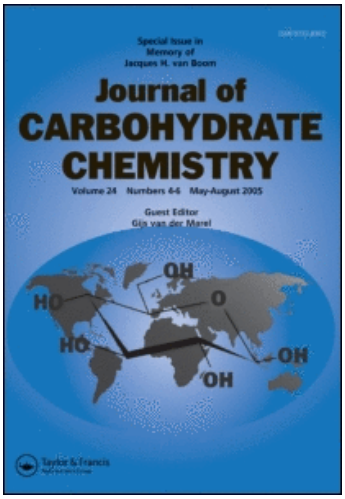

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STUDIES ON THE REGIOSELECTIVITY OF HORNER-WADSWORTH-EMMONS (HWE) REACTIONS ON 3,4-ENULOSES. FURTHER EVIDENCE OF PHOSPHONATE-PHOSPHATE REARRANGEMENTS THROUGH FIVE MEMBERED CYCLIC INTERMEDIATES.

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ABSTRACT

The Horner-Wadsworth-Emmons (HWE) reaction was performed on methyl 3,6-di-*O*-benzoyl-2-deoxy-α-D-*glycero*-hex-2-enopyranosid-4-ulose (**1**) with the potassium enolates of dimethyl [(methoxycarbonyl)methyl]phosphonate (**2**) or diethyl [(ethoxycarbonyl) methyl]phosphonate (**3**) under different conditions (metallic cation and solvent) in order to study regio- and stereochemical aspects of the reaction. In the presence of lithium ions, no reaction took place. When sodium enolates were employed, 1,2-addition was the main reaction in chelating solvents, whereas the 1,4-adduct is favoured in the less polar, non chelating toluene. Only 1,2-addition was observed with potassium enolates. Evidence of phosphonate-phosphate rearrangements through five membered cyclic intermediates is described.

INTRODUCTION

When the Horner-Wadsworth-Emmons (HWE) reaction was performed on methyl 3,6-di-*O*-benzoyl-2-deoxy-α-D-*glycero*-hex-2-enopyranosid-4-ulose (**1**) using the potassium enolates of dimethyl [(methoxycarbonyl)methyl]phosphonate (**2**) or diethyl [(ethoxycarbonyl)methyl]phosphonate (**3**) in toluene, anomalous results were obtained. As expected, 1,2-addition to the carbonyl group was observed, but in all cases, 3-*O*-phosphorylated products were obtained.[1] A mechanism involving a phosphonate-phosphate like rearrangement through a five membered cyclic intermediate followed by benzoate elimination was suggested to explain this fact. We now report the results obtained when different metal cations and/or solvents were employed. It was observed that changes in the nature of solvent and metal cation can induce major changes in the course of the reaction, resulting in 1,4-addition in some cases. Deschamps and Seyden-Penne[2] have reported 1,4-addition in reactions of 3-alkyl (or 3-aryl) alicyclic α-enones with phosphorylated anions. The regio- and stereochemical aspects of the attack of enolates of **2** and **3** on ulose **1** were analyzed, and a correlation between the effects of both solvent and metal on the regioselectivity of these additions was established. The fact that 3-*O*-phosphorylation was observed in the 1,4-addition products provides additional evidence for the occurrence of phosphonate-phosphate rearrangements through five membered cyclic intermediates.

RESULTS AND DISCUSSION

The reaction of enulose **1** with enolates of **2** or **3** afforded either products of 1,2- or 1,4-addition depending on the experimental conditions. Results are shown in Table 1. All yields reported are those of isolated products. When a solution of enulose **1** was treated with the lithium enolates of **2** or **3** in toluene, no reaction at all was observed and the original enulose was recovered unchanged. When the reaction was performed on **1** with the sodium enolate of phosphonate **2** using toluene as solvent, two products were isolated (Scheme 1). The minor product (28%) was methyl 6-*O*-benzoyl-3-*O*-dimethoxyphosphoryl-4-*C*-[*E*-(methoxycarbonyl)methylene]-2,4-dideoxy-α-D-*glycero*-hex

