (75 mL) in a separatory funnel, and the mixture was shaken gently for 5 min. The organic phase was dried ($MgSO_4$) and evaporated. The residue was dissolved in dry 1:1 dioxane–DMF (25 mL), and D-glucose (1.82 g, 10.1 mmol) was added. The mixture was then heated at 90 °C for 3 h, cooled to room temperature, and then evaporated. The residue was shaken with a mixture of water (100 mL) and CH_2Cl_2 (100 mL), and the resulting emulsion was allowed to stand for at least 24 h, at which time the solid product had collected at the interface of the two immiscible liquids. The material was filtered off and recrystallized from MeOH–H_2O (by dissolution in hot MeOH, followed by addition of water until the mixture became cloudy), affording **14** (3.29 g, 85%): mp 139–140 °C; $[\alpha]_D$ −12.6° (*c* 1.1, MeOH); FTIR (MeOH cast) 1715, 1657 cm^{-1}; ^1H NMR (Me_2SO-d_6, 300 MHz): δ 3.31–3.69 (m, 5 H), 4.22–4.36 (m, 2 H, H-4 and OH), 4.39 (d, *J* 7 Hz, 1 H), 4.44 (d, *J* 6 Hz, 1 H), 4.56 (d, *J* 6 Hz, 1 H), 5.18 (d, *J* 4.5 Hz, 1 H), 6.13 (dd, *J* 16, *J* 2 Hz, 1 H, H-2), 6.85 (s, 1 H, C*H*Ph_2), 7.13 (dd, *J* 16, *J* 5 Hz, 1 H, H-3), 7.22–7.46 (m, 10 H, ArH); ^{13}C NMR (Me_2SO-d_6, 75.5 MHz): δ 63.32 (t′, C-8), 70.65 (d′), 71.23 (d′), 72.14 (d′), 72.30 (d′), 76.09 (d′, O*C*HPh_2), 119.24 (d′, C-2), 126.46 (d′), 126.50 (d′), 127.72 (d′), 128.51 (d′), 140.60 (s′, quaternary aromatic carbon), 150.94 (d′, C-3), 164.80 (s′, C-1) (expected 17 peaks); HRMS: *m/z* calcd for $C_{21}H_{22}O_6$ [M − H_2O] 370.1416, found 370.1389. Anal. Calcd for $C_{21}H_{24}O_7$: C, 64.94; H, 6.23. Found: C, 64.76; H, 6.08.

Diphenylmethyl 2,3-dideoxy-D-manno-*oct-2-enonate* (**15**) .—Reagent **7**, prepared as described for the preparation of **14**, and on the same scale, was dissolved in dry dioxane (30 mL), and D-mannose (1.82 g, 10.1 mmol) was added. The mixture was then heated at 90 °C for 6 h, cooled to room temperature, and then evaporated. The residue was shaken with a mixture of water (100 mL) and CH_2Cl_2 (100 mL), and the resulting emulsion was allowed to stand for at least 24 h, by which time the solid product had collected at the interface of the two immiscible liquids. The material was filtered off and recrystallized from MeOH–H_2O (by dissolution in hot MeOH, followed by addition of water until the mixture became cloudy), to give **15** (2.84 g, 73%): mp 152–155 °C; $[\alpha]_D$ 12.6° (*c* 0.65, MeOH); FTIR (MeOH cast) 1717, 1653 cm^{-1}; ^1H NMR (Me_2SO-d_6, 300 MHz) traces of the *Z* isomer visible in the spectrum: δ 3.33–3.68 (m, 5 H), 4.15–4.23 (m, 1 H), 4.28 (d, *J* 7.2 Hz, 1 H), 4.34 (dd, *J* 5.5, 5.5 Hz, 1 H), 4.44 (d, *J* 5 Hz, 1 H), 4.56 (d, *J* 7.2 Hz, 1 H), 5.23 (d, *J* 6 Hz, 1 H), 6.16 (dd, *J* 15.5, 1.75 Hz, 1 H), 6.88 (s, 1 H), 7.21–7.45 (m, 11 H); ^{13}C NMR (Me_2SO-d_6, 75.5 MHz): δ 63.81 (t′, C-8), 69.66 (d′), 69.91 (d′), 71.13 (d′), 72.09 (d′), 76.12 (d′, *C*HPh_2), 118.98 (d′, C-2), 126.50 (d′), 127.76 (d′), 128.55 (d′), 140.62 (s′, quaternary aromatic carbon), 153.42 (d′, C-3), 164.89 (s′, C-1) (17 signals expected); CIMS: *m/z* calcd for $C_{21}H_{24}O_7$ 388, found 406 [M + 18]. Anal. Calcd for $C_{21}H_{24}O_7$: C, 64.94; H, 6.23. Found: C, 64.92; H, 6.28.

