Tetrahedron Vol 47, No 36, pp 7663-7672, 1991
Printed in Great Britain

0040-4020/91 $3 00+ 00

CARBOCYCLES FROM CARBOHYDRATES: SYNTHESIS OF SOME POLYFUNCTIONALIZED CYCLOHEXANE DERIVATIVES. PREPARATION OF USEFUL CHIRAL BUILDING BLOCKS

José Marco-Contelles* and Angeles Martínez-Grau

Instituto de Química Orgánica General (CSIC), Juan de la Cierva 3, 28006-Madrid, Spain.

(*Received in UK 29 May* 1991)

Abstract.- *Starting from diacetone glucose the synthesis of the polyfunctionalized cyclohexane derivatives* **1**, **2**, *and* **16** *is described.*

INTRODUCTION

In the last years the synthesis of carbocycles has attracted considerable interest.[1] The free radical route is an extremely efficient strategy for the cyclization of carbohydrate derivatives.[2] Most of these processes have involved the cyclization of 5-hexenyl radicals mediated by tributyltin hydride;[3] only a relative restricted number of examples of 6-membered ring construction by radical cyclization have been published.[4]

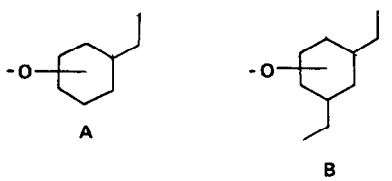
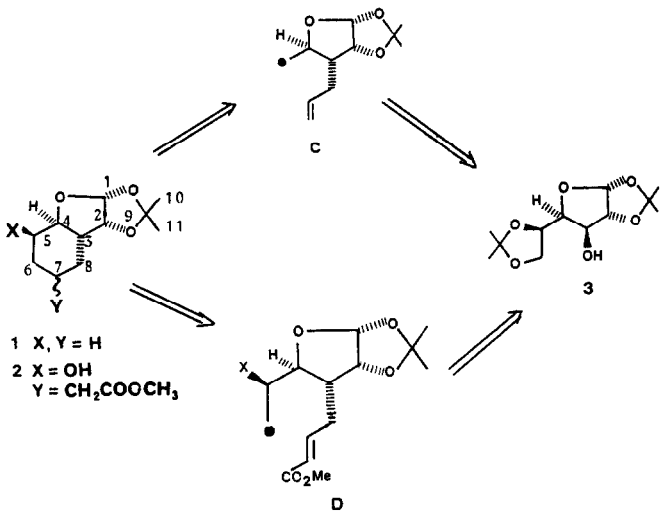


Fig 1

In the context of a program directed towards enantioselective total synthesis of natural products containing a cyclohexane ring, we needed building blocks type **A** and **B** (Fig. 1); compounds **1** and **2** (Scheme I), respectively, are good examples of this type of structures. In our *retro-radical synthetic analysis*,[5] compound **1** could be obtained by 6-*endo* mode of cyclization of radical C, and compound **2** by a 6-*exo* cyclization of radical D (Scheme I). In this paper we describe the successfull accomplishment of these objectives.[6]

RESULTS AND DISCUSSION

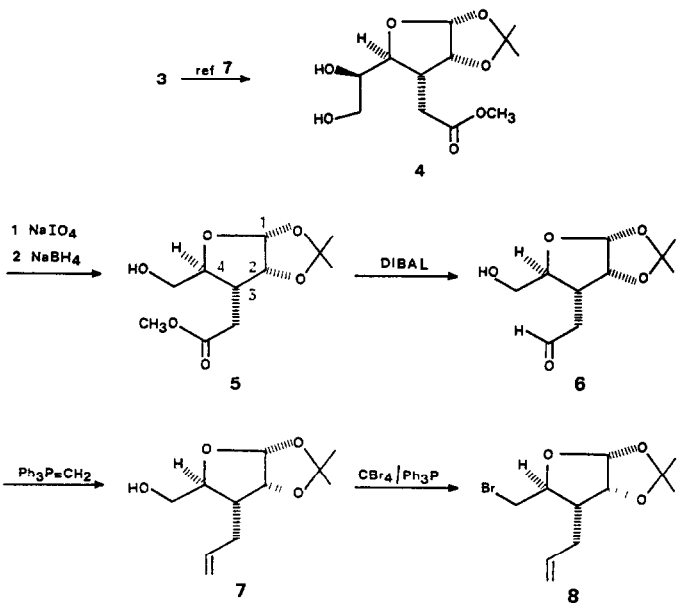
The radical precursors have been obtained from readily available diacetone glucose **3** by known or standard procedures. Compound **8** has been obtained from intermediate **4**[7] following



