Tetrahedron Vol. 43, No. 8, pp. 1895 to 1901, 1987
Printed in Great Britain.

0040-4020/87 $3.00+.00
Pergamon Journals Ltd.

THE REACTION OF CARBOHYDRATE-DERIVED ALKOXYALDEHYDES WITH METHOXYCARBONYLMETHYLENETRIPHENYLPHOSPHORANE: STEREOSELECTIVE SYNTHESIS OF β-UNSATURATED ESTERS

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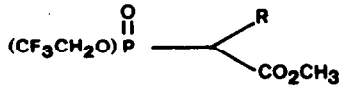
(*Received in UK 6 February* 1987)

ABSTRACT - *The reaction of several carbohydrate-derived alkoxyaldehydes with methoxycarbonylmethylenetriphenylphosphorane affords α,β-unsaturated esters with Z-stereoselectivity. The stereoselectivity depends on the substrate structure and the nature of the solvent used.*

As a part of our synthetic studies on naturally occurring α,β-unsaturated-δ-lactones[1], the stereoselective synthesis of Z-α,β-unsaturated esters was needed. The α,β-unsaturated esters are useful synthetic intermediates as Michael acceptors[2] and as precursors of allylic alcohols[3] and there is a necessity of obtaining them stereoselectively. Both the Wittig[4] and the Wittig-Horner[5] reaction using alkoxycarbonylphosphoranes or phosphonates generally yield the α,β-unsaturated esters with E-configuration and there are only a few methods which afford the Z-isomer. The bis(trifluoroethyl)phosphone ester 1 have been used to obtain di- and tri-substituted α,β-unsaturated esters with good stereoselectivity[6] and ethyl α-(dimethylphosphono) propionate (2) also gave primarily the Z-isomers[7]. It has been recently shown using long-chain alkyl derivatives of these phosphonocarboxylates that the stereoselectivity strongly depends on the nature of the substituent in the α-position[8]. A four step sequence has also been used[11c] to prepare α,β-unsaturated esters with good Z-stereoselectivity, although the overall yield is not encouraging. We now report on the Z-stereoselectivity of the reaction of carbohydrate-derived alkoxyaldehydes with methoxycarbonylmethylene phosphorane[9] in methanol at room temperature. The α,β-unsaturated esters thus prepared are being used as precursors of higher-order carbohydrates[10]. Methanol has been used occasionally as a solvent in the Wittig rection of stabilized ylides[11] but its influence on the reaction stereoselectivity has not been investigated.



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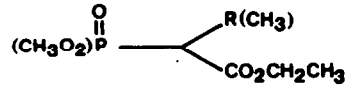

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RESULTS AND DISCUSSION

The reaction of the alkoxyaldehydes 4 with 3 molar equivalents of methoxycarbonylmethylene-triphenylphosphorane (3) in methanol at room temperature gave the corresponding α,β-unsaturated esters in

good yield. Reaction times were generally short with the exception of aldehyde **4a** probably due to the fact that this compound exists mainly in the hydrated form. (*see Scheme*). The results are summarized in Table 1.

SCHEME

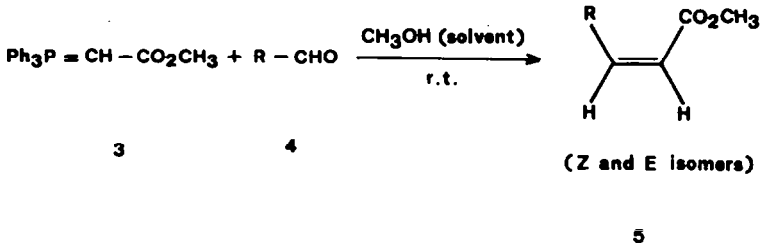


Table 1. Reaction conditions for the Wittig condensation of aldehydes[19] **4** and the phosphorane **3**.