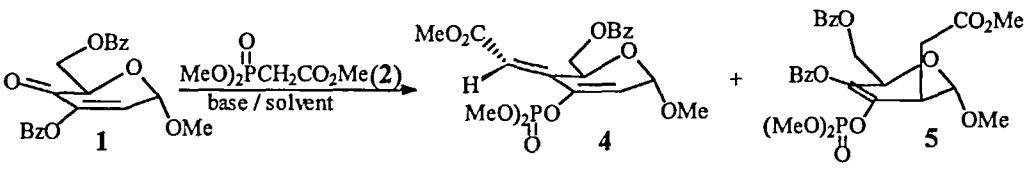
Table 1.

Phosphonate	Base	Solvent	% (1,4-addition)	% (1,2-addition)
2	LiBr : NaH = 2 : 1	PhMe	-----	-----
2	NaH	PhMe	47 (5)	28 (4)
2	NaH	DME	-----	73 (4)
2	KOtBu	PhMe	-----	67 (4)
2	NaH	DMF	7 (5)	56 (4)
3	LiBr : NaH = 2 : 1	PhMe	-----	-----
3	NaH	PhMe	61 (7)	30 (6)
3	NaH	DME	-----	84 (6)
3	KOtBu	PhMe	-----	79 (6)

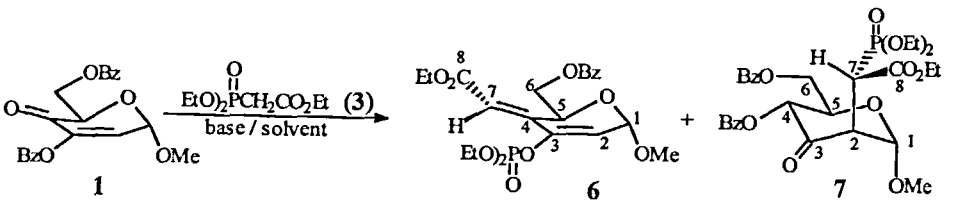
-2-enopyranoside (4).[1] The major product (47%) was identified as methyl 4,6-di-*O*-benzoyl-2-deoxy-2-*C*-[(methoxycarbonyl)methyl]-3-*O*-dimethoxyphosphoryl-α-D-*threo*-hex-3-enopyranoside (**5**).

The signal for H-1 in the ^{1}H NMR spectrum of **5** was a singlet centered at 4.86 ppm while the corresponding signal for H-2 appeared as a doublet of doublets due to the couplings with H-7 and H-7'. This fact would be the consequence of an equatorial-equatorial relationship between H-1 and H-2 and of the axial orientation of the (methoxycarbonyl)methyl branch attached at C-2. The ^{13}C NMR spectrum of **5** showed two signals for olefinic carbons at 131.9 and 135.1 ppm, with coupling constants of 7.0 and 9.0 Hz respectively due to the coupling with the phosphorus atom[3] indicating 3-*O*-phosphorylation. Furthermore, the absence of signals with large, characteristic one bond ^{13}C-^{31}P coupling[4] in the 2.5-3 ppm region, suggested the absence of a dimethoxy-phosphoryl group in the C-2 appendix moiety.

Compound **5** would be obtained as the result of a conjugate addition of the HWE reagent to the less hindered face of compound **1** followed by O3 → O4 migration of the



Scheme 1



Scheme 2

benzoyl group and a phosphonate-phosphate rearrangement through a five membered cyclic intermediate in a similar way to the mechanism described for 1,2 addition.[1]

When the reaction was performed with the sodium enolate of **3** in toluene, methyl 6-*O*-benzoyl-3-*O*-diethoxyphosphoryl-4-*C*-[*E*-(ethoxycarbonyl)methylene]-2,4-dideoxy-α-D-*glycero*-hex-2-enopyranoside (**6**)[1] was obtained as a minor product (30%) as a consequence of 1,2-addition. Conjugate addition was also the main reaction, but the product obtained was methyl 4,6-di-*O*-benzoyl-2-deoxy-2-*C*-[(1-ethoxycarbonyl-1-diethoxyphosphoryl)methyl]-α-D-*arabino*-hexopyranosid-3-ulose (**7**) (61%, Scheme 2).