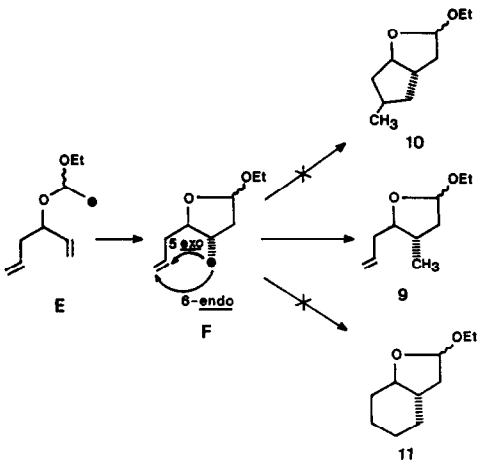
Scheme I

the steps shown in Scheme II. Under typical conditions for free radical cyclization (See Experimental Part) **8** gave the desired carbocycle **1** (Scheme I) in 71 % yield; we could not detect the reduced form of compound **8**. So, it is clear that being the 5-*exo* cyclyzation difficult as it would lead to a congested *trans*-diquinane compound, the 6-*endo* product is formed in good yield giving a stable *trans* annulated furanose **1**.

During the course of this work we had notice of a report about the free radical cyclization of bromoacetals of 3-hydroxyhexa-1,5-dienes;[8] in the case shown in Scheme III, the initial radical E undergoes 5-*exo* cyclization to produce intermediate F; as the authors state "owing to steric repulsion the carbon bearing the radical has a tendency to remain *trans* to the allyl group in the cyclized product F, and the only detected product is **9**; the 5-*exo* cyclized product **10** is prevented as it would led to a strained compound" and the annulated furanose **11** is absent. In view of these results, the formation of compound **1**, very analogous to **11**, during the cyclization of precursor **8**, seems to us very interesting. It is not easy to explain the different behaviour of radicals C (Scheme I) and F (Scheme III), but



Scheme II

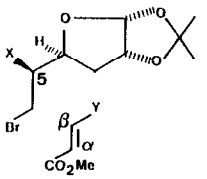
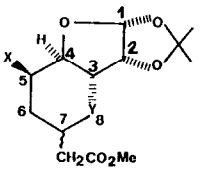


Scheme III

it is probably related to stereoelectronic effects in the preferred conformations of these radicals in the transition states.

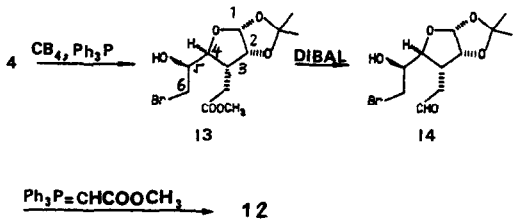
The radical precursor **12** (see Table I) has been synthesized from compound **4** (Scheme II) by bromination, reduction and Wittig reaction (see Scheme IV), in this process we isolated only one product, the expected *E* isomer, as it could be confirmed by ^{1}H NMR analysis ($\delta H_\alpha = 5.90$; $\delta H_\beta = 7.02$; $J_{\alpha,\beta} = 16.0$ Hz). The cyclization of substrate **12** gave compound **2** in good yield and diastereoselectivity (see Table I). After careful flash chromatography[9] the α/β isomers could be separated and analyzed. The absolute configuration at C-7 in the major α isomer is *S*; this could be established in the ^{1}H NMR spectrum (see Table II); H_7 appears at δ 2.34, with vicinal coupling constants $J_{7,6ax} = J_{7,8ax} = 12.5$ Hz. The minor isomer β shows. $\delta H_7 = 2.37$, $J_{7,8ax} = 6.1$ Hz and $J_{7,6eq} = J_{7,8eq} = 3.3$ Hz, in good accordance with the absolute configuration 7*R*.

Table I

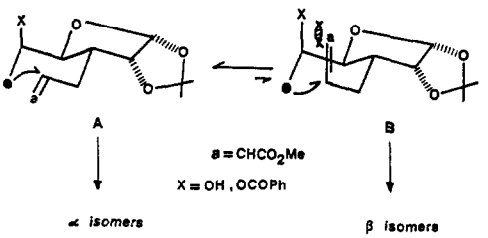
Radical Precursor	Products (yield %)[a]	∝/β ratio[b]
		
12 X = OH , Y = CH_2	2 (82)	85 15
15 X = OBz Y = CH_2	16 (80)	80 20
17 X = OH Y = O	18	only ∝

a) Combined isolated yields . b) The isomer ratios were determined by ^{1}H NMR (300 MHz) on the crude reaction mixtures

It was interesting to analyze the effect of the substitution at C-5 in compound **12** over the radical cyclization. So, we have synthetized the benzoate **15** (Table I). The benzoylation of compound **12** gave the expected compound as a mixture of *E* and *Z* isomers (7.5 : 1), that were separated by flash chromatography. The cyclization of compound **15** under the same conditions



