Enantioselective Synthesis of Medium-Sized Ring-Bridged Oxabicycles by Ring-Closing Metathesis

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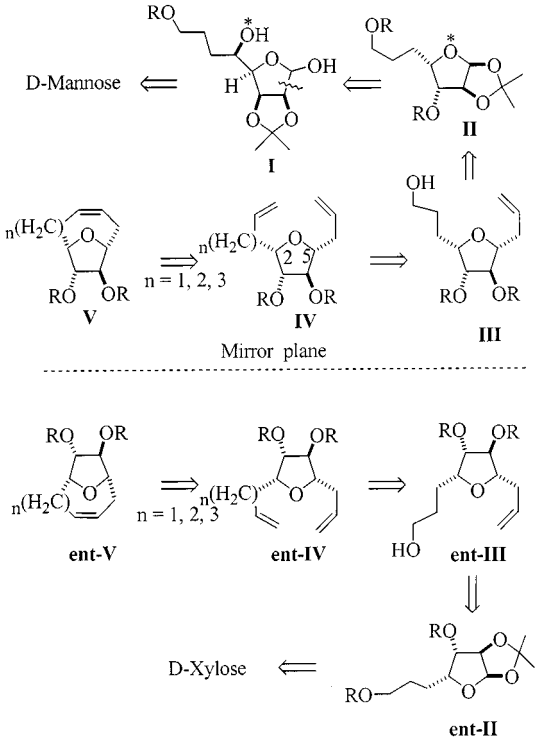
Dedicated to Professor Marcial Moreno-Mañas on the occasion of his 60th birthday

Keywords: Metathesis / Glycosides / Cyclizations / Carbohydrates

A flexible strategy is described for the enantioselective construction of both optical antipodes of the oxabicyclo[4.2.1]-, -[5.2.1]-, and -[6.2.1]alkenes by a ring-closing metathesis reaction of the suitable 2,5-*cis*-dialkenyltetrahydrofuran derivatives.

Introduction

Ring-closing metathesis (RCM) catalysed by carbene transition metal complexes[1,2] has become one of the most popular synthetic methods for the formation of a C−C bond. Commercially available Grubbs' catalyst[3] is widely used because of its tolerance of a wide range of functional groups and its easy bench handling. While the RCM reaction has found a wide use in the construction of medium ring-sized carbo- and heterocycles, its use in the construction of medium-sized bridged compounds is scarce.[4] In this paper we report on a flexible strategy for the enantioselective synthesis of the medium-sized bridged oxabicyclo[*n*.-2.1]alkenes **V** and ***ent*-V** (n = 4, 5, 6) (Scheme 1) by an RCM reaction of the conformationally constrained dienes **IV** and ***ent*-IV**, respectively. Bridged oxabicyclic compounds are not only a synthetic target in their own right, but also because of their use as templates and building blocks in organic synthesis.[5] In addition, the bridged 11-oxabicyclo[6.2.1]undecane is a central and common sub-structural motif of the cembranoids,[6] a pharmacologically important family of marine metabolites with a wide spectrum of biological activity.



Scheme 1. Retrosynthetic analysis for the synthesis of both antipodes of medium-sized bridged oxabicyclo[*n*.2.1]alkenes **V** and ***ent*-V** (n = 1, 2, 3)

Results and Discussion

The strategy is outlined in Scheme 1. We proposed to build the enantiomeric medium-sized bridged oxabicycles **V** and ***ent*-V** through the ring-closing metathesis reactions of dienes **IV** and ***ent*-IV**, respectively. The 2,5-*cis* geometry of the alkenyl chains must bring the diene termini into close proximity and so reduce the entropic cost associated with the ring-closing process. The *exo*-directed allylation[7] of the bicyclic acetals **II** and ***ent*-II** should permit access to olefins **III** and ***ent*-III**, respectively, as diastereomerically pure compounds. The bicyclic acetal **II** is obtained from diol **I** through the Suárez protocol,[8,9] which relocates the original anomeric position of D-mannose to the new one created by β-fragmentation at the anomeric position, and traps the intermediate by the secondary hydroxy group placed on the chain (*-marked oxygen atom). Finally, the enantiom-

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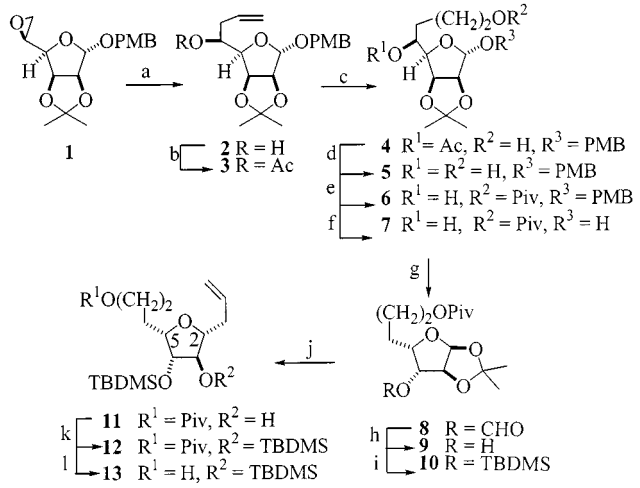
eric acetal ***ent*-II** is directly obtained from D-xylose by simple protecting groups manipulation.

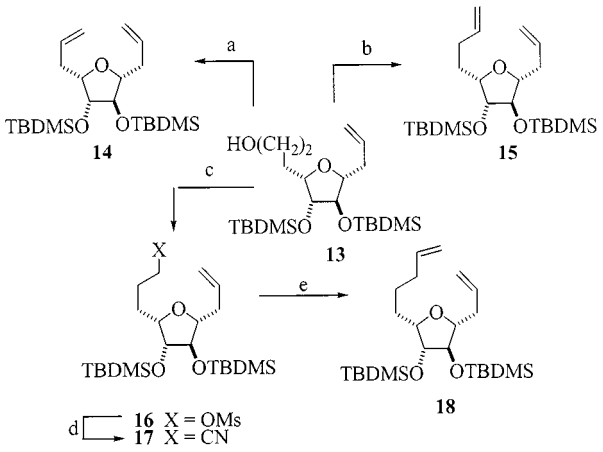
Synthesis of the Dienes

Epoxide **1**[10] (Scheme 2) was treated with vinylmagnesium chloride in the presence of CuI[11] to give alcohol **2** in 98% yield. Protection and oxidative hydroboration gave the alcohol **4** in 90% yield. Hydrolysis and regioselective protection of the primary hydroxy group as its pivaloyl ester gave the alcohol **6** in 92% yield.



