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Diacetone D-Glucose : Efficient Chiral Building Block for Asymmetric Photodeconjugation

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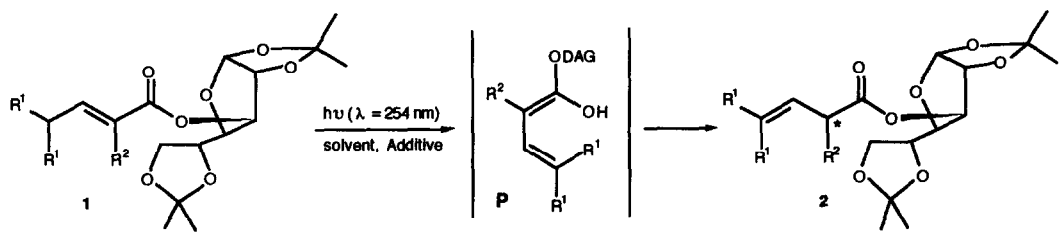
Abstract: *Irradiation of α-substituted, α,β-unsaturated esters of 1,2;5,6-di-O-isopropylidene-α-D-glucofuranose leads to the formation of β,γ-isomers with high d.e. (up to 98%) whatever the substitution of the chain. A very strong dependence of the nature of the protonating agent upon the selectivity and the configuration of the new chiral center is observed.*

High diastereoselective photodeconjugation of α,β-unsaturated esters has been reported from this laboratory [1,2] using monoprotected diols derived from camphor [3] or 8-phenylmenthol [4]. Unfortunately these chiral agents are relatively expensive or need multistep synthesis. Otherwise, 1,2;5,6-di-O-isopropylidene-α-D-glucofuranose (commonly known as diacetone D-glucose, DAGOH) [5], a very cheap and commercially available reagent, has been avantageously used recently to obtain high asymmetric induction during protonation of enolates [6], Reformatsky reactions [7], aldolisations [8], additions of chiral allyltitanate to aldehydes [9], reductions [10], enantioselective alkylations [11], [2+2] Paterno-Büchi reactions [12], diastereoselective halogenation of silylketene acetals [13], synthesis of chiral methylsulfoxides [14] and finally Diels-Alder cycloadditions [15]. With the purpose of making asymmetric photodeconjugation more attractive in synthesis, the use of DAGOH as a chiral auxiliary appeared very promising.

We have now found that this reagent can play the role of chiral inductor very efficiently during the asymmetric protonation of photodienol P (Scheme 1).

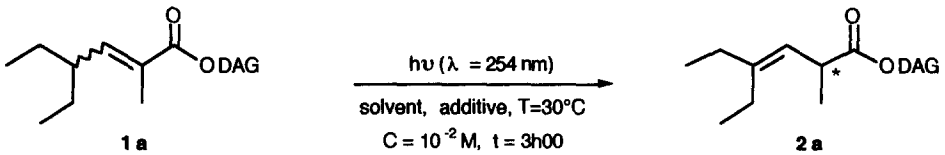


Scheme 1

Esters 1 obtained in high yields from the α,β-unsaturated acids, according to the standard procedure[16] were submitted to irradiation at 254 nm in the presence of various additives and in different solvents. Reaction of **1a** (Table1) in the presence of an achiral alcohol such as t-butanol gave after 3 hours the expected product with moderate diastereoselectivity (42%) and incomplete conversion. When performed in the presence of a base (diisopropylamine), the reaction occured more rapidly [17] and the d.e. was slightly improved (54% for the same solvent). Interestingly the ratio R/S was reversed indicating that one face of the photodienol is selectively protonated in the presence of alcohols and the other face by the means of amines. When both an alcohol and an amine are present the protonation occured preferentially on the same face as with the amines, as shown by the

ratio observed. Due to the high acidity of the photodienolic proton [18b] the intermediate presumably interacts more efficiently with any amine present. Finally, the d.e reached to 82% for the deconjugation of **1a** in methylene chloride at room temperature, in the presence of an achiral agent bearing both an hydroxy group and an amino function such as N,N-dimethylaminoethanol **I**. Similar synergism between an hydroxy and an amino group has been already observed during other enantioselective processes [18]. The excess can be improved (d.e.= 88%) when the reaction is conducted in an alkane instead of methylene chloride as solvent. In this solvent, photolysis of methylene chloride in the presence of amines at 254 nm is known to produce the weakly acidic ammonium salts [19], which interact with the photodienol on the reverse face compared with the amine. Interestingly, only catalytic amounts of protonating agent (0.1 eq.) are required to perform the reaction with the same efficiency.

Table 1. Photodeconjugation of ester **1a** in the presence of additive.