The ^{1}H and ^{13}C NMR spectra of compound **7** were completely assigned using 2 D homo and heteronuclear correlation experiments. The appearance of a signal at 197.2 ppm confirmed the presence of a ketone carbonyl. The presence of the phosphonoacetate moiety was indicated by the signals for H-7 (3.45 ppm) and C-7 (42.16 ppm) which showed large coupling constants of 21.2 and 128.9 Hz respectively with the ^{31}P nucleus, in agreement with literature data.[5]

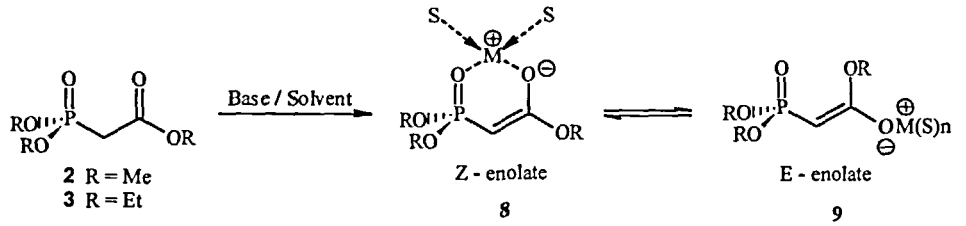
The presence of only one signal in the 2.5-3 ppm region suggested the formation of one of the two possible diastereomers on C-7, although its absolute configuration was not determined. The *arabino* configuration of **7** was assigned on the basis of its ^{1}H NMR and

NOESY spectra. The *trans* axial-axial three-bond coupling constant of 10.3 Hz between H-4 and H-5 indicated an equatorial orientation of the benzoyloxy group at C-4 in a $^4C_1$ conformation. Moreover, the significant NOE observed between H-4 and H-7 suggested the axial orientation of the branch at C-2.

Compound **7** would be the result of a conjugate addition in a similar way as that observed for compound **5**, but, in this case, no phosphonate-phosphate rearrangement occurred, and reketonization took place. This fact might be due to the greater steric hindrance of the diethoxyphosphoryl group compared with the dimethoxyphosphoryl one.[6] Different behaviour of dimethyl and diethylphosphonates has already been observed for other reactions.[7] Reversibility of the addition reaction is unlikely since when one molar equivalent of KO*t*-Bu was added to compound **7** in toluene, neither the starting 3,4-enulose **1** nor the 1,2-addition product **6** could be observed after several days at room temperature. Additional evidence was the formation of a tri-deuterated analog of **7** (at C-2, C-4 and C-7) as the only product by treatment of **7** with D_2O / THF / LiBr / Et_3N (see experimental). The retro-Michael reaction would be avoided by the O-3 → O-4 benzoyl migration observed when 1,4-addition occurs.

When DME was used as solvent instead of toluene in the reaction of the enulose **1** with the enolates of **2** or **3**, a change in regioselectivity took place. Only 1,2-addition was observed to give products **4** (73%) or **6** (84%) respectively. When enulose **1** was treated with the sodium enolate of **2** in DMF at room temperature, two products were isolated by column chromatography. The major product was characterized as compound **4**, the 1,2-addition product (56%), and the minor product was identified as the 1,4-addition product **5** (7%).

