The Wittig-Horner Reaction on 2,3,4,6-Tetra-*O*-benzyl-D-mannopyranose and 2,3,4,6-Tetra-*O*-benzyl-D-glucopyranose

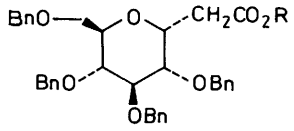
Pietro Allevi,* Pierangela Ciuffreda, and Diego Colombo
Dipartimento di Chimica e Biochimica Medica, Facoltà di Medicina e Chirurgia, Università di Milano, Via Saldini 50, I-20133 Milano, Italy
Diego Monti,* Giovanna Speranza, and Paolo Manitto
Centro Studi per le Sostanze Organiche del CNR and Dipartimento di Chimica Organica ed Industriale, Via Venezian 21, Milano, Italy

The synthetic utility of the Wittig-Horner reaction in the synthesis of C-glycosides is illustrated by the preparation of the α-and β-glycosyl acetates of the 2,3,4,6-tetra-*O*-benzyl-D-mannopyranose and of the 2,3,4,6-tetra-*O*-benzylglucopyranose. A partial epimerization of the C-2 carbon of the starting protected carbohydrate is observed.

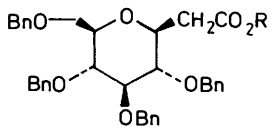
Wittig reactions on sugars are key to an efficient synthetic route to *C*-glycosides and were widely used in recent years.[1] In a previous preliminary paper[2] some of us reported a simple and convenient method for obtaining ethyl 2,3,4,6-tetra-*O*-benzyl-D-glucopyranosyl acetates as a mixture of isomers (**1a**), and (**2a**) employing the Wittig-Horner reaction of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose with triethyl phosphonoacetate followed by spontaneous cyclization of the initially formed α,β-unsaturated ester in the reaction medium. Other authors reported[3] that an analogue Wittig reaction afforded only the diene (**3**).† To test the general applicability of the method reported we attempted the synthesis of the isomeric acetates (**4a**), and (**5a**) derived from 2,3,4,6-tetra-*O*-benzyl-D-mannopyranose. Synthesizing the isomer (**4a**) by this method appeared of particular interest since it was reported[4] that only the β-isomer (**5a**) is obtainable in profitable yield by a three-step synthetic procedure. This affords the isomers (**4a**), and (**5a**) in a 1:3 ratio while neither of them is obtainable by the Wittig reaction.[3]

Thus the tetra-*O*-benzylmannopyranose, after optimisation of the reaction conditions, reacting with triethyl phosphonoacetate sodium salt in tetrahydrofuran at 50 °C afforded a mixture of four compounds (**1a**), (**2a**), (**4a**), and (**5a**) in a ratio (h.p.l.c.) of 2.3:1:21:9 and with a total yield of 86%. They were easily separated by rapid chromatography to the two pairs (**1a**), (**2a**) and (**4a**), (**5a**) (obtained in 8.6 and 77% yield respectively). The isolation by preparative t.l.c. of the single compounds required three elutions of the microplates with the same eluant.

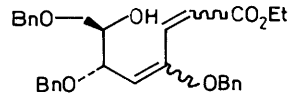
Assignment of the structure of the glucosyl derivative (**1a**) was by examination of spin-spin coupling constants for the ring protons in the 300 MHz ^{1}H n.m.r. spectrum. In particular the equatorial-axial relationship of the proton on C-1 and that on C-2 was derived from the observed coupling constant for these protons ($J_{1,2}$ 5.5 Hz, predicted[5] $J_{1,2}$ 5.4 Hz). Compound (**2a**) showed all the spectroscopic data in agreement with the assigned structure, which stereochemistry was clear from the ^{1}H n.m.r. spectrum. Appropriate physicochemical properties were observed also for the mannosyl derivatives (**4a**) and (**5a**). In addition, examination of the spin-spin coupling constants for their ring protons in the 300 MHz ^{1}H n.m.r. spectra showed that compound (**4a**) was the α-anomer in a $^1C_4$ conformation with the bulky anomeric substituent in an equatorial orientation as predictable[6] for this isomer. Compound (**5a**) was the β-anomer with a $^4C_1$ conformation.[6] In agreement with these assignments



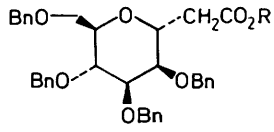
(**1**)