Diphenylmethyl 2,3-dideoxy-D-galacto-*oct-2-enonate* (**16**).—Reagent **7**, prepared as described for the preparation of **14**, and on the same scale, was dissolved in dry 1:1 dioxane–DMF (25 mL), and D-galactose (1.82 g, 10.1 mmol) was added. The mixture was then heated at 90 °C for 3 h, cooled to room temperature, and then evaporated. The residue was shaken with a mixture of water (100 mL) and CH_2Cl_2 (100 mL), and the resulting emulsion was allowed to stand for at least 24 h, at which time the solid product had collected at the interface of the two immiscible liquids. The material was filtered off and recrystallized from MeOH–H_2O (by dissolution in hot MeOH, followed by addition of water until the mixture became cloudy), affording **16** (2.32 g, 60%): mp 171–172 °C; $[\alpha]_D$ $-11°$ (*c* 0.67, MeOH); FTIR (MeOH cast) 1712 cm^{-1}; ^1H NMR (Me_2SO-d_6, 300 MHz): δ 3.36–3.60 (m, 4 H), 3.68–3.77 (m, 1 H), 4.23 (d, *J* 7, 1 H), 4.25 (d, *J* 7, 1 H), 4.44–4.60 (m, 3 H), 4.90 (d, *J* 7 Hz, 1 H), 6.17 (dd, *J* 16, *J* 2 Hz, 1 H, H-2), 6.87 (s, 1 H, C*H*Ph_2), 7.17 (dd, *J* 16, *J* 4 Hz, 1 H, H-3), 7.24–7.47 (m, 10 H); ^{13}C NMR (Me_2SO-d_6, 75.5 MHz): δ 63.02 (t′, C-8), 69.57 (d′), 69.88 (d′), 70.11 (d′), 71.87 (d′), 76.13 (d′, O*C*HPh_2), 119.48 (d′, C-2), 126.48 (d′), 126.55 (d′), 127.75 (d′), 128.54 (d′), 140.65 (s′, quaternary aromatic carbon), 153.04 (d′, C-3), 164.78 (s′, C-1) (17 signals expected); CIMS: *m/z* calcd for $C_{21}H_{24}O_7$ 388, found 406 [M + 18]. Anal. Calcd for $C_{21}H_{24}O_7$: C, 64.94; H, 6.23. Found: C, 65.23; H, 6.17.

*Preparation of 2,3-dideoxy-*D-manno*-octanono-1,4-lactone* (**18**).—A 2:1 mixture of *tert*-butyl (*E*)- and (*Z*)-2,3-dideoxy-2-D-*manno*-oct-2-enonate (**9**) (0.920 g, 3.31 mmol) in absolute EtOH (100 mL) was hydrogenated in a Parr shaker at 55 psi using 10% Pd–C (100 mg). After 16 h the catalyst was filtered off and TFA (10 mL) was added. The resulting solution was refluxed for 1 h, cooled to room temperature and evaporated. The residue was covered with 1:1 EtOH–toluene (25 mL), and evaporation then gave the crude product, which was recrystallized from EtOH, to afford **18** (0.671 g, 98%): mp 155–156 °C [lit. [7] mp 156–157 °C]; $[\alpha]_D$ $-15°$ (*c* 0.52, EtOH) [lit. [7] $-16.6°$ (EtOH)]; FTIR (MeOH cast) 1770, 1737 cm^{-1}; ^1H NMR (D_2O, 400 MHz): δ 2.27–2.37 (m, 1 H, H-3), 2.39–2.51 (m, 1 H, H-3), 2.64–2.77 (m, 2 H, H-2), 3.67–3.72 (m, 2 H), 3.77–3.82 (m, 1 H), 3.89 (dd, *J* 11.5, 3 Hz, 1 H), 4.02 (dd, *J* 6.5, 1.5 Hz, 1 H), 4.77 (ddd, *J* 7, 7, *J* 7 Hz, 1 H); ^{13}C NMR (D_2O, 100 MHz): δ 23.31 (t′, C-3), 28.18 (t′, C-2), 62.85 (t′, C-8), 69.78 (d′), 70.19 (d′), 70.56 (d′), 81.05 (d′), 181.71 (s′, C-1); HRMS: *m/z* calcd for $C_8H_{15}O_6$ [M + H] 207.0869, found 207.0864. Anal. Calcd for $C_8H_{14}O_6$: C, 46.60; H, 6.84. Found: C, 46.64; H, 6.74.

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References

[1] O. Isler, H. Gutmann, M. Montavon, R. Rüegg, G. Ryser, and P. Zeller, *Helv. Chim. Acta*, 40 (1957) 1242–1249.

[2] (a) Y.A. Zhdanov, Y.E. Alexeev, and V.G. Alexeeva, *Adv. Carbohydr. Chem. Biochem.*, 27 (1972) 227–299. (b) F. Nicotra, F. Ronchetti, G. Russo, and L. Toma, *Tetrahedron Lett.*, 25 (1984) 5697–5700. (c) F. Nicotra, F. Ronchetti, and G. Russo, *J. Org. Chem.*, 47 (1982) 5381–5382. (d) N.K. Kochetkov and B.A. Dmitriev, *Tetrahedron*, 21 (1965) 803–815.

[3] R.D. Dawe and B. Fraser-Reid, *J. Org. Chem.*, 49 (1984) 522–528.

[4] (a) Cf. T.H. Webb, L.M. Thomasco, S.T. Schlachter, J.J. Gaudino, and C.S. Wilcox, *Tetrahedron Lett.*, 29 (1988) 6823–6826.

[5] L. Dheilly, C. Lièvre, C. Fréchou, and G. Demailly, *Tetrahedron Lett.*, 34 (1993) 5895–5898.

[6] W. Flitsch and E. Mukidjam, *Chem. Ber.*, 112 (1979) 3577–3588.

[7] P.M. Collins, W.G. Overend, and T. Shing, *J. Chem. Soc., Chem. Commun.*, (1981) 1139–1140.

[8] B. Giese and T. Linker, *Synthesis*, (1992) 46–48.

[9] D.L.J. Clive, T.L.B. Boivin, and A.G. Angoh, *J. Org. Chem.*, 52 (1987) 4943–4953.

[10] J.B. Miller, *J. Org. Chem.*, 24 (1959) 560–561.