The observed behaviour of the reaction of enulose **1** with enolates of **2** or **3**, is consistent with known properties of the chelates. In the presence of lithium ions, of high chelating ability, no reaction took place because of the low reactivity of the strong chelate formed with the enolates and the cation. When sodium ions are employed, of intermediate chelating ability, the course of the reaction is determined by the nature of the solvent employed. When toluene was the solvent, the chelates were stronger because of the absence of solvent competence for the metallic cation. In this case, the carbanionic



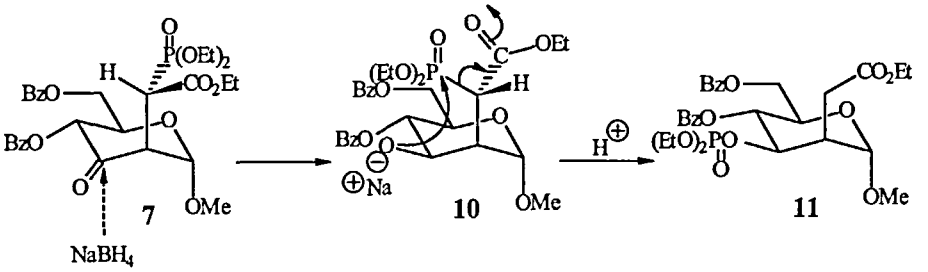
Scheme 3

character of C-1 is diminished as the negative charge is more delocalized. As a result, the interaction between frontier orbitals become more important than electrostatic interactions and favour conjugate addition.[2,8] In the case of DME, the high sequestrating power of the solvent makes the chelate weaker, which enhances the negative charge on C-1 of the enolate favouring 1,2-addition.

When DMF was used as a solvent, the amount of the conjugate product obtained may be explained by the presence of a small proportion of the less reactive *E*-enolate in the equilibrium (Scheme 3). The ratio of enolate *E* to enolate *Z* (10:1) was estimated from the intensity of H-1 in the ^{1}H NMR spectrum. In this case, the high chelating power of DMF results in partial dissociation of the *Z*-enolate which is stabilized by complexation with the metal cation, producing the small proportion of the *E*-isomer observed. These observations agree with the results reported by Seyden-Penne *et al.*[5] in their studies on the metallic complexes of diethyl[(carbomethoxy)methyl]phosphonate.

In the ^{13}C NMR spectrum, both species **8** and **9** are characterized by large $^1J_{C1,P}$ coupling constants. The signal for C-1 of **8** appears at 37.9 ppm, while the corresponding signal in the *E*-enolate **9** C-1 appears at higher field (41.8 ppm), thus showing a better negative charge delocalization. Since C-1 in the *Z*-enolate **8** becomes harder than C-1 in the *E*-enolate **9**, carbonyl attack is favoured with the former. Thus, enolate **9** should undergo 1,4-addition. This conclusion is confirmed by the similarity between the 1,2-:1,4-addition ratio of the products (**4** : **5** ≅ 8 : 1) and the measured ratio of sodium enolate reagents (**8** : **9** ≅ 10 : 1). The low chelating ability of potassium ions explains that only 1,2-addition was observed in all the cases analyzed.

Phosphonate-phosphate rearrangements through five membered cyclic intermediates were observed both in 1,2- and 1,4-additions when the methyl phosphonate



Scheme 4

2 was used. As we mentioned above, this rearrangement was not observed in the 1,4-addition of the ethyl analogue **3**. The enhancement of the nucleophilicity of the anionic center could induce the rearrangement. Therefore, γ-ketophosphonate **7** was treated with sodium borohydride in *t*BuOH / PhMe affording an anionic intermediate (**10**) which led to methyl 4,6-di-*O*-benzoyl-2-deoxy-3-*O*-diethoxyphosphoryl-2-*C*-[(ethoxycarbonyl) methyl]-α-D-mannopyranoside (**11**) as the only product in 92% yield (Scheme 4).