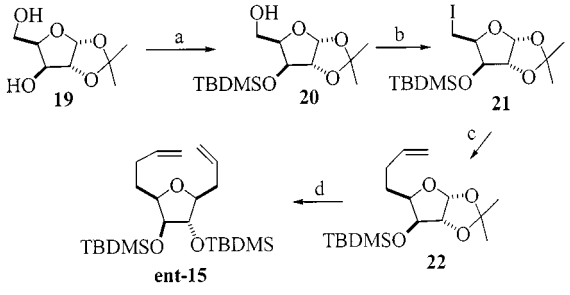
Scheme 2. Reagents and conditions: (a) $CH_2CHMgCl/CuI$, THF, −30 °C to −15 °C, 15 min, 98%; (b) Ac_2O, Py; (c) (1) 9-BBN, THF, room temp., 1 h, (2) $NaOH/H_2O_2$, room temp., 0.5 h, 90%; (d) KOH, MeOH, 15 min, room temp., quant.; (e) PivCl, Et_3N, CH_2Cl_2, 0 °C, 1 h, 92%; (f) DDQ, H_2O/CH_2Cl_2, room temp., 16 h, 91%; (g) PhIO, I_2, CH_2Cl_2, 6 h, 70%; (h) Na_2CO_3, MeOH, room temp., 10 min, 99%; (i) TBDMSCl, imidazole, DMF, 60 °C, 16 h, 91%. (j) $(CH_3)_3SiCH_2CH{=}CH_2$, $BF_3.Et_2O$, CH_2Cl_2, room temp., 6 h, 85%; (k) TBDMSCl, imidazole, DMF, 60 °C, 16 h, 90%; (l) DIBAL, CH_2Cl_2, −78 °C, 1 h, 95%

Deprotection at the anomeric position by reaction with DDQ gave the diol **7**, which was easily transformed into the bicyclic acetal **8** by the Suárez protocol. Therefore, treatment of lactol **7** with iodosylbenzene and iodine resulted in oxidative β-fragmentation of the anomeric oxygen-centred radical, affording the formyl derivative **8** in 70% yield. Basic hydrolysis and reprotection of the hydroxy group as its *tert*-butyldimethylsilyl ether gave the acetal **10** in a yield of 91%. The *exo*-directed allylation[7] of this bicyclic acetal gave the alkene **11** as a unique diastereomer in 85% yield. Protection of the secondary hydroxy group as its *tert*-butyldimethylsilyl ether followed by DIBAL deprotection of the primary pivaloyl ester gave the alcohol **13** in a yield of 86%. Synthetic manipulation of the primary hydroxy group of **13** allowed the installation of the required second alkenyl chain (Scheme 3). Therefore, Grieco elimination of the primary hydroxy group gave diene **14** in a 75% yield. Swern oxidation, followed by a Wittig olefination efficiently transformed **13** into the diene **15** (70%). Finally, mesylate formation, cyanide displacement, DIBAL reduction of the cyanide group to the imine, followed by hydrolysis to the aldehyde, and Wittig olefination afforded diene **18** in a 40% overall yield.



Scheme 3. Reagents and conditions: (a) (1) *o*-$NO_2C_6H_4SeCN$, Bu_3P, THF, room temp., 16 h, (2) H_2O_2, THF, 0 °C, 3 h, 75% two steps; (b) (1) Swern oxidation, (2) Ph_3PCH_3I, *n*BuLi, THF, 0 °C, 1 h, 70% two steps: (c) MsCl, Et_3N, CH_2Cl_2, 0 °C, 30 min, 100%; (d) KCN, DMF, 50 °C, 10 h, 68%; (e) (1) DIBAL, CH_2Cl_2, −78 °C, 1 h, (2) aq. HCl (1 N), (3) Ph_3PCH_3I, *n*BuLi, THF, 0 °C, 1 h, 56% for the three steps

As the representative example of the enantiomeric series, we chose the readily accessible diene ***ent*-15**, which was easily synthesised from commercial 1,2-*O*-isopropylidene-D-xylofuranose (**19**) through the synthetic sequence outlined in the Scheme 4. Selective monoprotection of the secondary hydroxy group of **19**[12] as its *tert*-butyldimethylsilyl ether gave the alcohol **20** in a 54% yield. Treatment of **20** with molecular iodine and triphenylphosphane/imidazole gave the iodine derivative **21**, which was transformed into alkene **22** by radical allylation with allyltri-*n*-butylstannane and azobis(isobutyronitrile) (86%). The *exo*-directed allylation of this bicyclic acetal followed by hydroxy group protection gave the diene ***ent*-15** as the unique diastereomer in 55% of yield.



Scheme 4. Reagents and conditions: (a) (1) $(Bu_3Sn)_2O$, toluene, reflux, 12 h and then *p*MeOBzCl, reflux, 62 h, 80%; (2) TBDMSCl, imidazole, DMF, 60 °C, 16 h, 85%; (3) DDQ, CH_2Cl_2/H_2O, room temp., 2 h, 80%; (b) I_2, Ph_3P, imidazole, C_6H_6, 2 h, reflux, 90%; (c) $nBu_3SnCH_2CH{=}CH_2$, AIBN cat., toluene, reflux, 16 h, 86%; (d) (1) $(CH_3)_3SiCH_2CH{=}CH_2$, $BF_3{\cdot}Et_2O$, CH_2Cl_2, room temp., 3 h; (2) TBDMSCl, imidazole, DMF, 60 °C, 16 h, 55% two steps

Ring-Closing Metathesis Reactions

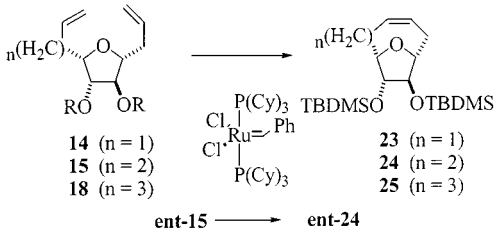
Initial metathesis reactions were carried out with the diene **14** to obtain the 9-oxabicyclo[4.2.1]non-3-ene (**23**)

Table 1. Conditions for ring-closing metathesis of dienes **14**, **15**, ***ent*-15**, and **18**

Entry	Substrate	Solvent	*T* [°C]	*t* [h]	[M][a][b]	Yield (%)	RSM[c] (%)	Product
1	**14**	CH_2Cl_2	room temp.	24	A	–	100	–
2	**14**	CH_2Cl_2	reflux	24	A	–	100	–
3	**14**	C_6H_6	40	16	A	–	100	–
4	**14**	C_6H_6	reflux	16	A	64	8	**23**
5	**14**	C_6H_6	reflux	16	C	61	7	**23**
6	**15**	CH_2Cl_2	room temp.	24	A	–	100	–
7	**15**	CH_2Cl_2	reflux	24	A	–	100	–
8	**15**	$C_2H_4Cl_2$	reflux	16	A	24	7	**24**
9	**15**	C_6H_6	reflux	16	A	45	18	**24**
10	**15**	C_6H_6	reflux	16	B	41	12	**24**
11	**15**	C_6H_6	reflux	16	C	46	3	**24**
12	***ent*-15**	C_6H_6	reflux	16	A	40	10	***ent*-24**
13	**18**	C_6H_6	reflux	16	A	53	8	**25**
14	**18**	C_6H_6	reflux	16	B	40	9	**25**
15	**18**	C_6H_6	reflux	16	C	50	15	**25**

[a] In all cases 20 mol % of $[(Pcy_3)_2RuCHPh]Cl_2$ was used. [b] (A) 0.02 M in diene. (B) 0.003 M. (C) 0.02 M and the catalyst added in two portions at eight hour intervals. [c] RSM = Recovered Starting Material.

