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Influence of the Protective Groups on the Ring Closure of *gluco*-Octenoates

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Among the procedures for the synthesis of *C*-glycopyranosides and *C*-glycofuranosides, two classes of compounds which are of interest for their relationship to the *C*-nucleosides, the Wittig reaction has recently been widely employed.[1-5] The procedure requires the cyclization of the Wittig reaction product to a *C*-glycosyl derivative. In the case of α,β-unsaturated methyl and ethyl enoates, such a ring closure generally requires treatment with base;[1,3] the only known exception is that of the systems in which a preexisting five-membered ring strongly favors the spontaneous formation of a second fused five-membered ring.[3-5]

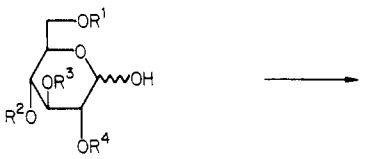
We now report some unexpected results on the behavior of α,β-unsaturated ethyl octenoates toward the cyclization to *C*-glucopyranosides.

The *gluco*-octenoate **8**, obtained by treatment of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (**7**) with 2 equiv of (carbethoxymethylene)triphenylphosphorane, was unexpectedly stable to base: after treatment with sodium methoxide, either at room temperature or under reflux, no cyclization occurred, and **8** was recovered unchanged. Treatment of **8** with a catalytic amount of *p*-toluenesulfonic acid or with iodine did not lead to the corresponding *C*-glucopyranoside but, in both cases, to the furano derivative **11**. The presence of the conjugated carboxylate is essential for this aromatization, as it was not observed when the product of the reaction of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose with methylenetriphenylphosphorane[2] was treated as above.

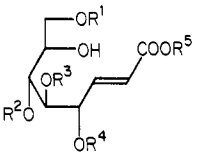
A quite different behavior was observed when 2,3,4,6-tetra-*O*-acetyl-D-glucopyranose (**1**) was treated with (carbethoxymethylene)triphenylphosphorane: a 1:1 mixture[6] of the α- and β-*C*-glucopyranosyl derivative **3** was obtained, whereas the enoate **2** was present only in small amounts (Scheme I). The conversion of the enoate **2** into a furano derivative, attempted as described for **8**, was unsuccessful.

In the light of these facts it is clear that the nature of the protecting groups plays a striking role in the cyclization of such enoates. In the case of the tetra-*O*-benzyl derivative **8**, a possible explanation of its behavior could be that, owing to the steric hindrance of the benzyl group and to the conformational mobility of the molecule, the conformation required for the Michael-type ring closure can be attained only with difficulty; however, **8** can undergo an easy acid-catalyzed rearrangement with loss of benzyl alcohol and formation of a furano derivative (Scheme II). In the case of the ethylidene derivative **4**, described by Fraser-Reid et al.,[1] the proper conformation can be at-

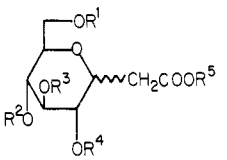
Scheme I

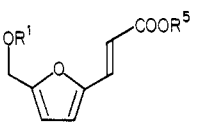


1, $R^1 = R^2 = R^3 = R^4 = Ac$
4, $R^1, R^2 = CH_3CH$; $R^3 = R^4 = H$
7, $R^1 = R^2 = R^3 = R^4 = Bzl$
9, $R^1 = R^2 = R^3 = Ac$; $R^4 = Bzl$



2, $R^1 = R^2 = R^3 = R^4 = Ac$; $R^5 = Et$
5, $R^1, R^2 = CH_3CH$; $R^3 = R^4 = H$; $R^4 = H$; $R^5 = Me$
8, $R^1 = R^2 = R^3 = R^4 = Bzl$; $R^5 = Et$
10, $R^1 = R^2 = R^3 = Ac$; $R^4 = Bzl$; $R^5 = Et$