No ketone carbonyl group was observed in the ^{13}C NMR spectrum of compound **11** and C-7 appeared as a singlet, indicating the absence of a diethoxyphosphoryl group at C-2. The presence of a diethoxyphosphoryloxy group at C-3 was evident through C-3-^{31}P coupling.The equatorial orientation of this phosphorylated group at C-3 was assigned by a *trans* axial-axial three-bond coupling constant of 9.4 Hz between H-3 and H-4 in the ^{1}H NMR spectrum of compound **11**. Reduction of **7** with $NaBH_4$ gives only axial attack. This high stereoselectivity can be explained taking into account the steric interactions generated by the axial C-2 substituent. The enhanced nucleophilicity and the more favoured geometry of the γ-hydroxyphosphonate anion **10** would induce the phosphonate-phosphate rearrangement to yield compound **11**.

These results suggest the generality of phosphonate-phosphate rearrangements through five membered cyclic intermediates and provide additional evidences for the mechanism proposed[1] for the formation of 3-*O*-phosphorylated products.

EXPERIMENTAL

General Remarks. All air and moisture sensitive reactions were carried out under nitrogen using oven-dried glassware. Dimethyl [(methoxycarbonyl)methyl]phosphonate

and diethyl [(ethoxycarbonyl)methyl]phosphonate were used as supplied commercially. Column chromatography was performed on silicagel 60. TLC was carried out on precoated aluminum plates (0.1 mm) of silicagel 60 F-254; detection was effected by exposure to UV light and by spraying the plates with 5 % (v/v) H_2SO_4 in ethanol followed by heating. ^1H NMR spectra were recorded at 200.13 MHz in $CDCl_3$. ^{13}C NMR spectra were recorded at 50.13 MHz in $CDCl_3$. Chemical shifts are given in ppm from TMS. FABMS (positive-ion mode from glycerol) spectra were obtained employing a ZAB-VSEQ hybrid mass spectrometer.

General technique for reaction of potassium enolates of dimethyl(methoxycarbonyl)methyl phosphonate (2) or diethyl(ethoxycarbonyl) methyl phosphonate (3) and methyl 3,6-di-*O*-benzoyl-2-deoxy-α-D -*glycero*-hex-2-enopyranosid-4-ulose (1). To 7.82 mmole of base in the corresponding solvent (25 mL) at 0 °C, 7.82 mmol of phosphonate **2** or **3** was added. The mixture was stirred during 45 min, and 2.60 g (6.80 mmole) of enulose **1** in 45 mL of the same solvent was then added. After 30 min the reaction mixture was poured over 250 mL of ethyl acetate, and washed with saturated $NaHCO_3$, NaH_2PO_4 (10 %) and NaCl (10 %). The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure to give, after column chromatography (ethyl acetate-hexane 2:1), the corresponding compounds. Compounds **4** and **6** were described previously.[1]

Methyl 4,6-di-*O*-benzoyl-2-deoxy-2-*C*-[(methoxycarbonyl)methyl]-3-*O*-dimethoxyphosphoryl-α-D-*threo*-hex-3-enopyranoside (5). $[\alpha]_D$ = +52.4° (*c* 1.95, $CHCl_3$), IR.: ν_{max} (cm^{-1}): 1735 and 1733 (C=O, benzoate), 1726 (C=O ethoxycarbonyl), 1295 (P=O), ^1H NMR δ 7.35 - 8.13 (m, 10H, H_{aryl}), 4.89 (m, 1H, H-5), 4.86 (s, 1H, H-1), 4.61 (dd, 1H, $J_{5,6'}$ = 3.4 Hz, $J_{6,6'}$ = 11.9 Hz, H-6'), 4.49 (d, 1H, $J_{5,6}$ = 4.4 Hz, H-6), 3.70 (d, 3H, $J_{H,P}$ = 2.1 Hz, O<u>C</u>H_3 methoxyphosphoryl), 3.65 (s, 3H, O<u>C</u>H_3 methoxycarbonyl), 3.59 (d, 3H, $J_{H,P}$ = 1.2 Hz, O<u>C</u>H_3 methoxyphosphoryl), 3.54 (s, 3H, O<u>C</u>H_3 C-1), 3.17 (dd, 1H, $J_{2,7}$ = 10.6 Hz, $J_{2,7'}$ = 3.1 Hz, H-2), 2.93 (dd, 1H, $J_{7,7'}$ = 16.8 Hz, H-7'), 2.61 (dd, 1H, H-7). ^{13}C NMR δ 171.7 (C=O, C-8), 166.1 and 166.3 (<u>C</u>=O, benzoyl), 135.1* (d, $J_{C,P}$ = 9.0 Hz, C-3), 131.9* (d, $J_{C,P}$ = 7.0 Hz, C-4), 128.3-133.8 (C_{aryl}), 100.3 (C-1), 66.6 (C-5), 63.3 (C-6), 56.0 (O<u>C</u>H_3, C-1), 55.1 (O<u>C</u>H_3, methoxyphosphoryl), 51.8 (O<u>C</u>H_3, methoxycarbonyl), 40.3 (C-2); 34.6 (C-7). * the signals may be interchanged.