Scheme IV



Scheme V

Table II ^{1}H-NMR parameters for 2α,β

	2α		2β	
	δ/ppm	J/Hz	δ/ppm	J/Hz
H-1	5.72(d)	3 4	5 76(d)	3 5
H-2	4.07(t)	3 4	4 55(t)	3 5
H-3	1.80(m)	-	2 00(m)	-
H-4	3.66(dd)	$J_{4,3}$ = 10 8 $J_{4,5}$ = 2 4	3 60(dd)	$J_{4,3}$ = 11 5 $J_{4,5}$ = 2 6
H-5	4 23(m)	-	4 29(m)	$J_{5,6ax}$ = 3 0 $J_{5,6eq}$ = 1 8
H-6eq	1 80(m)	J_{gem} = -14 9	1 85(m)	$J_{6ec,8eq}$ = 1 7
H-6ax	0 79(m)		1 58(m)	J_{gem} = -15-2
H-7	2 34(m)	$J_{7,6ax}$ = 12 5	2 37(m)	$J_{7,6ax}$ = 6 1 $J_{7,6eq}$ = 3 3
H-8eq	1 80(m)	J_{gem} = -14 0	1 72 - 1 62	$J_{8eq,7}$ = 3 3
H-8ax	1 13(m)	$J_{8ax,7}$ = 12 5	1 28(m)	$J_{8ax,7}$ = 6 1
CH_3 CH_3-C- CH_3	1 44(s) 1 15(s)	-	1 44(s) 1 26(s)	-
2H-12	1 95(d) 1 92(d)	-	2 66(dd) 2 55(dd)	J_{gem} - 15 9 $J_{12,7}$ = 7 4 $J_{12',7}$ - 8 0
O-CH_3	3 56(s)	-	3 61(s)	-
OH	2 18(s)	-	2 92(s)	-

used for the cyclization of compound **12** gave the carbocycle **16** (Table I) in good yield, in almost equal diastereoselectivity (see Table I). The ratio of isomers were determined by integration of the methoxy signals in the ^{1}H NMR spectrum (δ 3.64, s, for the major α isomer, and δ 3.54, s, for the minor β isomer). Unfortunately we could not separate these isomers, but simple benzoylation of the major **2** isomer gave pure major **16** α.

In Scheme V we show a possible rationale for the stereochemical results obtained in these 6-*exo* cyclizations: assuming that in the transition state the radical cyclizes in a chair-like conformation,[10] the 1,3-diaxial unfavourable interactions in B drives the equilibrium to the A rotamer, thus giving the α isomer as the major product. However, increasing the steric repulsion by putting a benzoate at C-5 does not lead to a major proportion

of the α isomer; we cannot exclude the significance of the potential electronic effects of the aryl ester.[2b]

The stereochemical results obtained in this work are also in accordance with the reported transformation of compound **17** into **18**[11] (see Table I); only one isomer was detected; this is probably due to the fact that the C-O bonds being shorter than the C-C bonds,[12] the 1,3-diaxial interactions between OH-C_5 and the alkene moiety in the transition state leading to the β isomer are stronger in compound **17** than in **12** or **15**.

In summary, we have described the synthesis of some polyfunctionalized cyclohexane rings in enantiomerically pure form *via* free radical cyclization of intermediates derived from carbohydrates. In some of these processes a new stereocenter has been formed at *off template site*[13] with good diastereoselectivity.

EXPERIMENTAL

Melting points are uncorrected and were determined in a Kofler apparatus. Optical rotations were measured with a Perkin-Elmer 241 polarimeter with a 1-dm cell. Elemental analyses were carried out in Madrid with the help of a Perkin-Elmer 240 analyzer. IR spectra were determined on a Perkin-Elmer 257 spectrometer. ^{1}H NMR spectra were measured on a Varian EM 390, Varian XL-300 or a Bruker AM-200 spectrometer using tetramethylsilane as internal standard. Mass spectra were obtained with a AEI MS 50 spectrometer. For column chromatography, the flash chromatography technique on silica gel was used.[9]

3-Deoxy-1,2-*O*-isopropylidene-3-*C*-(methoxycarbonylmethyl)-α-D-ribofuranose (5).- Compound **4**[7] (2.6 g, 10.5 mmol) dissolved in methanol (100 mL) and cooled at 0°C was treated with an aqueous solution (40 mL) of sodium metaperiodate (3.96 g, 18.5 mmol, 1.1 eq.), the mixture was stirred at room temperature for 45 min. The solvent was removed and the residue suspended in water and extracted several times with ethyl acetate. The organic extract was washed with brine and dried. The solvent was removed and the residue dissolved in methanol (40 mL), cooled at 0°C and treated with sodium borohydride (704 mg, 18.5 mmol, 1.1 eq.). The mixture was stirred at room temperature, under argon, for 1 h. After 1 h, brine was added and the methanol evaporated; the residue was extracted several times with ethyl acetate, the organic extract was washed with brine and dried. Evaporation and flash chromatograpphy (hexane/ethyl acetate 1:1:5) gave **5** (1.62 g, 63 %) as an oil: $[\alpha]_D^{25}$ +63° (c 2.4, $CHCl_3$), IR (film) ν: 3480, 2995, 2960, 2945, 2890, 1740, 1445, 1420, 1390, 1380, 1345, 1220, 1170, 1140, 1120, 1020, 880 cm^{-1}, ^{1}H NMR (90 MHz, $CDCl_3$) δ: 5.95 (d, J = 3.6 Hz, 1H, H-1), 4.92 (t, J = 3.6 Hz, 1H, H-2), 4.03 (m, 2H, CH_2-OH), 3.85 (s, 3H, OCH_3), 3.8-3.6 (m, 1H, H-4), 3.0-2.2 (m, 4H, H-3, OH, COH_2-$COOCH_3$), 1.62 (s, 3H), 1.45 (s, 3H), MS (70 eV) *m/e*: 231 (M^+-15,33), 215(8), 157(100), 139 (16), 111(12), 97(51), 83(13), 59(48), 43(69). Anal. Calcd. for $C_{11}H_{18}O_6$: C, 53.65; H, 7.37. Found. C, 53.55, H, 7.50 %.