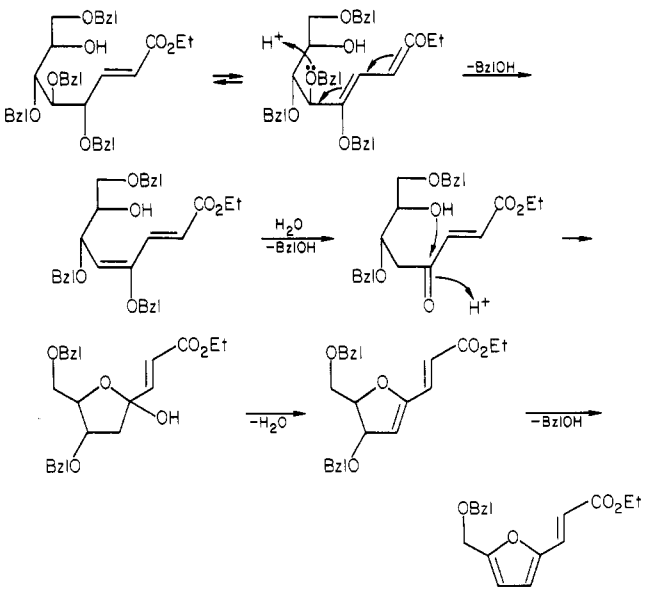




11, $R^1 = Bzl$; $R^5 = Et$

3, $R^1 = R^2 = R^3 = R^4 = Ac$; $R^5 = Et$
6, $R^1, R^2 = CH_3CH$; $R^3 = R^4 = H$; $R^5 = Me$

Scheme II



(1) Fraser-Reid, B.; Dawe, R. D.; Bhandu Tulshian, D. *Can. J. Chem.* **1979**, *57*, 1746.
(2) Pougny, J. R.; Nassr, M. A. M.; Sinäy, P. *Chem. Commun.* **1981**, 375.
(3) Ohrui, H.; Jones, G. H.; Moffatt, J. G.; Maddox, M. L.; Christensen, A. T.; Byram, S. K. *J. Am. Chem. Soc.* **1975**, *97*, 4606.
(4) Chu, C. K.; Wempen, I.; Watanabe, K. A.; Fox, J. J. *J. Org. Chem.* **1976**, *41*, 2793.
(5) Collins, P. M.; Overend, W. G.; Shing, T. S. *Chem. Commun.* **1982**, 297.
(6) As deduced from ^1H and ^{13}C NMR, see Experimental Section.

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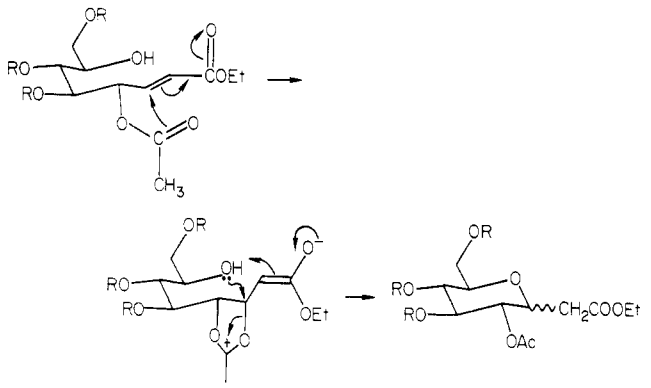
Scheme III



tained more easily, and the Michael-type ring closure can occur by treatment with sodium methoxide. In the case of the tetra-*O*-acetyl derivative **2**, the direct cyclization to the *C*-glucopyranosyl derivative **3** may rely on the "participation" of the acyloxy substituent at C-4 (Scheme III), as happens in the glycosidation reaction. In agreement with this last hypothesis, 2-*O*-benzyl-3,4,6-tri-*O*-acetyl-D-glucopyranose (**9**), which differs from **1** by the presence of a "nonparticipating" benzyl-protecting group at the required position, when submitted to the Wittig reaction with (carbethoxymethylene)triphenylphosphorane, yielded the enoate **10** but no *C*-glucopyranosyl derivative.

