Pergamon

Tetrahedron: Asymmetry, Vol. 7, No. 1, pp. 219-226, 1996

0957-4166/96 $15.00 + 0.00

0957-4166(95)00438-6

Elimination *versus* Diastereoselective Alkylation in Homochiral 2-(β-Ethoxy Carbonyl) Acetals

Mercedes Caballero, María García-Valverde, Rafael Pedrosa,* and Martina Vicente

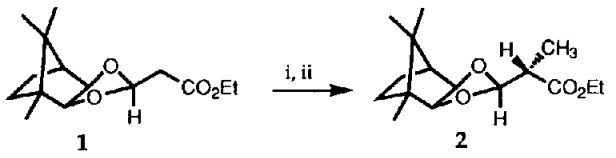
Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Valladolid, Doctor Mergelina s/n. 47011-Valladolid, Spain.

Abstract: The reaction of the homochiral 2-(β-ethoxycarbonyl) dioxolane derived from (-)-*exo*-camphanediol with methyl iodide in the presence of one equivalent of LDA lead to the alkylated product in very good chemical yield and poor diastereomeric excess. 2-(β-Ethoxycarbonyl)-1,3-dioxanes derived from 2,4-pentanediol behave in a different way, whereas the diequatorial form is alkylated in excellent chemical yield, the equatorial-axial diastereoisomer yields a mixture of alkylation and elimination products.

Nucleophilic ring opening of homochiral acetals directed to diastereoselective synthesis is a widely used and well documented reaction.[1] Recently the complementary diastereoselective elimination in cyclic ketals has received much attention as a way to asymmetrization of *meso* cyclic ketones,[2,3] and asymmetric alkylation of β-ketoesters.[4-6] This process has been observed in reactions promoted by both organometallics[2] or lithium amides,[3-6] but in the latter case only ketals have been studied. As a part of work on the reactivity of homochiral lithium enolates[7] we report now our study on the reaction of 2-β-ethoxycarbonyl dioxolane and 1,3-dioxanes with lithium amides, and subsequent treatment with electrophiles.

The reaction of ethyl 3,3-diethoxypropionate with an equimolar amount of (-)-*exo*-camphanediol, in the presence of boron trifluoride etherate for 30 min. in benzene, yielded the dioxolane **1** in 85 per cent chemical yield and 96 per cent d.e. Dioxolane **1** was deprotonated by reaction with one equivalent of lithium amides at -78ºC in THF, and then treated with an excess of methyl iodide allowing the reaction to rise room temperature. In these conditions, the alkylation product **2** was obtained in good chemical yield and poor to modest diastereomeric excess (Scheme 1 and table 1).

There are two remarkable aspects from the data collected in table 1. By the one side, although the chemical yields are similar for all the reactions, the diastereofacial discrimination diminished with increasing the bulkiness of the base (compare entry 2 where lithium di*iso*propyl amide was used as base versus entries 3 and 4 where the bases used were lithium dicyclohexyl amide and lithium hexamethyldisilazide respectively); by the other, the diastereoselectivity of the alkylation increases in more diluted solutions (compare entries 2 versus 1).



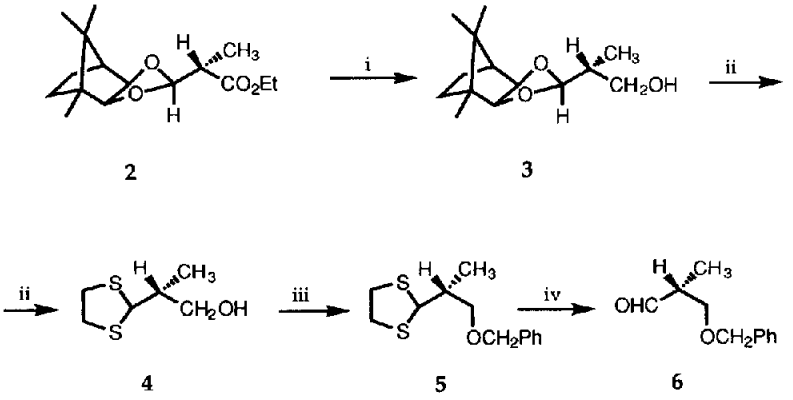
Scheme 1: Reaction conditions: i: Base, THF, -78°C. ii: MeI excess, -78°C to 20°C