1a **2a**

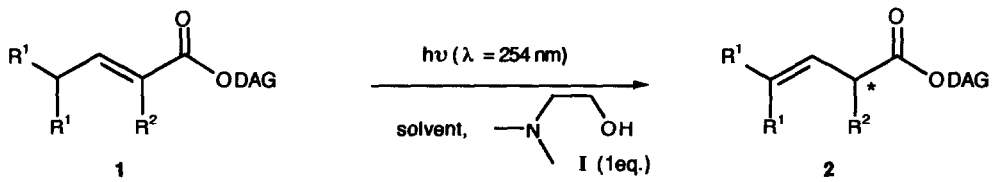
Solvent	Additive	(a) Conversion	(b) Yields (%)	d.e. (%)	(c) Ratio
MeOH	-	80%	44 (55)	15	(57/43)
CH_2Cl_2	i-PrOH (1eq.)	65%	35 (54)	42	(29/71)
CH_2Cl_2	t-BuOH (1eq.)	85%	61 (71)	41	(29.5/70.5)
CH_2Cl_2	1-Adamantol (1eq.)	38%	not det.	12	(44/56)
CH_2Cl_2	$(iPr)_2CHOH$ (1eq.)	57%	34 (60)	20	(40/60)
CH_2Cl_2	$HO-(CH_2)_2-OH$ (1eq.)	60%	27 (45)	42	(29/71)
CH_2Cl_2	DAGOH (1eq.)	55%	30 (54)	22	(39/61)
CH_2Cl_2	$Bu_4N^+ Cl^-$ (1eq.)	>98%	41	23	(38.5/61.5)
CH_2Cl_2	iPr_2NH (2.5eq.)	>98%	72	54	(77/23)
CH_2Cl_2	t-$BuNH_2$ (1 eq.)	>98%	73	74	(86.5/13.5)
CH_2Cl_2	$Me_2N-(CH_2)_2-OH$ (1eq)	>98%	90	82	(91/9)
CH_2Cl_2	Et_3N (1eq) + MeOH (1eq)	86%	44	32	(66/34)
n-hexane	iPr_2NH (2.5eq.)	94%	76	61	(80.5/19.5)
n-hexane	$Me_2N-(CH_2)_2-OH$ (1eq)	>95%	69	87	(93.5/6.5)
n-hexane	$Me_2N-(CH_2)_2-OH$ (0.1eq)	>98%	85	88	(94/6)
Et_2O	$Me_2N-(CH_2)_2-OH$ (1eq)	65%	57	77	(88.5/11.5)
CH_3CN	$Me_2N-(CH_2)_2-OH$ (1eq)	>98%	68	61	(69.5/30.5)

(a) conversion determined with ^{1}H- NMR on the crude product.
(b) isolated yields of pure product.
(c) ratio determined with ^{1}H-NMR.

Decreasing the temperature and in the presence of the same hindered and achiral aminoalcohol **I**, diastereoselection increased considerably (Table 2). Finally the reaction has been generalized to other α,β-

unsaturated esters and the corresponding β,γ-isomers have been obtained in good yields and high d.e. (superior to 98%) whatever the nature of the chain. Substitution of n-hexane by n-octane to increase the viscosity of the solvent results in a slight improvement of the diastereoselectivity.

Table 2. Photodeconjugation of esters 1 in the presence of N,N-dimethylaminoethanol **I** .

