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Strategies and Tactics for Free Radical Carbocyclization: Synthesis of Polyfunctionalized Cyclopentanoid Molecules from Carbohydrates

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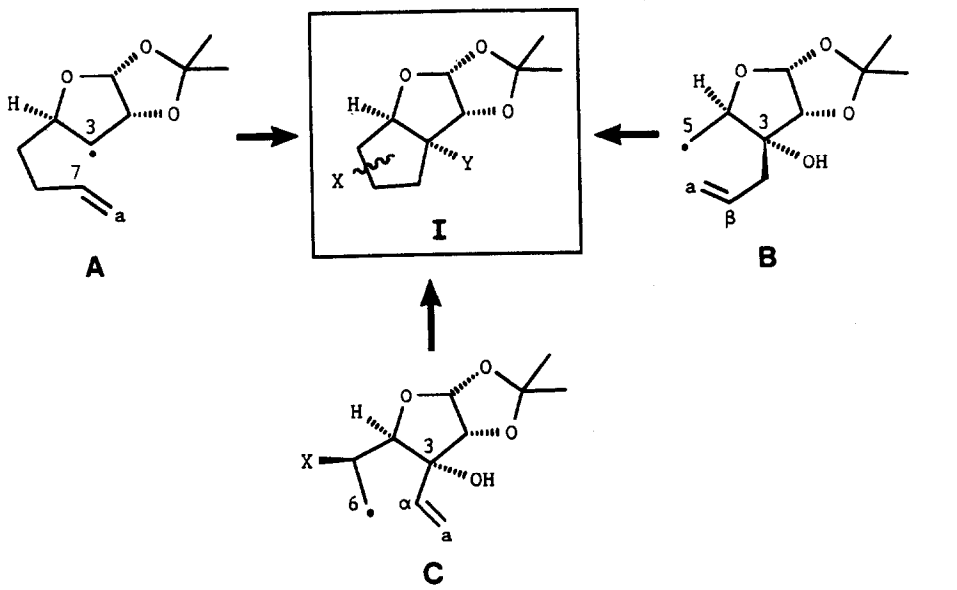
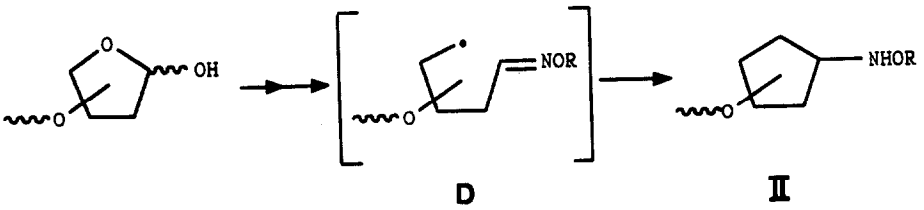
Abstract: The tributyltin hydride + azobisisobutyronitrile (AIBN) mediated free radical carbocyclization of precursors **1-9**, **48** and **49** is described. The resulting carbocycles have been obtained in moderate yield and good diastereoselectivity. These polyfunctionalized, enantiomerically pure cyclopentane derivatives are useful intermediates for further manipulation.

INTRODUCTION

In the last years free radical chemistry has emerged as a powerful method for the synthesis of carbocycles.[1] The seminal studies reported by Wilcox,[2] RajanBabu[3] and Bartlett[4] have established useful strategies for the preparation of chiral, polyfunctionalized cyclopentanoid molecules from readily available carbohydrate type precursors. Current methods for free radical carbocyclization from sugars involve: a) functionalization of glycosides by preparation of branched chains having the leaving group and the radical trap conveniently located; this leads to annulated sugars,[5] and b) opening the sugar, functionalization and cyclization[2-4] on acyclic free radical precursors.

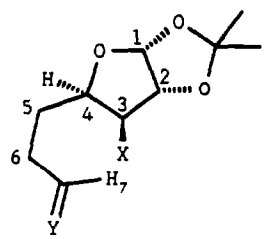
In this context, the synthesis of carbocycles from sugars has been an area of continuous interest in our laboratory.[6] Following the first synthetic strategy, we have very recently reported the intramolecular 5-*exo*-trig cyclization of an endocyclic C3 radical onto an electron-deficient exocyclic unsaturated chain in furanose templates[7] (Scheme 1, **A**); the resulting annulated furanoses **I** are chiral, diversely functionalized and potential useful intermediates for a general approach to related and important cyclopentanoid molecules as polyquinanes, iridoids and prostanoids.[8] Following the second tactic we have also shown that carbon centred radicals of type **D** (Scheme 1), easily available from D-ribonolactone, give polyhydroxycyclopentylamines **II**[9] in moderate yield and excellent diastereoselectivity. These compounds are critical intermediates for the synthesis of enantiomerically pure carbocyclic nucleosides of high current pharmacological interest.[10]



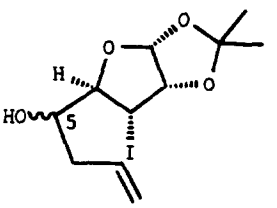


Scheme 1

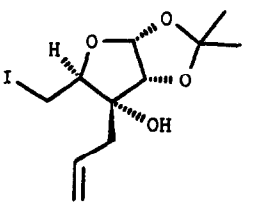
In this paper we report in full detail our preliminary communications.[7,9] In addition and regarding the synthesis of annulated furanoses,[5] we have extended this methodology to other related radical precursors and describe now here complementary free radical strategies involving: a) 5-*exo* intramolecular cyclization of a carbon centred radical at C5 onto a radical trap located at Cß position on C3 (Scheme 1, **B**), and b) 5-*exo* intramolecular cyclization of a carbon centred radical at C6 on a radical trap located at Cα position on C3 (Scheme 1, **C**).[11] As prototypes of these *radicochirons* we have selected and synthesized the radical precursors **1-9**.



1 X = OC(S)Im
Y = NOBn
2 X = OC(S)Im
Y = $CHCO_2CH_3$
3 X = OC(S)SCH_3
Y = $CHCO_2CH_3$
4 X = OC(S)Im
Y = $C(CH_3)CO_2CH_2CH_3$
5 X = OC(S)SCH_3
Y = $C(CH_3)CO_2CH_2CH_3$
(Im = Imidazole)



6 [C5(*S*+*R*)]



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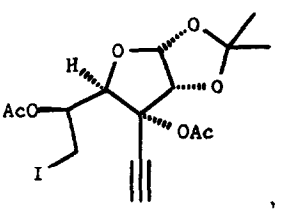

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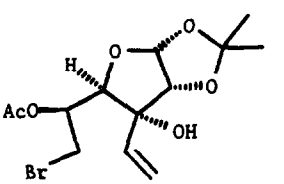
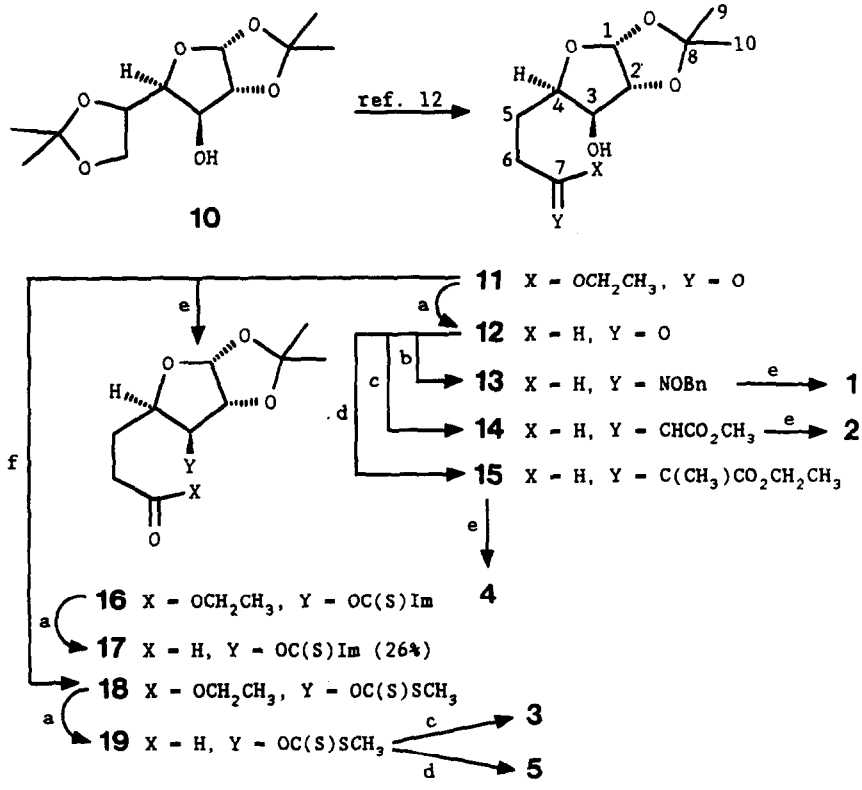


9

RESULTS AND DISCUSSION

These products have been prepared from a common, readily available starting material, diacetone glucose **10** (Schemes 2-6). Precursors **1-5** have been synthesized as shown in Scheme 2. The known ester **11**[12] was reduced with DIBALH giving the aldehyde **12**, that was conveniently functionalized for locating the radical trap at C7 and the leaving group at C3. The subsequent transformation of **12** into **13-15** followed the standard conditions. The final reaction with 1,1'-thiocarbonyldiimidazole provided in good yield the desired carbohydrates (**1, 2, 4**). Compounds **2** and **4** have been also prepared, albeit in low yield, from ester **11** by reaction with 1,1'-thiocarbonyldiimidazole followed by DIBALH reduction and Wittig reaction. This protocol, however, gave good results for the synthesis of the precursors **3** and **5**, where a xanthate has been

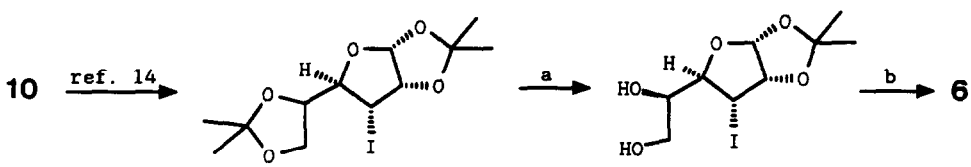
used as leaving group at C3. *S*-Methyl dithiocarbonate formation followed by DIBALH reduction (Scheme 2) and final Wittig reaction of aldehyde **19** with the corresponding ylide gave compounds **3** or **5** in good overall yield. All new compounds gave satisfactory analytical and spectroscopic data, in accordance with their structures (see **Experimental Part**). The *O*-benzyl oximes **13** and **1** have been obtained as a mixture of *E* and *Z* isomers (72:28) that we could not separate [^{1}H NMR: δH7(*E*) 7.46 (t, $J_{7,6}$=5.6 Hz), δH7(*Z*) 6.72 (t, $J_{7,6}$=5.6 Hz)]. The radical precursors **2** and **3** have been prepared as a mixture of *E*/*Z* isomers in a 94:6 ratio [^{1}H NMR: δH7(*E*) 6.92 (dt, $J_{7,8}$=15.6 Hz, $J_{7,6}$=6.9 Hz), δH8(*E*) 5.86 (dt, $J_{8,6}$=1.5 Hz)] that we could not separate. In the synthesis of precursors **4** and **5** major *E* compounds have been detected (*E*/*Z*::95/5; we could not separate these isomers) [^{1}H NMR δH7 6.76 (tq, $J_{7,6}$=7.3 Hz, $J_{7,CH}$ =1.4 Hz)]; this result is in good agreement with other observations reported in literature for this type of ylide, solvent and aldehyde.[13]



Reagents. a: DIBALH, toluene, -78°C (98%); b: $BnONH_3Cl$, pyridine, H_2O/CH_2Cl_2, reflux (69%); c: $Ph_3P{=}CHCO_2CH_3$, toluene, 80°C (78%); d: $Ph_3P{=}C(CH_3)CO_2CH_2CH_3$, toluene, 80°C (96%); e: 1,1'-Thiocarbonyldiimidazole, CH_2Cl_2, reflux (98%); f: NaH, S_2C, CH_3I (82%).

Scheme 2

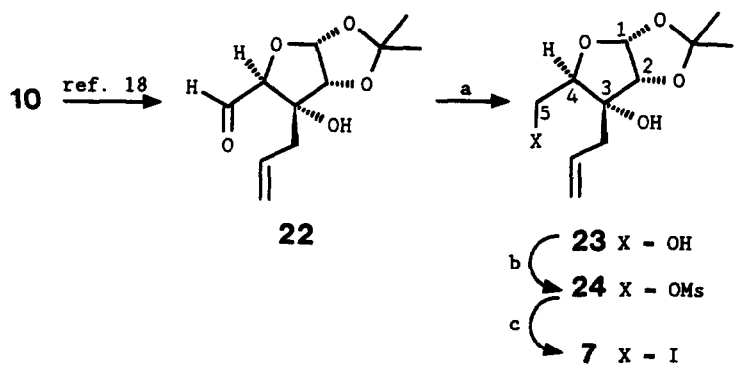
The obtention of compound **6** was approached from iodide **20**[14] (Scheme 3) by acid hydrolysis, periodate cleavage[15] followed by treatment of the crude aldehyde with allylmagnesium bromide[16] (31%) or allyltrimethylsilane + BF_3 Et_2O[17] (86%). In both cases we have isolated a mixture of isomers at C5, in ratio 1:3, that we could not separate and were processed together.



20 **21**

Reagents. a: $AcOH/H_2O$ (7/3; v/v) (83%);
b: i, $NaIO_4$; ii, $(CH_2{=}CH\text{-}CH_2)Si(CH_3)_3$, $BF_3.Et_2O$ (75%).