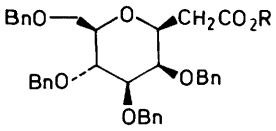
(**2**)



(**3**)



(**4**)



a; R = Et
b; R = Me

(**5**)

the 80 MHz ^{1}H n.m.r. spectra of the compounds (**2a**), (**4a**), and (**5a**) were superimposable with those of the same compounds reported by Y. Kishi and available as supplementary material.[4]

In order to circumvent the tiresome separation of the ethyl acetates (**1a**), (**2a**), and (**4a**), (**5a**), and to enhance their synthetic availability, we performed the Wittig-Horner reaction with trimethyl phosphonoacetate. In fact, our previous experience had shown that *C*-glucopyranosyl acetates methyl esters (**1b**) and (**2b**) were separable by column chromatography more easily than the corresponding ethyl esters. In this way we succeeded in producing pure *C*-glucopyranoside methyl esters (**1b**) and (**2b**) and the *C*-mannopyranoside methyl esters (**4b**) and (**5b**) with the same yields observed for the ethyl esters. Also the observed coupling constants of the relevant protons in the 300 MHz ^{1}H n.m.r. spectra of the methyl esters (**1b**), (**2b**), (**4b**), and (**5b**) were in complete accord with the proposed structures and with literature reports.[4]

† The diene (**3**) was also obtained[2] as a by-product of the Wittig-Horner reaction in DMF when an excess of NaH was used. Its structure, however, was erroneously represented as an homologous alkene.

The obtention of *C*-glucopyranosides starting from tetra-*O*-benzylmannopyranose was unexpected although the Wittig-Horner reagent could theoretically induce C-2 epimerization at the level of the starting tetra-*O*-benzylmannopyranose and/or of the α,β-unsaturated ester mixture before its Michael-like cyclization. However, the second possibility was rejected on the basis of the h.p.l.c. evidence. In fact, the starting tetra-*O*-benzylmannopyranose partially isomerized to the corresponding tetra-*O*-benzylglucopyranose just a few minutes after having mixed the reagents. On the other hand, the *C*-mannopyranosides/*C*-glucopyranosides ratio measured during the first stages of the reaction remained unchanged until the end and the ratio between the α- and β-anomer for each pair (**1b**), (**2b**) and (**4b**), (**5b**) was constant throughout the reaction. Additional support for the complete initial isomerization of the tetra-*O*-benzylmannopyranose was obtained by treating the pure isolated four *C*-glycopyranosides (**1b**), (**2b**), (**4b**), and (**5b**) with trimethyl phosphonoacetate sodium salt (5 mequiv.) in tetrahydrofuran at 50 °C for 4 h. Under these conditions no isomerization of α- to the β-anomers or C-2 epimerization was observed and the compounds were recovered unchanged in quantitative yields.

In the light of these results it appeared necessary to re-examine the Wittig-Horner reaction of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose with triethyl phosphonoacetate[2] using the conditions described above. Thus, also in this case, the epimerization of the starting material was found to occur with formation of 2,3,4,6-tetra-*O*-benzyl-D-mannopyranose and consequently of a mixture of the *C*-glycopyranosides (**1a**), (**2a**), (**4a**), and (**5a**) (total yield 86%, ratio 13.2:5.6:2.3:1). The total yield and the ratio of the esters were the same starting with trimethyl phosphonoacetate. This suggested that a mistake was reported in the previous paper[2] and that the compounds isolated and characterised were indeed ethyl 2-(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl)acetate (**2a**) and ethyl 2-(2,3,4,6-tetra-*O*-benzyl-β-D-mannopyranosyl)acetate (**5a**).

The structure of the ethyl 2-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)acetate (**1a**) was erroneously attributed to the latter substance.[2] The complete isomerization of α-anomers into β-anomers induced by an excess of sodium hydride can reasonably account for the absence of α-isomers (under the previous reaction conditions[2]).

In conclusion, the Wittig-Horner reaction using trimethyl phosphonoacetate represents a useful reaction for obtaining gluco- and manno-pyranosyl acetates in one step. It represents a satisfactory replacement of the Wittig reaction which does not afford useful results.[3] The unexpected isomerization of tetra-*O*-benzylglucopyranose into tetra-*O*-benzylmannopyranose (and *vice versa*) under Wittig-Horner reaction conditions suggests that the α-carbon of other enolizable α-alkoxy aldehydes may also epimerize. This would require a rigorous demonstration of the stereochemistry of the resulting products.