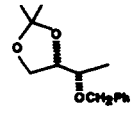
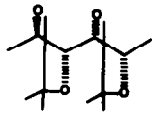
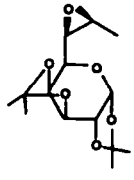
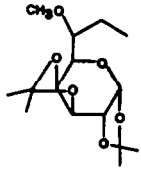
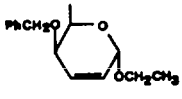
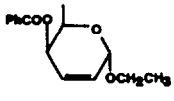
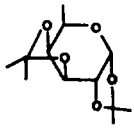
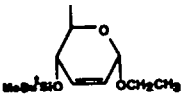
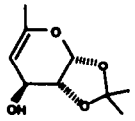
Product	Reaction time (hours)	Overall yield (%)	Ratio[a] Z/E	R (Reference)	
5a	24	77	11 : 1		(1)
5b	1	70	7 : 1		(16)
5c	0.75	82	4.3 : 1		(17)
5d	2.25	88	5 : 4		(21)
5e	2	82	3.7 : 1		(22)
5f	3	78	100 : 1[b]		(16)
5g	2	76	90 : 1		(16)
5h	4	80	20 : 1		(18)

Table 1. (cont.)

5i	1	92	1 : 3.5		(16)
5j	1.5	73	1 : 1.7		(16)

[a] The isomers ratio was determined by isolation of the products, except in the reaction of aldehyde **4b**, which was determined by ^{1}H-NMR and ^{13}C-NMR. In the reaction of **4g**, the E-isomer of **5g** was detected in a minor fraction of the flash chromatography of the reaction crude, along with the Z-isomer. The analysis of the ^{1}H-NMR spectrum of this fraction allowed to estimate the amount of the E-isomer formed in this reaction.

[b] The E-isomer was not detected in this reaction. It was prepared by the reaction of **4f** with **3** in toluene solution.

The stereoselectivity of the process seems to strongly depend on the structure of the starting alkoxyaldehyde. With acyclic aldehydes (**4a-4e**) the stereoselectivity ranged from moderate to good. In the case of hexopiranosides *cis*-substituted relative to the formyl group (**4f-4h**) the selectivity was excellent. When the alkoxy substituent was *trans*-orientated relative to the formyl group (**4i**), the stereoselectivity was only moderate but reversed with respect to the previous cases. The reaction of **4j**, in which position 4 is unsubstituted, did not show any stereoselectivity, but even in these last two cases, there were a clear departure from the E-stereoselectivity expected when working in an inert solvent.

The steric course of the reaction also depends on the solvent, as indicated by the reaction of aldehyde **4f** with **3** in toluene at room temperature to give a 1:1 mixture of Z and E isomers in 62% yield. The use of large volumes of methanol and longer reaction times resulted in the addition of methanol to the double bond. Thus when aldehyde (**4h**) (1 mmol) was treated with three molar equivalents of **3** in methanol (10 mL) at room temperature for 24 h, compound **6** (only one diastereomer, no stereochemistry assigned) was obtained in 60% yield. The use of anhydrous methanol (4 mL per mmol of aldehyde) seems to be necessary to attain high yield and good stereoselectivity since the presence of small amounts of water resulted in the lowering of both yield and stereoselectivity. The effect of ethanol and isopropanol as solvents and the influence of the temperature, were also investigated in the reaction of the aldehyde **4h** with **3**, and the results are summarized in Table 2. All these experiments were carried out for 24 h, the conversion being practically quantitative (^{1}H-NMR evidence) and both yield and isomer ratio were determined by g.l.c. Apparently, isopropanol and ethanol are not as convenient as methanol, the reaction rate being slower and the yield lower when using these solvents. The stereoselectivity in ethanol is similar to that in methanol. As expected, the stereoselectivity in methanol increased as temperature decreased but the reaction time was much longer. In one case (**4e**) the reaction has been carried out in three different solvents (*see Table 3*); the highest yield of Z-isomer was obtained in methanol as expected.