It is noteworthy that the acetyl protecting group, which was considered unsuitable for the synthesis of *C*-glycosides via the described procedure, owing to the basic condition employed for the cyclization of the Wittig reaction product, could become the protecting group of choice, if present at C-2 in the starting aldehydo sugar, because of its capability to induce the spontaneous formation of the *C*-glucopyranosides.

Experimental Section

General Methods. Column chromatography was performed using 230–400 mesh Merck silica gel. Thin-layer chromatography (TLC) was done on Merck silica gel HF-254 plates, using hexane–ethyl acetate, 2:1 (a) or 1:1 (b), as eluant. The spots were detected with UV light and/or by spraying with 50% aqueous sulfuric acid and heating at 110 °C. NMR spectra were obtained on a Varian XL-100 spectrometer. IR spectra were obtained on a Perkin-Elmer 681 instrument. Melting points are uncorrected. Usual workup refers to diluting with an organic solvent, washing with water to neutrality, drying over Na_2SO_4, and evaporating under reduced pressure.

Reaction of 2,3,4,6-Tetra-*O*-benzyl-D-glucopyranose (7) with (Carbethoxymethylene)triphenylphosphorane. 2,3,4,6-Tetra-*O*-benzyl-D-glucopyranose[7] (5.4 g, 10 mmol) in CH_3CN (50 mL) was refluxed with (carbethoxymethylene)triphenylphosphorane (6.7 g, 20 mmol). After 16 h the solvent was removed under reduced pressure, and the residue, submitted to chromatography (hexane–ethyl acetate 2:1), afforded **8** (5.2 g, oil): IR (Nujol) ν_{max} 3450, 1735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.30 (t, J = 7 Hz, CH_3), 3.87 (m, H-7), 4.26 (q, J = 7 Hz, OCH_2CH_3), 3.52, 4.48, 4.66, and 4.76 (OCH_2Ph), 4.1–4.6 (H-5, H-6, H-8, H-8'), 5.53 (d, J = 9 Hz, H-4), 6.20 (d, J = 16 Hz, H-2), 7.20 (d, J = 16 Hz, H-3), 7.3 (Ar H); ^{13}C NMR ($CDCl_3$) 119.71 (=CHCOO), 139.56 (CH=), 166.32 (COO) ppm.

Attempted Cyclization of 8. (a) Compound **8** (100 mg) was treated with sodium ethoxide (0.1 M, 0.5 mL); after 30 min at room temparature, TLC analysis (eluant a) showed the presence of only unreacted **8**; the same result was obtained after 15 min under reflux.

(b) **8** (200 mg) in CH_2Cl_2 (5 mL) was treated with *p*-toluenesulfonic acid (50 mg). After 30 min at room temperature TLC analysis (eluant a) showed the formation of a single product, which was recovered by usual workup (91 mg) and crystallized from hexane (mp 61 °C). Structure **11** was assigned to this product: ^1H NMR ($CDCl_3$) δ 1.30 (t, J = 7 Hz, CH_3), 4.25 (q, J = 7 Hz, OCH_2CH_3), 4.49 (s, OCH_2C=), 4.56 (s, OCH_2C=), 6.33 (d, J = 15 Hz, H-3), 6.40 (d, J = 4 Hz, H-5 or H-6), 6.56 (d, J = 4 Hz, H-5 or H-6), 7.41 (d, J = 15 Hz, H-2); mass spectrum, m/e 286, 179, 151, 91. Anal. Calcd for $C_{17}H_{18}O_4$: C, 71.31; H, 6.34. Found: C, 71.36; H, 6.25.

(c) To a solution of **8** (100 mg) in CH_2Cl_2 (10 mL), a saturated solution of $NaHCO_3$ (5.5 mL) was added. The mixture was stirred at room temperature, and a solution of iodine (81 mg) in CH_2Cl_2 (5 mL) was added dropwise. After 2 h, TLC analysis (eluant a) showed the quantitative formation of the furano derivative **11** as in method b.