3-Deoxy-3-*C*-(formylmethyl)-1,2-*O*-isopropylidene-α-*O*-ribofuranose (6).- Compound **5** (2.6 g,

10.5 mmol) dissolved in dry toluene (30 mL), cooled at -78°C, under argon and stirring, was treated dropwise with diisobutylaluminium hydride (19 mL, 19 mmol , 1.0 M in hexane, 1.8 eq.); after 30 min, methanol (50 mL) was added slowly and the mixture warmed at room temperature. The mixture was filtered over Celite, the solvent evaporated and the residue submitted to flash chromatography (hexane/ethyl acetate, 2:3) giving compound **15** as an oil (1.5 g, 67%); $[\alpha]_D^{25}$ +72° (c 1.1, $CHCl_3$), IR (film) ν: 3440, 2990, 2940, 2880, 2730, 1725, 1455, 1420, 1385, 1375, 1330, 1250, 1215, 1170, 1110, 1020, 875 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ: 9.9 (s, 1H, *H*CO), 5.90 (d, *J*=3.4 Hz, 1H, H-1), 4.85 (t, *J*=3.4 Hz, 1H, H-2), 4.03-3.70 (m, 4H, H-4, 2H-5, O*H*), 2.9-2.65 (m, 3H, H-3, CH_2)-CHO), 1.53 (s, 3H), 1.35 (s, 3H); MS (70 eV) *m/e*: 201 (M^+ -15,70), 185(11), 141(19), 127(64), 99(16), 83(30), 69(69), 59(71), 43(100). Anal. Calcd. for $C_{10}H_{16}O_5$: C, 55.54; H, 7.46. Found. C, 55.15; H, 7.34 %.

3-Deoxy-1,2-*O*-isopropylidene-3-*C*-(2-propenyl)-α-D-ribofuranose (7).- To a solution of $Ph_3P{=}CH_2$ (21 mmol, 3 eq) in dry tetrahydrofuran (30 mL), under argon, and stirring at -20°C, a solution of compound **6** (1.52 g, 7 mmol) in dry tetrahydrofuran (20 mL) was added dropwise. After 1 h the mixture was warmed at room temperature overnight. Acetone was added and stirred for 10 min, the solution was diluted with methylene chloride and washed with a saturated aqueous solution of sodium bicarbonate and brine. The solution was dried, evaporated and submitted to chromatography (hexane/ethyl acetate, 1:1). Compound **7** was obtained as an oil (1.0 g, 71%); $[\alpha]_D^{25}$ +86° (c 2.1 $CHCl_3$), IR (film) ν: 3450, 3080, 2990, 2940, 2880, 1645, 1440, 1385, 1375, 1250, 1220, 1170, 1110, 915, 875 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ: 5.92 (d, *J*=3.6 Hz, 1H, H-1), 6.06-5.8 (m, 1H, C*H*=CH_2), 5.33-5.1 (m, 2H, CH_2=CH), 4.75 (t, *J*=3.6 Hz, 1H, H-2), 4.03 (m, 2H, CH_2OH), 3.83-3.5 (m, 1H, H-4), 2.73 (s, 1H, O*H*), 2.5-2.0 (m, 3H, H-3, CH_2-CH=CH_2), 1.6 (s, 3H), 1.43 (s, 3H). MS (70 eV) *m/e*: 199 (M^+-15,100), 125(97), 79(54), 59(45), 43(73). Anal. Calcd. for $C_{11}H_{18}O_4$. C, 61.66, H, 8.47. Found: C, 61.55; H, 8.49 %.