Scheme 3



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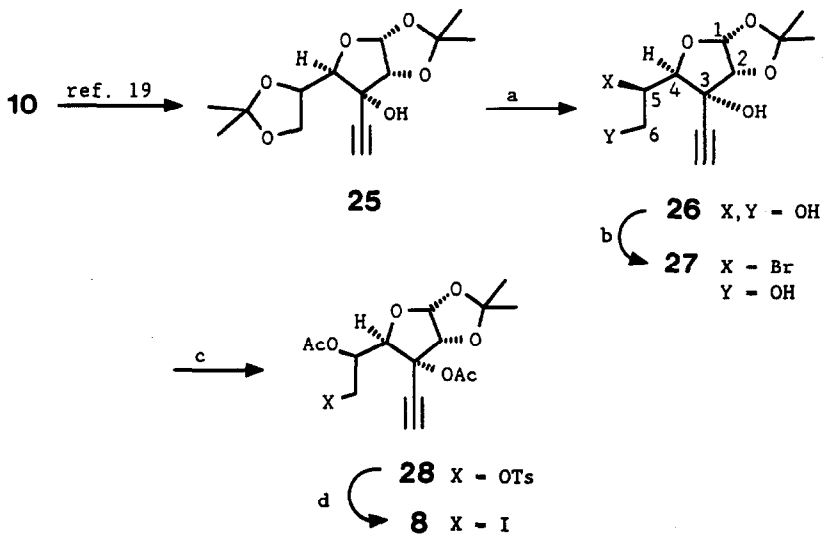
Reagents. a: $NaBH_4$, MeOH, 0°C (75%); b: MsCl, Et_3N, CH_2Cl_2 (95%);
c: NaI, DMF (16%).

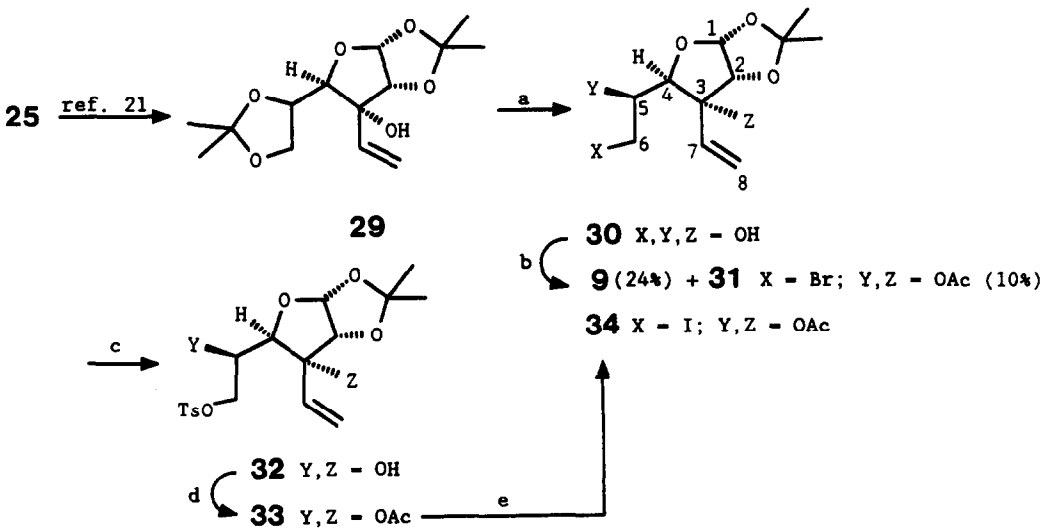
Scheme 4

The iodide **7** has been synthesized from aldehyde **22**[18] as shown in Scheme 4. Subsequent reduction gave the diol **23**. Unfortunately, this compound resisted direct bromination or iodination at C5; in these experiments (CBr_4, Ph_3P or I_2, Ph_3P, imidazole[14]) only complex mixtures were obtained. Thus, we turned out to a two step sequence: mesylation and treatment with sodium iodide. The desired product was finally prepared, albeit in a low yield that we could not improve. In spite of this, the synthetic path is short and allowed us to manipulate convenient quantities of the precursor. As in the other cases, all new compounds showed good analytical and spectroscopic data, in full agreement with the proposed structures.



Reagents. a: AcOH/H_2O (7:3) (99%); b: Br_4C, Ph_3P (30%); c: i. ClTs, pyridine; ii. Ac_2O, pyridine (84%); d: NaI, DMF (79%).

Scheme 5

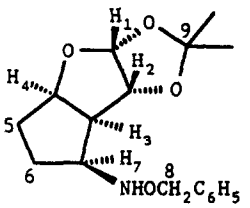


Reagents. a: AcOH/H_2O (7:3) (83% yield from **25**). b: i, CBr_4, Ph_3P; ii, Ac_2O/pyridine; c: ClTs/pyridine, 0°C (61%); d: Ac_2O, pyridine, 60°C (49%); e: NaI, DMF, 80°C (17%).

Scheme 6

The radical precursor **8** has been synthesized from diacetone glucose **10** as shown in Scheme 5. From the alkynyl branched chain sugar **25**,[19] after acid hydrolysis and direct bromination,[20] a poor yield (30%) of compound **27** was obtained. Then, we attempted "one pot" tosylation of the primary hydroxyl group followed by peracetylation (**26** → **28**; 84% overall yield). Final sodium iodide/dimethylformamide reaction provided the desired radical precursor **8** in good yield (79 %).

The synthesis of the analogous precursor **9** has been performed following a similar pathway (Scheme 6). Starting from compound **25** (Scheme 5) alcohol **29** was obtained as described.[21] After mild acid hydrolysis triol **30** was isolated. "One-pot" bromination + acetylation provided the monoacetate (**9**) and diacetate (**31**) derivatives in 24% and 10% yield, respectively. An alternative route: monotosylation (**30** → **32**) followed by peracetylation (**32** → **34**) and sodium iodide treatment gave compound **34** (Scheme 6) in poor overall yield. Then, we selected the first route and choose radical **9** as radical precursor.



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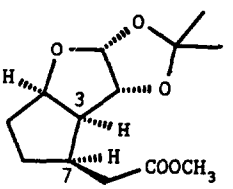

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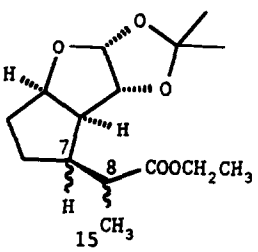
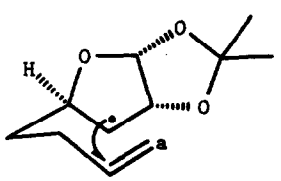
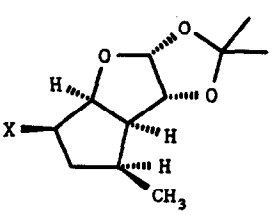


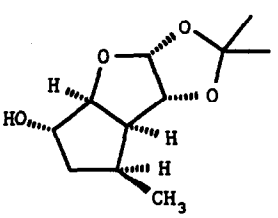
37



a: $NOCH_2C_6H_5$, $CHCO_2R$
$C(CH_3)CO_2R$



38 X = OH
40 X = H



39

Figure 1

With products **1-9** in hands we have studied their radical intramolecular cyclization. Following the general protocol (see **Experimental Part**), the tributyltin hydride + AIBN mediated free radical cyclization of precursor **1** gave the expected carbocycle **35** in 45% yield and 74% diastereomeric excess (d.e.) (determined by ^1H NMR in the crude mixture). Only the major isomer [**35**(C7 *S*)] could be isolated pure

Table 1. ^{1}H and ^{13}C NMR Data for Compound **35**.

^{13}C (ppm, $CDCl_3$)		^{1}H (ppm, $CDCl_3$)	
C1	106.85	H1	5.73, d $J_{1,2}$=3.7 Hz
C2	85.04*	H2	4.92, d
C3	52.24	H3	2.70, dd $J_{3,4}$=5.0 Hz $J_{3,7}$=9.1 Hz
C4	82.19*	H4	4.81
C5	29.88**	H5 H5'	1.90, m 1.62, m
C6	28.48**	H6 H6'	1.79, m 1.58, m
C7	60.98	H7	3.57
C8	75.81		
C9	110.66		
C10,11	27.28, 26.60	H10,11	1.51*, 1.32*, s, s
Aromatics	137.43 128.44-127.85	$OCH_2C_6H_5$ C_6H_5 $NHOC_6H_5$	4.74,4.66, d, J=11.7 Hz 7.27, m 5.41

Table 2. ^{1}H and ^{13}C NMR Data for Compound **36**.

^{13}C (ppm, $CDCl_3$)		^{1}H (ppm, $CDCl_3$)	
C1	106.24	H1	5.71, d $J_{1,2}$=3.6 Hz
C2	85.64*	H2	4.55, d
C3	35.89	H3	2.77, dd $J_{3,4}$=5.2 Hz $J_{3,7}$=9.7 Hz
C4	82.86*	H4	4.86
C5	32.03**	H5 H5'	1.90, m 1.50, m
C6	30.76**	H6 H6'	1.82, m 1.29, m
C7	23.22	H7	2.50-2.30, m
C8	36.27	2H8	2.50-2.30, m
C9	110.93		
C10,11	27.31, 26.60	H10,11	1.50*, 1.31*, s, s
C12	172.63		
C13	51.43	H13	3.70, s

(The values with asterisk can be interchanged)

after chromatography. The analytical and spectroscopic data (see Table 1) are in good agreement with the assigned structure; particularly significant are the chemical shifts of C3 (52.24 ppm) and H3 (2.70 ppm, dd, $J_{3,4}$=5.0 Hz, $J_{3,7}$=9.1 Hz) in the ^{13}C and ^{1}H NMR spectra. The absolute configuration at the new formed stereocenter during the carbocyclization has been established after a detailed analysis of the ^{1}H NMR spectrum and the observed enhancements in the n.O.e. experiments. In effect, we have found n.O.e,s between H4-H3 (10.6%) and H3-H7 (8.7%) that clearly determined the absolute stereochemistry at C7 as *S* and then, the formation of major *cis* isomer during the ring closure.

The carbocyclization of compound **2** (or **3**) provided compound **36** in 88% (or 73%) yield. The diastereomeric excesses, determined in the crude reaction mixture by ^{1}H NMR, were 76%. After purification by chromatography only the major isomer could be isolated in 80% of diastereomeric excess. The absolute configuration at the new stereocenter has been assigned as C7 *R* after careful inspection of the spectroscopic data and comparison with the corresponding values for **35**. In effect, in the ^{1}H NMR spectrum of this diastereomeric enriched mixture (see Table 2), H3 appears, as expected, at 2.77 ppm (dd, $J_{3,4}$=5.2 Hz and $J_{3,7}$=9.7 Hz).

In the case of the analogous precursor **4** (or **5**) the free radical cyclization provided the desired carbocycle **37** in 76% (or 83%) yield. After chromatography we have isolated a mixture of the four possible isomers, that we could not separate, in 12-6-68-14 (%) ratio, almost similar to the ratio observed in the crude. We have determined these values in the ^{1}H NMR spectrum integrating the signals for H1 (δ 5.83, d, $J_{1,2}$=3.6 Hz; 5.81, d, J=5.8 Hz; 5.73, d, J=4.0 Hz; 5.67, d, J=3.7 Hz); in the rest of the spectrum we have observed clear signals for H3 at 2.75 ppm, $J_{3,4}$=5.9 Hz, $J_{3,7}$=9.6 Hz, indicating that, as in compounds **35** or **36**, we have also obtained now major *cis* isomers. This has been also confirmed in the analysis of the ^{13}C NMR spectrum of the mixture. The major isomer shows C3 and C7 at 41.46 and 23.30 ppm, respectively [compare with C3 (35.89), C7 (23.12) in **36**]. Regarding the absolute configuration at C8 in the major isomer (^{13}C NMR δ C8, 44.73; C15, 16.50) we could not establish it.

From these results we conclude that the 5-*exo*-trig cyclization of precursors **1-5** give the corresponding carbocycles in good yield ($\approx$75%) and excellent diastereoselectivity (d.e. $\approx$78%). And this is independent of the type of leaving group at C3. In all these cases, the major formed compound is the (C2,3-C7,8) *cis* isomer. This is not unexpected and is coherent with the general rule that 1-alkyl substituted 5-hexenyl radicals (Fig. 1) cyclize to give major *cis*-1,2-cyclopentanes.[22] This also agrees with other reported results in this area.[23]

In order to analyze the effect of an hydroxyl group at C5 in this process, precursor **6** was submitted to cyclization. In the usual conditions and after careful chromatography, compounds **38** (d.e.: 95%) and **39** (d.e.: 95%) have been obtained (1:3 ratio; 64% overall yield) and separated. The spectroscopic data (Table 3) confirmed these structures and established that these compounds are *cis* cyclized products [^{1}H NMR δH3 (**38**) 2.72, dd, $J_{3,4}$=5.1 Hz, $J_{3,7}$=10 Hz; H3 (**39**) 2.88, dd, $J_{3,4}$=5.1 Hz, $J_{3,7}$=10.3 Hz); [^{13}C NMR δC3

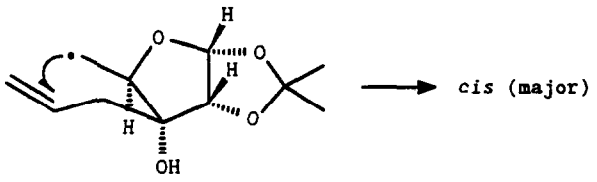


Figure 2

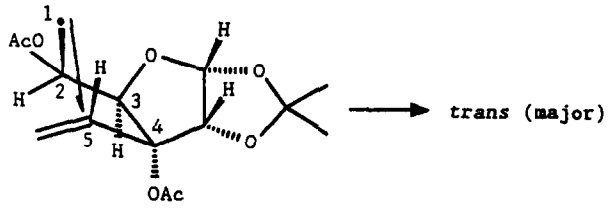
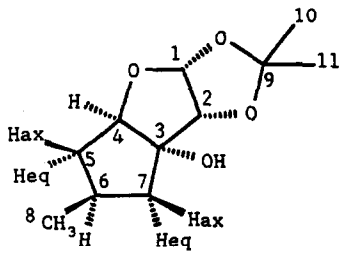
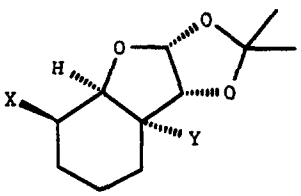


Figure 3

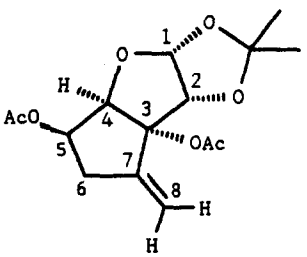


41 [C6(*S*)]



42 X = H; Y = OH

47 X,Y = $OCOCH_3$



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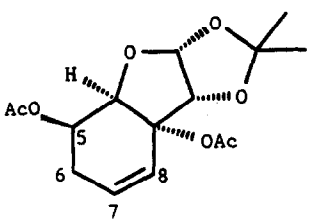

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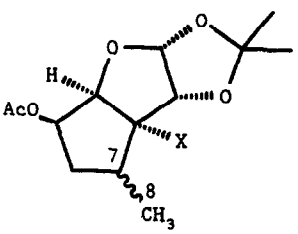


45 X = OH

46 X = $OCOCH_3$

(**38**) 45.64, C3 (**39**) 50.56; compare with C3 (**40**)[7] 52.33, C7 (**38**) 29.45, C7 (**39**) 31.04; compare with C7 (**40**)[7] 33.30, C8 (**38**) 16.78; C8 (**39**) 16.89; compare with C8 (**40**)[7] 16.93]. As expected, these compounds are only different in the absolute configuration at C5 [^{1}H NMR δH5 (**38**) 3.91, m; H5 (**39**) 4.19, d, $J_{5,6}$=4.1 Hz]. Then, precursor **6** behaves (independently of the absolute configuration of the hydroxyl group at C5) as compounds **1-5** giving major *cis* cyclized products in large diastereomeric excess and good yield. In addition no products arising from the 6-*endo* mode of cyclization were detected.