Experimental

Conditions and equipment used in the syntheses and in the analyses were those described in the preceding paper.

Wittig-Horner Reaction: General Procedure.—To a suspension of sodium hydride (10 mmol, washed three times with pentane) in tetrahydrofuran (40 ml) at 0 °C triethyl or trimethyl phosphonoacetate (10 mmol) was slowly added under N_2 and the resulting mixture was allowed to warm to 23 °C. After the mixture had been stirred for 5 h at this temperature, 2,3,4,6-tetra-*O*-benzyl-D-mannopyranose or 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (2 mmol) in tetrahydrofuran (5 ml) was added and the mixture was stirred at 50 °C for 4 h. It was then evaporated and the residue dissolved in ethyl acetate; this solution was washed with water, dried (Na_2SO_4), and evaporated and the residue was chromatographed.

Wittig-Horner Reaction of 2,3,4,6-*Tetra*-O-*benzyl*-D-*mannopyranose with Triethyl Phosphonoacetate.*—2,3,4,6-Tetra-*O*-benzyl-D-mannopyranose[7] (1.08 g, 2 mmol) was treated with triethyl phosphonoacetate sodium salt (10 mmol). Rapid chromatography of the residue (1.17 g) gave two material fractions. The first-eluted material (105 mg, 8.6%), R_F 0.26 (hexane–ethyl acetate, 8:2), showed by h.p.l.c. analysis two components with R_t 12.5 and 13.3 min, in a relative ratio of 2.3:1. A portion of this mixture (50 mg) was separated by preparative t.l.c. eluting three times with hexane–ethyl acetate (8:2), to give the less polar *ethyl* 2-(2,3,4,6-*tetra*-O-*benzyl*-β-D-*glucopyranosyl*)*acetate* (**2a**) (14.5mg): R_t 13.3 min; m.p. 43.5—45 °C (from light petroleum) (Found: C, 74.6; H, 6.9. Calc. for $C_{38}H_{42}O_7$: C, 74.7; H, 6.9%); $[\alpha]_D^{20}$ − 2.3° (*c* 1); $\nu_{max.}$ 1 732 cm^{-1}; δ_H(300 MHz) 1.19 (3 H, t, *J* 7.0 Hz, CO_2CH_2Me), 2.46 (1 H, dd, $J_{2a,2b}$ 15.5 and $J_{2a,1'}$ 8.3 Hz, 2a-H), 2.73 (1 H, dd, $J_{2b,2a}$ 15.5 and $J_{2b,1'}$ 3.5 Hz, 2b-H), 3.36 (1 H, dd, $J_{2',1'}$ 9.5, and $J_{2'3'}$ 9.5 Hz, 2′-H), 3.45 (1 H, ddd, $J_{5',4'}$ 9.5, $J_{5',6'a}$ 3.0, and $J_{5',6'b}$ 3.0 Hz, 5′-H), 3.66 (1 H, dd, $J_{4',3'}$ 9.5 and $J_{4',5'}$ 9.5 Hz, 4′-H), 3.69 (2 H, d, *J* 3.0 Hz, A_2 part of A_2X system, 6′a- and 6′b-H), 3.72 (1 H, dd, $J_{3',2'}$ 9.5 and $J_{3',4'}$ 9.5, Hz, 3′-H), 3.75 (1 H, ddd, $J_{1',2'}$ 9.5, $J_{1',2a}$ 8.3, and $J_{1',2b}$ 3.5 Hz, 1′-H), 4.08 (2 H, q, *J* 7.0 Hz, OCH_2Me), 4.51, 4.57, 4.61, 4.63, 4.81, 4.87, 4.91, 4.92 (8 H, 8 × d, *J* 10.5—11.0 Hz, benzylic), and 7.10—7.65 (20 H, m, ArH); *m/z* 610 (M^+), 518 (M^+ − 92), 412 (M^+ − 198), and 304 (M^+ − 306).