Table 1: Alkylation of the dioxolane **1** with MeI[a]

Entry	Base	Yield(%)	d.e.(%)[b] (abs.config.)
1	LDA	87	20(S)
2	LDA[c]	85	32(S)
3	LDCA	83	9(S)
4	LHMDS	85	4(S)

[a]The reaction were carried out at concentration 3.10^{-2} M of dioxolane. [b]Measured by GC on the reaction mixture. [c]The reaction was carried out at $1.5.10^{-2}$ M of dioxolane.

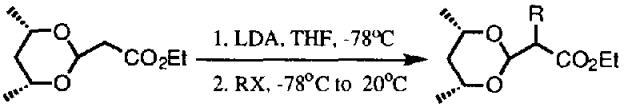
The absolute configuration at the new created stereocenter was determined as *S* by correlation with the known[8] 3-benzyloxy-2-methylpropionaldehyde **6** as shown in scheme 2. Thus, lithium aluminium hydride reduction of **2** led to alcohol **3** in 89 per cent yield, that was transformed into the dithiolane **4** by transthioacetallization by stirring with ethanodithiol in the presence of a catalytic amount of methanosulfonic acid.[9] Compound **4** was converted into 3-benzyloxy-2-methylpropionaldehyde **6** by benzylation,[10] followed by treatment with a solution of methyl iodide in acetonitrile, in the presence of calcium carbonate.[11]



Scheme 2 : Reaction conditions: i: $LiAlH_4$, Et_2O, 30°C, 3h. Then aqueous NaOH. ii: $HSCH_2CH_2SH$, $MeSO_3H$, CH_2Cl_2, r.t. iii: NaH, $PhCH_2Br$, Bu_4NI. iv: MeI, $CaCO_3$, CH_3CN.

Comparison of the sign and value of the specific rotation of **6** with those previously reported[8] showed that our compound was a mixture where the major enantiomer (31% e.e.) was R-configured (the *S* configuration at the alkylation product is a consequence of a change in the priority of the substituents at **2**).

The behaviour of 1,3-dioxanes derived from 2,4-pentanediol was quite different from that shown by the dioxolane **3**. In fact, the *meso* 1,3-dioxane **7**, prepared by reaction[12] of *meso* 2,4-pentanediol and ethyl 3-ethoxyacrylate, reacted with excess of methyl iodide or benzyl bromide in the presence of an equimolar amount of lithium di*iso*propylamide, leading to the alkylation products **8a** and **8b** respectively in excellent chemical yields (Scheme 3).

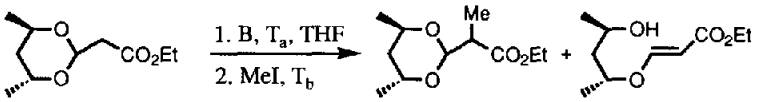


7

8a: R=CH_3 (85%)
8b: R=$C_6H_5CH_2$ (80%)

Scheme 3

On the contrary, racemic 1,3-dioxane (*rac*-**9**) reacted with methyl iodide leading to a mixture of alkylation product *rac*- **10** and the elimination hydroxyalkene (*rac*-**11**) in different experimental conditions. (Scheme 4 and table 2). Moreover, when an equimolar mixture of *meso*- **7** and *rac*-**9** was treated with excess of methyl iodide in presence of one equivalent of LDA, at -78°C for 20 min., the *meso* form was completely transformed into **8a**, whereas *rac* -**9** was only alkylated in 20 per cent yield. This reaction showed that, as expected,[1a] the *meso* form is more reactive in the alkylation process but lesser in the elimination reaction than *rac*- **9**.



rac - **9** *rac* - **10** *rac* - **11**

Scheme 4

The data summarized in table 2 showed some interesting aspects of the reaction. First of all, was the fact that the alkylation product was formed as a single compound in the reaction where TMEDA was used as co-solvent (entries 2 and 4), whereas the change of lithium to magnesium as counterion led to the formation of the elimination hydroxyalkene *rac*-**11** (entry 5). Otherwise, the elimination reaction competes with the alkylation in any experimental condition, being dominant as the temperature increases (compare entries 1 versus 3).