The free radical cyclization of compound **7** gave a complex mixture of cyclized products in 55% yield. After purification the major **41** [C6 *S*] isomer was isolated pure. In the crude reaction and by ^{1}H NMR analysis, we could determine the ratio 5-*exo* (**41**) (δH1 5.83, d, $J_{1,2}$=4.0 Hz)/6-*endo* (**42**) δH1 5.80, d, $J_{1,2}$=3.9 Hz) as 85:15. The ratio **41** (C6 *S*/*R*) is 76/24. These isomers showed in the ^{1}H NMR spectrum identical shifts for H1, but significant differences for H2, H4 and C(8)H_3. For **41** (C6 *R*), H2 appears at 4.83 ppm; H4 at 4.57 as a broad doublet ($J_{4,5}$=5.7 Hz), while in **41** (C6 *S*) H2 appears at 4.31 ppm and H4 4.19 (see **Experimental Part**). Unfortunately we could not isolate pure **42** nor minor **41** (C6 *R*).The absolute configuration at C6 (new stereocenter) in the major isomer has been assigned by a detailed high field ^{1}H NMR analysis, including ^{1}H-^{1}H NOESY experiments. The formation of major *cis* isomer can also be explained assuming that in the transition state the carbon centred radical adopts a chair-like conformation where substituents occupy preferred pseudoequatorial positions (Fig. 2). In fact, it is known that 3-alkyl substituted 5-hexenyl radicals give major *cis* 1,3-disubstituted cyclopentanes.[22]

Radical precursor **8** has a terminal triple bond as radical trap,[24] and when this compound was submitted to the cyclization conditions gave a mixture of **43**+**44** (ratio: 7/3; determined by ^{1}H NMR) that we could not separate. Compound **43** is the normal 5-*exo*-dig and **44** the 6-*endo*-dig cyclization product. In the ^{1}H NMR spectrum of the mixture major **43** showed typical signals at δ 5.83 (d, $J_{1,2}$=3.5 Hz, 1 H, H1), 5.80 (t, J=2.5 Hz, 1 H, H8), 5.41 (br s, 1 H, H8'), 5.29 (m, 1 H, H5), 5.16 (d, 1 H, H2), 4.65 (d, $J_{4,5}$=3.4 Hz, 1 H, H4). In minor isomer **44** we could observe in the ^{1}H NMR spectrum H7 at 5.96 ppm (ddd, $J_{7,8}$=10 Hz, $J_{7,6}$=2.1 Hz, $J_{7,6'}$=4.9 Hz) and H8 at 6.00 ppm (br d, $J_{7,8}$=10 Hz) (note that we could unequivocally assign the ratio and type of cyclized compound by simply analyzing the coupling constants for the vinyl protons in the spectrum of the mixture); in addition, other signals are: 5.73 ppm (d, $J_{1,2}$=3.7 Hz, 1 H, H1), 5.13 (m, 1 H, H5), 4.90 (d, 1 H, H2), 4.38 (br s, 1 H, H4). In the ^{13}C NMR (50 MHz, $CDCl_3$, δ) spectrum we could also easily assign the signals: **43** [143.81 (C7), 119.16 (C8), 113.28 (C1), 105.92 (C1), 88.55 (C3), 34.45 (C6)]; **44** [131.78, 122.08 (C7, C8), 112.92 (C9), 104.90 (C1), 82.47 (C3), 25.54 (C6)]. Normal 5-hexynyl free radical cyclizations give 5-*exo*-dig products.[25] The formation of major 6-*endo*-dig compounds was observed in the annulation reactions of ß-lactams[26] or pyrrolidones.[27] The unexpected obtention of large quantities of compound **44** from cyclization of precursor **8** can be explained by the relatively high steric compression present in compound 5-*exo*-dig **43**.

Free radical cyclization of precursor **9** gave product **45** in 31% yield (64% diastereomeric excess)

Table 3. ^{1}H and ^{13}C NMR Data for Compounds **38** and **39**.

38				
^{13}C		^{1}H		
C1	106.51	H1	5.75, d	$J_{1,2}$=3.5 Hz
C2 C4	85.30 85.23	H2 H4	4.71-4.60 m	
C3	49.64	H3	2.72, dd	$J_{3,4}$=5.1 Hz $J_{3,7}$=10 Hz
C5	73.79	H5	3.91, m	
C6	40.33	H6 H6'	1.65, m 2.15-2.00	
C7	29.45	H7	2.15-2.00	
C8	16.38	H8	1.05, d	J=6.9 Hz
C9	111.88			
C10 C11	27.62 26.87	H10 H11	1.52, s 1.32, s	

39				
^{13}C		^{1}H		
C1	106.49	H1	5.67, d	$J_{1,2}$=3.5 Hz
C2	82.71	H2	4.66, d	
C3	50.56	H3	2.88, dd	$J_{3,4}$=5.1 Hz $J_{3,7}$=10.3 Hz
C4	90.61	H4	4.59, d	$J_{3,4}$=5.1 Hz
C5	75.34	H5	4.19, d	$J_{5,6}$=4.1 Hz
C6	41.31	H6' H6	1.83, dd 1.45, ddd	$J_{6',7}$=7.0 Hz $J_{6,6'}$=13.6 Hz $J_{6,5}$=4.1 Hz $J_{6,7}$=11.1 Hz
C7	31.01	H7	2.54, m	
C8	16.89	H8	1.02, d	J=7.3 Hz
C9	111.27			
C10 C11	27.51 26.70	H10 H11	1.51, s 1.33, s OH, br s	

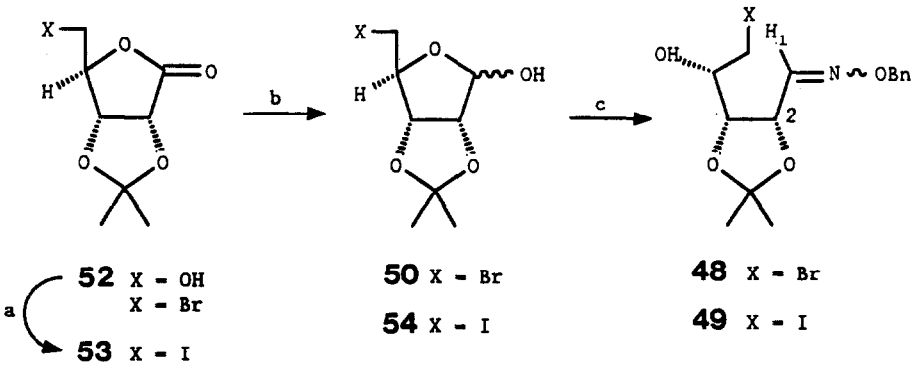
as the only isolated and correctly characterized compound. The reaction mixture is very complex and other more polar compounds were detected, but we could not identify them. For this reason we cannot rule out the formation of the 6-*endo* cyclization carbocycle. Compound **45** was fully analyzed as the peracetate **46**, obtained as a mixture of isomers at C7 that we could not separate. In the ^{1}H NMR spectrum the major isomer showed typical signals at 5.87 ppm, (d, $J_{1,2}$=3.7 Hz, 1 H, H1), 4.92 (d, 1 H, H2), 4.66 (d, $J_{4,5}$=4.4 Hz, 1 H, H4), 1.00 (d, J=7.1 Hz, 3 H, CH_3). The minor isomer showed also well resolved signals in the ^{1}H NMR spectrum [5.84 (d, $J_{1,2}$=4.7 Hz, 1 H, H1), 5.07 (d, 1 H, H2), 4.56 (d, $J_{4,5}$=3.3 Hz, 1 H, H4), 1.22 (d, J=7.0 Hz, CH_3)]. In the ^{13}C NMR spectrum major isomer showed C8 and C7 at 16.07 and 36.92 ppm, respectively; in turn, minor isomer showed C8 and C7 at 16.64 and 39.09 ppm. The absolute configuration at C7 in the major isomer has been assigned as *R* after extensive ^{1}H NMR analysis and ^{1}H-^{1}H NOESY experiments and confirmed by the observed chemical shifts for C-7 and C-8 in the ^{13}C NMR spectrum; in effect, as would be expected on grounds of steric compression, the major isomer has the methyl group *endo*.[28] The formation of a major *trans* product in the cyclization of a 4-substituted hex-5-enyl precursor such as **9** is coherent with the general guidelines proposed by Beckwith.[29] As noted by RajanBabu[28] the allylic local *O*-substituted portion of the molecule is an important factor in controlling the stereochemistry. In the present case (precursor **9**) as the C4 (radical numbering; Fig. 3) is disubstituted having a tertiary acetate, it is not clear which is the more stable conformer that minimizes 1,3-allylic strain,[30] and a balance should result. In Figure 3 we show a possible chairlike preferred transition state that accounts for the formation of the major *trans* product.

In order to correlate products the mixture **43**+**44** was hydrogenated to give a mixture of **46** (C7 *S*)/ **46** (C7 *R*) and **47** in 1.2:1.1:1 ratio. Unfortunately, after chromatography we could not separate and obtain pure each isomer. However, in the ^{1}H NMR spectrum of the mixture the signals observed for the 5-*exo* products obtained in the cyclization + acetylation of precursor **9** were clearly analyzed and identified.

In summary, in the cyclopentane annulation of precursors **1**-**9** we have observed moderate yields in the cyclization with good diastereoselectivities. This is thus an interesting example of how a chiral substrate can induce high levels of diastereoselectivity at "off template site".[31]

Regarding the second tactic (see above) we have selected as prototypes of the carbon centred radical **D** (Scheme 1) the compounds **48** and **49**. Oximes **48/49** have been synthesized from lactol **50**[2,32] and compound **52** (Scheme 7), readily available from D-ribonolactone.[33]

Compounds **48** and **49** have been isolated as a mixture of *syn* and *anti* isomers that we could not separate [^{1}H NMR *anti*:δH1 7.45,d, $J_{1,2}$=7.5 Hz; *syn*:δH1 6.70,d, $J_{1,2}$=6.0 Hz]. In the typical free radical cyclization conditions (see **Experimental Part**) precursor **48** gave the 5-*exo* cyclized product **51** in 74% yield. This process has been carefully analyzed and we have found optimal conditions (see Table 4). Then, a good yield and excellent diastereoselectivity was found in this carbocyclization. Conversely, the cyclization of product **49**, in the conditions of the experiment 1 (see Table 4), gave product **51** in lower yield (26%).



Reagents. a: I_2, Ph_3P, imidazole (50%); b: DIBALH, toluene, -78°C (77%); c: $BnONH_3Cl$/ pyridine (76%).

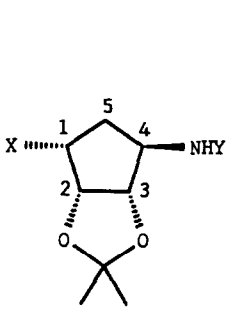
Scheme 7

Table 4. Free Radical Cyclization of Precursor **48**.

Exp	Solvent	Conc (M)	Hydride (equiv)	Addition (time)	Yield (%)
1	benzene	0.01	2.4	5 h 30 min	47
2	benzene	0.01	2.4	15 h 30 min	22
3	benzene	0.02	2.4	5 h	47
4	benzene	0.02	1.5	5 h	32
5	toluene	0.02	2.4	4 h	75

The configuration at the new stereocenter in **51** has been established after careful analysis of the ^1H NMR spectrum. The observed vicinal coupling constant $J_{3,4}$=0 Hz is a very significant structural diagnostic; in effect, this value is typical for a *trans* orientation of H3/H4 in related cyclopentanes,[34] and justifies the *exo* position of the benzylhydroxylamine moiety. The formation of the *exo* product **51** in the cyclization of precursors **48/49** is in good agreement (and can be explained in the same terms) with the results reported by Wilcox[2] for an analogous substrate in similar carbocyclization conditions.