The more polar *ethyl* 2-(2,3,4,6-*tetra*-O-*benzyl*-α-D-*glucopyranosyl*)*acetate* (**1a**) as an oil (33.5 mg) showed: R_t 12.5 min (Found: C, 74.8; H, 6.7. $C_{38}H_{42}O_7$ requires C, 74.7; H, 6.9%); $[\alpha]_D^{20}$ + 35.1° (*c* 1); $\nu_{max.}$ 1 732 cm^{-1}; δ_H(300 MHz) 1.18 (3 H, t, *J* 7.0 Hz, CO_2CH_2Me), 2.68 (1 H, dd, $J_{2a,2b}$ 15.0 and $J_{2a,1'}$ 9.5 Hz, 2a-H), 2.75 (1 H, dd, $J_{2b,2a}$ 15.0 and $J_{2b,1'}$ 5.5 Hz, 2b-H), 3.58—3.76 (5 H, overlapping, 3′-, 4′-, 5′-, 6′a-, and 6′b-H), 3.78 (1 H, dd, $J_{2',1'}$ 5.5 and $J_{2',3'}$ 9.0 Hz, 2′-H), 3.98—4.15 (2 H, AB part of ABX_3 system, CO_2CH_2Me), 4.45, 4.47, 4.60, 4.78, 4.80, 4.90 (6 H, 6 × d, *J* 11.0—12.0 Hz, benzylic), 4.65 (2 H, s, benzylic), 4.67 (1 H, ddd, $J_{1',2'}$ 5.5, $J_{1',2b}$ 5.5, and $J_{1',2a}$ 9.5 Hz, 1′-H), and 7.1—7.65 (20 H, m, ArH); *m/z* 610 (M^+).

The second-eluted material (940 mg, 77%), R_F 0.18 (hexane–ethyl acetate 8:2), showed by h.p.l.c. analysis two components with R_t 8.4 and 9.2 min, in relative ratio of 2.3:1. A portion of this mixture (50 mg) was separated by preparative t.l.c. eluting three times to give, as less polar compound the *ethyl* 2-(2,3,4,6-*tetra*-O-*benzyl*-α-D-*mannopyranosyl*)*acetate* (**4a**) as an oil (33 mg), R_t 8.4 min (Found: C, 74.9; H, 6.8. $C_{38}H_{42}O_7$ requires C, 74.7; H, 6.9%); $[\alpha]_D^{20}$ + 8.4° (*c* 1); $\nu_{max.}$ 1 732 cm^{-1}; δ_H(300 MHz) 1.20 (3 H, t, *J* 7.0 Hz, CO_2CH_2Me), 2.54 (1 H, dd, $J_{2a,2b}$ 15.0 and $J_{2a,1'}$ 8.0 Hz, 2a-H), 2.66 (1 H, dd, $J_{2b,2a}$ 15.0 and $J_{2b,1'}$ 5.0 Hz, 2b-H), 3.65 (1 H, dd, $J_{2',1'}$ 6.5 and $J_{2',3'}$ 3.0 Hz, 2′-H), 3.76—3.88 (4 H, overlapping, 3′-, 4′-, 6′a-, and 6′b-H), 3.92 (1 H, ddd, $J < 1$, *J* 10.0, and *J* 5.0 Hz, 5′-H), 4.10 (2 H, q, *J* 7.0 Hz, CO_2CH_2Me), 4.50 (1 H, ddd, $J_{1',2'}$ 6.5, $J_{1',2a}$ 8.0, and $J_{1',2b}$ 5.0 Hz, 1′-H), 4.51, 4.54, 4.54 (6 H, 3 × s, benzylic), 4.53, 4.61 (2 H, 2 × d, *J* 11.5 Hz, benzylic), and 7.10—7.65 (20 H, m, ArH); *m/z* 610 (M^+). The more polar *ethyl* 2-(2,3,4,6-*tetra*-O-*benzyl*-β-D-*mannopyranosyl*)*acetate* (**5a**) as an oil (15 mg) showed: R_t 9.2 min (Found: C, 74.8; H, 6.7. $C_{38}H_{42}O_7$ requires C, 74.7; H, 6.9%); $[\alpha]_D^{20}$ 0.0° (*c* 1); $\nu_{max.}$ 1 732 cm^{-1}; δ_H(300 MHz) 1.23 (3 H, t, *J* 7.0 Hz, CO_2CH_2Me), 2.61 (1 H, dd, $J_{2a,2b}$ 16.5 and $J_{2a,1'}$ 7.5 Hz, 2a-H), 2.73 (1 H, dd, $J_{2b,2a}$ 16.5 and $J_{2b,1'}$ 6.3 Hz, 2b-H), 3.50 (1 H, ddd, $J_{5',4'}$ 9.5, $J_{5',6'a}$ 5.0, and $J_{5',6'b}$ 2.0 Hz, 5′-H), 3.69 (1 H, dd, $J_{6'a,5'}$ 5.0 and $J_{6'a,6'b}$ 11.0 Hz, 6′a-H), 3.70 (1 H, dd, $J_{3',4'}$ 9.5 and $J_{3',2'}$ 2.8 Hz, 3′-H), 3.76 (1 H, dd, $J_{6'b,5'}$ 2.0 and $J_{6'b,6'a}$ 11.0 Hz, 6′b-H), 3.82 (1 H, ddd, $J_{1',2'}$ 1.0, $J_{1',2b}$ 6.3, and $J_{1',2a}$ 7.5