(Scheme 5). After attempting to modify several experimental conditions including solvent, catalyst charge,[13] and temperature (Table 1, Entries 1–5), refluxing benzene (0.02 M) with a 20 mol % of Grubbs' catalyst charge were found to be the best conditions, affording **24** in 64% yield. Remarkably, in spite of the known difficulty in forming eight-membered rings by this reaction,[4a,4c] dienes **15** and ***ent*-15** gave the 10-oxabicyclo[5.2.1]dec-3-enes **24** and ***ent*-24** in a 45% and 40% yield, respectively (Entries 9 and 12). Unfortunately, the efficiency of the reaction could not be improved by changes in the experimental conditions (Entries 6–11).



Scheme 5. Ring-closing metathesis reaction of dienes **14**, **15**, ***ent*-15**, and **18** to give the oxabicycles **23**, **24**, ***ent*-24**, and **25**.

Diene **18** also underwent the RCM reaction with acceptable efficiency, affording the (1*S*,8*R*,9*S*,10*S*)-9,10-di-*tert*-butoxy-11-oxabicyclo[6.2.1]undec-3-ene (**25**) in 53% yield (Entries 13–15). Although this 53% yield is susceptible to improvement by the use of other catalysts,[14] this is still good enough for synthetic use.

Conclusion

Some features of this methodology are noteworthy: Firstly, it opens a synthetic access to the medium-sized oxabicyclo[4.2.1]non-3-ene, -[5.2.1]dec-3-ene, and -[6.2.1]undec-3-ene in both their enantiomerically pure forms and with a moderate to good yield; secondly, dienes **14**, **15**, and **18** and their enantiomers ***ent*-14**, ***ent*-15**, and ***ent*-18** are easily synthesised from cheap and commercially available carbohydrates by means of standard reactions and in a highly chemo- and stereoselective mode; thirdly, the synthetic protocol admits a wide functional group presence on both alkenyl chains, which is very important in order to apply this methodology to the synthesis of more elaborated targets; and finally, the RCM reactions are carried out with the aid of a commercial and bench stable Grubbs' catalyst with moderate to good efficiency. It is hoped that the new family of more reactive Grubbs' catalysts[14] (still not commercially available) could improve the chemical efficiency of these cyclizations.

Experimental Section

General Remarks: Melting points are uncorrected and were determined in a Reichter Thermovar apparatus. ^1H NMR and ^{13}C NMR spectra of $CDCl_3$ solutions were recorded either at 200 and 50 MHz or at 500 and 125 MHz (Bruker Ac 200 and AMX2-500), respectively. FT-IR spectra were measured in chloroform solutions using a Shimadzu IR-408 spectrophotometer. Mass spectra (low resolution) (EI/CI) were obtained with a Hewlett-Packard 5995 gas chromatograph/mass spectrometer. High-resolution mass spectra were recorded with a Micromass Autospec mass spectrometer. Microanalyses were performed with a Fisons Instruments EA 1108 carbon, hydrogen, and nitrogen analyser. Optical rotations were determined at room temperature with a Perkin -Elmer 241 polarimeter and are referenced to the D-line of sodium. Analytical thin-layer chromatography plates used were E. Merck Brinkman UV-active silica gel (Kieselgel 60 F254) on aluminium. Flash column chromatography was carried out with E. Merck silica gel 60 (particle size less than 0.020 mm) using appropriate mixtures of ethyl acetate and hexanes as eluent. All reactions were performed in oven-dried glassware under nitrogen unless otherwise stated in the text. Tetrahydrofuran, benzene, and toluene were distilled from sodium metal/benzophenone ketyl. Dichloromethane, dimethyl sulfoxide, dimethylformamide, and triethylamine were distilled from CaH_2.

Bis(tricyclohexylphosphane)benzylideneruthenium(IV) dichloride (Grubbs' catalyst) was purchased from Strem Chemicals, and used under nitrogen with standard Schlenk techniques.

4-Methoxybenzyl 6,7,8-Trideoxy-2,3-*O*-(1-methylethylidene)-α-D-*manno*-oct-7-enofuranoside (2): In an oven-dried round-bottomed flask was placed CuI (1.29 g, 6.76 mmol) and the flask was purged with nitrogen. Dry THF (20 mL) was added and the suspension was cooled at −30 °C. Vinylmagnesium chloride (1.7 M in THF) (8 mL, 13.6 mmol) was added and the mixture was stirred at −30 °C for 15 min. Then, epoxide **1** (2.18 g, 6.8 mmol) in dry THF (40 mL) was added via cannula and the mixture was slowly warmed from −30 °C to −10 °C during 2 h. Aqueous saturated NH_4Cl was added to destroy the reagent excess and the mixture was transferred to a decantation funnel with the aid of more ethyl acetate. The organic phase was washed with H_2O (3×), 1 N HCl (3×), aqueous saturated $NaHCO_3$ (3×), and aqueous saturated NaCl (3×), dried with Na_2SO_4, filtered and concentrated to give a gummy residue. Flash chromatography (eluent gradient: ethyl acetate/hexanes from 2:8 to 4:6) gave pure alcohol **2** (yield 2.34 g, 95%). IR ($CHCl_3$): $\tilde{\nu}$ = 3514, 3007 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 9.0 Hz, 2 H), 6.87 (d, *J* = 9.0 Hz, 2 H), 5.87 (m, 1 H), 5.19 (dd, *J* = 7 and 2 Hz, 1 H), 5.14 (s, 1 H, H-1), 5.13 (dd, *J* = 10 and 2 Hz, 1 H), 4.75 (dd, *J* = 6 and 3 Hz, 1 H), 4.64 (d, *J* = 6.0 Hz, 1 H), 4.61 and 4.41 (d, 1 H each, *J* = 11.0 Hz), 4.11 (dd, *J* = 11 and 4 Hz, 1 H), 3.89 (app. t, 1 H, *J* = 6 and 4 Hz), 3.80 (s, 3 H), 2.41 (m, 1 H), 1.47 (s, 3 H), 1.29 (s, 3 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 159.2, 134.3, 129.6 (2 C), 129.1, 117.3, 113.6 (2 C), 112.4, 104.5, 85.3, 80.8, 80.2, 69.3, 66.4, 55.0, 37.7, 25.7, 24.2. LRMS (EI): *m*/*z* (%) = 350 (0.9) [M^+], 335 (1.4), 229 (2.9), 171 (8.4), 121 (100), 91 (2), 83 (3.6), 69 (2.7). HRMS (EI): calcd. for $C_{19}H_{26}O_6$ 350.172939, found 350.174675. The alcohol was acetylated with Ac_2O/Py to give the acetate **3**, which was directly used in the next experiment.