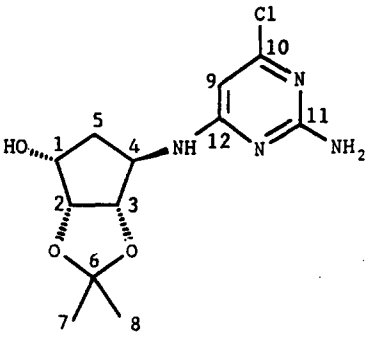
With compound **51** we have accomplished a series of transformations. Hydrogenation (Pd/C 10%) was very sluggish, even at high pressure (60 psi, 48 h) and a poor conversion was detected. Reduction with lithium aluminium hydride in tetrahydrofuran was effective and gave aminoalcohol **55** in modest yield (40%). Peracetylation of the crude mixture provided product **56**. Finally, reaction of **55** with 2-amino-4,6-dichloropyrimidine gave the carbocyclic nucleoside **57**, whose spectroscopic data are in good agreement with reported data for similar compounds.[35]



51 X = OH, Y = OBn

55 X = OH, Y = H

56 X = $OCOCH_3$
Y = $COCH_3$



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In summary, all the transformations reported here prove the high efficiency of the free radical mediated carbocyclizations for the synthesis of carbocycles.

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EXPERIMENTAL PART

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.[36]

General Procedure for Selective Acid Hydrolysis of Acetals. The product was dissolved in acetic acid/water (7:3/v:v) and the solution stirred overnight at room temperature. The solvents were evaporated and the residue submitted to chromatography.

General Procedure for Cleavage of 1,2-Diols.[15] To a suspension of silica gel in methylene chloride, an aqueous solution of sodium periodate (0.65 M, 1.3 equiv) was slowly added. To this stirred mixture the diol (1 equiv) was added; after 40 min at room temperature, the cake was filtered over Celite-545, washed with methylene chloride, evaporated and submitted to chromatography. The aldehyde was transformed without further purification.

Reduction of Esters to Aldehydes. To a solution of the ester (1 equiv) in dry toluene (0.05 M), cooled at -78°C, under argon and stirring, DIBALH (1.5 equiv, 1.0 M in hexane) was added dropwise.

After 30 min the reaction was complete, and methanol was slowly added, the mixture warmed at room temperature and the salts filtered over Celite-545. The filtrate was concentrated in vacuo and the residue submitted to chromatography.

Synthesis of *O*-Thiocarbonylimidazole Derivatives. The alcohol dissolved in dry methylene chloride (0.08 M) was treated with 1,1'-thiocarbonyldiimidazole (2 equiv). Refluxing was continued for 2 h. The mixture was cooled, diluted with methylene chloride, washed with brine, dried and evaporated. The residue was submitted to flash chromatography.

Formation of Xanthates. To a suspension of sodium hydride (1.7 equiv) in dry tetrahydrofuran, carbon disulfide (1.5 equiv), methyl iodide (1 equiv) and imidazole (cat.) were added. The mixture was cooled at -30°C, and under argon and stirring the alcohol (1 equiv) dissolved in dry tetrahydrofuran was slowly added. After 2 h the reaction is over, the mixture quenched with acetic acid, the tetrahydrofuran evaporated, and the residue diluted with ethyl acetate, washed with 5% aqueous sodium bicarbonate solution and brine. After drying and evaporation, the residue was purified by chromatography.

General Procedure for Wittig Reaction. The aldehyde was dissolved in toluene and treated with the corresponding ylide (1.1 equiv) at room temperature and with stirring (overnight) or at 80°C (bath temperature) for 2 h. The solvent was removed and the residue submitted to chromatography.

General Method for Acetylations. The compound was treated with acetic anhydride/pyridine (1:1/v:v) for 24 h at room temperature. The solvents were removed in vacuo and the residue purified.

General Method for Free Radical Cyclization. To a solution of the radical precursor in toluene (0.03 M), that has been deoxygenated with argon for 1 h, a solution of tributyltin hydride (2 equiv) and AIBN (cat.) in toluene (8 M) was slowly (*via* "syringe pump") added in the indicated time in each case. The flask was cooled and the solvents removed, the residue dissolved in ethyl ether and stirred overnight with a 20% aqueous potassium fluoride solution. The organic phase was recuperated, dried and evaporated. Flash chromatography gave the products.

5,6-Dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-heptodialdo-1,4-furanose (12). Following the general procedure ester **11**[12] (500 mg, 1.9 mmol) was reduced to aldehyde **12** (obtained in the hemiacetal form) [flash chromatography (hexane/EtOAc, 1:1); 409 mg, 98%]: mp 102-105°C; $[\alpha]_D^{25}$ +82 (*c* 0.33, $CHCl_3$); IR (Nujol) ν : 3430, 2970, 2875, 1460, 1390, 1380, 1185, 1215, 1085, 905 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (major anomer, α): 5.91 (d, $J_{1,2}$=3.9 Hz, 1H, H1), 5.22 (m, $W_{h/2}$=6.2 Hz, 1H, H7), 4.47 (d, $J_{1,2}$=3.9 Hz, 1H, H2), 4.24 (br s, 2H, H3, H4), 2.93 (dd, $J_{OH,7}$=3 Hz, J=2 Hz, 1H, OH), 2.25-2.09 (m, 1H, H6), 2.00-1.82 (m, 2H, H6', H5), 1.60-1.45 (m, 1H, H5'), 1.50, 1.32 (s, s; 3H, 3H); MS (70 eV) *m/z*: 201 (M^+-15, 66), 183 (4), 169 (2), 159 (2), 141 (47), 123 (7), 100 (33), 87 (35), 71 (32), 59 (100), 43 (84). Anal. Calcd. for $C_{10}H_{16}O_5$: C, 55.54; H, 7.46. Found: C, 55.34; H, 7.77.

***O*-Benzyl Oxime of Aldehyde 12 (13).** A solution of compound **12** (409 mg, 1.89 mmol) in methylene chloride (15 mL) was treated with *O*-benzylhydroxylamine chloride (360 mg, 2.26 mmol, 1.2 equiv), pyridine (0.2 mL, 2.26 mmol) and water (7 drops). The mixture was refluxed for 50 min, cooled, diluted with methylene chloride, washed with diluted aqueous solution of sodium bicarbonate and brine. After drying, evaporation and chromatography (hexane/EtOAc, 4:1), the oxime **13** (420 mg, 69%) was isolated: mp 58-63°C; IR (film) ν : 3600-3100, 3080, 3060, 2980-2930, 1495, 1455, 1380, 1370, 1215, 1165, 1100-1000, 800 cm^{-1}; MS (70 eV) *m/z*: 306 (M^+-15, 3), 274 (2), 245 (1), 149 (3), 141 (3), 100 (6), 91 (100), 59 (16), 43 (15). Anal. Calcd. for $C_{17}H_{23}NO_5$: C, 63.53; H, 7.21; N, 4.36. Found: C, 63.28; H, 7.40; N, 4.40.

Radical Precursor (1). Following the general procedure compound **13** (420 mg, 1.31 mmol) was transformed into **1** [flash chromatography (hexane/EtOAc, 60:40); 538 mg, 95%]: Oil; IR (film) ν : 3120, 3060, 3020, 2980, 1765, 1530, 1465, 1390, 1150, 1280, 1230, 1160, 1090, 1025 cm^{-1}; MS (70 eV) *m/z*:

322 (2), 306 (2), 246 (1), 199 (2), 91 (100), 59 (9), 43 (9). Anal. Calcd. for $C_{21}H_{25}N_3SO_5$: C, 58.46; H, 5.84; N, 9.74; S, 7.43. Found: C, 58.31; H, 5.79; N, 9.60; S, 7.22.

Methyl 1,2-*O*-Isopropylidene-5,6,7,8-tetradeoxy-α-D-*xylo*-nona-7-ene-furanuronate (14). Compound **12** (1.0 g, 4.6 mmol) has been converted according to the general method into ester **14** [flash chromatography (hexane/EtOAc, 4:1); 980 mg, 78%]: mp 93-97°C; IR (Nujol) ν : 3400, 2970, 2930, 2890, 1715, 1660, 1500, 1385, 1380, 1225, 1090, 860 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (major isomer E): 7.00 (dt, $J_{7,8}$=15.7 Hz, $J_{7,6}$=6.9 Hz, 1H, H7), 5.91-5.83 (m, 2H, H1, H8), 4.51 (d, $J_{1,2}$=3.6 Hz, 1H, H2), 4.20-4.00 (m, 2H, H4, H3), 3.72 (s, 3H, CO_2CH_3), 2.50-2.25 (m, 2H, 2H6), 1.95-1.75 (m, 2H, 2H5), 1.48, 1.31 (s, s; 3H, 3H); MS (70 eV) *m/z*: 257 (M^+-15, 6), 254 (7), 225 (4), 197 (57), 165 (56), 147 (11), 143 (31), 137 (25), 119 (18), 109 (52), 95 (69), 59 (83), 43 (100). Anal. Calcd. for $C_{13}H_{20}O_6$: C, 57.34; H, 7.40. Found: C, 57.39; H, 7.70.

Radical Precursor (2). From compound **14** (225 mg, 0.82 mmol) and following the standard method, after chromatography (hexane/EtOAc, 6:4) compound **2** was prepared (300 mg, 97%): Oil; $[\alpha]_D^{25}$ -5° (*c* 0.49, $CHCl_3$); IR (film) ν : 3110, 3080, 2990, 2970, 2890, 1725, 1660, 1535, 1470, 1440, 1385, 1380, 1225, 1170, 1020 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (major isomer E): 8.33, 7.60, 7.07 (m, m, m; 1H, 1H, 1H, imidazole), 6.92 (dt, $J_{7,8}$=15.6 Hz, $J_{7,6}$=6.9 Hz, 1H, H7), 5.97 (d, $J_{1,2}$=3.9 Hz, 1H, H1), 5.86 (dt, $J_{7,8}$=15.6 Hz, $J_{8,6}$=1.5 Hz, 1H, H8), 5.78 (d, $J_{3,4}$=2.8 Hz, 1H, H3), 4.72 (d, $J_{1,2}$=3.9 Hz, 1H, H2), 4.41 (ddd, $J_{3,4}$=2.8 Hz, $J_{4,5}$=5.3 Hz, $J_{4,5'}$=8.3 Hz, 1H, H4), 3.71 (s, 3H, CO_2CH_3), 2.50-2.25 (m, 2H, 2H6), 2.00-1.75 (m, 2H, 2H5), 1.55, 1.34 (s, s; 3H, 3H); MS (70 eV) *m/z*: 257 (4), 165 (6), 143 (10), 137 (3), 123 (3), 111 (14), 100 (10), 83 (15), 59 (79), 43 (100). Anal. Calcd. for $C_{17}H_{22}N_2SO_6$: C, 53.40; H, 7.33; N, 7.33; S, 8.38. Found: C, 53.20; H, 5.65; N, 7.36, S, 8.10.

Ethyl 1,2-*O*-Isopropylidene-8-*C*-methyl-5,6,7,8-tetradeoxy-α-D-*xylo*-nona-7-enofuranuronate (15). From aldehyde **12** (1.0 g, 4.6 mmol) and following the standard procedure for the Wittig reaction, after chromatography (hexane/EtOAc, 4:1) alcohol **15** (1.32 g, 96%) was isolated: mp 86-89°C; $[\alpha]_D^{25}$ -20° (*c* 0.19, $CHCl_3$); IR (Nujol) ν : 3420, 3060, 2950, 2870, 1710, 1655, 1460, 1390, 1380, 1270, 1165, 1090, 860 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.76 (tq, $J_{7,10}$=1.4 Hz, $J_{7,6}$=7.3 Hz, 1H, H7), 5.89 (d, $J_{1,2}$=3.8 Hz, 1H, H1), 4.50 (d, $J_{1,2}$=3.8 Hz, 1H, H2), 4.19 (q, J=7.1 Hz, 2H, $CO_2CH_2CH_3$), 4.12 (ddd, $J_{3,4}$=2.6 Hz, $J_{4,5}$=7.7 Hz, $J_{4,5'}$=6.0 Hz, 1H, H4), 4.05 (dd, $J_{3,4}$=2.6 Hz, $J_{3,OH}$=6.5 Hz, 1H, H3), 2.40-2.25 (m, 2H, 2H6), 1.85 (d, $J_{10,7}$=1.4 Hz, 3H, CH_3), 1.92-1.70 (m, 3H, OH, 2H5), 1.48, 1.31 (s, s; 3H, 3H), 1.28 (t, J=7.1 Hz, 3H, $CO_2CH_2CH_3$); MS (70 eV) *m/z*: 285 (M^+-15, 6), 225 (14), 196 (4), 179 (14), 171 (28), 141 (14), 137 (20), 133 (11), 125 (100), 97 (28), 59 (81), 43 (79). Anal. Calcd. for $C_{15}H_{24}O_6$: C, 59.98; H, 8.05. Found: C, 59.77; H, 8.12.

Radical Precursor (4). From alcohol **15** (1.53 g, 5.10 mmol), and following the general procedure, after chromatography (hexane/EtOAc, 7:3) ester **4** (2.05 g, 98%) was isolated as a mixture of E/Z (91:9) isomers: Oil; $[\alpha]_D^{25}$ -10° (*c* 0.62, $CHCl_3$); IR (film) ν : 3130, 2990, 1710, 1650, 1530, 1470, 1270, 1225, 1090 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (major isomer E): 8.33, 7.60, 7.07 (m, m, m; 1H, 1H, 1H, imidazole), 6.69 (tq, $J_{7,10}$=1.4 Hz, $J_{7,6}$=7.5 Hz, 1H, H7), 5.96 (d, $J_{1,2}$=3.9 Hz, 1H, H1), 5.77 (d, $J_{3,4}$=2.7 Hz, 1H, H3), 4.71 (d, $J_{1,2}$=3.9 Hz, 1H, H2), 4.39 (ddd, $J_{3,4}$=2.7 Hz, $J_{4,5}$=5.1 Hz, $J_{4,5'}$=8.3 Hz, 1H, H4), 4.17 (q, J=7.1 Hz, 2H, $CO_2CH_2CH_3$), 2.35 (m, 2H, 2H6), 2.00-1.96 (m, 1H, H5), 1.83 (d, J=1.4 Hz, 3H, CH_3), 1.82-1.75 (m, 1H, H5'), 1.55, 1.34 (s, s; 3H, 3H), 1.27 (t, J=7.1 Hz, 3H, $CO_2CH_2CH_3$); MS (70 eV) *m/z*: 303 (3), 282 (13), 258 (5), 225 (54), 195 (14), 179 (77), 99 (55), 59 (43), 43 (100). Anal. Calcd. for $C_{19}H_{26}N_2SO_6$: C, 55.60; H, 6.39; N, 6.83; S, 7.81. Found: C, 55.35; H, 6.18; N, 6.66; S, 7.59.