5-Bromo-3,5-dideoxy-1,2-*O*-isopropylidene-3-*C*-[2-propenyl]-α-D-ribofuranose (8).- A solution of **7** (1.0 g, 4.67 mmol), carbon tetrabromide (4.65 g, 14 mmol, 3 eq.) in dry tetrahydrofuran (25 mL), cooled at 0°C, under argon, was treated with triphenylphosphine (3.67 g, 14 mmol, 3 eq.). The mixture was stirred at room temperature overnight, the solvent removed and the residue submitted to chromatography (hexane/ethyl acetate, 19.1), giving compound **8** (858 mg, 69%) as an oil: $[\alpha]_D^{25}$ +68° (c 2.3 $CHCl_3$); IR (film) ν: 3080, 2990, 2940, 2850, 1645, 1455, 1440, 1425, 1375, 1250, 1220, 1170, 1110, 1035, 1010, 920, 875 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ: 5.87 (m, J_{cis}= 10.05 Hz, J_{trans}= 17.4 Hz, 1H, C =CH_2), 5.81 (d, $J_{1,2}$= 3.7 Hz, 1H, H-1), 5.15 (m, J_{gem}= 1.68 Hz, 1H, CH=C*H*$_2$), 5.07 (m, J_{gem}= 1.68 Hz, 1H, CH=C*H*$_2$), 4.63 (t, *J* = 3.7 Hz, 1H, H-2), 3.98 (m, *J*=9.49, 4.37 and 2.79 Hz, 1H, H-4), 3.72 (dd, *J*=11.42 and 2.79 Hz, 1H, CH_2-Br), 2.4 (m, *J*=13.44, 12.8 and 7.57 Hz, 1H, C $_2$-CH=CH_2), 2.17 (m, *J*=13.44, 12.8 and 5.94 Hz, 1H, C*H*$_2$-CH=CH_2), 2.05 (m, *J*=12.8, 9.49 and 3.7 Hz, H-3), 1.5 (s, 3H), 1.32 (s, 3H); MS (70 eV) *m/e*. 211, 263 (M^+-15,90), 219, 221(13), 201, 203(22), 161(8), 139(21), 125(33), 93 (70), 81(74), 43(100). We could not obtain a satisfactory elemental analysis.

Cyclization of compound 8: Compound **8** (886 mg, 3.2 mmol) dissolved in benzene (160 mL, 0.02

M) was degassed with argon 1 h and treated, at reflux, with tributyltin hydride (2.15 mL, 8 mmol , 2.5 eq.), AIBN (cat.) in benzene (10 mL), added *via* syringe pump in 18 h. The solvent was removed and the residue dissolved in ether, treated with 10% potassium fluoride aqueous solution overnight; the organic phase was separated, dried and evaporated. Flash chromatography gave compound **1** (435 mg, 71%): mp 36-38°C; $[\alpha]_D^{25}$ +14° (c 1.3, $CHCl_3$); IR (KBr) ν: 2980, 2960, 2940, 1890, 1870, 1455, 1385, 1375, 1255, 1215, 1170, 1120, 1020, 885 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ. 5.79 (d, J=3.7 Hz, 1H, H-1), 4.55 (t, J=3.7 Hz, 1H, H-2), 3.54 (td, J= 3.9 and 10.3 Hz, 1H, H-4), 2.30-2.10 (m, 1H, H-3), 1.82-1.75 (m, 2H), 1.51 (s, 3H), 1.32 (s, 3H), 1.45-1.10 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 110.84 (C-9), 104.98 (C-1), 80.25, 78.39 (C-2, C-4), 49.18 (C-3), 30.38, 25.64, 23.71, 23.40 (C-5, C-6, C-7, C-8), 25.87, 25.23 (C-10, C-11), MS (70 eV) *m/e*: 183 (M^+-15, 100), 137(14), 123(59). Anal. Calcd. for $C_{11}H_{18}O_3$: C, 66.64, H, 9.15. Found: C, 66.57; H, 9.21 %.

6-Bromo-3,6-dideoxy-3-*C*-(methoxycarbonylmethyl)-1,2-*O*-isopropyldene-α-D-allofuranose (13).- Compound **4**[7] (400 mg, 1.4 mmol) and carbon tetrabromide (1.39 g, 4.2 mmol) were dissolved in dry tetrahydrofuran (10 mL) and cooled in an ice bath. Triphenylphosphine (1.1 g, 4.2 mmol) was added and the reaction stirred at room temperature overnight. The solvent was evaporated; flash chromatography (hexane/ethyl acetate 4:1) gave compound **13** (289 mg, 60%) as an oil: $[\alpha]_D^{25}$ -11° (c 2.1, $CHCl_3$); IR (film) ν: 3600-3200, 2950, 1740, 1380, 1220 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ. 5.78 (d, J=3.6 Hz, 1H, H-1), 4.75 (t, J=3.6 Hz, 1H, H-2), 3.80-3.30 (m, 4H, 2H-6, H-5, H-4), 3.70 (s, 3H, $-CO_2CH_3$), 2.85-2.65 (m, 2H, $-CH_2-CO_2CH_3$), 2.00-1.65 (m, 2H, OH, H-3), 1.50 (s, 3H, $-O-CMe_2-O-$), 1.32 (s, $-O-CMe_2-O-$), MS (70 EV) *m/e*: 305(3), 134, 136 (48), 106, 108(12), 95(10), 80, 82(50), 55(100), 41(15). Anal. Calcd. for $C_{12}H_{19}BrO_6$: C, 42.49; H, 5.64; Br, 23.55. Found: C, 42.40; H, 5.39, Br, 23.31 %.