4-Methoxybenzyl 5-*O*-Acetyl-6,7-dideoxy-2,3-*O*-(1-methylethylidene)-α-D-*manno*-octofuranoside (4): Alkene **3** (1.88 g, 4.8 mmol) in dry THF (20 mL) was stirred with 9-BBN (0.5 M THF) (19 mL, 9.5 mmol) at room temperature for 45 min. 3 N NaOH solution (1.6 mL) and 30% H_2O_2 (3 mL, 27 mmol) were cautiously added and the resulting mixture was stirred for 30 min. The excess reagent was destroyed by addition of aqueous saturated $NaHSO_3$ solution, and the solvent was distilled off. Ethyl acetate was added and the solution was transferred to a decantation funnel. The organic phase was washed with aqueous saturated solutions of $NaHSO_3$ and NaCl, dried with Na_2SO_4, filtered and concentrated to give a gummy residue. Flash chromatography (eluent gradient: ethyl acetate/hexanes from 2:8 to 6:4) gave pure **4** (yield 1.78 g, 90%). $[\alpha]_D$ = 43 (*c* = 0.221, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ =3500, 1735 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 7.24 (d, *J* = 9.0 Hz, 2 H), 6.88 (d, *J* = 9.0 Hz, 2 H), 5.36 (m, 1 H), 5.08 (s, 1 H), 4.71 (dd, *J* = 6 and 4 Hz, 1 H), 4.62 (d, *J* = 6.0 Hz, 1 H), 4.58 and 4.40 (d each, *J* = 11.0 Hz, 2 H each), 4.00 (dd, *J* = 9 and 4 Hz, 1 H), 3.81 (s, 3 H), 3.7 (m, 1 H), 2.12 (s, 3 H), 1.44 (s, 3 H), 1.29 (s, 3 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 170.5, 159.1, 129.6 (2 C), 129.2, 113.5 (2 C), 104.8, 85.1, 80.9, 79.5, 71.5, 68.4, 61.7, 55.1, 27.7, 26.8, 25.9, 24.8, 21.0. LRMS (EI): *m*/*z* (%) = 410 (1.6) [M^+], 257 (2.3), 242 (0.8), 231 (9.4), 213 (0.9), 197 (1.8), 185 (4), 171 (6.7), 155 (2.6), 143 (8), 135 (8.2), 125 (15.8), 121 (100). $C_{21}H_{30}O_8$: calcd. C 61.45, H 7.37; found C 61.586, H 7.556.

4-Methoxybenzyl 6,7-Dideoxy-8-*O*-(2,2-dimethylpropanoyl)-2,3-*O*-(1-methylethylidene)-α-D-*manno*-octofuranoside (6): Acetate **4** (1.78 g, 4.4 mmol) was stirred with KOH (3 g, 54 mmol) in MeOH (45 mL) for 15 min. The solvent was distilled off and the residue was taken up in CH_2Cl_2/H_2O. The mixture was decanted and the aqueous phase extracted with CH_2Cl_2. The combined organic phases were washed with aqueous saturated NaCl, dried with Na_2SO_4, filtered, and concentrated to give diol **5** as a crystalline solid. The crude diol **5** in dry CH_2Cl_2 (30 mL) and dry Et_3N (3.4 mL, 24.4 mmol) was cooled at 0 °C and stirred with pivaloyl chloride (1.8 mL, 14.5 mmol) and a catalytic amount of DMAP for 1 h at this temperature. The solution was transferred to a decantation funnel and the organic phase was consecutively washed with 1 N HCl, aqueous saturated $NaHCO_3$ and aqueous saturated NaCl, dried with Na_2SO_4, filtered, and concentrated to give a solid residue. Flash chromatography (eluent gradient: ethyl acetate/hexanes from 1:9 to 4:6) gave pure **6** (yield 1.83 g, 92%). M.p. 38.3−38.8 °C (ethyl acetate/hexane). $[\alpha]_D$ = 56.2 (*c* = 0.26, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$): δ = 7.24 (d, *J* = 9.0 Hz, 2 H), 6.87 (d, *J* = 9.0 Hz, 2 H), 5.12 (s, 1 H), 4.73 (dd, *J* = 6 and 4 Hz, 1 H), 4.60 (d, *J* = 11.0 Hz, 2 H), 4.43 (d, *J* = 11.0 Hz, 2 H), 4.05 (m, 2 H), 3.83 (dd, *J* = 5 and 4 Hz, 1 H), 3.8 (s, 3 H), 1.75 (m, 4 H), 1.46 (s, 3 H), 1.28 (s, 3 H), 1.20 (s, 9 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 178.3, 159.2, 129.6 (2 C), 129.1, 113.5 (2 C), 112.4, 104.5, 85.2, 82.0, 80.1, 69.4, 66.5, 63.9, 55.0, 38.5, 29.1, 26.8 (3 C), 25.7, 24.6, 24.2. LRMS (EI): *m*/*z* (%) = 452 (0.16) [M^+], 437 (0.3), 315 (0.2), 299 (0.3), 273 (6.4), 258 (1.4), 229 (3.8), 227 (1.8), 183 (4.5), 171 (3.6), 163 (1.8), 143 (1.6), 137 (2.1), 125 (10), 121 (100), 85 (7.2), 71 (10.3), 57 (32). $C_{24}H_{36}O_8$: calcd. C 63.70, H 8.02; found C 63.804, H 8.022.

6,7-Dideoxy-8-*O*-(2,2-dimethylpropanoyl)-2,3-*O*-(1-methylethylidene)-α-D-*manno*-octofuranose (7): Alcohol **6** (2 g, 4.4 mmol) in CH_2Cl_2 (90 mL) and H_2O (4.5 mL) was vigorously stirred with DDQ (1.5 g, 6.6 mmol) at room temperature for 16 h. Aqueous saturated $NaHCO_3$ (1 mL) was added and the resulting mixture stirred for 15 min. Filtration through a pad of Celite and concentration gave a solid residue that was purified by flash chromatography (eluent gradient: ethyl acetate/hexanes from 2:8 to 6:4) to give pure hemiacetal **7** (yield 1.33 g, 91%). M.p. 83.7−84.7 °C (ethyl acetate/hexane). $[\alpha]_D$ = 7.98 (*c* = 0.038, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$): δ = 5.37 (s, 1 H), 4.69 (dd, *J* = 6 and 3 Hz, 1 H), 4.57 (d, *J* = 6.0 Hz, 1 H), 4.07 (app. t, 2 H, *J* = 7 and 6 Hz), 3.97 (m, 2 H), 1.7 (m, 4 H), 1.41 (s, 3 H), 1.25 (s, 3 H), 1.17 (s, 9 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 178.6, 112.3, 100.5, 85.8, 82.9, 79.1, 69.7, 64.0, 38.6, 28.6, 26.7 (3 C), 25.8, 24.6, 24.4. LRMS (EI): *m*/*z* (%) = 317 (55.5) [M^+ − 15], 299 (19.1), 255 (5), 227 (6.4), 215 (21.9), 212 (73.5), 202 (18.1), 197 (6.4), 189 (17.5), 183 (17.3), 173 (84.7), 171 (26), 159 (18), 155 (55.6), 143 (20.5), 137 (42.2), 131 (19.7), 129 (17.7), 126 (46.7), 121 (10.3), 114 (11.6), 113 (35.5), 109 (25.2). $C_{16}H_{28}O_7$: calcd. C 57.82, H 8.49; found C 57.994, H 8.58.