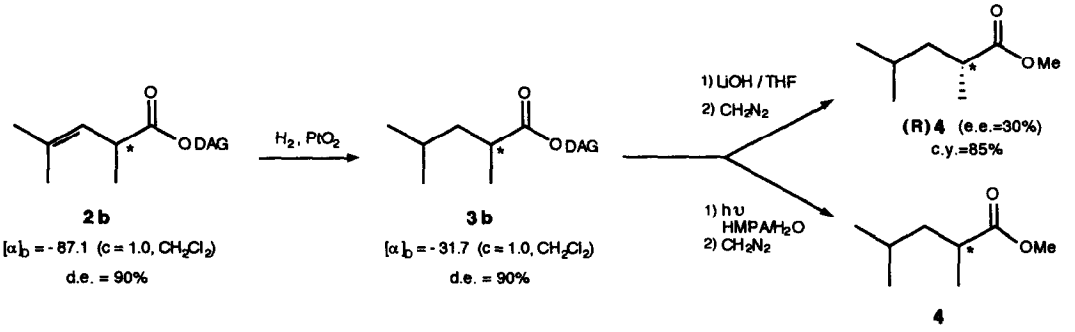


Ester	R^1	R^2	Solvent	Temperature	c.y. [a]	d.e. [b]	conf. [c]
1a	Et	Me	CH_2Cl_2	-35°C	79	83	R
			n-hexane	-35°C	84	96	R
			n-octane	-35°C	88	>97	R
1b	Me	Me	CH_2Cl_2	+30°C	60	80	R
			CH_2Cl_2	-35°C	57	84	R
			CH_2Cl_2	-50°C	63	91	R
			n-hexane	+30°C	57	90	R
			n-hexane	-35°C	63	93	R
			n-hexane	-50°C	55	96	R
			n-octane	-35°C	55	>98	R
1c	H	Me	CH_2Cl_2	+30°C	77	82	R
			n-hexane	+30°C	73	86	R
			n-hexane	-35°C	79	89	R
1d	Me	Et	CH_2Cl_2	+30°C	78	86	R
			CH_2Cl_2	-35°C	71	93	R
			CH_2Cl_2	-50°C	71	94	R
			n-hexane	+30°C	72	88	R
			n-hexane	-35°C	73	94	R
			n-hexane	-50°C	79	>96	R
			n-octane	-35°C	73	>98	R

(a) yields of pure isolated material. (b) d.e. measured with ^{1}H NMR.
(c) configuration established by chemical synthesis for **2b**, see text.

Determination of the configuration of the new chiral center was achieved by conversion of the ester **2b** to the corresponding saturated methyl ester **4** (Scheme 2). Hydrogenation of deconjugated ester **2b** in diethylether afforded the saturated compound **3b** which has been saponified using LiOH [13, 20] to the corresponding acid and further esterified by diazomethane. Unfortunately, significant epimerisation occurred, probably during the

alkaline step. To avoid this problem, ester **3b** was submitted to mild photoreductive conditions [21]. But in this case, even after irradiation over a long time, conversion was still very low.

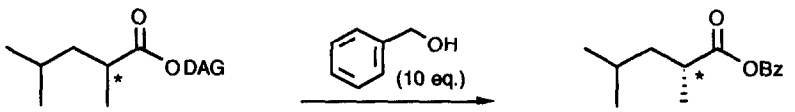


2b
$[\alpha]_D$ = - 87.1 (c = 1.0, CH_2Cl_2)
d.e. = 90%

3b
$[\alpha]_D$ = - 31.7 (c = 1.0, CH_2Cl_2)
d.e. = 90%

Scheme 2

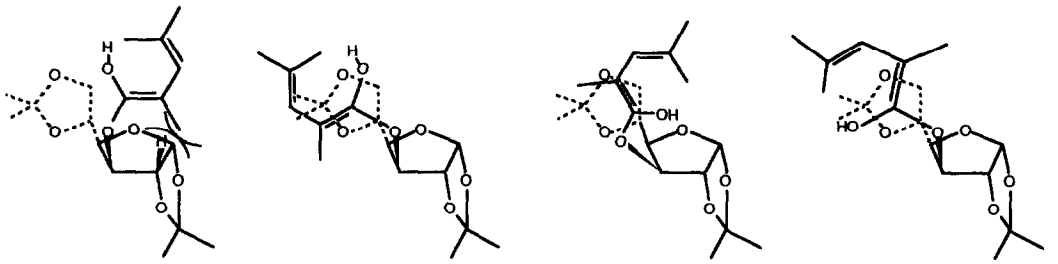
Finally, ester **3b** was completely transesterified with benzyl alcohol according to Seebach's method [22] using $Ti(OiPr)_4$ as catalyst without epimerisation of the asymmetric center. The chiral esters **4** and **5** thus obtained, were compared with authentic samples already synthezised via the enantioselective process [18c].



3b
$[\alpha]_D$ = - 31.7 (c = 1.0, CH_2Cl_2)
d.e. = 90%

(R)-5
$[\alpha]_D$ = - 8.0 (c = 1.1, CH_2Cl_2)
e.e. = 88%

By comparison of the sign of the $[\alpha]_D$ value [23, 24], attribution of the R configuration to the new created chiral center is thus possible. The approach of the protic agent **I** during the protonation of the photodienol **P** can also be defined from this result and from studying molecular models. Four plausible conformations of the dienol are depicted in the following schemes.

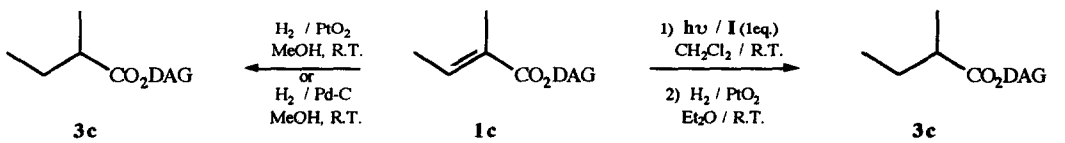


Conformation **A**, which could lead preferentially to the S-diastereomer, can be totally excluded, due to the interaction between the hydrogen on carbon 2 of the sugar and the substituent in the α-position of the acid chain. In the second conformation **B**, one face is considerably shielded by the isopropylidene group and the protonation of the less hindered face could lead to the R-isomer, predominantly observed.