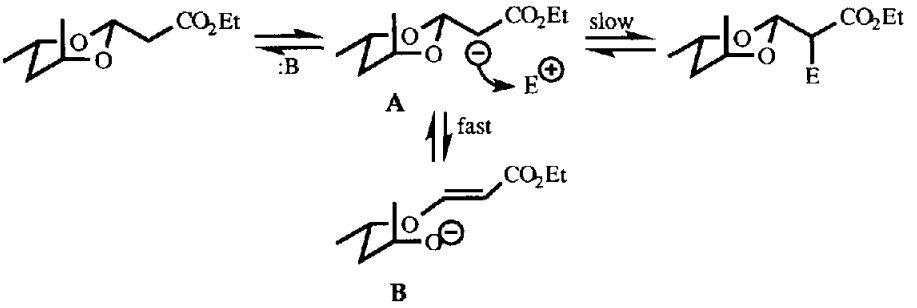
It is worth noting that the stereochemistry of the double bond in the hydroxyalkene *rac* **-11** was *E* as demonstrated by the coupling constant of the vinylic protons (J = 12.3 Hz), and that the alkylation occurs without any facial discrimination.

Table 2. Reaction of 1,3-dioxane *rac* **-9** with MeI in the presence of 1 equivalent of base

Entry	T_a(°C)[a]	T_b(°C)[b]	Products (Yield)[c]		
			rac - **9**	*rac* -**10**	*rac* -**11**
1	-78	-78 to -20	45	29	26
2	-78[d]	-78 to -20	69	31	---
3	-78	-78 to 0	27	29	40
4	-78[d]	-78 to 20	37	63	---
5	-78[e]	-78 to 20	53	---	47
6	0	-78	54	23	23
7	0	0	43	38	19

[a]T_a refers to the temperature of deprotonation. [b]T_b refers to the final temperature of alkylation. [c]Measured by integration of the signals in the ^{1}H-NMR spectra. [d]TMEDA was added as cosolvent. [e]Magnesium diisopropyl amide was used as base.

On the other hand, the elimination product *rac*-**11** can be obtained as a single component when the deprotonation was carried out at 0°C, the methyl iodide added at this temperature, and the reaction quenched with water after 15 min. of stirring. This experiment and the different reactivity of *rac*-**9** compared with *meso*-**7** allow us to propose a possible pathway for the reaction of both diastereoisomers as follows. The fast deprotonation of 1,3-dioxanes lead to a carbanion that, in the case of the *meso*-**7** is stable enough to be alkylated by the electrophile; in contrast, for *rac*-**9** the carbanionic specie **A** is immediately equilibrated with the open oxyanion **B** by an E1bc mechanism and the alkylation, a much slower process, occurs on the intermediate **A** as shown in scheme 5.



Scheme 5

Otherwise, the elimination on the intermediate formed from *rac*-**9** shows the same regio- and stereochemical outcome than that previously described for $S_{N'}$ substitution in acetals derived from α,β-unsaturated aldehydes.[13-15] The fast elimination on the intermediate formed from *rac*-**9** and not on the *meso*-**7** could be explained because the cleavage of the C-O bond next to the axial methyl group in the former release the 2,4-steric interactions present in the heterocycle,[16,17] and it has been also found in the nucleophilic ring opening reactions promoted by alkylcopper in the presence of boron trifluoride.[1]