6-Bromo-3,6-deoxy-1,2-*O*-isopropylidene-3-*C*-[*E*-(methoxycarbonyl)-2-propenyl]-α-D-allofuranose (12).- Compound **13** (672 mg, 2 mmol) dissolved in dry toluene (10 mL), cooled at -78°C, under argon, was treated with DIBAL (6 mL, 6 mL, 1.0 M in hexane). After 30 min the reaction was complete and an excess of methanol was added. The reaction was stirred at room temperature and filtered over Celite. The solvent was evaporated; flash chromatography (hexane/ethyl acetate 1.5:1) gave compound **14** (556 mg, 90%). This product (171 mg, 0.55 mmol) dissolved in toluene (7 mL) was treated with (methoxycarbonylmethylen)triphenylphosphoran (274 mg, 0.82 mL) at room temperature during 18 h. Concentration and flash chromatography (hexane/ethyl acetate 2:1) gave compound **12** (171 mg, 83%) as an oil; $[\alpha]_D^{25}$ +109° (c 2.5, $CHCl_3$, IR (film) ν: 3600-3200, 2990, 2960, 2940, 1725, 1660, 1440, 1385, 1375, 1220, 1170, 1040, 880 cm^{-1}, ^1H NMR (90 MHz, $CDCl_3$) δ 7.02 (dt, J=16.0 y 7.0 Hz, 1H, $-CH$=CH-$COOCH_3$), 5.90 (dt, J=16.0 and 1.5 Hz, 1H, -CH=C -$COOCH_3$), 5.78 (d, $J_{1,2}$=3.6 Hz, 1H, H-1), 4.60 (t, J=3.6 Hz, 1H, H-2), 4.00-3.50 (m, 4H, 2H-6, H-5, H-4), 3.70 (s, 3H), 2.70-2.40 (m, 3H, -CH=CH-CH_2-, OH), 2.20-2.00 (m, 1H, H-3), 1.49 (s, 3H); MS (70 eV) *m/e* 305,307(60), 263(9), 241(23), 231(53), 183(100), 151 (50), 123(51), 95(82), 79(38), 59(89), 43(53). Anal. Calcd. for $C_{14}H_{21}BrO_6$: C, 46.04; H, 5.79, Br, 21.87. Found: C, 45.99, H, 5.78; Br, 21.66 %.

Cyclization of compound 12: To a solution of compound **12** (138 mg, 0.37 mmol) in toluene (12 mL, 0.03 M), under argon, at reflux, a solution of tributyltin hydride (0.12 mL, 0.44 mmol), AIBN (cat) in toluene (3 mL) was added in 3 h *via* syringe pump. The reaction was refluxed 30 min more and the solvent evaporated. The residue was dissolved in acetonitrile, extracted several times with hexane and the solvent evaporated. Flash chromatography (hexane/ethyl acetate 3:2) gave **2α** (77 mg) and **2β** (17 mg). The total yield was **82 %**.

2α: mp 98-100°C; $[\alpha]_D^{25}$ +22.6° (c 1.5, $CHCl_3$); IR (KBr) ν: 3490, 2995, 2980, 2960, 2940, 2910, 2870, 1740, 1455, 1435, 1420, 1385, 1375, 1250, 1225, 1160, 1125, 1090, 1025, 870 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): (see Table II); MS (70 eV) *m/e*: 271 (M^+-15,100), 210(27), 179(26), 151(13), 91(22), 79(19), 59(21), 43(77). Anal. Calcd. for $C_{14}H_{22}O_6$: C, 58.73; H, 7.75. Found: C, 58.81; H, 7.91 %.

2β: mp 94-96°C; $[\alpha]_D^{25}$ +4.1° (c 0.58, $CHCl_3$); IR (KBr) ν: 3495, 2990, 2980, 2940, 2910, 2870, 1735, 1455, 1435, 1420, 1385, 1375, 1250, 1225, 1160, 1125, 1010, 890 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): (see Table II); MS (70 eV) *m/e*: 287 ($M+1^+$, 8), 271(65), 239(10), 210 (30), 193(100), 179(29), 151(28), 119(27), 95(36), 79(37), 59(35), 43(41). Anal. Calcd. for $C_{14}H_{22}O_6$: C, 58.73; H, 7.75. Found: C, 59.06; H, 7.58 %.

5-*O*-Benzoyl-6-bromo-3,6-dideoxy-1,2-*O*-isopropylidene-3-C-[(*E*)-(methoxycarbonyl)-2-propenyl]-α-D-allofuranose (15).- To a solution of compound **12** (205 mg, 0.56 mmol) in dry pyridine (3 mL), cooled in an ice bath, benzoyl chloride (0.1 mL, 0.84 mmol) was added dropwise. The reaction was stirred at room temperature 20 h, treated with ice, extracted with ethyl acetate several times, washed with brine and dried. Evaporation of the solvent and flash chromatography (hexane/ethyl acetate 4·1) gave isomers **15-(*Z*)** (23 mg, 8%) and **15-(*E*)** (155 mg, 59%).