HRMS Calcd for $C_{26}H_{30}O_{12}P$ (M+H): 565.4946. Found: 565.4945.

Methyl 4,6-di-*O*-benzoyl-2-deoxy-2-*C*-[(1-diethoxyphosphoryl)ethoxycarbonylmethyl]-α-D-*arabino*-hexopyranosid-3-ulose (7). $[\alpha]_D$ = + 77.3° (*c* 2.08, $CHCl_3$), IR (NaCl) ν_{max} (cm^{-1}): 1750 (C=O, ethoxycarbonyl), 1730 (C=O, benzoate), 1720 (C=O, ketone), 1260 (P=O). ^1H NMR δ 7.39 - 8.13 (m, 10H, H_{aryl}), 5.68 (d, 1H, $J_{4,5}$ = 10.3 Hz, H-4), 5.63 (d, 1H, $J_{1,2}$ = 3.7 Hz, H-1), 4.74 (dd, 1H, $J_{5,6'}$ = 4.7 Hz, $J_{6,6'}$ = 14.3 Hz, H-6'), 4.56 (dd, 1H, $J_{5,6}$ = 5.0 Hz, H-6), 4.87 (ddd, 1H, H-5), 4.05-4.30 (m, 6H, $C\underline{H}_2O$ ethoxyl), 3.77 (dd, 1H, $^3J_{H,P}$ = 6.2 Hz, H-2), 3.47 (s, 3H, $OC\underline{H}_3$), 3.45 (d, 1H, $^2J_{H,P}$ = 21.2 Hz, H-7), 1.24-1.42 (m, 9H, $C\underline{H}_3$ ethoxyl). ^{13}C NMR δ 197.2 (d, $J_{C,P}$ = 17.6 Hz, C-3), 167.7 ($J_{C,P}$ = 6.5 Hz, C-8), 166.2 and 164.7 ($\underline{C}$=O benzoyl), 128.5-133.8 (C_{aryl}), 100.8 (C-1), 73.0 (C-4), 70.5 (C-5), 63.5 (C-6), 63.3 (d $J_{C,P}$ = 6.5 Hz, $\underline{C}H_2O$ ethoxyphosphoryl); 63.1 (d, $J_{C,P}$ = 7.1 Hz, $\underline{C}H_2O$ ethoxyphosphoryl), 61.8 ($\underline{C}H_2O$ ethoxycarbonyl), 55.5 ($O\underline{C}H_3$), 53.3 (d, $J_{C,P}$ = 3.3 Hz, C-2), 42.2 (d, $J_{C,P}$ = 128.9 Hz, C-7), 16.4 and 16.3 ($\underline{C}H_3$, ethoxyphosphoryl), 13.9 ($\underline{C}H_3$, ethoxycarbonyl).

Anal. Calcd for $C_{29}H_{35}O_{12}P$: C, 57.42; H, 5.82. Found: C, 57.05; H, 6.26.