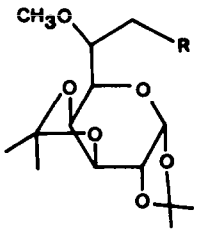
Table 2. Conditions for the reaction of **4h** and **3**

Solvent	temperature	yield (%)	Z/E ratio
Isopropanol	25ºC	56	10 : 1
Ethanol	25ºC	48	22 : 1
Methanol	0ºC	60	35 : 1
Methanol	-8ºC	68	> 100 : 1

In general, there are two main factors which can influence the final result of the Wittig reaction; the nature of the ylide (stabilized or nonstabilized) and the solvent. In nonpolar aprotic solvents, stabilized ylides stereoselectively yield the E-olefin, while nonstabilized ylides yield the Z-olefin. The intermediacy of betaines, oxaphosphetanes and zwitterious has been proposed[12]. The presence of oxa-

Table 3. Conditions for the reaction of **4e** and **3**

Solvent	temperature	yield (%)	Z/E ratio
Methanol	r.t.	82	3.7 : 1
Toluene	r.t.	81	1 : 1
Dichloromethane	r.t.	80	1 : 2



6 R = CO_2CH_3

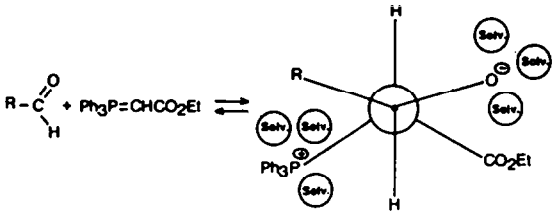
7 R = CH_2OH

phosphetanes, in the case of nonstabilized ylides, has been recently proved by NMR spectroscopy[12], and zwitterious has been postulated[13] as intermediates that would explain the high E-stereoselectivity observed for stabilized ylides.

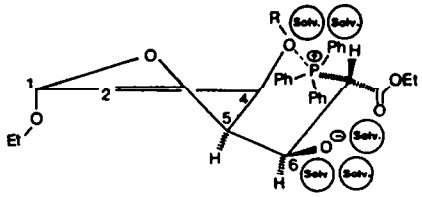
As indicated previously, the Wittig reaction of stabilized ylides in methanol as solvent[11] has been occasionally carried out. In all the reported cases it is observed a departure of the stated rule which would predict high E-stereoselectivity of the olefin formed, and considerable amounts of Z-olefin has always been obtained.

Furthermore, the prevailing stereoselectivity is Z when, besides using methanol as solvent, there is an alkoxy group at the carbon atom β to the carbonyl group. Apparently both factors contribute to increase the Z-stereoselectivity of the reaction (*see* **4f-4h**).

To explain those results we assume that, in the Wittig condensation of stabilized ylides in methanol as solvent, the "*anti*" betaine is partially stabilized through solvation; conformers such as "**A**" can be



A



B

postulated[11d,20] and these would undergoe *syn*-elimination to afford *cis*-olefins such as it is experimentally experimentally observed.

The presence of a β-alkoxy substituent can enhance this mechanism through the participation of the alkoxy group in the solvation phenomena, as indicated in "**B**" for the case of β-alkoxy-hexenopyranosides.

EXPERIMENTAL

Column chromatography was performed on silica gel 60, 70-230 mesh (Merck). T.l.c. was carried out on plates of silica gel 60 F_{254} (Merck). ^1H- and ^{13}C-NMR spectra were measured for $CDCl_3$ solutions with a Varian XL-300 (300 MHz) and a Brücker WP-80 (20 MHz) spectrometer, respectively. M.p.s. were determined on a Kofler hot-stage apparatus and are uncorrected. Optical rotations were determined with a Perkin-Elmer 141 polarimeter.

Wittig reaction of alkoxyaldehydes **4** *with methoxycarbonylmethylenetriphenylphosphorane* (**3**). *General procedure.*

The alkoxyaldehyde **4** (1 mmol) in anhydrous methanol (4 mL) was treated with methoxycarbonylmethylenetriphenylphosphorane (3 equivalents) and the mixture stirred at room temperature for the time indicated in Table 1. The solvent was then evaporated under vacuum and the residue was dissolved in the

minimum amount of methylene chloride and directly transformed to the head of a flash-chromatography column[12]. The column was eluted with hexane:ethyl acetate mixtures in the proportions required to place the fastest moving product at Rf 0.25 in an analytical t.l.c. plate; in all cases the two isomers (Z and E) were easily separated, except compounds **5b** *(see below)*. The configuration of the olefinic double bond was assigned based on ^{1}H-NMR spectral data.