15-(*E*): Oil; $[\alpha]_D^{25}$ +36.3° (c 2.1, $CHCl_3$), IR (film) ν: 3100, 3080, 3050, 2990, 2960, 2940, 2880, 1725, 1645, 1605, 1590, 1495, 1455, 1445, 1430, 1420, 1390, 1375, 1270,1175, 1010, 870 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 8.10-8.05 (m, 2H), 7.61 (m, 1H), 7.48 (m, 2H), 6.91 (td, J=7.3 and 15.6 Hz, 1H, $-CH_2-CH=CH-COOCH_3$), 5.82 (d, $J_{1,2}$=3.4 Hz, 1H, H-1), 5.76 (dt, J=1.0 and 15.6 Hz, 1H, $-CH=CH-COOCH_3$), 5.30 (m, 1H, H-5), 4.63 (t, J=3.4 Hz, 1H, H-2), 4.17 (dd, J=10.0 and 6.8 Hz, 1H, H-4), 3.79 (m, 2H, 2H-6), 3.70 (s, 3H), 2.58 (m, 1H, $-CH_2-$CH=CH-), 2.35 (m, 1H, $-CH_2-$CH=CH-), 2.15 (m, 1H, H-3), 1.53 (s, 3H), 1.33 (s, 3H), MS (70 eV) *m/e*: 453,455(8), 241(23), 183(39), 151(16), 105(100), 77(18). Anal. Calcd. for $C_{21}H_{25}BrO_7$: C, 53.74, H, 5.36, Br, 17.02. Found: C, 53.59; H, 5.47, Br, 16.85%.

15-(*Z*): mp 81-83°C; $[\alpha]_D^{25}$ +76° (c 0.42, $CHCl_3$), IR (KBr) ν: 2990, 1730, 1725, 1645, 1605, 1590, 1495, 1445, 1385, 1370, 1315, 1260, 1180, 1110, 1010, 870 cm^{-1}, ^1H NMR (90 MHz, $CDCl_3$) δ: 8.20-8.00 (m, 2H), 7.60-7.40 (m, 3H), 6.35 (dt, J=6.5 and 11.5 Hz, 1H, $-CH=CH-COOCH_3$), 5.83 (dt, J=1.0 and 11.5 Hz, 1H, $-CH=CH-COOCH_3$), 5.80 (d, $J_{1,2}$=3.5 Hz, 1H, H-1), 5.40 (m, 1H, H-5), 4.62 (t, J=3.5 Hz, 1H, H-2), 4.25 (dd, J=6.0 and 10.0 Hz, 1H, H-4), 3.80 (d, J=4.5 Hz, 2H, 2H-6), 3.53 (s, 3H), 3.20-2.53 (m, 2H), 2.40-2.10 (m, 1H), 1.53 (s, 3H), 1.33 (s, 3H), MS (70 eV) *m/e*. 453,455(8), 267(5), 241(23), 209(7), 183(33), 165(56), 151(38), 105(100), 77(32). Anal. Calcd. for $C_{21}H_{25}BrO_7$: C, 53.74; H, 5.36, Br, 17.02. Found: C, 53.6, H,

5.61; Br, 16.90 %.

Cyclization of compound 15-(*E*): Compound **15-(*E*)** (132 mg, 0.29 mmol) was cyclized using the same procedure for the cyclization of compound **12**. Flash chromatography (hexane/ethyl acetate 4.1) gave a mixture of **16α,β** (95 mg, 82 %) that we could not separate.

Compound **2α** was benzoylated using the standard protocol giving compound **16α** (77 %) as an oil· $[\alpha]_D^{25}$ +5.5° (c 2.2, $CHCl_3$); IR (film) ν: 3070, 2990, 2940, 2880, 1730, 1605, 1590, 1490, 1455, 1440, 1420, 1385, 1375, 1275, 1220, 1170, 1115, 1030, 870, 715 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 8.03-7.44 (m, 5H), 5.81 (d, *J* = 3.5 Hz, 1H, H-1), 5.72 (m, 1H, H-5), 4.61 (t, *J* = 3.5 Hz, 1H, H-2), 3.81 (dd, *J* = 11.0 and 2.6 Hz, 1H, H-4), 3.64 (s, $-CO_2Me$), 2.40-2.00 (m, 7H, H-3, 2H-6, H-7, H-8eq, 2H-12), 1.45-1.25 (m, 1H, H-8ax), 1.45 (s, 3H, $-O-CMe_2-O-$), 1.37 (s, 3H, $-O-CMe_2-O-$), ^{13}C NMR (25.2 MHz, $CDCl_3$) δ: 177.55 (O-*CO*-Ph), 165.47 (*C*OOCH$_3$), 137.66, 129.71, 129.64, 128.13 (aromatics), 111.59 (C-9), 105.70 (C-1), 79.67, 78.75 (C-5, C-4), 68.74 (C-2), 51.48 (O-CH_3), 42.12, 40.15 (C-7, C-3), 35.07 (C-12), 29.77, 28.18 (C-10, C-11), 26.18, 25.87 (C-6, C-8), MS (70 eV) *m/e*. 375 M^+-15.19), 315(9), 269(6), 210(11), 193(16), 105(100), 77(38). Anal. Calcd. for $C_{21}H_{26}O_7$. C, 64.60; H, 6.71. Found: C, 64.93, H, 7.00 %.