Experimental

General. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Bruker AC 300 spectrometer with tetramethylsilane as internal standard. IR spectra were recorded on a Philips PU 9706 Spectrometer, as film. Optical rotations were measured on a Perkin-Elmer 241 Polarimeter in a 1 dm cell, and concentrations are given in g/100ml. Organic extracts were dried over Na_2SO_4 and filtered before removal of the solvent under reduced pressure. Dry tetrahydrofuran (THF) and Et_2O were distilled from sodium metal in presence of benzophenone ketyl. All reactions employing "dry" solvents were run under a nitrogen or argon atmosphere. 3,3-Diethoxypropionaldehyde, ethyl β-ethoxyacrylate and 2,4-hexanediol are commercially available and (-)-*exo*-camphanediol[18] were prepared as previously described. Dioxolane **1** was prepared by condensation of (-)-*exo*-camphanediol with 3,3-diethoxypropionaldehyde, whereas 1,3-dioxanes **7** and **9** by reaction[12] of the corresponding diol with ethyl 3-ethoxyacrylate.

(1R,2S,4R,6S,7S)-4-(1'-Ethoxycarbonylmethylen)-1,10,10-trimethyl-3,5-dioxa-tricyclo [3.2.1.0^{2,6}] decane (1). Colorless oil. B.p. 172-173°C (0.9 mmHg). $[\alpha]_D^{23}$ = -13.3 (c = 1, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$) δ : 0.81 - 2.04 (m, 17H), 2.76 (d, 2H, H-1', J = 5.4 Hz), 3.77 and 3.97 (dd, 2H, H-2 and H-6, J = 6.7 Hz), 4.10 (q, 2H, J = 7.1 Hz), 5.06 (t, 1H, H-4, J = 5.4 Hz). ^{13}C-NMR (75 MHz, $CDCl_3$) δ : 10.8 (CH_3), 14.0 (CH_3), 19.8 (CH_3), 22.4 (CH_3), 23.3 (CH_2), 31.7 (CH_2), 38.1 (C-1'), 45.9 (C quat.), 47.2 (C quat.), 47.3 (CH), 60.5 (CH_2), 83.7 (CH), 87.7 (CH), 99.9 (C-4), 169.2 (CO_2). IR (neat) ν: 1730. MS (m/z, %): 268 (M^+, 1), 239 (100). Anal. Calcd. for $C_{15}H_{24}O_4$: C, 67.13; H. 9.01. Found: C, 67.32; H, 9.22.

***meso*-4,6-Dimethyl-2-(1'-ethoxycarbonylmethylen)-1,3-dioxane (7).** Colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ : 1.13 - 1.65 (m, 11H), 2.65 (d, 2H, H-1', J = 5.5 Hz), 3.52 - 3.97 (m, 2H, H-4 and H-6), 4.16 (q, 2H, CH_2CH_3, J = 7.1 Hz), 5.00 (t, 1H, H-2, J = 5.5 Hz). ^{13}C-NMR (75 MHz, $CDCl_3$) δ :13.7 (CH_3), 21.1 (2 x CH_3), 39.7 (CH_2), 40.4 (CH_2), 60.1 (CH_2), 72.1 (C-4 and C-6), 97.7 (C-2), 169.4 (CO_2). IR (neat) ν: 1735. MS (m/z, %): 202 (M^+, 1), 115 (100), 69 (85). Anal. Calcd. for $C_{10}H_{18}O_4$: C, 59.38; H, 8.97. Found: C, 59.57; H, 8.74.

***rac*-4,6-Dimethyl-2-(1'-ethoxycarbonylmethylen)-1,3-dioxane (9).** Colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ : 1.15 - 2.02 (m, 11H), 2.59 (d, 2H, H-1', J = 5.5 Hz), 3.88 - 4.48 (m, 4H), 5.33 (t, 1H, H-2, J = 5.5 Hz). ^{13}C-NMR (75 MHz, $CDCl_3$) δ : 13.9 (CH_3), 16.8 (CH_3), 21.5 (CH_3), 36.3 (CH_2), 40.8 (CH_2), 60.2 (CH_2), 67.5 (CH), 68.0 (CH), 91.2 (C-2), 169.5 (CO_2). IR (neat) ν: 1730. MS (m/z, %): 202 (M^+,1), 115 (100), 69 (68). Anal. Cald. for $C_{10}H_{18}O_4$: C, 59.38; H, 8.97. Found: C, 59.16; H, 8.72.