Compounds **5a**.- From **4a** and **3**. Z-Isomer (thick oil), $|\alpha|_D^{20}$+32º (c 0.9, chloroform). ^{1}H-NMR data: δ 1.35 (3H, s), 1.42 (3H, s), 3.70 (3H, s), 3.95 (2H, d, J 5 Hz), 4.27 (1H, m), 4.48 (1H, d, J 12 Hz), 4.67 (1H, d, J 12 Hz), 5.19 (1H, dd, J 8 Hz, 4 Hz), 5.90 (1H, d, J 11 Hz), 6.20 (1H, dd, J 11 Hz, 4 Hz), 7.30 (5H, s). ^{13}C-NMR data: δ 25.6, 26.2, 51.5 (q each), 65.3 (t), 71.5 (t), 74.4 (d), 77.7 (d), 109.8 (s), 123.1, 127.6, 127.8,128.3 (d each), 138.1 (s), 146.2 (d), 166.1 (s). (Found: C, 67.02; H, 7.29. Calcd. for $C_{17}H_{22}O_5$: C, 66.67; H, 7.19).

E-Isomer: M.p. 48-50ºC (hexane), $|\alpha|_D^{20}$ +28º (c 1.3, chloroform). ^{1}H-NMR data: δ 1.30, 1.35, 3.72 (3H, s each), 3.80-4.70 (6H, m), 6.10 (1H, d, J 15 Hz), 6.85 (1H, dd, J 15 Hz, 6 Hz), 7.30 (5H, s). ^{13}C-NMR data: δ 25.1, 26.3, 51.7, (q each), 65.3 (t), 71.5 (t), 76.7 (d). 78.2 (d), 109.8 (s), 124.0, 127.8, 127.9, 128.5, 137.6, 143.8 (d), 166.2 (s). (Found: C, 66.59; H, 7.28).

Compounds **5b**.- From **4b** and **3**. The Z- and E-isomers could not be separated and the isomers ratio was determined by ^{1}H- and ^{13}C-NMR spectroscopy. Z-Isomer, ^{1}H-NMR data: δ 5.90 (d, J 11 Hz), 6.05 (d, J 11 Hz). E-Isomer, ^{1}H-NMR data: δ 6.20 (dd, J 15, 2 Hz), 6.85 (dd, J 15, 6 Hz).

Compound **5c**.- From **4c** and **3**. Z-Isomer (thick oil), $|\alpha|_D^{20}$ +103º (c 0.3, chloroform), ^{1}H-NMR data: δ 1.33 (6H, s), 1.48 (3H, s), 1.50 (3H, s), 3.56 (2H, s), 3.78 (3H, s), 4.06 (1H, dd, J 7.8, 1 Hz), 4.32 (1H, dd, J 4.9, 2.6 Hz), 4.55 (2H, m), 5.59 (1H, d, J 4.9 Hz), 5.86 (1H, d, J 4.9 Hz), 6.04 (1H, dd, J 11.5, 3 Hz), 6.10 (1H, dd, J 11.5, 3 Hz). (Found: C, 57.55; H, 7.00. Calcd. for $C_{17}H_{24}O_8$: C, 57.30; H, 6.79).

E-Isomer, (thick oil), $|\alpha|_D^{20}$ -31º (c 0.3, chloroform). ^{1}H-NMR data: δ 1.25, 1.34, 1.46, 1.49 (3H, s each), 3.50 (1H, m), 3.70 (1H, m), 3.75 (3H, s), 3.81 (1H, m), 4.05 (1H, dd, J 7.9), 1.4 Hz), 4.33 (1H, dd, J 5, 2.6 Hz), 4.58 (1H, dd, J 7.9, 2.6 Hz), 5.59 (1H, d, J 5 Hz), 6.24 (1H, dd, J 15.5, 1.1 Hz), 6.89 (1H, dd, J 15.5, 5.5 Hz). (Found: C, 57.41; H, 6.81).

Compound **5d**.- From **4d** and **3**. Z-Isomer, (thick oil), $|\alpha|_D^{20}$ -37º (c 0.2, chloroform). ^{1}H-NMR data: δ 1.30 (6H, s), 1.45 (3H, s), 1.51 (3H, s), 3.05 (2H, m), 3.45 (3H, s), 3.80 (3H, s), 3.80 (2H, m), 4.25 (2H, m), 4.55 (1H, dd, J 7.5, 1.0 Hz), 5.60 (1H, d, J 4.5 Hz), 5.75 (1H, dt,J 10.5, 1.0 Hz), 6.40 (1H, m). (Found: C, 58.93; H, 7.73. Calcd. for $C_{19}H_{30}O_8$: C, 59.05; H, 7.82).