In conformation **C**, in which one face is shielded by the same isopropylidene group, the substituent in the

α-position of the chain can interact with the methyl of the isopropylidene group and this conformation is unfavourable, although it leads to the R-isomer. Otherwise, in conformation **D**, steric interactions can be developed between the isopropylidene group and the substituents of the acid chain in the γ-position: for these reasons, conformation **D** is excluded. **B** constitutes in our opinion the most favourable conformation. We assume that protonation using aminoalcohol **I** as protic agent occurs on the less hindered face with high efficiency. Finally this approach can be extrapolated to other prochiral photodienols derived from esters **1a**, **1c** or **1d** and configuration R has been attributed for each deconjugated species obtained under the above mentioned conditions. Furthermore, in the proton spectrum of the deconjugated ester **2b**, we have observed two doublets of unequal intensity at 4.41 ppm and 4.44 ppm, corresponding to the proton on the C-3 of the sugar of each diastereoisomer, respectively the S and the R isomers. The same phenomenum is observable in the proton spectra of the other esters **2** and confirms the assignment of the R configuration to the major diastereoisomer.

Compared with direct hydrogenation of chiral ester **1**, the two step sequence of asymmetric deconjugation, followed by reduction of the double bond of the β,γ-isomers constitutes a more powerful method. For example, ester **1c** was hydrogenated to **3c** in the presence of catalytic amounts of PtO_2 or Pd/C without significant induction: DAGOH thus appears as a poor inductor for the asymmetric hydrogenation of α,β-unsaturated esters, compared with other chiral alcohols already tested [25]. In contrast, irradiation at room temperature in the presence of the aminoalcohol **I** leads to the β,γ-unsaturated compound **2c** which was conveniently converted into the saturated ester **3c** with 75% d.e..



3c
d.e.= 0%
$[\alpha]_D$= -25.7
(c = 1.0, CH_2Cl_2)

1c

3c
(d.e. = 75 %)
$[\alpha]_D$= -31.2
(c = 1.1, CH_2Cl_2)

In conclusion, irradiation of chiral α,β-unsaturated esters derived from the cheap "diacetone D-Glucose" performed in the presence of an achiral aminoalcohol can lead to the formation of deconjugated compounds with very high diastereoselectivities and in good yields. Compared with previous work in this field, the diastereoselectivities are higher, whatever the nature of the acid chain. Application of this efficient method to the syntheses of more elaborate structures is currently in progress.

Experimental :

IR spectra were recorded in chloroform on a Philips SP-3-300 infrared spectrophotometer. ^1H and ^{13}C N.M.R. spectra were recorded on a Bruker AC 250 MHz spectrometer in deuteriochloroform using tetramethylsilane as internal standard, chemical shifts are expresed in ppm. Mass spectra were performed on a Jeol D 300 instrument. UV spectra were recorded on a Beckman Acta III. Optical rotations were measured on a Perkin-Elmer 241 polarimeter at 20°C. The microanalyses were obtained from the Service de microanalyse de la Faculté des Sciences de Reims.

General procedure for the preparation of esters 1:

The esters **1a-d** were prepared according to the method of Neises and Steglich[16] : To a solution of the α,β-unsaturated acid (10mmol.) in freshly distilled methylene chloride were added DMAP (100mg), 4Å molecular

sieves and diacetone D-glucose (11mmol.). The reaction mixture was cooled to 0°C (external ice-water bath), then a solution of dicyclohexylcarbodiimide (11mmol.) in methylene chloride (5ml) was added dropwise. After stirring 5 minutes at 0°C and overnight at room temperature, urea was filtered off and the solvent was removed by evaporation under reduced pressure. Esters **1** were purified by flash-chromatography [26] (ethyl acetate/petrol ether 10/90).

(1,2 ; 5,6-Di-O-isopropyliden-α-D-glucofuranose-3-O-yl) 4-ethyl, 2-methyl 2-hexenoate: **1a**