*Reaction of dioxolane **1** and 1,3-dioxanes **7** and **9** with methyl iodide in the presence of metal amides. General Method:* A solution of acetal (0.4 mmol) in dry THF (8 ml) was added dropwise to a stirred solution of LDA or magnesium diisopropyl amide during 15 minutes at the temperature shown in tables 1 and 2. The methyl iodide (0.5 mmol) was added to the enolate solution and the mixture was stirred until the reaction reached the temperatures shown in the tables. The resulting mixture was quenched with water, neutralized with aqueous hydrochloric acid, and extracted with diethyl ether. The organic layer was dried over anhydrous Na_2SO_4 and evaporated. The oily residue was purified by flash cromatography to afford the alkylated product.

(1R,1'S,2S,4R,6S,7S)-4-(1'-Ethoxycarbonylethyl)-1,10,10-trimethyl-3,5-dioxa-tricyclo [3.2.1.0^{2,6}] decane (2). Colorless oil. B.p. 183-185ºC (1 mmHg). $[\alpha]_D^{23}$= -0.4 (c = 5.8, MeOH).^{1}H-NMR (300 MHz, $CDCl_3$) δ : 0.80 - 2.06 (m, 20H), 2.55 - 2.90 (m, 1H, H-1'), 3.67 - 3.97 (m, 2H, H-2 and H-6), 4.16 (q, 2H, J = 6.9 Hz), 4.73 (d, 1H, H-4, J = 8.0 Hz). ^{13}C-NMR (75 MHz, $CDCl_3$) δ : 10.8 (CH_3), 13.9 (2 x CH_3), 19.9 (CH_3), 22.4 (CH_3), 23.3 (CH_2), 31.7 (CH_2), 43.3 (C-1'), 45.9 (C quat.), 47.3 (C quat.), 47.3 (CH), 60.3 (CH_2), 83.2 (CH), 87.9 (CH), 103.9 (C-4), 173.1 (CO_2). IR (neat) ν: 1730. MS (m/z, %): 282 (M^+, 1), 181 (100). Anal. Calcd. for $C_{16}H_{26}O_4$: C, 68.05; H, 9.28. Found: C, 68.27; H, 9.09.

***rac*-4,6-Dimethyl-2-(1'-ethoxycarbonylethyl)-1,3-dioxane (8a).** Colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ : 1.02 - 1.67 (m, 14H), 2.46 - 2.81 (m, 1H, H-1'), 3.55 - 3.95 (m, 2H, H-4 and H-6), 4.15 (q, 2H, CH_2CH_3, J = 7.1 Hz), 4.68 (d, 1H, H-2, J = 6.6 Hz). ^{13}C-NMR (75 MHz, $CDCl_3$) δ : 11.5 (CH_3), 13.8 (CH_3), 21.1 (2 x CH_3), 40.1 (C-5), 44.7 (C-1'), 59.8 (CH_2), 72.1 (C-4 and C-6), 101.1 (C-2), 173.0 (CO_2). IR (neat) ν: 1730. MS (m/z, %): 216 (M^+, 2), 115 (100). Anal. Calcd. for $C_{11}H_{20}O_4$: C, 61.08; H, 9.32. Found: C, 60.91; H, 9.46.