Acknowledgements. *We are grateful to C I C.Y.T. (Grant 8400/89) for financial support.*

REFERENCES AND NOTES

1. For some leading reviews: (a) Fraser-Reid, B., Anderson, A.C. *Prog. Chem. Org. Nat Prod* **1980**, *39*, 1 (b) Fraser-Reid, B. *Acc Chem. Res.* **1985**, *18*, 347; **1975**, *8*, 192. For recent examples, see: (c) Fleet, G.W.J.; Shing, T.K.M., Warr, S.M. *J. Chem. Soc., Perkin Trans 1* **1984**, 904. (d) Ferrier, R.J., Prasit, P.; Tyler, P.C. *Ibid.* **1983**, 1641 (e) Verheyden, J. P.H., Richardson, A.C.; Bhatt, R.S.; Grant, B.D.; Fitch, W.L., Moffatt, J.G. *Pure Appl. Chem.* **1978**, *50*, 1363. (f) Lichtenthaler, F.W. *Angew. Chem. Int Ed. Engl.* **1964**, *3*, 211.
2. (a) RajanBabu, T.V. *J. Am. Chem Soc.* **1987**, *119*, 609. (b) Wilcox, C.S., Thomasco, L.M. *J. Org. Chem.* **1985**, *50*, 546. (c) Nugent, W.A.; RajaBabu, T.V. *J Am Chem. Soc.* **1988**, *110*, 8561. (d) RajanBabu, T.V., Fukunaga, T., Reddy, G.S. *J. Am. Chem. Soc.* **1989**, *111*, 1759. (e) Wilcox, C.S., Gaudino, J.J. *J Am. Chem. Soc* **1986**, *108*, 3102. (f) RajanBabu, T.V. *J Org. Chem.* **1988**, *53*, 4522. (g) Bartlett, P.A., McLaren, K.L., Ting, P.C. *J. Am. Chem. Soc* **1988**, *110*, 1633.
3. (a) Giese, B. *Radicals in Organic Synthesis Formation of Carbon-Carbon Bonds*, Pergamon Press; New York, 1986. (b) Curran, D.P. *Synthesis* **1989**, Part 1, p. 417, Part 2, p. 489.
4. (a) Tsang, R., Fraser-Reid, B. *J Am Chem. Soc* **1986**, *108*, 2116. (b) Sugawara, T., Otter, B.A., Ueda, T. *Tetrahedron Lett.* **1988**, *29*, 75. (c) Vité, G.D.; Alonso, R., Fraser-Reid, B. *J Org. Chem* **1989**, *54*, 2271. (d) Yeung, B.W.A., Contelles, J.L.M., Fraser-Reid, B. *J. Chem. Soc., Chem Commun.* **1989**, 1160. (e) Yeung, B.W.A., Alonso, R.; Vité, G.D., Fraser-Reid, B. *J Carbohydr. Chem.* **1989**, *8*, 413. (f) Dickson, J.K.; Tsang, R., Llera, J. M., Fraser-Reid, B. *J Org. Chem* **1989**, *54*, 5350.

5. Curran, D.P. *Synlett* **1991**, 63.
6. Part of this work has been reported as preliminary communication: Marco-Contelles, J.L.; Martínez-Grau, A.; Bernabé, M.; Martín, N.; Seoane, C. *Synlett* **1991**, 165.
7. Rosenthal, A.; Nguyén, L. *J. Org. Chem.* **1969**, *34*, 1029.
8. Yadav, J.S., Gadgil, V.R. *J. Chem. Soc., Chem Commun.* **1989**, 1824.
9. Still, W.C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 1923.
10. Hanessian, S.; Dhanoa, O.S.; Beaulieu, P. *Can. J. Chem.* **1987**, *65*, 1859.
11. Araki, Y.; Endo, T.; Arai, Y.; Tanji, M.; Ishido, Y. *Tetrahedron Lett.* **1989**, *30*, 2829.
12. Beckwith, A.L.J.; Schiesser, C.H. *Tetrahedron* **1985**, *41*, 3925.
13. (a) Rama Rao, A.W.; Yadav, J.S. Srinivas Rao, C.; Chandrasekhar, S. *J. Chem. Soc., Perkin Trans 1* **1990**, 211, (b) Rashid, A.; Mark Taylor, G., Wood, W.W. *Ibid.* **1991**, 1289.