Ethyl 5,6-Dideoxy-1,2-*O*-Isopropylidene-3-*O*-thiocarbonylimidazole-α-D-*xylo*-hepto-furanuronate (16). From ester **11** (330 mg, 1.27 mmol) and following the general protocol, after flash chromatography (hexane/EtOAc, 7:3) compound **16** was obtained (464 mg, 98%): mp 63-65°C; $[\alpha]_D^{25}$ +53° (*c* 0.45, $CHCl_3$); IR (film) ν : 3120, 3060, 2990, 2960, 1735, 1535, 1470, 1395, 1380, 1290, 1230, 1165, 1090, 1020 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.33, 7.60, 7.04 (m, m, m; 1H, 1H, 1H, imidazole), 5.95 (d,

$J_{1,2}$=3.6 Hz, 1H, H1), 5.77 (d, $J_{3,4}$=2.5 Hz, 1H, H3), 4.72 (d, $J_{1,2}$=3.6 Hz, 1H, H2), 4.45 (m, 1H, H4), 4.11 (q, J=7.2 Hz, 2H, $CO_2CH_2CH_3$), 2.60-2.30 (m, 2H, 2H6), 2.10-1.90 (m, 2H, 2H5), 1.54, 1.32 (s, s; 3H, 3H), 1.23 (t, J=7.2 Hz, 3H, $CO_2CH_2CH_3$); MS (70 eV) *m/z*: 339 (2), 263 (2), 243 (3), 217 (4), 213 (13), 199(13), 197 (13), 184 (51), 179 (10), 167 (50), 157 (25), 139 (36), 111 (41), 101 (64), 83 (26), 55 (49), 43 (100). Anal. Calcd. for $C_{16}H_{22}N_2SO_6$: C, 51.88; H, 5.99; N, 7.56; S, 8.65. Found: C, 51.67; H, 5.87; N, 7.89; S, 8.40.

Ethyl 5,6-Dideoxy-1,2,-*O*-isopropylidene-3-*O*-(*S*-methyl-thiocarbonate)-α-D-*xylo*-hepto-furanuronate (18). From ester **11** (4.0 g, 16.6 mmol) and following the standard conditions, after flash chromatography (hexane/EtOAc, 9:1), ester **18** (4.5 g, 82%) was obtained: Oil; $[\alpha]_D^{25}$ +10° (*c* 0.16, $CHCl_3$); IR (film) ν : 2990, 2920, 1735, 1420, 1380, 1375, 1200, 1080, 1020, 920 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.93 (d, $J_{1,2}$=3.9 Hz, 1H, H1), 5.89 (d, $J_{3,4}$=2.8 Hz, 1H, H3), 4.65 (d, $J_{1,2}$=3.9 Hz, 1H, H2), 4.39 (ddd, $J_{3,4}$=2.9 Hz, $J_{4,5}$=5.3 Hz, $J_{4,5'}$=8.2 Hz, 1H, H4), 4.13 (q, J=7.1 Hz, 2H, $CO_2CH_2CH_3$), 2.59 (s, 3H, $OC(S)SCH_3$), 2.55-2.35 (m, 2H, 2H6), 2.10-1.90 (m, 2H, 2H5), 1.53, 1.32 (s, s; 3H, 3H), 1.25 (t, J=7.1 Hz, 3H, $CO_2CH_2CH_3$); MS (70 eV) *m/z*: 335 (M^+-15, 1), 305 (3), 293 (4), 275 (5), 247 (9), 213 (7), 197 (19), 184 (100), 167 (16), 155 (27), 139 (23), 127 (16), 111 (32), 100 (59), 91 (53), 85 (16), 43 (28). Anal. Calcd. for $C_{14}H_{22}S_2O_6$: C, 48.00; H, 6.33; S, 18.29. Found: C, 47.82; H, 6.21; S, 18.10.

Radical Precursors 3 and 5. From ester **18** (1.0 g, 3 mmol) and following the standard protocol (reduction with DIBALH) and after flash chromatography (hexane/EtOAc, 4:1) compound **19** (750 mg, 80%) was obtained: Oil; $[\alpha]_D^{25}$ +21° (*c* 0.71, $CHCl_3$); IR (film) ν : 2990, 2940, 1725, 1380, 1375, 1210, 1165, 1080, 1020, 850 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.79 (t, J=1.1 Hz, 1H, H7), 5.92 (d, J=3.4 Hz, 2H, H1, H3), 4.64 (d, $J_{1,2}$=3.4 Hz, 1H, H2), 4.37 (ddd, $J_{3,4}$=2.8 Hz, $J_{4,5}$=5.6 Hz, $J_{4,5'}$=8.0 Hz, 1H, H4), 2.70-2.55 (m, 2H, 2H6), 2.59 (s, 3H, $OC(S)SCH_3$), 2.10-2.09 (m, 2H, 2H5), 1.52, 1.31 (s, s; 3H, 3H); MS (70 eV) *m/z*: 273 (11), 259 (8), 248 (4), 231 (5), 203 (9), 191 (17), 155 (10), 140 (45), 133 (10), 111 (58), 91 (73), 83 (66), 57 (79), 43 (100). Anal. Calcd. for $C_{12}H_{18}S_2O_5$: C, 47.06; H, 5.92; S, 20.92. Found: C, 47.14; H, 6.10; S, 20.70.

From this aldehyde (321 mg, 1.05 mmol), after Wittig reaction and chromatography (hexane/EtOAc, 4:1) precursor **3** (335 mg, 87%) was prepared: Oil; $[\alpha]_D^{25}$ +9° (*c* 0.52, $CHCl_3$); IR (film) ν : 2990, 2950, 1725, 1660, 1440, 1385, 1380, 1225, 1200, 1170, 1050, 850 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (major isomer E): 6.95 (dt, $J_{7,8}$=15.7 Hz, $J_{7,6}$=7.0 Hz, 1H, H7), 5.93 (d, $J_{1,2}$=3.9 Hz, 1H, H1), 5.89 (d, $J_{3,4}$=2.4 Hz, 1H, H3), 5.85 (dt, $J_{7,8}$=15.7 Hz, $J_{8,6}$=1.5 Hz, 1H, H8), 4.64 (d, $J_{1,2}$=3.9 Hz, 1H, H2), 4.34 (ddd, $J_{3,4}$=2.8 Hz, $J_{4,5}$=5.8 Hz, $J_{4,5'}$=7.9 Hz, 1H, H4), 3.72 (s, 3H, CO_2CH_3), 2.59 (s, 3H, $OC(S)SCH_3$), 2.50-2.15 (m, 2H, 2H6), 2.00-1.70 (m, 2H, 2H5), 1.52, 1.32 (s, s; 3H, 3H); MS (70 eV) *m/z*: 347 (M^+-15, 2), 331 (15), 305 (13), 273 (2), 257 (6), 227 (5), 196 (22), 179 (15), 165 (47), 137 (17), 113 (100), 91 (82), 81 (51), 43 (29). Anal. Calcd. for $C_{15}H_{22}S_2O_6$: C, 49.72; H, 6.12; S, 17.69. Found: C, 49.64; H, 6.42; S, 17.20.

From aldehyde **19** (324 mg, 1.06 mmol) and following the general procedure the radical precursor **5** (390 mg, 94%; hexane/EtOAc, 9:1) was synthesized: Oil; $[\alpha]_D^{25}$ +1° (*c* 0.27, $CHCl_3$); IR (film) ν : 2990, 2950, 1710, 1650, 1440, 1380, 1375, 1260, 1200, 1160, 1070, 1020, 870 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.72 (tq, $J_{7,10}$=1.46 Hz, $J_{7,6}$=7.5 Hz, 1H, H7), 5.92 (d, $J_{1,2}$=3.8 Hz, 1H, H1), 5.88 (d, $J_{3,4}$=2.8 Hz, 1H, H3), 4.62 (d, $J_{1,2}$=3.8 Hz, 1H, H2), 4.32 (ddd, $J_{3,4}$=2.8 Hz, $J_{4,5}$=7.8 Hz, $J_{4,5'}$=5.8 Hz, 1H, H4), 4.16 (q, J=7.1 Hz, 2H, $CO_2CH_2CH_3$), 2.57 (s, 3H, $OC(S)SCH_3$), 2.40-2.20 (m, 2H, 2H6), 1.95-1.80 (m, 1H, H5), 1.78 (s, 3H, CH_3), 1.80-1.70 (m, 1H, H5'), 1.51, 1.31 (s, s; 3H, 3H), 1.27 (t, J=7.1 Hz, 3H, $CO_2CH_2CH_3$); MS (70 eV) *m/z*: 357 (1), 332 (3), 285 (4), 224 (16), 206 (15), 195 (9), 179 (29), 167 (13), 149 (24), 113 (28), 99 (49), 91 (92), 75 (64), 43 (100). Anal. Calcd. for $C_{17}H_{26}S_2O_6$: C, 49.72; H, 6.12; S, 17.69. Found: C, 49.64; H, 6.42; S, 17.20.

3-Deoxy-3-iodo-1,2-*O*-isopropylidene-α-D-*allo*-furanose (21). From iodide **20**[14] (2.34 g, 6.1 mmol) after mild acid hydrolysis according to the general procedure and chromatography (hexane/EtOAc, 1:1) iodide **21** (1.79, 83%) was obtained: mp 103-105°C $[\alpha]_D^{25}$ +76° (*c* 0.37, $CHCl_3$); IR (Nujol) ν : 3440, 3320, 2980, 2920, 1460, 1385, 1380, 1225, 1165, 1020, 870 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.82 (d,

$J_{1,2}$=3.5 Hz, 1H, H1), 4.62 (d, $J_{1,2}$=$J_{2,3}$=3.5 Hz, 1H, H2), 4.31 (dd, $J_{3,4}$=10.1 Hz, $J_{4,5}$=3.0 Hz, 1H, H4), 4.08 (m, 1H, H6), 3.92 (dd, $J_{3,4}$=10.1 Hz, $J_{3,2}$=3.5 Hz, 1H, H3), 3.90 (m, 1H, H6'), 3.78 (m, 1H, H5), 2.66 (br d, J=4.7 Hz, 1H, OH), 2.24 (br d, 1H, OH), 1.57, 1.38 (s, s; 3H, 3H); MS (70 eV) *m/z*: 330 (M^+-15, 24), 269 (100), 211 (13), 185 (90), 155 (4), 113 (13), 85 (25), 59 (55), 43 (99). Anal. Calcd. for $C_9H_{15}IO_5$: C, 32.74; H, 4.58; I, 38.44. Found: C, 33.00; H, 4.80; I, 38.20.

Radical Precursor (6). Starting from diol **21** (311 mg, 0.94 mmol) and following the general method for periodate cleavage, the corresponding aldehyde [flash chromatography (hexane/EtOAc, 4:6)] (245 mg, 87%) was obtained. Without further analysis, this aldehyde was inmediately dissolved in dry methylene chloride (7 mL), mixed with boron trifluoride etherate (1.23 mmol, 0.15 mL, 1.5 equiv), cooled at -78°C, and treated with allyltrimethylsilane (1.02 mmol, 0.16 mL, 1.25 equiv). After 3 h the mixture was warmed at room temperature and stirred for 1h 30 min. The reaction was quenched with aqueous saturated solution of sodium bicarbonate and extracted with methylene chloride; the organic extract was washed with brine, dried, concentrated and the residue purified by chromatography giving **6** (238 mg, 86%): Oil; IR (film) ν : 3450, 3070, 2990, 1640, 1385, 1370, 1230, 1160, 1100, 1005, 870 cm^{-1}; EM (70 eV) *m/z*: 341 (M^++1, 5), 324 (37), 299 (79), 269 (92), 211 (14), 185 (98), 155 (13), 113 (18), 59 (100), 43 (75). Anal. Calcd. for $C_{11}H_{17}IO_4$: C, 38.84; H, 5.03; I, 37.30. Found: C, 38.60; H, 5.32; I, 37.05.

3-*C*-Allyl-1,2-*O*-isopropylidene-α-D-*ribo*-furanose (23). Compound **22**[18] (349 mg, 1.52 mmol) was dissolved in methanol (8 mL), cooled in an ice bath, and treated with sodium borohydride (116 mg, 3.06 mmol). After 45 min the solvent was removed, the residue dissolved in methylene chloride and washed with brine. The organic layer was dried, evaporated and purified by chromatography (hexane/EtOAc, 1:4) giving compound **23** (3.2 mg, 87%): mp 70-73°C; $[\alpha]_D^{25}$ +48° (*c* 0.47, $CHCl_3$); IR (KBr) ν : 3470, 3250, 3080, 2990, 2970, 1643, 1380, 1375, 1225, 1115, 1040, 870 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.89 (m, 1H, C*H*=CH_2), 5.79 (d, $J_{1,2}$=3.8 Hz, 1H, H1), 5.20-5.10 (m, 2H, CH=CH_2), 4.31 (d, 1H, H2), 4.00-3.75 (m, 3H, H4, 2H5), 2.73 (br s, 1H, OH), 2.42 (dd, J=14.7 Hz, J=5.9 Hz, 1H, CH_2CH=CH_2), 2.13 (dd, J=14.7 Hz, J=8.0 Hz, 1H, CH_2CH=CH_2), 1.95 (br s, 1H, OH), 1.58, 1.35 (s, s; 3H, 3H; O-C(CH_3)$_2$-O); MS (70 eV) *m/z*: 215 (M^+-15, 7), 171 (4), 125 (15), 99 (77), 84 (59), 71 (76), 59 (65), 43 (100). Anal. Calcd. for $C_{11}H_{18}O_5$: C, 57.38; H, 7.88. Found: C, 57.40; H, 7.65.