5,6-Dideoxy-7-*O*-(2,2-dimethylpropanoyl)-3-*O*-formyl-1,2-*O*-(1-methylethylidene)-α-D-*xylo*-heptofuranose (8): Hemiacetal **7** (720 mg, 2.16 mmol) in dry CH_2Cl_2 (43 mL) was heated at reflux with I_2 (576 mg, 2.3 mmol) and PhIO (freshly prepared) (475 mg, 2.16 mmol) for 1 h. More PhIO was added (475 mg, 2.16 mmol) and the heating continued for 1 h further. The same amount of PhIO was again added and the heterogeneous mixture was heated under reflux for further 3 h. After cooling, the mixture was filtered through a pad of Celite, diluted with more dichloromethane, washed with aqueous $Na_2S_2O_3$ until complete decolouration was observed, dried with Na_2SO_4, and concentrated to give a gummy residue. Flash chromatography (eluent gradient: ethyl acetate/hexane from 1:9 to 4:6) gave pure **8** (yield 500 mg, 70%). $[\alpha]_D$ = 2.4 (*c* = 0.287, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ =1731, 1724 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 8.07 (s, 1 H), 5.88 (d, *J* = 4.0 Hz, 1 H), 5.24 (d, *J* = 3.0 Hz, 1 H), 4.50 (d, *J* = 4.0 Hz, 1 H), 4.25 (m, 1 H),

4.04 (app. t, J = 6.0 Hz, 2 H), 1.6 (m, 4 H), 1.49 (s, 3 H), 1.29 (s, 3 H), 1.16 (s, 9 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 178.3, 159.5, 111.8, 104.2, 83.3, 78.3, 75.4, 63.7, 38.6, 27.1 (3 C), 26.4, 26.0, 25.2, 24.5. LRMS (EI): *m*/*z* (%) = 315 (51.9) [M^+ − 15], 227 (30.3), 187 (10.4), 125 (29.8), 121 (28.1), 107 (10.9), 97 (15), 85 (23), 71 (60.7), 57 (100). HRMS (EI): calcd. for $C_{15}H_{23}O_7$ [M^+ − 15] 315.144378, found 315.144325.

5,6-Dideoxy-7-*O*-(2,2-dimethylpropanoyl)-1,2-*O*-(1-methylethylidene)-α-D-*xylo*-heptofuranose (9): Formate **8** (800 mg, 2.4 mmol) in Na_2CO_3 saturated MeOH (25 mL) was stirred for 10 min. The solvent was evaporated and the residue dissolved in ethyl acetate, washed with aqueous saturated NaCl, dried with Na_2SO_4, and concentrated to give the crude alcohol **9**. Crystallization from ethyl acetate/hexane gave pure alcohol **9** (yield 812 mg, quant.). $[\alpha]_D$ = 14.6 (c = 0.268, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3500, 1721 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.90 (d, J = 4.0 Hz, 1 H), 4.51 (d, J = 4.0 Hz, 1 H), 4.1 (m, 3 H), 1.8 (m, 2 H), 1.6 (m, 2 H), 1.5 (s, 3 H), 1.31 (s, 3 H), 1.20 (s, 9 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 178.8, 111.3, 104.2, 85.3, 79.9, 75.1, 64.2, 29.7, 27.1 (3 C), 26.6, 26.1, 25.3, 24.2. LRMS (EI): *m*/*z* (%) = 287 (21) [M^+ − 15], 227 (10.9),173 (14), 159 (7.9), 143 (9.3), 125 (17.6), 100 (11.2), 85 (15.5), 71 (100), 57 (66.1), 55 (10.5). $C_{15}H_{26}O_6$: calcd. C 59.58, H 8.67; found C 59.385, H 8.829.

3-*O*-(*tert*-Butyldimethylsilyl)-5,6-dideoxy-7-*O*-(2,2-dimethylpropanoyl)-1,2-*O*-(1-methylethylidene)-α-D-*xylo*-heptofuranose (10): Alcohol **9** (720 mg, 2.4 mmol) in dry DMF (15 mL) was stirred with imidazole (326 mg, 4.8 mmol) and TBDMSCl (544 mg, 3.6 mmol) at 60 °C for 6 h. After cooling, diethyl ether was added and the mixture was transferred to a decantation funnel with the aid of more diethyl ether. The organic phase was washed with H_2O (3×), dried with Na_2SO_4, and concentrated to give an oily residue. Flash chromatography (eluent gradient: ethyl acetate/hexane from 5:95 to 2:8) gave pure **10** (yield 910 mg, 91%). $[\alpha]_D$ = 13.2 (c = 0.205, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 1719 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.87 (d, J = 4.0 Hz, 1 H), 4.36 (d, J = 4.0 Hz, 1 H), 4.07 (m, 3 H), 1.75 (m, 2 H), 1.49 (s, 3 H), 1.31 (s, 3 H), 1.19 (s, 9 H),.9 (s, 9 H), 0.12 (s, 3 H), 0.08 (s, 3 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 178.5, 111.3, 104.6, 85.6, 80.6, 76.4, 64.3, 38.7, 27.2 (3 C), 26.7, 26.2, 25.8 (3 C), 25.7, 25.0, 18.0, −4.7, −5.1. LRMS (EI): *m*/*z* (%) = 401 (4.6) [M^+ − 15], 359 (3.9), 283 (3.7), 215 (6.9), 199 (29.2), 183 (9.3), 171 (5.6), 159 (100), 157 (17.4), 129 (74.1), 125 (9.3), 117 (5.4), 75 (22.3), 73 (28.5), 57 (51.9). $C_{21}H_{40}O_6Si$: calcd. C 60.54, H 9.68; found C 60.22, H 10.04.

(1*S*)-1,4-Anhydro-2-*O*-(*tert*-butyldimethylsilyl)-5,6,7-trideoxy-1-[3-(2,2-dimethylpropanoyloxy)propyl]-D-*arabino*-hept-6-enitol (11): The 1,2-*O*-isopropylidene derivative **10** (920 mg, 2.2 mmol) in dry CH_2Cl_2 (20 mL) was cooled to 0 °C and allyl trimethylsilane (1.4 mL, 8.8 mmol) and boron trifluoride−diethyl ether (freshly distilled) (0.6 mL, 4.7 mmol) were added. After 15 min at this temperature, the mixture was allowed to warm to room temperature and stirred for a further 6 h. Aqueous saturated $NaHCO_3$ was added and the organic phase decanted. The aqueous phase was extracted with more CH_2Cl_2, and the combined organic phases were washed with aqueous saturated NaCl, dried with Na_2SO_4, and concentrated to give an oily residue. Flash chromatography (eluent gradient: ethyl acetate/hexane from 1:9 to 2:8) gave pure alcohol **11** (yield 750 mg, 85%). $[\alpha]_D$ = 13.8 (c = 0.42, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3472, 3023, 1719, cm^{-1}. The NMR data were determined for the acetate derivative. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.8 (m, 1 H); 5.08 (ddd, 1 H, J = 17, 2 and 2 Hz), 4.07 (t, J = 6.0 Hz, 2 H), 3.93 (dd, J = 3 and 1 Hz, 1 H), 3.84 (ddt, 1 H, J = 5, 3 and 2 Hz), 3.81 (td, 1 H, J = 7 and 2 Hz), 2.44 (m, 1 H), 2.07 (s, 3 H), 1.77−1.57 (m, 4 H), 1.2 (s, 9 H), 0.9 (s, 9 H), 0.13 (s, 3 H), 0.06 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.5, 169.9, 134.3, 117.0, 82.6 (2 C), 81.4, 76.8, 64.3, 38.6, 38.3, 27.1 (3 C), 25.8 (3 C), 25.7 (2 C), 20.9, 18.0, −4.7, −5.5. LRMS (EI): *m*/*z* (%) = 343 (2.4) [M^+ − C_4H_9], 325 (1), 299 (0.6), 283 (0.7), 257 (1.6), 241 (3.2), 227 (2.6), 187 (7.7), 171 (12.4), 159 (100), 75 (15.2), 57 (53.1). $C_{21}H_{40}O_5Si$: calcd. C 62.96, H 10.06; found C 63.36, H 9.69.