E-Isomer, (thick oil), $|\alpha|_D^{20}$ -61º (c 0.2, chloroform). ^{1}H-NMR data: δ 1.30 (6H, s), 1.43 (3H, s), 1.49 (3H, s), 2.55 (2H, m), 3.45 (3H, s), 3.70 (3H, s), 3.70 (2H, m), 4.25 (2H, m), 4.60 (1H, dd, J 7.5, 1.0 Hz), 5.60 (1H, J 4.5 Hz), 5.93 (dt, J 15.0, 1.0 Hz), 7.06 (1H, m). (Found: C, 59.00; H, 7.91).

Compound **5e**.- From **4e** and **3**. Z-Isomer, (oil), $|\alpha|_D^{20}$ +36º (c 0.6, chloroform), ^{1}H-NMR data: δ 1.33 (3H, d, J 6.0 Hz), 3.70 (3H, s), 4.46 (2H, s), 5.15 (1H, m), 5.80 (1H, d, J 12.6 Hz), 6.20 (1H, dd, J 12.0, 8.0 Hz), 7.30 (5H, s).

E-Isomer, (oil), $|\alpha|_D^{20}$ -44º (c 0.2, chloroform). ^{1}H-NMR data: δ 1.30 (3H, d, J 6.0 Hz), 3.75 (3H, s), 4.10 (1H, m), 4.50 (2H, q, J 12 Hz), 6.00 (1H, d, J 15.0 Hz), 6.90 (1H, dd, J 15.0, 5.0 Hz).

Compound **5f**.- From **4f** and **3**. Z-Isomer, (thick oil), $|\alpha|_D^{20}$ -255º (c 0.2, chloroform). ^{1}H-NMR data: δ 1.22 (3H, t, J 6 Hz), 3.53 (1H, m), 3.70 (3H, s), 3.77 (1H, m), 4.05 (1H, dd, J 5.2, 2.8 Hz), 4.51 (1H, d, J 12.1 Hz), 4.58 (1H, d, J 12.1 Hz), 5.08 (1H, dd, J 3.1, 0.8 Hz), 5.49 (1H, m), 5.93 (1H, dd, J 12, 1.6 Hz), 5.98 (1H, dd, J 10, 3.1 Hz), 6.11 (1H, ddd, J 10, 5.2 Hz), 6.44 (1H, dd, J 12, 7 Hz), 7.29 (5H, s). ^{13}C-NMR data: δ 15.2 (q), 51.3 (q), 63.8 (t), 68.5 (d), 68.9 (d), 71.2 (t), 93.9 (d), 120.0, 127.1, 127.7, 127.9, 128.3, 129.3 (d), 138.5 (s), 147.3 (d), 166.0 (s) ppm. (Found: C, 68.09; H, 7.02. Calcd. for $C_{18}H_{22}O_5$: C, 67.91; H, 6.97).

E-Isomer, (thick oil), $|\alpha|_D^{20}$ -161º (c 0.5, chloroform). ^{1}H-NMR data: δ 1.18 (3H, t, J 6 Hz), 3.27-3.60 (3H, m), 3.70 (3H, s), 4.47 (2H, s), 4.70 (1H, m), 5.07 (1H, d, J 2 Hz), 5.99 (2H, m), 6.20 (1H,

dd, J 16, 3 Hz, 7.00 (1H, dd, J 16, 5 Hz), 7.27 (5H, s). ^{13}C-NMR data: δ 15.3 (q), 51.6 (q), 64.0 (t), 68.5 (d),69.8 (d), 70.8 (t), 94.1 (d), 121.6, 126.8, 127.8, 127.9, 128.5,129.8, 144.7 (d), 166.8 (s) ppm. (Found: C, 68.16; H, 7.21).