Yield: 73 % (mixture of E, Z isomers). I.R.: 3000, 2960, 2920, 1710, 1640, 1385, 1375, 1240-1200, 1165, 1090, 1080, 1025. ^{1}H-NMR: Z-isomer: 0.84 (t, 7.4, 6H); 1.22-1.28 (m, 2H); 1.30 (s, 3H); 1.31 (s, 3H); 1.41 (s, 3H); 1.40-1.55 (m, 2H); 1.53 (s, 3H); 1.93 (d, 1.3, 3H); 2.80-3.05 (m, 1H); 4.02 (dd, 1.8, 4.7, 1H); 4.08 (dd, 1.8, 4.7, 1H); 4.27 (m, 2H); 4.54 (d, 3.7, 1H); 5.31 (d, 2.2, 1H); 5.66 (dd, 1.3, 10.5, 1H); 5.88 (d, 3.7, 1H). E-isomer: 0.86 (t, 7.4, 6H); 1.20-1.60 (m, 4H); 1.30 (s, 3H); 1.31(s, 3H); 1.41(s, 3H); 1.53 (s, 3H); 1.85 (d, 1.3, 3H); 2.10-2.35 (m, 1H); 3.94-4.12 (m, 2H); 4.15-4.37 (m, 2H); 4.55 (d, 3.7, 1H); 5.30 (d, 1.7, 1H); 5.90 (d, 3.7, 1H); 6.51 (dq, 10.5, 1.7, 1H). ^{13}C-NMR: Z-isomer: 166.66; 148.99; 126.64; 112.28; 109.32; 105.08; 83.51; 80.10; 75.96; 72.52; 67.45; 41.75; 27.77; 26.78; 26.22; 25.17; 20.75; 11.86. E-isomer: 166.78; 148.52; 127.18; 112.15; 109.17; 105.08; 83.35; 80.06; 75.55; 72.65; 67.17; 42.28; 27.53; 26.68; 26.17; 25.13; 12.85; 11.82. M.S. : 383 ($M^{+\cdot}$ -15, 20); 340 (15); 129 (80); 101 (100). U.V. (EtOH): 217nm (ε=11000); 254 (ε=480). $[\alpha]_D$ = -32.4 (c= 1.0, CH_3OH) (E-isomer).
Analysis $C_{21}H_{34}O_7$: C 63.29, H 8.60 %. Found: C 63.47 , H 9.04 %.

(1,2 ; 5,6-Di-O-isopropyliden-α-D-glucofuranose-3-O-yl) 2,4-dimethyl 2-pentenoate: **1b**

Yield: 82 % . I.R.: 2960, 2940, 1710, 1640, 1385, 1375, 1260-1200, 1080, 1020. ^{1}H-NMR: E-isomer: 1.01 (d, 6.6, 3H); 1.02 (d, 6.6, 3H); 1.31 (s, 6H); 1.41 (s,3H); 1.53 (s, 3H); 1.84 (d, 1.3, 3H); 2.64 (dqq, 9.7, 6.6, 6.6, 1H); 3.99-4.13 (m, 2H); 4.24-4.30 (m, 2H); 4.54 (d, 3.7, 1H); 5.27 (d, 2.2, 1H); 5.90 (d, 3.7, 1H); 6.58 (dd, 1.3, 9.7, 1H). ^{13}C-NMR: E-isomer: 167.03; 150.35; 125.05; 112.21; 109.24; 105.08; 83.35; 79.98; 76.31; 72.65; 67.20; 27.98; 26.74; 26.19; 25.23; 21.84; 12.27. M.S. : 356 ($M^{+\cdot}$ -14, 25); 210 (27); 111 (100); 101 (73). U.V. (EtOH): 216nm (ε=10050); 254 (ε=350). $[\alpha]_D$ = -38.0 (c = 0.2, CH_2Cl_2) (E-isomer).
Analysis $C_{19}H_{30}O_7$: C 61.60, H 8.16 %. Found: C 61.21, H 8.24 %.

(E)-(1,2 ; 5,6-Di-O-isopropyliden-α-D-glucofuranose-3-O-yl) 2-methyl 2-butenoate: **1c**

Yield: 69 %. I.R.: 2980, 1710, 1645, 1385, 1375, 1255, 1135, 1080, 1020. ^{1}H-NMR: 1.30 (s, 3H); 1.31 (s, 3H); 1.41 (s, 3H); 1.53 (s, 3H); 1.80 (d, 7.1, 3H); 1.84 (s, 3H); 4.03-4.10 (m, 2H); 4.26 (t, 3.7, 2H); 4.52 (d, 3.7, 1H); 5.29 (d, 1.2, 1H); 5.88 (d, 3.7, 1H); 6.88 (dq, 1.2, 7.1, 1H). ^{13}C-NMR: 166.50; 138.44; 128.17; 112.15; 109.20; 105.013; 83.31; 79.88; 76.12; 72.55; 67.11; 26.70; 26.13; 25.21; 14.39; 11.96. M.S. : 327 ($M^{+\cdot}$ -15, 20); 101 (79); 83(100). U.V. (EtOH): 217nm (ε=10500); 254 (ε=340). $[\alpha]_D$ = -40.4 (c = 1.2, CH_2Cl_2). Analysis $C_{17}H_{26}O_7$: C 59.64, H 7.65 %. Found: C 59.22, H 7.74 %.