***rac*-4,6-Dimethyl-2-(1'-ethoxycarbonyl-2'-phenylethyl)-1,3-dioxane (8b).** Colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ : 1.03 (t, 3H, J = 7.1 Hz), 1.17 - 1.55 (m, 8H), 2.83 - 2.96 (m, 2H), 3.09 - 3.12 (m, 1H), 3.68 - 3.81 (m, 1H), 3.99 (q, 2H, CH_2CH_3, J = 7.1 Hz), 4.73 (d, 1H, H-2, J = 6.8 Hz), 7.13 - 7.27 (m, 5H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ : 13.9 (CH_3), 21.4 (CH_3), 21.5 (CH_3), 33.7 (CH_2), 40.3 (CH_2), 52.8 (CH), 60.1 (CH_2), 72.5 (CH), 72.7 (CH), 100.9 (CH), 126.1 (CH_{Arom}), 128.1 (CH_{Arom}), 128.9 (CH_{Arom}), 138.8 (C_{Arom}), 172.1 (CO_2). Anal. Calcd. for $C_{17}H_{24}O_4$: C, 69.83; H, 8.27. Found: C, 69.21; H, 8.48.

***rac*-4,6-Dimethyl-2-(1'-ethoxycarbonylethyl)-1,3-dioxane (10).** Colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ : 1.10 - 2.01 (m, 14H), 2.45 - 2.81 (m, 1H, H-1'), 3.70 - 4.50 (m, 4H), 4.98 (d, 1H, H-2, J = 6.7 Hz). ^{13}C-NMR (75 MHz, $CDCl_3$) δ : 12.1 (CH_3), 14.1 (CH_3), 16.93(CH_3), 21.7 (CH_3), 36.7 (C-5), 45.3 (C-1'), 60.3 (CH_2), 67.7 (CH), 68.1 (CH), 97.5 (C-2), 173.4 (CO_2). IR (neat) ν: 1725. MS (m/z, %): 216 (M^+, 1), 115 (100), 69 (77). Anal. Calcd. for $C_{11}H_{20}O_4$: C, 61.08; H, 9.32. Found: C, 61.26; H, 9.53.

Ethyl β-(1,3-dimethyl-3-hydroxypropoxy)-acrylate. (11). Colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ : 1.11 - 1.75 (m, 11H), 2.40 - 2.50 (s br, 1H, OH), 3.75 - 4.51 (m, 4H), 5.25 (d, 1H, H-α, J = 12.3 Hz), 7.55 (d, 1H, H-β, J = 12.3 Hz). ^{13}C-NMR (75 MHz, $CDCl_3$) δ : 14.4 (CH_3), 20.6 (CH_3), 23.3 (CH_3), 45.7 (C-2), 59.7 (CH_2), 64.9 (C-3), 77.1 (C-1), 97.0 (C-α), 162.6 (C-β), 168.5 (CO_2). IR (neat) ν: 3410, 1725, 1630. MS (m/z, %): 202 (M^+, 0.5), 69 (100).

Synthesis of aldehyde 6. A solution of **3** (0.40 mmol) in dry ether (5 ml) was added dropwise to a stirred suspension of LAH (0.44 mmol) in dry ether (3 ml). The mixture was stirred under reflux for 3h, cool and the excess LAH was destroyed by the addition of water. The mixture was filtered and dried, and the organic solution was concentrated *in vacuo*. The residue was purified by flash cromatography to give **3** (89%). Colorless oil. $[\alpha]_D^{23}$= -10.1 (c=1.4, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$) δ : 0.81 - 2.22 (m, 18H), 2.75 - 2.97 (m, 1H, H-1'), 3.48 - 3.67 (m, 2H, H-2'), 3.74 - 4.01(m, 2H, H-2 and H-6), 4.42 (d, 1H, H-4, J = 7.9 Hz). ^{13}C-NMR (75 MHz, $CDCl_3$) δ : 10.9 (CH_3), 12.8 (CH_3), 20.0 (CH_3), 22.4 (CH_3), 23.4 (CH_2), 31.8 (CH_2), 38.8 (C-1'), 46.0 (C quat.), 47.3 (C quat.), 47.4 (CH), 65.4 (C-2'), 82.9 (CH), 88.1 (CH), 107.7 (C-4). IR (neat) ν: 3420. MS (m/z, %): 240 (M^+, 0.22), 81 (41), 41 (100).