3-*C*-Allyl-1,2-*O*-isopropylidene-5-*O*-methanosulphonyl-α-D-*ribo*-furanose (24). Compounds **23** (277 mg, 1.2 mmol) was dissolved in dry methylene chloride (7 mL), triethylamine (0.67 mL, 4.8 mmol, 4 equiv), and the mixture cooled at 0°C. Then, methanesulphonyl chloride (0.11 mL, 1.4 mmol, 1.2 equiv) was added dropwise. The mixture was stirred 30 min and quenched with water, extracted with methylene chloride; the organic phase was dried, concentrated and the residue purified by chromatography (hexane/EtOAc, 7:3) giving **24** (350 mg, 94%): mp 51-53°C; $[\alpha]_D^{25}$ +33° (*c* 0.63, $CHCl_3$); IR (KBr) ν : 3440, 3020, 2970, 1380, 1375, 1360, 1170, 990 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.87 (m, 1H, C*H*=CH_2), 5.75 (d, $J_{1,2}$=3.4 Hz, 1H, H1), 5.25-5.11 (m, 2H, CH=CH_2), 4.50-4.00 (m, 4H, H2, H4, 2H5), 3.07 (s, 3H, OSO_2CH_3), 2.74 (s, 1H, OH), 2.35 (dd, J=14.3 Hz, J=5.2 Hz, 1H, CH_2CH=CH_2), 2.15 (dd, J=14.3 Hz, J=7.6 Hz, 1H, CH_2CH=CH_2), 1.57, 1.35 (s, s; 3H, 3H; O-C(CH_3)$_2$-O); MS (70 eV) *m/z*: 309 (M^++1, 3), 293 (M^+-15, 19), 291 (14), 251 (40), 233 (43), 179 (18), 169 (42), 155 (23), 141 (25), 111 (35), 100 (100), 71 (50), 43 (71). Anal. Calcd. for $C_{12}H_{20}SO_7$: C, 46.75; H, 6.54; S, 10.38. Found: C, 46.41; H, 6.60; S, 10.25.

Radical Precursor (7). Compound **24** (288 mg, 0.93 mmol), dissolved in dry dimethylformamide (7 mL), was treated with sodium iodide (210 mg, 1.4 mmol) with stirring, at 60°C for 56 h. The mixture was cooled and the solvent removed under vacuum. The residue was dissolved in water and extracted several times; the combined organic phase was washed with brine, dried and evaporated. Flash chromatography (hexane/EtOAc, 7:3) gave **7** [150 mg, 16% (21%)] and unreacted **24** (70 mg). **7**: mp 128-131°C; $[\alpha]_D^{25}$ +27° (*c* 0.29, $CHCl_3$); IR (KBr) ν : 3450, 3020, 2980, 1642, 1380, 1220, 1010 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.83 (m, 1H, C*H*=CH_2), 5.75 (d, $J_{1,2}$=3.7 Hz, 1H, H1), 5.19-5.10 (m, 2H, CH=CH_2), 4.38 (d, 1H, H2), 4.06 (dd, $J_{4,5}$=1.9 Hz, $J_{4,5'}$=12.6 Hz, 1H, H4), 3.33 (dd, $J_{5,5'}$=12.6 Hz, 1H, H5), 3.16 (t, $J_{5,5'}$=$J_{4,5'}$=12.6 Hz, 1H, H5'), 2.72 (s, 1H, OH), 2.44 (dd, J=14.3 Hz, J=5.2 Hz, 1H,

$CH_2CH=CH_2$), 2.11 (dd, J=14.3 Hz, J=7.6 Hz, 1H, $CH_2CH=CH_2$), 1.58, 1.35 (s, s; 3H, 3H; O-$C(CH_3)_2$-O); MS (70 eV) *m/z*: 325 (M^+-15, 3), 283 (4), 265 (6), 223 (2), 195 (2), 169 (17), 155 (19), 127 (11), 111 (59), 69 (100), 43 (68). Anal. Calcd. for $C_{11}H_{17}IO_4$: C, 38.83; H, 5.03. Found: C, 38.75; H, 4.87.

3-*C*-Ethynyl-1,2-*O*-isopropylidene-α-D-*allo*-furanose (25). Compound **25**[19] (525 mg, 1.83 mmol) was selectively hydrolyzed in the standard mild acid conditions; after flash chromatography (AcOEt), triol **26** (435 mg, 99%) was isolated: mp 95-97°C; $[\alpha]_D^{25}$ +30° (*c* 0.51, $CHCl_3$); IR (KBr) ν: 3450, 3260, 3080, 3060, 3030, 2940, 2120, 1460, 1380, 1375, 1110, 1040, 875 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.84 (d, $J_{1,2}$=3.6 Hz, 1H, H1), 4.61 (d, 1H, H2), 4.12-4.07 (m, 1H, H5), 3.88 (d, $J_{4,5}$=8.6 Hz, 1H, H4), 3.87 (m, 1H, H6), 3.75 (dd, $J_{5,6'}$=4.8 Hz, $J_{6,6'}$=11.7 Hz, 1H, H6'), 2.70 (s, 1H, C=CH), 2.35, 2.08 (s, s; 1H, 1H; OH, OH), 1.59, 1.37 [s, s; 3H, 3H; O-$C(CH_3)_2$-O]; MS (70 eV) *m/z*: 229 (M^+-15, 4), 187 (2), 155 (7), 149 (5), 128 (4), 109 (16), 97 (69), 59 (100), 43 (44). Anal. Calcd. for $C_{11}H_{16}O_6$: C, 54.09; H, 6.60. Found: C, 54.38; H, 6.90.

3,5-Di-*O*-acetyl-3-*C*-ethynyl-1,2-*O*-isopropylidene-6-*O*-*p*-toluenesulphonyl-α-D-*allo*-furanose (28). Compound **26** (317 mg, 1.3 mmol), was dissolved in dry pyridine (7 mL), cooled at 0°C and tosyl chloride (462 mg, 2.4 mmol, 1.9 equiv) was added slowly; after 1 h the mixture was warmed at room temperature and stirred for 6 h. Then, the mixture was cooled with an excess of acetic anhydride (6 mL). After overnight at room temperature, was processed as usual. Flash chromatography (hexane/EtOAc, 7:3) gave **28** (567 mg, 84%): Oil; $[\alpha]_D^{25}$ +36° (*c* 0.63, $CHCl_3$); IR (film) ν : 3270, 2980, 2940, 2120, 1755, 1600, 1380, 1230, 1170, 1080, 920 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, J=8.4 Hz, 2H, aromatic), 7.34 (d, J=8.4 Hz, 2H, aromatic), 5.79 (d, $J_{1,2}$=3.6 Hz, 1H, H1), 5.29 (ddd, $J_{5,6}$=2.2 Hz, $J_{5,6'}$=4.0 Hz, $J_{4,5}$=8.6 Hz, 1H, H5), 5.13 (d, 1H, H2), 4.41 (dd, $J_{6,6'}$=11.2 Hz, $J_{6,5}$=2.2 Hz, 1H, H6), 4.33 (d, 1H, H4), 4.18 (dd, 1H, H6'), 2.62 (s, 1H, C=CH), 2.45 (s, 3H, $CH_3C_6H_4SO_2$), 2.11, 2.04 (s, s; 3H, 3H; 2 $OCOCH_3$), 1.53, 1.34 (s, s; 3H, 3H; 2 O-$C(CH_3)_2$-O); MS (70 eV) *m/z*: 467 (M^+-15, 2), 366 (15), 329 (6), 287 (3), 193 (3), 155 (14), 152 (11), 139 (10), 115 (15), 110 (14), 91 (23), 43 (100). Anal. Calcd. for $C_{22}H_{26}SO_{10}$: C, 53.05; H, 5.26; S, 6.42. Found: C, 52.90; H, 5.30; S, 6.12.

Radical Precursor (8). Compound **28** (567 mg, 1.1 mmol) dissolved in dimethylformamide (6 mL) was treated with sodium iodide (825 mg, 5.5 mmol, 5 equiv) at 80°C for 6 h. The solvent was removed in vacuo and the residue dissolved in methylene chloride, washed with brine, dried, concentrated and purified (flash chromatography: hexane/EtOAc, 4:1) giving **8** (359 mg, 79%): mp 123-125°C; $[\alpha]_D^{25}$ +13° (*c* 1.7, $CHCl_3$); IR (KBr) ν : 3275, 2990, 2940, 2120, 1755, 1380, 1240, 1170, 1075, 870 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.85 (d, $J_{1,2}$=3.7 Hz, 1H, H1), 5.17 (d, 1H, H2), 4.90 (ddd, $J_{5,6}$=3.2 Hz, $J_{5,6'}$=4.3 Hz, $J_{5,4}$=8.6 Hz, 1H, H5), 4.27 (d, 1H, H4), 3.64 (dd, $J_{6,6'}$=11.3 Hz, 1H, H6), 3.49 (dd, 1H, H6'), 2.69 (s, 1H, C=CH), 2.13, 2.12 (s, s; 3H, 3H; 2 $OCOCH_3$), 1.57, 1.34 [s, s; 3H, 3H; O-$C(CH_3)_2$-O]; MS (70 eV) *m/z*: 423 (M^+-15, 2), 322 (7), 311 (5), 153 (4), 101 (3), 93 (5), 53 (6), 43 (100). Anal. Calcd. for $C_{15}H_{19}IO_7$: C, 41.11; H, 4.37. Found: C, 41.03; H, 4.60.

1,2-*O*-Isopropylidene-3-*C*-vinyl-α-D-*allo*-furanose (30). The crude **29**[21] [obtained from **25** (1.8 g, 6.33 mmol) after $LiAlH_4$ reduction] was submitted to acid hydrolysis in the usual conditions, to give, after flash chromatography (AcOEt), **30** (1.3 g, 83% yield from **25**): mp 156-158°C; $[\alpha]_D^{25}$ -11° (*c* 0.17, $CHCl_3$); IR (KBr) ν : 3600-3100, 3100, 2990, 2940, 1430, 1380, 1375, 1220, 1100, 1020, 880 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.91 (dd, $J_{7,8}$=10.98 Hz, $J_{7,8'}$=17.3 Hz, 1H, H7), 5.79 (d, $J_{1,2}$=3.7 Hz, 1H, H1), 5.62 (dd, $J_{8,8'}$=1.4 Hz, 1H, H8'), 5.39 (dd, 1H, H8), 4.24 (d, 1H, H2), 3.87 (d, $J_{4,5}$=8.4 Hz, 1H, H4), 3.78 (m, 2H, H6, H5), 3.66 (dd, $J_{5,6'}$=5.6 Hz, $J_{6,6'}$=12.4 Hz, 1H, H6'), 3.34 (br s, 1H, OH), 2.95-2.70 (br s, 2H, OH), 1.61, 1.35 (s, s; 3H, 3H; O-$C(CH_3)_2$-O); MS (70 eV) *m/z*: 247 (M^++1, 1), 231 (M^+-15, 2), 185 (2), 171 (3), 153 (4), 130 (4), 111 (12), 98 (72), 85 (18), 71 (38), 59 (81), 100 (43). Anal. Calcd. for $C_{11}H_{18}O_6$: C, 53.64; H, 7.37. Found: C, 53.64; H, 7.37.

Radical Precursor 9 and Compound 31. Compound **30** (1.3 g, 5.5 mmol) was dissolved in dry methylene chloride, triphenylphosphine (2.29 g, 8.8 mmol, 1.6 equiv) was added and the mixture cooled

in an ice bath; then, carbon tetrabromide (2.91 g, 8.8 mmol, 1.6 equiv) was slowly added. After 31 h at room temperature, the reaction was acetylated under the standard conditions (36 h, r.t.) to give, after flash chromatography (hexane/EtOAc, 85:15) **31** (224 mg, 10% yield) and **9** (465 mg, 24%). **31**: Oil; $[\alpha]_D^{25}$ -17° (*c* 1.3, $CHCl_3$); IR (KBr) ν : 2990, 1750, 1430, 1375, 1230, 1115, 1020, 870 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.23 (s, 1H, H1), 5.99 (dd, $J_{7,8}$=17.0 Hz, $J_{7,8'}$=10.7 Hz, 1H, H7), 5.49 (dd, $J_{8,8'}$=1.4 Hz, 1H, H8), 5.21 (dd, 1H, H8'), 4.96 (ddd, $J_{5,6}$=3.0 Hz, $J_{5,6'}$=4.0 Hz, $J_{5,4}$=10.3 Hz, 1H, H5), 4.42 (s, 1H, H2), 4.40 (d, 1H, H4), 3.66 (dd, $J_{6,6'}$=11.4 Hz, 1H, H6), 3.53 (dd, 1H, H6'), 2.12, 2.03 (s, s; 3H, 3H; 2 $OCOCH_3$), 1.56, 1.34 [s, s; 3H, 3H; O-C$(CH_3)_2$-O]; MS (70 eV) *m/z*: 379, 377 (M^+-15; 1, 1), 335, 333 (8, 8), 239, 237 (8, 8), 197, 195 (2, 2), 140 (8), 101 (12), 98 (21), 55 (12), 43 (100). Anal. Calcd. for $C_{15}H_{21}BrO_7$: C, 45.81; H, 5.38. Found: C, 46.00; H, 5.60. **9**: mp 48-51°C; $[\alpha]_D^{25}$ +38° (*c* 0.37, $CHCl_3$); IR (KBr) ν : 3480, 3040, 2990, 2950, 1740, 1635, 1380, 1255, 1225, 1110, 1005, 980 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.79 (m, 2H, H1, H7), 5.48 (d, $J_{7,8}$=17.18 Hz, 1H, H8), 5.33 (d, $J_{7,8'}$=9.5 Hz, 1H, H8'), 4.97 (ddd, $J_{5,4}$=8.7 Hz, $J_{5,6}$=3.6 Hz, $J_{5,6'}$=4.2 Hz, 1H, H5), 4.24 (d, $J_{1,2}$=3.6 Hz, 1H, H2), 4.13 (d, 1H, H4), 3.71 (dd, $J_{6,6'}$=11.3 Hz, 1H, H6), 3.59 (dd, 1H, H6'), 2.78 (br s, 1H, OH), 2.08 (s, 3H, $OCOCH_3$), 1.62, 1.37 [s, s; 3H, 3H; O-C$(CH_3)_2$-O]; MS (70 eV) *m/z*: 337, 335 (M^+-15; 2, 2), 271 (2), 195 (6), 155 (6), 112 (9), 98 (62), 71 (13), 43 (100). Anal. Calcd. for $C_{13}H_{19}BrO_6$: C, 44.36; H, 5.45. Found: C, 44.30; H, 5.70.