(1*S*)-1,4-Anhydro-2,3-bis-*O*-(*tert*-butyldimethylsilyl)-5,6,7-trideoxy-1-[3-(2,2-dimethylpropanoyloxy)propyl]-D-*arabino*-hept-6-enitol (12): Alcohol **11** (780 mg, 1.95 mmol) in dry DMF was stirred with imidazole (265 mg, 3.9 mmol) and TBDMSCl (4421 mg, 2.9 mmol) at 60 °C for 4 h and 30 min. After cooling, diethyl ether was added and the mixture was transferred to a decantation funnel with the aid of more diethyl ether. The organic phase was washed with H_2O (3×), dried with Na_2SO_4, and concentrated to give an oily residue. Flash chromatography (eluent gradient: ethyl acetate/hexane from 5:95 to 6:4) gave pure **12** (yield 970 mg, 97%). $[\alpha]_D$ = 12.3 (c = 0.86, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 1719 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.8 (m, 1 H), 5.06 (dd,1 H, J = 17 and 2 Hz), 5.03 (d, J = 10.0 Hz, 1 H), 4.06 (t, J = 6.0 Hz, 2 H), 3.92 (m, 1 H), 3.83 (s, 1 H), 3.72 (s, 1 H), 3.71 (t, J = 8.0 Hz, 1 H), 2.39 (m, 1 H), 2.31 (m, 1 H), 1.8−1.54 (m, 4 H), 1.16 (s, 9 H), 0.89 (s, 9 H), 0.85 (s, 9 H), 0.08 (s, 3 H), 0.06 (s, 3 H), 0.04 (s, 3 H), 0.02 (s, 3 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 178.5, 135.2, 116.9, 86.2, 81.1 (2 C), 79.5, 64.5, 38.7, 27.1 (3 C), 25.7 (2 C), 25.6 (3 C), −4.4, −4.5 (2 C), −5.2. LRMS (EI): *m*/*z* (%) = 499 (0.9) [M^+ − 15], 473 (2.4), 457 (24.2), 387 (4.6), 371 (3.8), 341 (14.5), 325 (10.8), 301 (8), 285 (16), 271 (3.9), 255 (2.8), 239 (11.1), 231 (4.6), 215 (15.4), 211 (18.9), 201 (18.9), 197 (13.5), 189 (1.7), 185 (9.4), 171 (3.7), 169 (2.1), 159 (100), 157 /6.9), 149 (14.6), 147 (21.5), 141 (12.5), 133 (5.1), 129 (7.8), 115 (8.7), 101 (5.1), 89 (3.9), 75 (30.4), 73 (93.1), 57 (61.8). HRMS (EI): calcd. for $C_{26}H_{51}O_5Si_2$ [M^+ − 15] 499.327507; found 499.328926.

(7*S*)-7-Allyl-4,7-anhydro-5,6-bis-*O*-(*tert*-butyldimethylsilyl)-1,2,3-trideoxy-D-*arabino*-hept-1-enitol (14): A solution of **12** (358 mg, 0.69 mmol) in dry CH_2Cl_2 was cooled to −78 °C, and DIBAL (0.9 mL, 0.9 mmol, 1 M in toluene) was added. The reaction mixture was stirred a −78 °C for 1 h and quenched with methanol (2−3 drops) and H_2O and extracted with CH_2Cl_2 (15 mL). The organic layer was dried with Na_2SO_4, and the solvent was removed under reduced pressure to give the alcohol **13**, which was used directly in the next synthetic step. − To a stirring THF solution of the alcohol **13** (300 mg, 0.7 mmol) and *o*-$O_2NC_6H_4SeCN$ (380 mg, 1.7 mmol) was added tributylphosphane (0.4 mL, 1.67 mmol) dropwise, and the deep wine-red solution was stirred at room temperature for 16 h, quenched with H_2O, and extracted with diethyl ether (25 mL). The organic layer was dried with Na_2SO_4, and the solvent was removed under reduced pressure. The residue was dissolved in THF (9 mL) at room temperature and then cooled to 0 °C. To this solution was added H_2O_2, and the resulting mixture was stirred at 0 °C for 3 h, quenched with H_2O (10 mL), and extracted with diethyl ether (20 mL). The combined extracts were dried with Na_2SO_4, the solvent was removed under reduced pressure and the residue was purified by flash chromatography (*n*-hexane/benzene: 7:3) to give **14** (yield 200 mg, 75% for two steps) as a colourless oil. $[\alpha]_D$ = +15.8 (c = 0.4, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 2954, 2858, 1643, 1471, 1257, 1102 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.58 (m, 4 H), (app. dq, 2 H, J = 17 and 2 Hz), 5.03 (dd, 2 H, J = 10 and 1 Hz), 3.97 (ddd, 1 H, J = 9, 6 and 3 Hz), 3.84 (s,1 H), 3.75 (d, J = 4.0 Hz, 1 H), 3.72 (app. t, J = 7.0 Hz, 1 H), 2.44−2.3 (m, 4 H), 0.9 (s, 9 H), 0.84 (s, 9 H), 0.059 (s, 3 H,), 0.054 (s, 3 H), 0.049 (s, 3 H), 0.04 (s, 3 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 135.4,

135.2, 116.8, 86.2, 81.0, 80.9, 79.1, 76.9, 38.6, 33.5, 25.6 (3 C), 25.5 (3 C), 18.0, 7.7, −4.3, −4.51, −4.55, −5.17. HRMS (EI): calcd. for $C_{22}H_{44}O_3Si_2$ 412.3120, found 412.3117.