To a solution of dioxolane **3** (0.4 mmol) in dry CH_2Cl_2 was added ethanedithiol (0.4 mmol) and a small amount of methanesulfonic acid, under an Ar atmosphere. The mixture was heated under reflux for 1h, and cooled. The solution was treated with K_2CO_3, filtered and concentrated. The residue was purified by flash cromatography to give **4** (92%). Colorless oil. $[\alpha]_D^{23}$ = -5.2 (c=1, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$) δ : 1.09 (d, 3H, CH_3, J = 6.9 Hz), 1.97 - 2.05 (m, 1H, H-1'), 2.60 (br s, 1H, OH), 3.16 - 3.25 (m, 4H, H-4 and H-5), 3.59 - 3.71 (m, 2H, H-2'), 4.64 (d, 1H, H-2, J = 6.5 Hz). ^{13}C-NMR (75 MHz, $CDCl_3$) δ : 15.3 (CH_3), 38.5 (CH_2), 38.6 (CH_2), 42.4 (C-1'), 56.8 (C-2), 66.7 (C-2'). IR (neat) ν: 3300, 1010. MS (m/z, %): 164 (M^+, 28), 105 (100).

To a solution of alcohol **4** (0.40 mmol) in dry THF (5 ml) was added sodium hydride (0.48 mmol) under an Ar atmosphere. After gentle reflux for 20 min. the mixture was cooled to room temperature, and the benzyl bromide (0.40 mmol) and the tetrabutyl ammonium iodide (0.04 mmol) were added. The solution was stirred overnight at room temperature. The solvent was removed under reduced pressure and the residue was treated with a satured sodium chloride solution. The mixture was extracted with dichloromethane and the combined extract was dried over sodium sulfate. The solvent was removed under reduced pressure to give **5** as a colorless oil.^{1}H-NMR (300 MHz, $CDCl_3$) δ : 1.10 (d, 3H, CH_3, J = 7.0 Hz), 2.09 - 2.18 (m, 1H, H-1'), 3.12 - 3.19 (m, 4H, H-4 and H-5), 3.45 (dd, 2H, H-2', J = 5.7 and 1.3 Hz), 4.49 (s, 2H, Ar-CH_2), 4.72 (d, 1H, H-2, J = 6.6 Hz), 7.22 - 7.36 (m, 5H, H_{Arom}). ^{13}C-NMR (75 MHz, $CDCl_3$) δ : 14.9 (CH_3), 38.5 (CH_2), 38.7 (CH_2), 40.8 (C-1'), 56.5 (C-2), 73.1 (CH_2), 74.3 (CH_2), 127.5 (CH_{Arom}), 127.7 (CH_{Arom}), 128.3 (CH_{Arom}), 128.5 (CH_{Arom}), 128.7 (CH_{Arom}), 138.4 (C_{Arom}) . MS (m/z,%): 254 (M^+, 4.4), 163 (54), 105 (100).

To a solution of ditiolane **5** (0.40 mmol) in an aqueous solution of acetonitrile (80%) was added $CaCO_3$ (0.40 mmol) and methyl iodide (2.40 mmol). The mixture was stirred overnight at room temperature, treated with dichloromethane and filtered over silica gel. The solvent was removed under reduced pressure to give **6** (79%) as a colorless oil. $[\alpha]_D^{23}$= -8.9 (c = 0.6, CHCl3), (e.e. 31%). (lit.[8] [α] = -28.2 (c = 1.4, $CHCl_3$)). ^{1}H-NMR (300 MHz, $CDCl_3$) δ : 1.16 (d, 3H, CH_3, J=7.1 Hz), 2.66 - 2.75 (m, 1H, H-2), 3.64 - 3.72 (m, 2H), 4.56 (s, 2H, Ar-CH_2), 7.28 - 7.41 (m, 5H, H_{Arom}), 9.76 (d, 1H, J = 1.5 Hz). ^{13}C-NMR (75 MHz, $CDCl_3$) δ : 10.7 (CH_3), 46.8 (C-2), 70.1 (CH_2), 73.3 (CH_2), 127.6 (CH_{Arom}), 127.7 (CH_{Arom}), 128.4 (CH_{Arom}), 128.8 (CH_{Arom}), 138.3 (C_{Arom}) 203.9 (CHO). IR(neat) ν: 2700, 1710. MS (m/z, %): 178 (M^+, 0.06), 107 (67), 91(100).