1,2-*O*-Isopropylidene-6-*O*-*p*-toluenesulphonyl-3-*C*-vinyl-α-D-*allo*-furanose (32). A solution of compound **30** (227, 0.92 mmol) in dry pyridine (8 mL) was cooled at 0°C and treated with tosyl chloride (228, 1.1 mmol, 1.3 equiv). After 22 h at r.t., the solvent was removed and the residue dissolved in methylene chloride, washed with brine, dried, evaporated and submitted to chromatography (hexane/EtOAc, 60:40) to give **32** (222 mg, 61%): Oil; $[\alpha]_D^{25}$ +28° (*c* 0.56, $CHCl_3$); IR (film) ν : 3600-3200, 3080, 2990, 1600, 1370, 1190, 1100, 920 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.79 (d, *J*=8 Hz, 2H, aromatic), 7.33 (d, 2H, aromatic), 5.82 (dd, $J_{7,8}$=17.3 Hz, $J_{7,8'}$=10.6 Hz, 1H, H7), 5.74 (d, $J_{1,2}$=3.7 Hz, 1H, H1), 5.59 (dd, $J_{8,8'}$=1.8 Hz, 1H, H8), 5.38 (dd, 1H, H8'), 4.25-4.22 (m, 2H, H2, H5), 4.10-3.90 (m, 2H, 2H6), 3.76 (d, $J_{4,5}$=8.9 Hz, 1H, H4), 3.01 (br s, 1H, OH), 2.56 (br s, 1H, OH), 2.44 (s, 3H, $CH_3C_6H_4SO_2$), 1.57, 1.34 (s, s; 3H, 3H; 2 O-C$(CH_3)_2$-O). MS (70 eV) *m/z*: 343 (7), 245 (24), 173 (38), 155 (35), 112 (25), 98 (100), 71 (24), 59 (51). Anal. Calcd. for $C_{18}H_{24}SO_8$: C, 53.99; H, 6.04; S, 8.01. Found: C, 53.80; H, 5.99; S, 7.80.

3,5-Di-*O*-acetyl-1,2-*O*-isopropylidene-6-*O*-*p*-toluenesulphonyl-3-*C*-vinyl-α-D-*allo*-furanose(33). Compound **32** (707 mg, 1.77 mmol) was acetylated (60°C; 36 h) under the standard conditions. After flash chromatography (hexane/EtOAc, 7:3) diacetate **33** (419 mg, 49%) was isolated: Oil; $[\alpha]_D^{25}$ +63° (*c* 1.1, $CHCl_3$); IR (film) ν : 3080, 2990, 1750, 1600, 1370, 1240, 1180, 1040, 870 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.77, 7.34 (d, d; *J*=8 Hz, 2H, 2H; aromatic), 5.74 (d, $J_{1,2}$=3.7 Hz, 1H, H1), 5.65 (dd, $J_{7,8}$=11.4 Hz, $J_{7,8'}$=17.7 Hz, 1H, H7), 5.32 (d, 1H, H8), 5.00 (d, 1H, H2), 5.05-4.99 (m, 2H, H5, H8'), 4.29 (d, $J_{4,5}$=8.9 Hz, 1H, H4), 4.28 (dd, $J_{6,6'}$=11.2 Hz, $J_{6,5}$=2.4 Hz, 1H, H6), 4.11 (dd, $J_{6,5'}$=4.8 Hz, 1H, H6'), 2.45 (s, 3H, $CH_3C_6H_4SO_2$), 2.09, 2.04 (s, s; 3H, 3H; 2 $OCOCH_3$), 1.54, 1.33 (s, s; 3H, 3H; 2 O-C$(CH_3)_2$-O). Anal. Calcd. for $C_{22}H_{28}SO_{10}$: C, 54.53; H, 5.82; S, 6.62. Found: C, 54.34; H, 5.70; S, 6.45.

6-Deoxy-3,5-di-*O*-acetyl-6-iodo-1,2-*O*-isopropylidene-3-*C*-vinyl-α-D-*allo*-furanose (34). Compound **33** (396 mg, 0.89 mmol) was dissolved in dry DMF (7 mL) and treated with sodium iodide (1.34 g, 8.9 mmol, 10 equiv) at 80°C for 30 h. The solvent was removed and the residue dissolved in methylene chloride and washed with brine, dried, evaporated and purified by chromatography (hexane/EtOAc, 7:3) giving **34** (58 mg, 14%): mp 138-141°C; $[\alpha]_D^{25}$ +54° (*c* 0.11, $CHCl_3$); IR (KBr) ν : 3080, 2990, 1750, 1740, 1380, 1245, 1020, 870 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.79 (d, $J_{1,2}$=3.9 Hz, 1H, H1), 5.72 (dd, $J_{7,8}$=11.4 Hz, $J_{7,8'}$=17.7 Hz, 1H, H7), 5.35 (d, 1H, H8), 5.00 (d, 1H, H8'), 5.04 (d, 1H, H2), 4.62 (ddd, $J_{5,6}$=3.2 Hz, $J_{5,6'}$=5.1 Hz, $J_{5,4}$=8.7 Hz, 1H, H5), 4.24 (d, 1H, H4), 3.53 (dd, $J_{6,6'}$=11.2 Hz, 1H, H6), 3.39 (dd, 1H, H6'); MS (70 eV) *m/z*: 383 (M^+-15, 1), 324 (13), 285 (12), 263 (4), 243 (7), 222 (6), 155 (11), 140 (10), 98 (34), 59 (15), 43 (100). Anal. Calcd. for $C_{13}H_{19}IO_6$: C, 39.21; H, 4.80. Found: C, 39.10; H, 4.65.

Free Radical Cyclization of Precursor 1. Compound **1** (900 mg, 2.08 mmol) in the usual carbocyclization conditions (addition in 3h) and after flash chromatography (hexane/EtOAc, 9:1) gave pure major **35** (C7 *S*) (289 mg, 45%): Oil; $[\alpha]_D^{25}$ +13° (*c* 2.1, $CHCl_3$); IR (film) ν : 3450, 3250, 3090, 3080, 3015, 2960, 2870, 1500, 1465, 1380, 1375, 1250, 1220, 1165, 1060, 1030 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) (see Table 1); ^{13}C NMR (50 MHz, $CDCl_3$) (see Table 1); MS (70 eV) *m/z*: 290 (M^+-15, 2), 247 (4), 156 (10), 110 (4), 107 (5), 91 (100), 67 (12), 43 (12). Anal. Calcd. for $C_{17}H_{23}NO_4$: C, 66.86; H, 7.59; N, 4.59. Found: C, 66.59; H, 7.81; N, 4.80.

Free Radical Cyclization of Precursor 2: Compound **2** (1.0 g, 2.6 mmol), after standard methodology (addition in 5 h 30 min) and flash chromatography (hexane/EtOAc, 9:1) gave **36** (591, 88%): Oil; $[\alpha]_D^{25}$ +11° (*c* 0.95, $CHCl_3$); IR (film) ν : 2995, 2960, 1740, 1460, 1440, 1385, 1375, 1250, 1220, 1170, 1065 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) (see Table 2); ^{13}C NMR (50 MHz, $CDCl_3$) (see Table 2); MS (70 eV) *m/z*: 241 (M^+-15, 96), 209 (31), 199 (34), 181 (11), 167 (79), 149 (40), 139 (17), 121 (41), 111 (15), 105 (16), 93 (41), 79 (46), 59 (37), 43 (100). Anal. Calcd. for $C_{13}H_{20}O_5$: C, 60.92; H, 7.87. Found: C, 61.14; H, 8.10.

Free Radical Cyclization of Precursor 4: Starting from **4** (537 mg, 1.3 mmol) and following the standard method (addition in 6 h 30 min), after chromatography (hexane/EtOAc, 9:1). Compound **37** (291 mg, 76%) was isolated: Oil; IR (KBr) ν : 2990, 2920, 1735, 1465, 1380, 1375, 1250, 1220, 1180, 1165, 1065, 1030, 870 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) (see text); ^{13}C NMR (50 MHz, $CDCl_3$) (see text); MS (70 eV) *m/z*: 269 (M^+-15, 41), 227 (21), 223 (30), 209 (11), 181 (76), 163 (22), 153 (12), 135 (34), 125 (15), 107 (53), 95 (56), 79 (34), 67 (42), 43 (100). Anal. Calcd. for $C_{15}H_{24}O_5$: C, 63.36; H, 8.51. Found: C, 63.40; H, 8.67.

Free Radical Cyclization of Precursor 6: Starting from alcohol **6** (as a mixture of C5 isomers in ratio 1:3) (180 mg, 0.53 mmol) and following the usual method (addition in 7 h), after chromatography (hexane/EtOAc, 7:1), we have isolated **38** (15 mg) **38** + **39** (20 mg) and **39** (39 mg). Total: 74 mg (64% yield). **38:** Oil; $[\alpha]_D^{25}$ +40° (*c* 3.9, $CHCl_3$); IR (film) ν : 3460, 2970, 1455, 1410, 1380, 1375, 1220, 1170, 1080, 870 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) (see Table 3); ^{13}C NMR (50 MHz, $CDCl_3$) (see Table 2); MS (70 eV) *m/z*: 214 (M^+, 26), 199 (100), 185 (3), 157 (7), 139 (4). Anal. Calcd. for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47. Found: C, 61.36; H, 8.81. **39:** Oil; $[\alpha]_D^{25}$ +9° (*c* 2.2, $CHCl_3$); IR (film) ν : 3470, 2975, 1455, 1415, 1380, 1375, 1240, 1215, 1105, 870 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) (see Table 3); ^{13}C NMR (50 MHz, $CDCl_3$) (see Table 3); MS (70 eV) *m/z*: 215 (M^++1, 12), 214 (M^+, 12), 199 (100), 157 (24), 139 (18), 121 (14), 109 (16), 81 (73), 58 (36), 43 (69). Anal. Calcd. for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47. Found: C, 61.89; H, 8.25.

Free Radical Cyclization of Precursor 7. In the usual free radical cyclization conditions (addition in 6 h) precursor **7** (102 mg, 0.29 mmol), after flash chromatography (hexane/EtOAc, 4:1), gave **41** [C8(*S*) 14 mg], **41** [*S*+*R*] and **42** (20 mg). Total: 34 mg (55% yield): **41** [C8(*S*)]: mp 85-87°C; $[\alpha]_D^{25}$ +83° (*c* 0.18, $CHCl_3$); IR (KBr) ν : 3495, 2950, 1460, 1380, 1375, 1260, 1210, 1170, 1110-1010, 870 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.85 (d, $J_{1,2}$=4.0 Hz, 1H, H1), 4.31 (d, 1H, H2), 4.19 (br d, $J_{4,5ax}$=1.7 Hz, $J_{4,5eq}$=6.0 Hz, 1H, H4), 2.73 (1H, OH), 2.52 (m, 1H, H6), 2.24 (m, $J_{5eq,5ax}$=14.6 Hz, $J_{5eq,6}$=9.3 Hz, $J_{5e,7e}$=1.1 Hz, 1H, H5eq), 1.93 (br dd, $J_{7eq,7ax}$=13.4 Hz, $J_{7eq,6}$=6.6 Hz, $J_{7eq,4}$=1.6 Hz, 1H, H7eq), 1.59 (s, 3H), 1.38 (s, 3H), 1.37 (m, $J_{5ax,6}$=7.7 Hz, 1H, H5ax), 1.38 (s, 3H), 1.25 (m, $J_{7ax,6}$=10.9 Hz, 1H, H7ax), 1.07 [d, *J*=6.8 Hz, 3H, CH_3(C8)]; ^{13}C NMR (50 MHz, $CDCl_3$) δ 111.96 (C9), 105.72 (C1), 88.11 (C3), 87.74, 81.13 (C2, C4), 42.96, 38.24 (C5, C7), 33.68 (C6), 26.87, 26.71 (C10, C11), 21.07 (C8); MS (70 eV) *m/z*: 199 (M^+-15, 31), 181 (5), 156 (57), 139 (65), 128 (10), 98 (100), 59 (55), 43 (97). Anal. Calcd. for $C_{11}H_{18}O_4$: C, 61.66; H, 8.46. Found: C, 61.73; H, 8.70.

Free Radical Cyclization of Precursor 8. Precursor **8** (359 mg, 0.82 mmol) in the usual conditions (addition in 5 h), after flash chromatography (hexane/EtOAc, 9:1), gave an unseparable mixture of **43** + **44** (178 mg, 69%): Oil; IR (film) ν :2990, 1750, 1650, 1445, 1380, 1240, 1080, 1040, 870 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) (see text); MS (70 eV) *m/z*: 297 (M^+-15, 5), 255 (6), 210 (3), 196 (27), 181 (2), 154

(58), 136 (43), 112 (12), 94 (100), 43 (93). Anal. Calcd. for $C_{15}H_{20}O_7$: C, 57.68; H, 6,46. Found: C, 57.45; H, 6.50.