The trideuterated analog of **7**, methyl 4,6-di-*O*-benzoyl-2-deoxy-2,4,7-tri-*C*-deutero-2-*C*-[(1-diethoxyphosphoryl)ethoxycarbonylmethyl]-α-D-*arabino*-hexopyranosid-3-ulose, was obtained by treatment of a solution of **7** (0.13 g; 0.21 mmol) in THF:D_2O = 3:2 (10 mL) with LiBr (0.91 g, 5 eq) and NEt_3 (88 μL, 3 eq) at 40 °C during 24 h. The mixture was diluted with dichloromethane (50 mL) and washed with water. The organic layer was dried (Na_2SO_4), filtered and the filtrate was concentrated to dryness. After purification by preparative thin-layer chromatography (EtOAc:hexane = 2:1), 0.105 g (83%) of a compound with $[\alpha]_D$ = + 76.2° (*c* 0.82; $CHCl_3$) was obtained. Its IR and NMR spectra were very similar with respect to the corresponding of compound **7**. ^1H NMR δ 7.35- 8.06 (m, 10H, H_{aryl}), 5.63 (s, 1H, H-1), 4.72 (dd, 1H, $J_{5,6'}$ = 2.3 Hz, $J_{6,6'}$ = 11.6 Hz, H-6'), 4.47-4.62 (m, 2H, H-5, H-6), 4.09-4.26 (m, 6H, $C\underline{H}_2O$ ethoxyl), 3.44 (s, 3H, $OC\underline{H}_3$), 1.25-1.43 (m, 9H, $C\underline{H}_3$ ethoxyl). ^{13}C RMN δ 197.5 (d, $J_{C,P}$ = 15 Hz, C-3), 167.8 ($\underline{C}$=O, $J_{C,P}$ = 6 Hz, C-8), 166.1 and 164.6 ($\underline{C}$=O, benzoyl), 128.3-133.4 (C_{aryl}), 100.8 (C-1), 70.4 (C-5), 63.5 (C-6), 63.2 (d, $J_{C,P}$ = 6.3 Hz, $\underline{C}H_2O$ ethoxyphosphoryl), 63.0 (d, $J_{C,P}$ = 6.9 Hz, $\underline{C}H_2O$ ethoxyphosphoryl), 61.7 ($\underline{C}H_2O$ ethoxycarbonyl), 55.5 ($O\underline{C}H_3$), 16.3 and 16.3 ($\underline{C}H_3$, ethoxyphosphoryl), 13.9 ($\underline{C}H_3$, ethoxycarbonyl).

***Z,E*-dimethyl(methoxycarbonyl)methyl phosphonate sodium salts (8, 9).** In a NMR tube containing NaH 80 % (13.75 mg, 0.46 mmol) under N_2, a solution of methyl phosphonoacetate **5** (91 μL; 0.55 mmol) in 0.5 mL of DMF-*d6* was added. After 2 h at room temperature with occasional shaking, the ^1H and ^{13}C NMR (sequence DEPT 135) spectra of the mixture of the sodium *Z*-(**8**) and *E*-(**9**) enolates and phosphonoester **5** were measured. ^1H NMR δ 3.72 (s, methoxyphosphoryl, **5**), 3.65 (s, C$\underline{H}_3$ methoxyl, **5**), 3.43-3.37 (s, C$\underline{H}_3$ methoxyphosphoryl, **8** and **9**), 3.35 (s, C$\underline{H}_3$ methoxycarbonyl, **9**), 3.29 (s, C$\underline{H}_3$ methoxycarbonyl, **8**), 3.17 (d, $J_{H,P}$ = 21.4 Hz, H-1, H-1', **5**), 2.27 (d, 1H, $J_{H,P}$= 14.2 Hz, **8**), 1.91 (d, $J_{H,P}$=15.1 Hz, H-1, **9**). ^{13}C NMR δ 52.7 and 52.6 (C$\underline{H}_3$ methoxyphosphoryl, **5**), 52.1 (C$\underline{H}_3$ methoxycarbonyl, **5**), 50.4 and 50.3 (C$\underline{H}_3$ methoxyphosphoryl, **8** and **9**), 49.1 (d, $J_{C,P}$= 2.9 Hz, C$\underline{H}_3$ methoxycarbonyl, **9**), 48.3 (d, $J_{C,P}$= 3.4 Hz, C$\underline{H}_3$ methoxycarbonyl, **8**), 41.8 (d, $J_{C,P}$= 215.9 Hz, C-1, **9**), 37.9 (d, $J_{C,P}$= 222.5 Hz, C-1, **8**), 32.03 (d, $J_{C,P}$= 131.77 Hz, C-1, **5**).