Hz, 1′-H), 3.93 (1 H, dd, $J_{4',3'}$ 9.5 and $J_{4',5'}$ 9.5 Hz, 4′-H), 3.93 (1 H, dd, $J_{2',1'}$ 1.0 and $J_{2',3'}$ 2.8 Hz, 2′-H), 3.93—4.15 (2 H, AB part of ABX_3 system, CO_2CH_2Me), 4.55, 4.57, 4.63, 4.66, 4.76, 4.83, 4.90, 5.04 (8 H, 8 × d, J 10.5—12.5 Hz, benzylic), and 7.10—7.65 (20 H, m, ArH); m/z 610 (M^+).

Wittig-Horner Reaction of 2,3,4,6-*Tetra*-O-*benzyl*-D-*mannopyranose with Trimethyl Phosphonoacetate.*—2,3,4,6-Tetra-*O*-benzyl-D-mannopyranose (1.08 g, 2 mmol) was treated with trimethyl phosphonoacetate sodium salt (10 mmol). The residue (1.132 g) showed by h.p.l.c. analysis four components with R_t 7.3, 8.0, 10.6, and 11.3 min, in relative ratio of 21:9:2.3:1. The residue was chromatographed (silica gel G-Celite, eluting with hexane–diethyl ether), to afford the following: (i) *methyl* 2-(2,3,4,6-*tetra*-O-*benzyl*-β-D-*glucopyranosyl*)*acetate* (**2b**) (31 mg): R_t 11.3 min; m.p. 65—66 °C (from light petroleum) (Found: C, 74.9; H, 6.8. $C_{37}H_{40}O_7$ requires C, 74.5; H, 6.75%); $[\alpha]_D^{20}$ − 3.5° (*c* 1); $\nu_{max.}$ 1 732 cm^{-1}; δ_H(300 MHz) 2.48 (1 H, dd, $J_{2a,2b}$ 15.0 and $J_{2a,1'}$ 8.0 Hz, 2a-H), 2.73 (1 H, dd, $J_{2b,2a}$ 15.0 and $J_{2b,1'}$ 4.0 Hz, 2b-H), 3.36 (1 H, dd, $J_{2',1'}$ 9.5 and $J_{2',3'}$ 9.5 Hz, 2′-H), 3.45 (1 H, ddd, $J_{5',4'}$ 9.5, $J_{5',6'a}$ 3.0, and $J_{5',6'b}$ 3.0 Hz, 5′-H), 3.60 (3 H, s, CO_2Me), 3.65 (1 H, dd, $J_{4',5'}$ 9.5 and $J_{4',3'}$ 9.5 Hz, 4′-H), 3.69 (2 H, d, J 3.0 Hz, A_2 part of A_2X system, 6′a- and 6′b-H), 3.72 (1 H, d, $J_{3',4'}$ 9.5 and $J_{3',2'}$ 9.5 Hz, 3′-H), 3.75 (1 H, ddd, $J_{1',2'}$ 9.5, $J_{1',2a}$ 8.0, and $J_{1',2b}$ 4.0 Hz, 1′-H), 4.50, 4.56, 4.60, 4.62, 4.81, 4.87, 4.91, 4.92 (8 H, 8 × d, J 10.5—12.0 Hz, benzylic), and 7.10—7.65 (20 H, m, ArH); m/z 596 (M^+), 504 (M^+ − 92), 398 (M^+ − 198), and 290 (M^+ − 306). (ii) *methyl* 2-(2,3,4,6-*tetra*-O-*benzyl*-α-D-*glucopyranosyl*)*acetate* (**1b**) (71.5 mg): R_t 10.6 min, m.p. 54—55 °C (from light petroleum) (Found: C, 