(7*R*)-4,7-Anhydro-7-(3-butenyl)-5,6-bis-*O*-(*tert*-butyldimethylsilyl)-1,2,3-trideoxy-L-*arabino*-hept-1-enitol (15): DMSO (0.07 mL, 0.96 mmol) was added dropwise to a solution of oxalyl chloride (0.04 mL, 0.48 mmol) in CH_2Cl_2 (2 mL) at −78 °C, and the resulting mixture was stirred for 20 min. A solution of alcohol **13** (see above) (104 mg, 0.24 mmol) in CH_2Cl_2 (2 mL) was added via cannula to the reaction mixture and the resulting mixture was stirred for 20 min at this temperature. Then, Et_3N (0.2 mL, 1.44 mmol) was added and the resulting mixture stirred for 10 min before being warmed to room temperature. The mixture was poured into H_2O and the two layers were separated. The aqueous layer was extracted with diethyl ether (2 × 2 mL) and the combined organic layers were dried with Na_2SO_4. The solvent was removed under reduced pressure, and the crude aldehyde was used in the next reaction without further purification. − A suspension of methyltriphenylphosphonium iodide (126 mg, 0.3 mmol) in THF (1.5 mL) was treated at 0 °C with *n*BuLi (0.2 mL, 0.3 mmol, 1.6 N in hexane). After stirring for 1 h at this temperature, the aldehyde (the residue from the previous step) in dry THF (1.5 mL) was added via cannula. After 1 h, the reaction was quenched with aqueous saturated NH_4Cl solution (1 mL), and extracted with diethyl ether (2 × 3 mL). The organic layer was dried with Na_2So_4, the solvent was removed under reduced pressure and the residue purified by flash chromatography (*n*-hexane/benzene: 7:3) to give **15** (yield 72 mg, 70% for the two steps) as a colourless oil. $[\alpha]_D = +22.5$ ($c = 0.14$, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3018, 2956, 2930, 2858, 1640, 1471, 1463, 1258 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 5.8 (m, 4 H), 5.0 (m, 2 H), 3.91(ddd, 1 H, J = 9, 8 and 3 Hz), 3.83 (s, 1 H), 3.75 (d, J = 3.0 Hz), 3.7 (d, J = 7.0 Hz, 1 H), 2.4 (m, 1 H), 2.3 (m, 1 H), 2.16 (m, 1 H), 2.07 (m, 1 H), 1.73 (m, 1 H), 1.62 (m, 1 H), 0.89 (s, 9 H), 0.08 (s, 3 H), 0.06 (s, 3 H), 0.005 (s, 3 H), 0.004 (s, 3 H), 0.002 (s, 3 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 138.4, 135.2, 116.7, 114.2, 86.0, 89.0 (2 C), 79.2, 38.6, 30.5, 28.1, 25.7 (3 C), 25.5 (3 C), 17.9, 17.7, −4.3, −4.5, −4.54, −5.1. HRMS (EI): calcd. for $C_{23}H_{46}O_3Si_2$ 426.298553; found 426.297256.

(7*R*)-4,7-Anhydro-5,6-bis-*O*-(*tert*-butyldimethylsilyl)-7-(3-cyanopropyl)-1,2,3-trideoxy-L-*arabino*-hept-1-enitol (17): To a solution of alcohol **13** (207 mg, 0.48 mmol) in dry CH_2Cl_2 (5 mL) was added dry Et_3N (0.33 mL, 2.4 mmol) and MsCl (0.07 mL, 0.96 mmol) and the resulting mixture was stirred at 0 °C for 30 min. More CH_2Cl_2 was added and the resulting solution was washed with 1 N HCl. The organic layer was dried with Na_2So_4 and the solvent removed under reduced pressure. The crude mesylate **16** was dissolved in dry DMF (3 mL) and stirred after addition of KCN (274 mg, 4.21 mmol) at 50 °C for 10 h. Then, the reaction mixture was allowed to cool, quenched with H_2O (10 mL), and extracted with diethyl ether (2 × 10 mL). The organic layer was dried with Na_2SO_4, the solvent was removed under reduce pressure and the residue was purified by flash chromatography (ethyl acetate/hexane: 10:90) to give the cyano derivative **17** (126 mg, 68%) as a colourless oil. $[\alpha]_D = +18.1$ ($c = 0.22$, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3079, 2955, 2930, 2858, 2249, 1641, 1471, 1361, 1257, 1111, 1078 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 5.01 (m, 1 H), 5.12 (m, 2 H), 3.93 (m, 1 H), 3.84 (s, 1 H), 3.74 (m, 2 H), 2.38 (m, 4 H), 1.79 (m, 4 H), 0.91 (s, 9 H), 0.88 (s, 9 H), 0.09 (s, 3 H), 0.07 (s, 3 H), 0.06 (s, 3 H), 0.02 (s, 3 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 135.1, 116.9, 86.3, 80.9, 80.5, 79.7, 38.6, 28.4 (2 C), 25.7 (3 C), 25.7 (3 C), 22.8, 17.9, 17.7, 17.2, −4.3, −4.4, −4.5, −5.0. HRMS (EI): calcd. for $C_{22}H_{42}NO_3Si_2$ [M^+ − 15] 424.270326; found 424.266037.

(7*R*)-4,7-Anhydro-5,6-bis-*O*-(*tert*-butyldimethylsilyl)-1,2,3-trideoxy-7-(4-pentenyl)-L-*arabino*-hept-1-enitol (18): A solution of **17** (80 mg, 0.18 mmol) in dry CH_2Cl_2 (3 mL) was cooled to −78 °C and DIBAL (0.7 mL, 0.7 mmol, 1 M in toluene) was added. The reaction mixture was stirred at −78 °C for 1 h and quenched with 1 N HCl (2 mL). The cooling bath was removed and the mixture was stirred for 1 h and extracted with CH_2Cl_2 (2 × 10 mL). The organic layer was dried with Na_2SO_4, the solvent was removed under reduced pressure and the crude aldehyde residue was directly used in the Wittig reaction. − A suspension of methyltriphenylphosphonium iodide (124 mg, 0.31 mmol) in THF (1.5 mL) was treated at 0 °C with *n*BuLi (0.3 mL, 0.3 mmol, 1.0 N in hexanes). After stirring for 1 h at this temperature, the aldehyde (the crude residue from the previous step), dissolved in dry THF (1.5 mL), was added via cannula. After 1 h, the reaction was quenched with aqueous saturated NH_4Cl solution (2 mL) and extracted with diethyl ether (2 × 4 mL). The organic layer was dried with Na_2SO_4, the solvent was removed under reduced pressure and the residue was purified by flash chromatography (*n*-hexane/benzene: 6:4) to give **18** (yield 45 mg, 56% for the two steps) as a colourless oil. $[\alpha]_D = +10$ (c = 0.1, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3077, 3018, 2955, 2930, 2858, 1642, 1474, 1361, 1257, 1220, 1101, 1005 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 5.8 (m, 2 H), 5.0 (m, 4 H), 3.99 (ddd, 1 H, J = 8, 5 and 3 Hz), 3.83 (s, 1 H), 3.71−3.69 (m, 2 H), 2.4 (m, 1 H), 2.3 (m, 1 H), 2.1 (m, 2 H), 1.63 (m, 1 H), 1.54 (m, 1 H), 1.4−1.23 (m, 2 H), 0.89 (s, 9 H), 0.86 (s, 9 H), 0.07 (s, 3 H), 0.04 (s, 3 H), 0.03 (s, 3 H), 0.02 (s, 3 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 138.6, 135.2, 116.2, 114.4, 86.0, 81.5, 81.0, 79.3, 38.6, 34.0, 28.6 (2 C), 25.7 (3 C), 25.6 (3 C), 16.0, 17.7, −4.3, −4.46, −4.5, −5.1. HRMS (EI): calcd. for $C_{24}H_{48}O_3Si_2$ 440.314203; found 440.318733.