(1,2 ; 5,6-Di-O-isopropyliden-α-D-glucofuranose-3-O-yl) 2-ethyl, 4-methyl 2-pentenoate: **1d**

Yield: 69 % (mixture of E / Z isomers). I.R.: 3000, 2970, 2940, 2860, 1700, 1640, 1520, 1450, 1385, 1240-

1200, 1170, 1080. ^{1}H-NMR: Z-isomer: 0.97-1.05 (m, 9H); 1.28 (s, 3H); 1.31 (s, 3H); 1.41 (s, 3H); 1.53 (s, 3H); 2.23 (q, 7.4, 2H); 3.11 (dqq, 9.7, 6.5, 6.5, 1H); 3.97-4.02 (m, 1H); 4.08-4.17 (m, 1H); 4.21 (t, 3.3, 2H); 4.51 (d, 3.7, 1H); 5.30 (d, 1.6, 1H); 5.66 (d, 9.7, 1H); 5.86 (d, 3.6, 1H). E-isomer: 1.00-1.06 (m, 9H); 1.31 (s, 6H); 1.42 (s, 3H); 1.54 (s, 3H); 2.32 (q, 7.5, 2H); 2.66 (dqq, 10.1, 6.6, 6.6, 1H); 3.99-4.04 (m, 1H); 4.09-4.14 (m, 1H); 4.27 (m, 2H); 4.55 (d, 3.7, 1H); 5.30 (d, 2.1, 1H); 5.90 (d, 3.7, 1H); 6.54 (d, 10.1, 1H). ^{13}C-NMR: Z-isomer: 166.71; 148.58; 130.59; 112.26; 109.32; 105.04; 83.41; 80.09; 75.99; 72.38; 67.52; 28.29; 27.42; 26.74; 26.19; 25.13; 22.72; 13.63. E-isomer: 166.71; 150.06; 131.11; 112.15; 109.20; 105.04; 83.29; 80.04; 76.18; 72.54; 67.26; 27.74; 26.68; 26.14; 25.13; 22.25; 20.13; 14.38. M.S. : 369 ($M^{+\cdot}$ -15, 21); 125 (79); 101 (100). U.V. (EtOH): 218nm (ε=8700); 254 (ε=390). $[\alpha]_D$ = -36.4 (c = 0.6, CH_2Cl_2) (Z-isomer). $[\alpha]_D$ = -33.0 (c = 0.8, CH_2Cl_2) (E-isomer).
Analysis $C_{20}H_{32}O_7$: C 62.48, H 8.39 %. Found: C 62.52, H 8.54 %.

Irradiation of α,β-unsaturated esters **1**. General procedure.

To a solution of the ester **1** (1mmol) in the appropriate solvent (100ml) was added N,N-dimethylaminoethanol **I** (1mmol). The mixture was poured into quartz tubes (10mm diameter) and deoxygenated with argon for 5mn. The tubes were placed around a short wave lamp (Rayonnet type system). The reaction was monitored by TLC. After total conversion, solvent was removed by evaporation and the crude product was purified by preparative thin-layer chromatography or by flash chromatography.

(1,2 ; 5,6-Di-O-isopropyliden-α-D-glucofuranose-3-O-yl) 4-ethyl, 2-methyl 3-hexenoate: **2a**

I.R.: 2980, 1730, 1380, 1370, 1240-1200, 1075. ^{1}H-NMR: 0.86-1.02 (m, 6H); 1.20 (d, 6.9, 3H); 1.27 (s, 3H); 1.29 (s, 3H); 1.38 (s, 3H); 1.49 (s, 3H); 1.95-2.30 (m, 4H); 3.38 (dq, 9.6, 7.1, 1H); 3.94-4.26 (m, 4H); 4.42 (d, 3.5, 1H); 5.06 (d, 9.6, 1H); 5.25 (s, 1H); 5.84 (d, 3.2, 1H). ^{13}C-NMR: 172.82; 145.40; 121.35; 112.21; 109.18; 105.05; 83.33; 80.13; 75.67; 72.24; 67.26; 38.55; 28.95; 26.70; 26.16; 25.15; 23.48; 18.07; 13.18; 12.55. M.S.: 384 ($M^{+\cdot}$ -14, 10); 139 (55); 113 (23); 101 (100). $[\alpha]_D$ = -85.0 (c = 0.7, CH_2Cl_2) d.e.>97% according to ^{1}H NMR.