Methyl 4,6-di-*O*-benzoyl-2-deoxy-3-*O*-diethoxyphosphoryl-2-*C*-[(ethoxycarbonyl)methyl]-α-D-mannopyranoside (11). To a solution of **7** (0.230 g, 0.38 mmol) of in *tert*-butyl alcohol (1.3 mL), toluene (0.5 mL) was added. The mixture was cooled to 5 °C and $NaBH_4$ (0.016 g, 0.42 mmol) was added. After 3 h at 5 °C, Dowex 50 (H^+) ion exchange resin in methanol was added, and the suspension was stirred for 5 min. The resin was filtered and the resulting solution was concentrated and purified by flash chromatography (hexane/ethyl acetate 2:1) to give chromatographically homogeneous methyl 4,6-di-*O*-benzoyl-2-deoxy-3-*O*-diethoxyphosphoryl-2-*C*-[(methoxycarbonyl) methyl]-α-D-mannopyranoside (**11**) in 92 % yield (0.212 g). $[\alpha]_D$ = +59.6° (*c* 2.13, $CHCl_3$). ^1H NMR δ 7.33-8.11 (m, 10H, H_{aryl}), 5.43 (dd, 1H, $J_{3,4}$ = 9.4 Hz, $J_{4,5}$ = 9.9 Hz, H-4), 4.94 (d, 1H, $J_{1,2}$ = 2.0 Hz, H-1), 4.78 (ddd, 1H, $J_{2,3}$=1.7 Hz, $J_{3,P}$ = 9.1 Hz, H-3), 4.51 (dd, 1H, $J_{5,6'}$=3.2 Hz, $J_{6,6'}$=12.1 Hz, H-6'), 4.39 (dd, 1H, $J_{5,6}$=5.0 Hz, H-6), 3.98-4.21 (m, 7H, H-5 and 3 C$\underline{H}_2$O), 3.38 (s, 3H, OC$\underline{H}_3$), 2.85 (m, 1H, $J_{7,7'}$ = 12.9 Hz, H-7'), 2.61 (m, 2H, H-2, H-7), 1.26 (m, 6H, C$\underline{H}_3$ ethoxyphosphoryl), 0.87 (t, 3H, C$\underline{H}_3$ ethoxycarbonyl). ^{13}C NMR δ 171.9 (C$\underline{=}$O, C-8), 166.2 and 165.5 (C$\underline{=}$O, benzoyl), 133.2 -128.3 (C_{aryl}), 99.3 (C-1), 77.1 (d, $J_{C,P}$ = 2.9 Hz, C-3), 71.2 (C-4), 67.8 (C-5), 63.9 (C$\underline{H}_2$ ethoxyphosphoryl), 63.5 (C$\underline{H}_2$ ethoxycarbonyl), 60.6 (C-6), 55.3 (OC$\underline{H}_3$, C-1), 47.2 (C-2), 32.0 (C-7), 15.9

(d, $J_{C,P}$ = 7.1 Hz, $\underline{C}H_3$ ethoxyphosphoryl), 15.4 (d, $J_{C,P}$ = 7.0 Hz, $\underline{C}H_3$ ethoxyphosphoryl), 14.2 ($\underline{C}H_3$ ethoxy-carbonyl).

Anal. Calcd for $C_{29}H_{37}O_{12}P$: C, 57.23; H, 6.13. Found: C, 57.05; H, 6.26.

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