74.7; H, 6.8. Calc. for $C_{37}H_{40}O_7$: C, 74.5; H, 6.75%); $[\alpha]_D$ + 46.8° (*c* 1) (lit.,[8] m.p. 54—55 °C; $[\alpha]_D^{20}$ + 46°); (iii) *methyl* 2-(2,3,4,6-*tetra*-O-*benzyl*-α-D-*mannopyranosyl*)*acetate* (**4b**) (644 mg): R_t 7.3 min; m.p. 39—40 °C (from light petroleum) Found: C, 74.5; H, 6.8. $C_{37}H_{40}O_7$ requires C, 74.5; H, 6.75%); $[\alpha]_D^{20}$ + 9.7° (*c* 1); $\nu_{max.}$ 1 732 cm^{-1}; δ_H(300 MHz) 2.53 (1 H, dd, $J_{2a,2b}$ 15.0 and $J_{2a,1'}$ 8.3 Hz, 2a-H), 2.67 (1 H, dd, $H_{2b,2a}$ 15.0 and $J_{2b,1'}$ 5.0 Hz, 2b-H), 3.61 (3 H, s, CO_2Me), 3.62 (1 H, dd, $J_{2',1'}$ 6.5 and $J_{2',3'}$ 3.0 Hz, 2′-H), 3.75—3.79 (4 H, overlapping, 3′-, 4′-, 6′a-, and 6′b-H), 3.91 (1 H, ddd, J < 1, J 5.0 and J 10.0 Hz, 5′-H), 4.46 (1 H, ddd, $J_{1',2'}$ 6.5, $J_{1',2b}$ 5.0, and $J_{1',2a}$ 8.3 Hz, 1′-H), 4.45, 4.47, 4.52, 4.58 (4 H, 4 × d, J 12.0 Hz, benzylic), 4.51, 4.52 (4 H, 2 × s, benzylic), and 7.10—7.65 (20 H, m, ArH); m/z 596 (M^+); (iv) *methyl* 2-(2,3,4,6-*tetra*-O-*benzyl*-β-D-*mannopyranosyl*)*acetate* (**5b**) an oil (274 mg); R_t 8.0 min (Found: C, 74.3; H, 6.8. $C_{37}H_{40}O_7$ requires C, 74.5; H, 6.75%); $[\alpha]_D^{20}$ + 8.5° (*c* 1); $\nu_{max.}$ 1 732 cm^{-1}; δ_H (300 MHz) 2.61 (1 H, dd, $J_{2a,2b}$ 16.5 and $J_{2a,1'}$ 7.5 Hz, 2a-H), 2.73 (1 H, dd, $J_{2b,2a}$ 16.5 and $J_{2b,1'}$ 6.0 Hz, 2b-H), 3.50 (1 H, ddd, $J_{5',6'a}$ 5.2, $J_{5',6'b}$ 2.0, and $J_{5',4'}$ 9.5 Hz, 5′-H), 3.61 (3 H, s, CO_2Me), 3.69 (1 H, dd, $J_{6'a,5'}$ 5.2 and $J_{6'a,6'b}$ 11.0 Hz, 6′a-H), 3.70 (1 H, dd, $J_{3',4'}$ 9.5 and $J_{3',2'}$ 3.0 Hz, 3′-H), 3.76 (1 H, dd, $J_{6'a,5'}$ 2.0 and $J_{6'a,6'b}$ 11.0 Hz, 6′b-H), 3.81 (1 H, ddd, $J_{1',2'}$ 1.0, $J_{1',2b}$ 6.0, and $J_{1',2a}$ 7.5 Hz, 1′-H), 3.93 (1 H, dd, $J_{2',1'}$ 1.0 and $J_{2',3'}$ 3.0 Hz, 2′-H), 3.93 (1 H, dd, $J_{4',3'}$ 9.5 and $J_{4',5'}$ 9.5 Hz, 4′-H), 4.55, 4.57, 4.63, 4.66, 4.76, 4.83, 4.90, 5.03 (8 H, 8 × d, J 11.0—12.0 Hz, benzylic), and 7.10—7.65 (20 H, m, ArH); m/z 596 (M^+).