Free Radical Cyclization of Precursor 9. Precursor **9** (158 mg, 0.45 mmol) was submitted to cyclization following the standard conditions (addition in 6 h). After chromatography (hexane/EtOAc, 9:1) compound **45** (38 mg, 31%) was obtained. This product was impurified with some minor unidentified material and was characterized as the peracetate **46** [obtained by treatment with acetic anhydride, pyridine, 60°C, 24 h, and standard work-up; after flash chromatography (hexane/EtOAc, 9:1) 19 mg (43 % yield) was obtained]: Oil; IR (film) ν : 2970, 1745, 1460, 1380, 1240, 1050, 880 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) (see text); ^{13}C NMR (50 MHz, $CDCl_3$) δ (major isomer) 170.56, 169.56 ($OCOCH_3$), 113.45 (C9), 106.57 (C1), 92.33 (C3), 85.12, 90.05, 72.13 (C2, C4, C5), 36.92 (C7), 36.40 (C6), 27.25, 26.98 (C10, C11), 20.92, 20.84 ($OCOCH_3$), 16.07 (C8); MS (70 eV) *m/z*: 299 (M^+-15, 4), 257 (10), 214 (5), 197 (6), 179 (4), 154 (18), 137 (13), 100 (24), 71 (31), 43 (10). Anal. Calcd. for $C_{15}H_{22}O_7$: C, 57.31; H, 7.05. Found: C, 57.60; H, 6.99.

5-Bromo-5-deoxy-2,3-*O*-isopropylidene-D-ribose *O*-Benzyl Oxime (48). Compound **50**[2,32] (200 mg, 0.79 mmol) was dissolved in methylene chloride (10 mL) and treated with *O*-benzyl hydroxylamine hydrochloride (18.9 mg, 1.18 mmol, 1.5 equiv), pyridine (0.2 mL) and water (25 drops). After 18 h at reflux, the mixture was diluted with methylene chloride and washed with brine, dried (Na_2SO_4), evaporated and purified by chromatography (hexane(EtOAc, 9:4) giving **53** (267 mg, 95%): Oil; IR (film) ν : 3480, 3090, 3060, 3030, 2990, 2940, 2040, 2880, 1495, 1455, 1380, 1370, 1245, 1220, 1165, 1065, 1020, 990, 925, 865, 800, 750, 735, 700 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ: 7.50 (d, J=7.5 Hz, 1H, H1 *anti*), 7.40-7.27 (m, 5H, aromatic), 6.85 (d, J=6 Hz, 1H, H1 *syn*), 5.30 (t, J=6 Hz, 1H, H2 *syn*), 5.15 (s, 2H, OCH_2Ph), 4.80 (t, J=6 Hz, 1H, H2 *anti*), 4.25 (t, J=6 Hz, 1H, H3 *syn*), 4.10 (dd, J=6 y 7.5 Hz, 1H, H3 *anti*), 3.70-3.40 (m, 3H, 2H5, H4), 2.80 (d, J=4.5 Hz, 1H, OH *syn*), 2.50 (d, J=4.5 Hz, 1H, OH *anti*), 1.45, 1.35 (s, s, CH_3). Anal. Calcd. for $C_{15}H_{20}NO_4$: C, 50.28; H, 5.58; N, 3.91. Found: C, 52.50; H, 6.24; N, 5.10.

(1*R*, 2*R*, 3*S*, 4*R*)-4-Benzyloxyamino-2,3-*O*-isopropylidene-1,2,3-cyclopentane triol (51). Compound **48** (2.3 g, 6.42 mmol), submitted to cyclization in the usual conditions (addition in 4 h and refluxing 2 h more), after flash chromatography (hexane/EtOAc, 1:1), gave **51** (1.3 g, 75 %): mp 40-42°C; $[\alpha]_D^{25}$ +4.8° (*c* 3.6, $CHCl_3$); IR (KBr) ν : 3600-3300, 3250, 3080, 3050, 3020, 2990, 1495, 1455, 1375, 1270, 1210, 1165, 1080, 1055, 870 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.19 (ddd, $J_{1,2}$=5.2 Hz, $J_{1,5\beta}$=7.6 Hz, $J_{1,5\alpha}$=8.0 Hz, 1H, H1), 4.39 (t, $J_{1,2}$=5.2 Hz, $J_{2,3}$=5.2 Hz, 1H, H2), 4.35 (d, $J_{2,3}$=5.2 Hz, 1H, H3), 3.42 (dd, $J_{4,5\beta}$=3.7 Hz, $J_{4,5\alpha}$=4.2 Hz, 1H, H4), 1.81 (m, 2H, 2H5); ^{13}C NMR (20 MHz, $CDCl_3$) δ 137.50, 128.61, 128.50, 127.89 (Aromatic), 111.03 (C7), 82.27, 78.88, 71.74 (C2, C3, C4), 76.72 (C6), 62.95 (C1), 35.87 (C5), 25.99, 24.31 (C8, C9); MS (70 eV) *m/z*: 279 (M^+), 269 (6), 268 (2), 267 (4), 266 (1), 265 (2), 213 (2), 211 (2), 177 (2), 155 (3), 91 (100), 84 (10), 51 (11), 41 (11). Anal. Calcd. for $C_{15}H_{21}NO_4$: C, 64.51; H, 7.52; N, 5.01. Found: C, 63.06; H, 8.06; N, 5.15.

5-Deoxy-5-iodo-2,3-*O*-isopropylidene-5-α-D-ribonolactone (53). Compound **52**[33] (1 g, 5.3 mmol) was dissolved in dry methylene chloride (20 mL) and treated with triphenylphosphine (2.79 g, 10.6 mmol, 2 equiv) and pyridine (2 mL). The mixture was cooled in an ice bath and iodine (2.69 g, 10.6 mmol, 2 equiv) was slowly added in small portions. After the addition the mixture was stirred at 5°C for 17 h. The reaction was quenched with water and the organic phase washed with 10% aqueous sodium thiosulfate solution, brine, dried and evaporated. Purification by flash chromatography (hexane/EtOAc, 7:3) gave **53**: mp 93-95°C; $[\alpha]_D^{25}$ -31° (*c* 0.9, $CHCl_3$); IR (KBr) ν : 3600-3100, 3040, 2995, 1730, 1375, 1345, 1275, 1190, 1075, 970 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 5.00 (d, J=6 Hz, 1H, H-2), 4.65 (m, 2H, H3, H4), 3.35 (d, J=4.5 Hz, 2H, CH_2I), 1.50, 1.39 (s, s, CH_3); Anal. Calcd. for $C_8H_{11}IO_4$: C, 32.21; H, 3.65. Found: C, 32.51; H, 3.69.

5-Deoxy-5-iodo-2,3-*O*-isopropylidene-D-ribofuranose (54). Product **53** (596 mg, 2 mmol) was dissolved in dry toluene, cooled at -78°C, and under argon and stirring was treated with DIBALH (1.7 mL,

2.4 mmol, 1.2 equiv, 1.5 M in hexane). After 1h methanol was added and the mixture warmed at r.t. The salts were filtered over Celite 545, washed and the solvent removed. Purification by flash chromatography (hexane/EtOAc, 3:2) gave **54** (456 mg, 77%): mp 83-86°C; $[\alpha]_D^{25}$ -29° (*c* 1.3, $CHCl_3$); IR (KBr) ν : 3390, 2950, 1430, 1380, 1375, 1250, 1215, 1165, 1070, 1015, 955, 870 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 5.55 (d, J=3 Hz, 1H, H-1ß), 4.85 (d, J=6 Hz, 1H, H-2), 4.78 (d, J=6 Hz, 1H, H-3), 4.40 (dd, J=7 and 9 Hz, 1H, H-4), 3.20 (m, 2H, 2H-5), 3.00 (d, J=3 Hz, 1H, OH), 1.50, 1.39 (s, s, CH_3); MS (70 eV) *m/z* 283 (M^+-15, 99), 85 (15), 69 (20), 43 (100). Anal. Calcd. for $C_8H_{13}IO_4$: C, 32.00; H, 4.33. Found: C, 32.10; H, 4.21.

5-Deoxy-5-iodo-2,3-*O*-isopropylidene-D-ribose *O*-benzyl Oxime (49). Following the same protocol for the preparation of compound **48**, compound **54** (365 mg, 1.22 mmol) was transformed into **49** (340 mg, 76%) (flash chromatography: hexane/EtOAc, 9:1): Oil; IR (film) ν : 3500, 3180, 3060, 3020, 2990, 1495, 1455, 1380, 1375, 1220, 1160, 1070, 1020, 815, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.46 (d, J=7.0 Hz, 1H, H1 *anti*), 7.40-7.27 (m, 5H, aromatic), 6.87 (d, J=5.8 Hz, 1H, H1 *syn*), 5.27 (t, J=6.0 Hz, 1H, H2 *syn*), 5.09 , 5.05 (s, s; 2H, 2H; OCH_2Ph *syn* and *anti*), 4.77 (dd, J=6 and 7 Hz, 1H, H2 *anti*), 4.18 (dd, J=7.7 and 6.3 Hz, 1H, H3 *syn*), 4.05 (dd, J=8.6 y 6.2 Hz, 1H, H3 *anti*), 3.50-3.05 (m, 3H, 2H5, H4), 1.88, 1.86 (s, s; 3H, 3H; 2 $OCOCH_3$), 1.46, 1.44, 1.35 (s, s, s; 3H, 3H, 3H; 3 CH_3). MS (70 eV) *m/z* [300]: 285 (M^+-15, 59), 196 (11), 127 (26), 115 (13), 98 (20), 69 (69), 59 (57), 43 (100). Anal. Calcd. for $C_{15}H_{20}INO_4$: C, 44.44; H, 4.93; N, 3.45. Found: C, 44.46; H, 4.50; N, 3.72.

(1*R*, 2*R*, 3*S*, 4*R*)-4-Amino-2,3-*O*-isopropylidene-1,2,3-cyclopentanetriol (55). Compound **48** (1.1 g, 4 mmol) was dissolved in dry tetrahydrofuran. Treated with lithium aluminium hydride (152 mg, 4 mmol, 1 equiv) and refluxed for 24 h. The usual work-up (quenching with water, 10% aqueous sodium hydroxide and water), filtration, evaporation and purification (CH_2Cl_2/MeOH, 4:1) gave **15** (285 mg, 40%): mp 47-49°C; $[\alpha]_D^{25}$ +33° (*c* 0.26, $CHCl_3$); IR (film) ν : 3600-3200, 2990, 2940, 1640, 1450, 1380, 1270, 1160, 1100, 1050, 870 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 4.60 (t, J=5.6 Hz, 1H, H3), 4.37 (dt, J=8.7 and 5.6 Hz, 1H, H4), 4.27 (d, J=5.6 Hz, 1H, H2), 3.39 (dd, J=2.4 and 4.5 Hz, 1H, H1), 1.89-1.80 (m, 2H, 2H5) 1.48, 1.34 (s, s; 3H, 3H; 2 CH_3). MS (70 eV) *m/z* [173]: 158 (M^+-15, 5), 115 (19), 98 (17), 72 (37), 43 (100). Anal. Calcd. for $C_8H_{15}NO_3$: C, 55.49; H, 8.67; N, 8.09. Found: C, 52.99; H, 9.07; N, 7.89.

(1*R*, 2*R*, 3*S*, 4*R*)-4-Acetamido-1-*O*-acetyl-2,3-*O*-isopropylidene-1,2,3-cyclopentanetriol (56). From aminoalcohol **55** (60 mg, 0.34 mmol) and following the standard acetylation conditions (24 h, r.t.), after flash chromatography (CH_2Cl_2/MeOH, 19:1) compound **56** (40 mg, 41%) was obtained: mp 187-190°C; $[\alpha]_D^{25}$ +79° (*c* 0.3, $CHCl_3$); IR (film) ν : 3600-3300, 3280, 3090, 2940, 1735, 1650, 1565, 1375, 1255, 1210, 1170, 1080, 1060, 990, 875 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 5.98 (d, J=5.5 Hz, 1H, N*H*Ac), 5.02 (qt, J=5.3, 1H, H4), 4.70 (t, J=5.3 Hz, 1H, H3), 4.49 (d, J=5.5 Hz, 1H, H2), 4.11 (t, J=6.1 Hz, 1H, H1), 2.27 (ddd, J=13.3, 11 and 6.4 Hz, 1H, H5), 2.13 (s, 3H, $OCOCH_3$), 1.98 (s, 3H, $OCOCH_3$), 1.95 (m, 1H, H5), 1.48, 1.29 (s, s; 3H, 3H; 2 CH_3). MS (70 eV) *m/z* [257]: 242 (M^+-15, 11), 199 (6), 157 (3), 140 (22), 98 (17), 85 (23), 60 (11), 43 (100). Anal. Calcd. for $C_{12}H_{19}NO_5$: C, 56.02; H, 7.44; N, 5.44. Found: C, 55.94; H, 7.31; N, 5.49.

Synthesis of Aminoalcohol 57. Compound **55** (285 mg, 1.6 mmol) was treated with 2-amino-4,6-dichloropyrimidine (360 mg, 2.2 mmol, 1.4 equiv), triethylamine (7 mL) in *i*-butanol (10 mL) at reflux for 30 h. The mixture was evaporated and the residue submitted to chromatography (EtOAc) giving nucleoside **57** (117 mg, 20%): mp 61-63°C; $[\alpha]_D^{25}$ +24° (*c* 0.15, $CHCl_3$); IR (KBr) ν : 3600-3100, 2980, 2940, 1620, 1580, 1470, 1380, 1210, 1050 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ: 5.87 (1H, H9), 5.27 (br s, 2H, NH_2), 5.08 (d, J=5.4 Hz, 1H, NH), 4.55 (t, $J_{3,2}$=$J_{2,1}$=5.4 Hz, 1H, H2), 4.46 (d, 1H, H3), 4.22 (m, 1H, H1), 3.94 (m, 1H, H4), 2.25-2.00 (m, 1H, H5), 2.00-1.80 (m, 1H), 1.51, 1.35 (s, s; 3H, 3H; 2 CH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ 163.64, 162.31 (C10, C11), 160.07 (C12), 112.12 (C6), 92.94 (C9), 83.57, 78.65, 71.34 (C1, C2, C3), 54.22 (C4), 36.73 (C5), 25.94, 24.31 (C7, C8); MS (70 eV) *m/z*: 301 (M^+, 14), 285 (15), 242-244 (30, 10), 225-227 (45, 15), 199 (17), 169 (100), 144 (14), 67 (20). Anal. Calcd. for $C_{12}H_{17}ClN_4O_3$: C, 47.92; H, 5.69; N, 18.62; Cl, 11.78. Found: C, 47.88; H, 5.40; N, 18.39; Cl, 11.60.

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