Reaction of 2,3,4,6-Tetra-*O*-acetyl-D-glucopyranose (1) with (Carbethoxymethylene)triphenylphosphorane. 2,3,4,6-Tetra-*O*-acetyl-D-glucopyranose[8] (1 g, 2.9 mmol) in CH_3CN (25 mL) was refluxed with (carbethoxymethylene)triphenylphosphorane (2 g, 5.8 mmol). After 20 h, TLC analysis (eluant b) showed the formation of two predominant products. The solvent was then removed under reduced pressure, and the residue was chromatographed (hexane–ethyl acetate, 2:1). To the higher R_f (0.40) predominant product (305 mg, oil) was assigned the structure of the *C*-glucopyranoside **3** (ca. 1:1 mixture of α and β isomers): ^1H NMR ($CDCl_3$) δ 2.47 (0.5-H, d, H-2), 2.6 (0.5-H, m, H-2 of the other isomer), 3.6–5.2 (9-H); ^{13}C NMR ($CDCl_3$) 37.27 and 33.20 (C-2 of the two isomers) ppm.

To the lower R_f (0.25) product (117 mg, oil) was assigned the structure **2**: ^1H NMR ($CDCl_3$) δ 1.30 (t, J = 7 Hz, CH_3), 2.0–2.1 (12-H, OAc), 3.65 (m, H-7), 4.1–4.5 (4-H, CH_2O), 5.1–5.5 (H-5 and H-6), 5.98 (dd, $J_{3,4}$ = 5 Hz, $J_{4,5}$ = 7 Hz, H-4), 6.29 (d, J = 5 Hz, H-2), 7.37 (d, J = 5 Hz, H-3).

Reaction of 2-*O*-Benzyl-3,4,6-tri-*O*-acetyl-D-glucopyranose (9) with (Carbethoxymethylene)triphenylphosphorane. 2-*O*-Benzyl-3,4.6-tri-*O*-acetyl-D-glucopyranose[9] (**9**; 120 mg, 0.3 mmol) in CH_3CN (5 mL) was refluxed with (carbethoxymethylene)triphenylphosphorane (209 mg, 0.6 mmol). After 20 h, the solvent was removed under reduced pressure, and the residue was purified by chromatography. The only detectable product was the enoate **10** (35 mg, oil): ^1H NMR ($CDCl_3$) δ 1.30 (t, J = 7 Hz, CH_3), 2.00, 2.05, and 2.05 (s, OAc), 3.65 (m, H-7), 4.0–4.2 (H-4, H-8, H-8'), 4.25 (q, J = 7 Hz, OCH_2CH_3), 4.83 (s, OCH_2Ph), 5.47 (d, J = 10 Hz, H-6), 5.83 (dd, $J_{5,6}$ = 10 Hz, $J_{4,5}$ = 5 Hz, H-5), 6.20 (d, J = 16 Hz, H-2), 7.10 (d, J = 16 Hz, H-3).

Registry No. **1**, 40437-08-9; **2**, 83232-14-8; α-**3**, 83232-12-6; β-**3**, 83232-13-7; **7**, 38768-81-9; **8**, 82933-07-1; **9**, 83232-15-9; **10**, 83232-16-0; **11**, 83232-11-5; (carboethoxymethylene)triphenylphosphorane, 1099-45-2.

(7) Tate, M. G.; Bishop, C. T. *Can J. Chem.* **1963**, *41*, 1801.

(8) Excoffier, G.; Gagnaire, D.; Utille, J. P. *Carbohydr. Res.* **1975**, *39*, 368.

(9) Brennan, S.; Finan, P. A. *J. Chem. Soc. c*, **1970**, 1742.

Reductive Cyclization Caused by Cobaloxime I. A New Method for the Synthesis of β-Methylene-γ-butyrolactones

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A β-methylene-γ-butyrolactone structural unit is present in some furanoid terpenes.[1] A few methods of synthesizing the unit have been reported. One method involves the reaction of an enol ether with the carbene derived from diazomalonate as a key step,[2] and the second method

(1) Devon, T. K.; Scott, A. I. "Handbook of Naturally Occurring Compounds"; Academic Press: New York, 1972; Vol. 2, p 172.

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