Acknowledgements

The financial support provided by the Spanish Dirección General de Investigación Científica y Técnica (Project PB92-0252), and by the Junta de Castilla y León (Project VA 55/93) is gratefully acknowledged. M. G.-V. also thanks the Ministerio de Educación y Ciencia for a Predoctoral Fellowship (PFPU).

References

(1) For recent rewiews see: (a) Alexakis, A.; Mangeney, P.; Ghribi, A.; Marek, I.; Sedrani, R.; Guir, C.; Normant, J. *Pure and Appl. Chem.* **1988**, *60*, 49. (b) Alexakis, A.; Mangeney, P. *Tetrahedron: Asymmetry* **1990**, *1*, 477.

(2) Naruse, Y.; Yamamoto, H. *Tetrahedron* **1988**, *44*, 6021.

(3) Underiner, T. L.; Paquette, L. A. *J. Org. Chem.* **1992**, *57*, 5438.

(4) (a) Kato, K.; Suemune, H.; Sakai, K. *Tetrahedron Lett.* **1992**, *33*, 247. (b) Sakai, K.; Suemune, H. *Tetrahedron: Asymmetry* **1993**, *4*, 2109.

(5) Suemune, H.; Watanabe, K.; Kato, K.; Sakai, K. *Tetrahedron: Asymmetry* **1993**, *4*, 1767.

(6) Suemune, H.; Maeda, K.; Kato, K.; Sakai, K. *J.Chem. Soc., Perkin Trans.1* **1994**, 3441.

(7) García-Valverde, M.; Pedrosa, R.; Vicente, M. *Tetrahedron: Asymmetry* **1995**, *6*, 1787.

(8) Meyers, A. I.; Babiak, K. A.; Campbell, H. L.; Comins, D. L.; Fleming, M. P.; Henning, R.; Heuschmann, M.; Hudspeth, J. P.; Kane, J. M.; Reider, P. J.; Roland, D. M.; Shimizu, K.; Tomioka, K.; Walkup, R. D. *J. Am. Chem. Soc.* **1983**, *105*, 5015.

(9) Hoppe, I.; Hoppe, D.; Wolff, C.; Engest, E.; Herbst, R. *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 67.

(10) Solladié, G.; Fernández, I.; Maestro, C. *Tetrahedron: Asymmetry* **1991**, *2*, 801.

(11) Bernardi, A.; Cardani, S.; Pilati, T.; Poli, G.; Scolastico, C.; Villa, R. *J. Org. Chem.* **1988**, *53*, 1600.

(12) Croxall, W. J.; Van Hook, J. O.; Cuckenbaugh, R. *J. Am. Chem. Soc.* **1949**, *71*, 2741.

(13) Maruoka, K.; Yamamoto, H.; *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 668.

(14) Ghribi, A.; Alexakis, A.; Normant, J. F. *Tetrahedron Lett.* **1984**, *25*, 3079.

(15) Mangeney, P.; Alexakis, A.; Normant, J. F. *Tetrahedron Lett.* **1986**, *27*, 3143.

(16) Barlett, P. A.; Johnson, W. S.; Elliott, J. D. *J. Am. Chem. Soc.* **1983**, *105*, 2088.

(17) Choi, V. M. F.; Elliott, J. D.; Johson, W. S. *Tetrahedron Lett.* **1984**, *25*, 591.

(18) Angyal, S. J.; Young, R. J. *J. Am. Chem. Soc.* **1959**, *81*, 5467.

(*Received in UK* 23 *October* 1995)