Wittig-Horner Reaction of 2,3,4,6-*Tetra*-O-*benzyl*-D-*glucopyranose with Triethyl Phosphonoacetate.*—2,3,4,6-Tetra-*O*-benzyl-D-glucopyranose (1.08 g, 2 mmol) was treated with triethyl phosphonoacetate sodium salt (10 mmol). The residue (1.16 g) was found to be a mixture of the compounds (**1a**), (**2a**), (**4a**), and (**5a**) in a relative ratio of 13.2:5.6:2.3:1 (h.p.l.c.). Analytical samples showing the correct physicochemical properties were obtained by preparative t.l.c. as described above.

Wittig-Horner Reaction of 2,3,4,6-*Tetra*-O-*benzyl*-D-*glucopyranose with Trimethyl Phosphonoacetate.*—2,3,4,6-Tetra-*O*-benzyl-D-glucopyranose (1.08 g, 2 mmol) was treated with trimethyl phosphonoacetate sodium salt (10 mmol) and afforded a mixture (1.14 g) of the compounds (**1b**), (**2b**), (**4b**), and (**5b**) in a relative ratio of 13.2:5.6:2.3:1 (h.p.l.c.). The mixture was subjected to a column chromatography as described above to afford: (i), compound (**2b**) (262 mg), m.p. 65—66 °C (from light petroleum); (ii) compound (**1b**) (615 mg), m.p. 54—55 °C (from light petroleum); (iii), compound (**4b**) (107 mg), m.p. 39—40 °C (from light petroleum); (iv) compound (**5b**) (46 mg) an oil; $[\alpha]_D^{20}$ + 8.7° (*c* 1). All compounds were identical with those described above.

Synthesis of Methyl 2-(2,3,4,6-*tetra*-O-*benzyl*-β-D-*mannopyranosyl*)*acetate* (**5b**).—The mixture (1.13 g) obtained by Wittig-Horner reaction from 2,3,4,6-tetra-*O*-benzyl-D-mannopyranose (1.08 g, 2 mmol) and trimethyl phosphonoacetate sodium salt (10 mmol) dissolved in dry tetrahydrofuran (4 ml), was added to a suspension of sodium hydride (2 mmol, washed three times with pentane) in dry tetrahydrofuran (30 ml). The mixture was stirred at room temperature for 24 h. Work-up and chromatography (silica gel G-Celite, eluting with hexane–diethyl ether) afforded in the sequence: (i) compound (**2b**) (101 mg, 8.5%); (ii) compound (**1b**) (4 mg, 0.35%); (iii) compound (**4b**) (39 mg, 3.3%); (iv) the title compound (**5b**) (903 mg, 75.8%); all compounds were identical with those obtained above.

Acknowledgements

We thank Miss Maria Filomena Urso for secretarial assistance. This work was supported by Ministero della Pubblica Istruzione.

References

1 A. G. M. Barrett and H. B. Broughton, *J. Org. Chem.*, 1986, **51**, 495; F. Nicotra, L. Panza, F. Ronchetti, G. Russo, and L. Toma, *Carbohydr. Res.*, 1987, **171**, 49; T. V. RajanBabu, *J. Am. Chem. Soc.*, 1987, **109**, 609; S. A. Babirad, Y. Wang, and Y. Kishi, *J. Org. Chem.*, 1987, **52**, 1370; A. B. Reitz, A. D. Jordan, Jr., and B. E. Maryanoff, *ibid.*, p. 4800; A. H. Davidson, L. R. Hughes, S. S. Qureshi, and B. Wright, *Tetrahedron Lett.*, 1988, **29**, 693.
2 D. Monti, P. Gramatica, G. Speranza, and P. Manitto, *Tetrahedron Lett.*, 1987, **28**, 5047.
3 F. Nicotra, F. Ronchetti, G. Russo, and L. Toma, *Tetrahedron Lett.*, 1984, **25**, 5697.
4 M. D. Lewis, J. K. Cha, and Y. Kishi, *J. Am. Chem. Soc.*, 1982, **104**, 4976.
5 C. Altona and C. A. G. Haasnoot, *Org. Magn. Reson.*, 1980, **13**, 417.
6 F. Nicotra, R. Perego, F. Ronchetti, G. Russo, and L. Toma, *Carbohydr. Res.*, 1984, **131**, 180.
7 S. Koto, N. Morishima, Y. Miyata, and S. Zen, *Bull. Chem. Soc. Jpn.*, 1976, **49**, 2639.
8 P. Allevi, M. Anastasia, P. Ciuffreda, A. Fiecchi, and A. Scala, *J. Chem. Soc., Chem. Commun.*, 1987, 101.

Received 3*rd May* 1988; *Paper* 8/01733F