Compound **5g**.- From **4g** and **3**. Z-Isomer, m.p. 80-82ºC (hexane), $|\alpha|_D^{20}$ -300º (c 0.3, chloroform): ^{1}H-NMR data: δ 1.20 (3H, t, J 6 Hz), 3.70 (3H,s), 3.45-3.90 (2H, m), 5.08 (1H, d, J 2 Hz), 5.30 (4H, m), 5.89 (1H, dd, J 11.8, 1.6 Hz), 6.34 (1H, dd, J 11.8, 7 Hz). ^{13}C-NMR data: δ 15.2 (q), 51.5 (q), 64.0 (t), 65.2 (d), 66.9 (d), 93.8 (d), 121.1, 125.6, 128.3, 129.7, 130.0, 130.5, 133.0, 145, 165.7 ppm. (Found: C, 65.02; H, 6.11. Calcd. for $C_{18}H_{20}O_6$: C, 65.05; H, 6.07.

The E-isomer could not be purified.

Compound **5h**.- From **4h** and **3**. Z-Isomer, $|\alpha|_D^{20}$ -136º (c 0.5, chloroform), lit.[15] $|\alpha|_D^{20}$ -135.7º. E-Isomer: $|\alpha|_D^{20}$ -140º (c 0.6, chloroform), lit.[15] $|\alpha|_D^{20}$ 135.7º.

Compound **5i**.- From **4i** and **3**. Z-Isomer, (thick oil), $|\alpha|_D^{20}$ +80º (c 0.7, chloroform). ^{1}H-NMR data: δ 0.10 (6H, s), 0.90 (9H, s), 1.28 (3H, t, J 6 Hz), 3.51 (1H, m), 3.73 (3H, s), 3.86 (1H, m), 4.03 (1H, m), 4.98 (1H, d, J 1.3 Hz), 5.39 (1H, m), 5.72 (1H, ddd, J 10.2, 5.6, 2.5 Hz), 5.89 (1H, ddd, J 10.2, 2.7, 1.3 Hz), 6.00 (1H, d, J 11 Hz), 6.05 (1H,dd, J 11, 7 Hz). ^{13}C-NMR data: δ -4.6,-4.4, 15.2 (q each), 17.9 (s), 25.6 (2C, q), 25.7 (q), 51.4 (q), 63.8 (t), 67.1 (d), 68.2 (d), 93.9 (d), 123.9 (d), 125.7 (d), 139.1 (d), 143.4 (d), 168.0 (s) ppm. (Found: C, 59.70; H, 8.62. Calcd. for $C_{17}H_{30}O_5Si$: C, 59.61; H, 8.83).

E-Isomer (thick oil), $|\alpha|_D^{20}$ +43º (c 0 2, chloroform). ^{1}H-NMR data: δ 0.10 (6H, s), 0.93 (9H, s), 1.25 (3H, t, J 6 Hz), 3.52 (1H, m), 3.78 (3H, s), 3.76-3.99 (1H, m), 4.01 (1H, m), 4.34 (1H, m), 5.04 (1H, d, J 2.4 Hz), 5.74 (1H, ddd, J 10.1, 4.6, 2.4 Hz), 5.89 (1H, ddd, J 10.1, 2.5, 1.2 Hz), 6.17 (1H, dd, J 15.8, 2 Hz), 7.13 (1H, dd, J 15.8, 4.3 Hz). ^{13}C-NMR data: δ -4.7, -4.4, 15.4 (q each), 18.0 (s), 25.7 (3C, q), 51.5 (q), 64.2 (t), 68.3 (d), 70.4 (d), 94.4 (d), 121.0 (d), 125.9 (d), 134.2 (d), 145.4 (d), 166.8 (s) ppm. (Found: C, 59.70; H, 8.62).

Compound **5j**.- From **4j** and **3**. Z-Isomer, (thick oil), $|\alpha|_D^{20}$ +11º (c 0.7, chloroform). ^{1}H-NMR data: δ 6.02 (1H, d, J 12.2 Hz), 5.89 (1H, d, J 12.2 Hz), 5.54 (1H, d, J 3.1 Hz), 5.26 (1H, dd, J 5.2 1 Hz), 4.36 (1H, broad s), 4.23 (1H, m), 3.77 (3H, s), 1.62 (1H, broad s), 1.46 (3H, s). (Found: C, 56.64; H, 6.24. Calcd. for $C_{12}H_6O_6$: C, 56.24; H, 6.29).