(1,2 ; 5,6-Di-O-isopropyliden-α-D-glucofuranose-3-O-yl) 2,4-dimethyl 3-pentenoate: **2b**

I.R.: 2990, 2940, 1735, 1450, 1385, 1375, 1260-1200, 1160, 1080-1060, 1030. ^{1}H-NMR: 1.20 (d, 6.9, 3H); 1.29 (s, 3H); 1.31 (s, 3H); 1.40 (s, 3H); 1.51 (s, 3H); 1.67 (d, 1.3, 3H); 1.71 (d, 1.2, 3H); 3.34 (dq, 9.3, 6.9, 1H); 3.97 (dd, 4.8, 8.3, 1H); 4.08-4.15 (m, 1H); 4.17-4.22 (m, 2H); 4.44 (d, 3.6, 1H); 5.12 (dq, 9.3, 1.3, 1H); 5.26 (d, 2.5, 1H); 5.87 (d, 3.6, 1H). ^{13}C-NMR: 173.72; 134.42; 123.26; 112.19; 109.17; 105.06; 83.35; 80.16; 75.74; 72.25; 67.31; 53.36; 38.99; 26.69; 26.16; 25.57; 25.14; 17.99; 17.62. M.S.: 355 ($M^{+\cdot}$-15, 20); 312 (15); 101 (82); 83 (100). $[\alpha]_D$ = -94.4 (c = 0.6, CH_2Cl_2) d.e.>98% according to ^{1}H NMR.

(1,2 ; 5,6-Di-O-isopropyliden-α-D-glucofuranose-3-O-yl) 2-methyl 3-butenoate: **2c**

I.R.: 2990, 2940, 1740, 1640, 1385, 1375, 1260-1200, 1160, 1080, 1025. ^{1}H-NMR: 1.25 (d, 6.6, 3H); 1.27 (s, 6H); 1.36 (s, 3H); 1.48 (s, 3H); 3.15 (dq, 7.2, 7.1, 1H); 3.90-3.96 (m, 1H); 4.03-4.09 (m, 1H); 4.17 (t,

3.2, 2H); 4.42 (d, 3.7, 1H); 5.06-5.24 (m, 3H); 5.84 (d, 3.7, 1H). ^{13}C-NMR: 172.70; 136.37; 116.38; 112.19; 109.18; 105.03; 83.26; 80.10; 75.95; 72.17; 67.38; 43.63; 26.64; 26.11; 25.11; 16.40. M.S.: 342 ($M^{+\cdot}$-14, 16); 101(69); 83(51); 55(100).

(1,2 ; 5,6-Di-O-isopropyliden-α-D-glucofuranose-3-O-yl) 2-ethyl, 4-methyl 3-pentenoate: **2d**

I.R.: 2980, 2940, 1730, 1385, 1375, 1240-1200, 1080, 1020. ^{1}H-NMR: 0.89 (t, 7.4, 3H); 1.29 (s, 3H); 1.30 (s, 3H); 1.39 (s, 3H); 1.51 (s, 3H); 1.42-1.52 (m, 1H); 1.65-1.85 (m, 1H); 1.66 (d, 1.0, 3H); 1.73 (s, 3H); 3.15 (dt, 9.5, 7.4, 1H); 3.94-3.99 (m, 1H); 4.05-4.11 (m, 1H); 4.18 (d, 3.7, 2H); 4.43 (d, 3.7, 1H); 5.07 (dq, 9.5, 1.1, 1H); 5.26 (d, 2.0, 1H); 5.86 (d, 3.7, 1H). ^{13}C-NMR: 173.12; 135.28; 121.92; 112.31; 109.16; 105.05; 83.37; 80.15; 75.68; 72.24; 67.35; 46.59; 26.72; 26.64; 26.17; 25.91; 25.66; 25.10; 18.15; 11.54. M.S.: 369 ($M^{+\cdot}$-15, 6); 101 (38); 97 (100); 55 (100).

$[\alpha]_D$ = -89.3 (c = 0.9, CH_2Cl_2) d.e.>98% according to ^{1}H NMR.

Determination of the absolute configuration of esters **2**

Hydrogenation of ester **2b** and **2c**:

The β,γ-unsaturated ester (0.5 mmol.) was dissolved in diethylether (10ml). A small amount of PtO_2 was added and the reaction mixture, stirred under hydrogen (1atm.). After complete conversion (^{1}H-NMR and TLC control), the catalyst was removed by filtration over celite. The solvent was evaporated and the product purified by flash-chromatography.