E-Isomer, (thick oil), $|\alpha|_D^{20}$ +27º (c 0.2, chloroform). ^{1}H-NMR data: δ 1.42 (3H, s), 1.43 (3H, s), 3.77 (3H, s), 4.28 (1H, m), 4.45 (1H, broad s), 4.80 (1H, dd, J 5.4, 1.4 Hz), 5.64 (1H, d, J 3.1 Hz), 6.35 (1H, d, J 15.4 Hz), 6.98 (1H, d, J 12.2 Hz). ^{13}C-NMR data: δ 24.5, 25.0, 26.0 (2C), (q each), 36.1 (t), 51.5 (q), 59.2 (q), 64.7 (d), 70.6 (d), 71.0 (2C, d), 77.7 (d), 96.6 (d), 108.6 (s), 109.3 (s), 171.8 (s). (Found: C, 56.42; H, 6.04).

Compound **6**.- Treatment of **4f** (1 mmol) with **3** (3 mol equiv.) in methanol (10 mL) at room temperature for 24 h, gave **6**, (60%). ^{1}H-NMR data: δ 1.34, 1.36, 1.48, 1.57 (3H, each, s), 2.61 (1H, dd, J 16, 6 Hz), 2.80 (1H, dd, J 16, 3Hz), 3.53 (3H, s), 3.74 (3H, s), 3.87 (1H, ddd, J 7.8, 6, 3 Hz), 3.93 (1H, dd, J 7.5, 2.1 Hz), 4.27 (1H, dd, J 7.9, 2.1 Hz), 4.30 (1H, dd, J 5.1, 2.1 Hz), 4.58 (1H, dd, J 7.5, 2.1 Hz), 5.60 (1H, d, J 5.1 Hz). ^{13}C-NMR data: δ 24.5 (q),25.0 (q),26.0 (2C, q), 36.1 (t), 51.5 (q), 59.2 (q), 69.7 (d), 70.6 (d), 71.0 (2C, d), 77.7 (d), 96.6 (d), 108.6 (s), 109.3 (s), 171.8 (s) ppm. (Found: C, 55.17; H, 7.51. Calcd. for $C_{16}H_{26}O_8$: C, 55.48; H, 7.57.

Compound **4d**.- The ester **6** (397 mg, 1.1 mmol) in THF (8 mL) was treated with $LiAlH_4$ (195mg, 5.0 mmol) in THF (10 mL) with stirring and under argon at 0ºC. The mixture was allowed to reach room temperature. After 4 hours the reaction was cooled again to 0ºC and a saturated solution of Na_2SO_4 in water was added. The solids formed were eliminated by filtration through celite and the filtrates were extracted with CH_2Cl_2/MeOH. Evaporation of this solvent left a residue which was subjected to short colum chromatography. Compound **7** (362 mg, 99% yield) was isolated. Compound **7** was a thick oil, $|\alpha|_D^{22}$ -80º (c 0.5, chloroform). ^{1}H-NMR data: δ 1.30 (6H, s), 1.40 (3H, s), 1.50 (3H, s), 1.90 (2H, m), 3.48 (3H, s), 3.75 (3H, m), 4.10 (1H, m), 4.25 (1H, m), 4.55 (1H, dd, J 6 Hz, 1.0 Hz), 5.53 (1H, d, J 5.0 Hz).

Without further characterization this alcohol was subjected to PCC oxidation in the presence of 4 Å molecular sieves to afford compound **4d** (83% yield). Compound **4d** was a thick oil, $|\alpha|_D^{22}$ -82º (c 0.4, chloroform). ^{1}H-NMR data: δ 1.28 (6H, s), 1.42 (3H, s), 1.50 (3H, s), 2.73 (2H, m), 3.40 (3H, s), 3.93 (1H, m), 4.27 (2H, m), 4.57 (1H, dd, J 6 Hz, 1 Hz), 5.54 (1H, d, J 5.0 Hz).

Acknowledgments.- We thank the CAICYT for financial support and the Ministerio de Educación y Ciencia for a fellowship (to B.H.).

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