(1,2 ; 5,6-Di-O-isopropyliden-α-D-glucofuranose-3-O-yl) 2,4-dimethyl pentanoate: **3b**

Yield: 98% I.R.: 2980, 2960, 1735, 1385, 1375, 1260-1200, 1170, 1155, 1080. ^{1}H-NMR: 0.89 (t, 6.9, 6H); 1.15 (d, 6.9, 3H); 1.15-1.40 (m, 2H); 1.31 (s, 6H); 1.40 (s, 3H); 1.52 (s, 3H); 1.55-1.75 (m, 1H); 2.54 (tq, 7.4, 6.9, 1H); 3.95-4.02 (m, 1H); 4.08-4.14 (m, 1H); 4.15-4.22 (m, 2H); 4.43 (d, 3.6, 1H); 5.27 (d, 2.2, 1H); 5.86 (d, 3.6, 1H). ^{13}C-NMR: 175.54; 112.25; 109.27; 105.09; 83.39; 80.19; 75.63; 72.34; 67.60; 42.93; 37.60; 26.72; 26.18; 25.76; 25.14; 22.47; 17.45. M.S.: 357 (M+. -15, 21); 113 (28); 101 (100); 85 (56). $[\alpha]_D$ = - 21.3 (c = 1.3, CH_2Cl_2). d.e. = 0%. $[\alpha]_D$ = - 31.7 (c = 1.0, CH_2Cl_2). d.e. = 90% (according to ^{13}C-NMR). Analysis $C_{19}H_{32}O_7$: C 61.27, H 8.66 %. Found: C 61.44, H 8.91 %.

(1,2 ; 5,6-Di-O-isopropyliden-α-D-glucofuranose-3-O-yl) 2-methyl butanoate: **3c**

Yield: 91%. I.R.: 2980, 1735, 1385, 1375, 1240-1200, 1080. ^{1}H-NMR: 0.92 (t, 7.5, 3H); 1.16 (d, 7.0, 3H); 1.31 (s, 6H); 1.36-1.56 (m, 1H); 1.40 (s, 3H); 1.52 (s, 3H); 1.58-1.73 (m, 1H); 2.40 (dq, 7.0, 7.0, 1H); 3.95- 4.02 (m, 1H); 4.08-4.17 (m, 1H); 4.20 (d, 2.3, 2H); 4.44 (d, 3.6, 1H); 5.28 (s, 1H); 5.87 (d, 3.6, 1H). ^{13}C-NMR: 174.94; 112.15; 109.17; 105.03; 83.38; 80.06; 75.55; 72.28; 67.47; 41.05; 26.63; 26.10; 25.07; 16.48; 11.47. M.S.: 329 ($M^{+\cdot}$ -15, 52); 113 (18); 101 (100); 85 (78); 57 (100). $[\alpha]_D$ = - 25.7 (c = 1.0, CH_2Cl_2). d.e. = 0 %. $[\alpha]_D$ = - 31.2 (c = 1.1, CH_2Cl_2). d.e. = 75 % (according to ^{13}C-NMR).
Analysis $C_{17}H_{28}O_7$: C 59.28, H 8.19 %. Found: C 59.12, H 8.35 %.

Hydrolysis [20] of ester **3b**:

To the ester **3b** (0.577g, 1.55mmol) in a mixture of THF/ H_2O (3:1), (32ml) at 5°C was added LiOH, H_2O

(0.130g, 3.10 mmol). The mixture was stirred over 4 days until total conversion and then hydrolyzed with HCl (1N) to pH 7. After extraction with petrol ether, the organic phase was dried over $MgSO_4$ and concentrated. The crude product was dissolved in diethylether (10ml) and treated with an excess of diazomethane. Unreactive CH_2N_2 was destroyed by addition of silica. After filtration, concentration and flash-chromatography, the methyl 2,4-dimethyl pentanoate **4** (0.190g, 1.32 mmol) was isolated. Yield : 85 %.

$[\alpha]_D$ = - 6.3 (c = 3.4, Et_2O). configuration (R), e.e. = 30 %.

Lit. [23] $[\alpha]_D$ = + 21.0 (c = 1.5, Et_2O). configuration (S), e.e. = 98 %.

Transesterification [22] of ester **3b** to benzyl ester **5**:

To the ester **3b** (0.225g, 0.60 mmol.) in toluene (3ml) was added benzyl alcohol (0.63ml, 6.04 mmol) and Titanium (IV) isopropoxide (0.18ml, 0.60mmol.). The mixture was heated at 120°C for 4 hours until complete disappearence of the starting material. After cooling to room temperature, the crude product was directly purified by flash-chromatography (AcOEt / Petrol ether: 5/95), affording the benzyl 2,4-dimethyl pentanoate **5** (0.123g, 0.56 mmol.). Yield : 93 %.

$[\alpha]_D$ = - 8.0 (c = 1.1, CH_2Cl_2). Configuration (R), e.e. = 88 %.

Lit. [24] $[\alpha]_D$ = -4.1 (c = 0.5, CH_2Cl_2). Configuration (R), e.e. = 45 %.

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