{[(3a*R*,5*R*,6*S*,6a*R*)-5-(3-Butenyl)-2,2-dimethyltetrahydrofuro[2,3-*d*]-[1,3]dioxol-6-yl]oxy}(*tert*-butyl)dimethylsilane (22): To a slurry of 3-*O*-(*tert*-butyldimethylsilyl)-1,2-*O*-isopropylidene-α-D-*xylo*-furanose (**20**) (500 mg, 1.6 mmol) in dry benzene (15 mL) was added imidazole (148 mg, 2.13 mmol) and Ph_3P (558 mg, 2.13 mmol). The mixture was then cooled to 0 °C and iodine (541 mg, 2.13 mmol) was added. After stirring for 2 h, the mixture was filtered through a pad of Celite and concentrated to give a gummy residue. Flash chromatography (ethyl acetate/hexane: 1:9) gave pure iodine derivative **21** (yield 638 mg, 90%), which was taken in dry toluene (15 mL) and heated at reflux with allyltributyltin (1.9 mL, 6.16 mmol) and a catalytic amount of AIBN overnight. The solvent was distilled off and the gummy residue purified by flash chromatography (ethyl acetate/hexane: 1:9) to give pure **22** (yield 389 mg, 86%). $[\alpha]_D = -13.8$ ($c = 0.36$, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3067, 1639 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 5.84 (d, J = 4.0 Hz, 1 H), 5.85−5.75 (m, 1 H), 5.01 (app. dq, 1 H, J = 17 and 2 Hz), 4.94 (app. dd, J = 10 and 1 Hz, 1 H), 4.32 (d, J = 4.0 Hz, 1 H), 4.08 (ddd, 1 H, J = 8, 6 and 3 Hz), 4.0 (d, J = 3.0 Hz, 1 H), 2.16 (m, 1 H), 2.08 (m, 1 H), 1.7 (m, 1 H), 1.6 (m, 1 H), 1.45 (s, 3 H), 1.28 (s, 3 H), 0.86 (s, 9 H), 0.1 (s, 3 H), 0.06 (s, 3 H).^{13}C NMR (50 MHz, $CDCl_3$): δ = 138.0, 114.7, 111.2, 104.4, 88.6, 86.3, 71.1, 30.2, 27.3, 26.7, 27.3 (3 C), 18.0, −4.6, −8.1. HRMS (EI): calcd. for $C_{15}H_{26}O_4Si_2$ [M^+ − 15] 313.183513; found 313.185493.

(1R)-1,4-Anhydro-1-(3-butenyl)-2,3-bis-*O*-(*tert*-butyldimethylsilyl)-5,6,7-trideoxy-L-*arabino*-hept-6-enitol (*ent*-15): The 1,2-*O*-isopropylidene derivative **22** (977 mg, 2.97 mmol) in dry CH_2Cl_2 (36 mL) was cooled to 0 °C, and allyltrimethylsilane (1.87 mL, 11.8 mmol) and boron trifluoride−diethyl ether (freshly distilled) (0.75 mL, 5.95 mmol) were added. After 15 min at this temperature, the mixture was allowed to warm to room temperature and stirred overnight. Aqueous saturated $NaHCO_3$ solution was added and the

organic phase decanted. The aqueous phase was extracted with more CH_2Cl_2, and the combined organic phases were washed with aqueous saturated NaCl solution, dried with Na_2SO_4 and concentrated to give an oily residue. Flash chromatography (eluent gradient: ethyl acetate/benzene from 5:95 to 1:9) gave the pure alcohol (yield 515 mg, 55%) which was transformed into the diene ***ent*-15** {$[\alpha]_D = -19$ ($c = 0.2$, $CHCl_3$)} using the same procedure as in the case of **12** (see above).

Synthesis of the Oxabicycles 23, 24, 25, and *ent*-24. – Method A: To a solution of the corresponding dienes **14**, **15**, **18**, and ***ent*-15** (0.23 mmol, 0.02 M) in dry degassed benzene was added the Grubbs' catalyst (20 mmol %). After stirring the reaction mixture for 16 h at reflux, the solvent was removed in vacuo and the residue was purified by flash chromatography (*n*-hexane/benzene: 7:3) to give the corresponding oxabicycles **23**, **24**, **25**, and ***ent*-24**, respectively. – **Method B:** The same as method A, but using more dilute conditions (0.003 M in diene). – **Method C:** To a solution of the corresponding dienes (0.23 mmol, 0.02 M) in dry degassed benzene was added the Grubbs' catalyst (10 mmol %). After stirring the reaction mixture for 8 h at reflux, a second charge of catalyst was added (10 mmol %) and the mixture further heated under reflux for 8 h. The solvent was removed in vacuo and the residue was purified by flash chromatography (*n*-hexane/benzene: 7:3) as in method A.

***tert*-Butyl({(1*S*,6*R*,7*S*,8*R*)-8-[(*tert*-butyldimethylsilyl)oxy]-9-oxabicyclo[4.2.1]non-3-en-7-yl}oxy)dimethylsilane (23):** $[\alpha]_D = +13.3$ ($c = 0.38$, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3013, 2956, 2930, 2857, 2358, 1711, 1471, 1252, 1103 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 5.6–5.5 (m, 2 H), 4.26–4.23 (m, 2 H), 4.0–3.98 (m, 2 H), 2.48 (m, 1 H), 2.35–2.27 (m, 3 H), 0.86 (s, 18 H), 0.06 (s, 3 H), 0.05 (s, 3 H), 0.03 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 129.2, 125.2, 83.7, 83.4, 82.0, 78.9, 36.2, 32.2, 25.7, 17.2 (2 C), −4.8, −4.6, −4.7, −4.1. $C_{20}H_{40}O_3Si_2$: calcd. C 62.44, H 10.48; found C 62.14, H 10.64.

***tert*-Butyl({(1*S*,7*R*,8*S*,9*R*)-9-[(*tert*-butyldimethylsilyl)oxy]-10-oxabicyclo[5.2.1]dec-4-en-8-yl}oxy)dimethylsilane (24):** $[\alpha]_D = +4.3$ ($c = 0.42$, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3012, 2959, 2934, 2928, 2859, 2854, 1471, 1463, 1361, 1257, 1210, 1101, 1083 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 5.82–5.53 (m, 2 H), 4.05 (app. d, J = 8.0 Hz, 1 H), 3.96–3.94 (m, 1 H), 3.81–3.76 (m, 2 H), 2.52–2.46 (m, 1 H), 2.45–2.22 (m, 3 H), 1.7–1.62 (m, 2 H), 0.9 (s, 3 H), 0.87 (s, 9 H), 0.08 (s, 3 H), 0.062 (s, 3 H), 0.05 (s, 3 H), 0.04 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 131.3, 127.6, 88.0, 83.6, 82.2, 79.5, 32.5 (2 C), 27.0, 26.0, 25.8, 18.1, 18.0, −4.3, −4.6, −4.95, −4.99. $C_{21}H_{42}O_3Si_2$: calcd. C 63.26, H 10.61; found C 62.9, H 10.21.

***ent*-24**: $[\alpha]_D = -5.5$ ($c = 0.18$, $CHCl_3$).

***tert*-Butyl({(1*S*,7*R*,8*S*,9*R*)-9-[(*tert*-butyldimethylsilyl)oxy]-10-oxabicyclo[5.2.1]dec-4-en-8-yl}oxy)dimethylsilane (25):** $[\alpha]_D = +10.9$ ($c = 0.22$, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3014, 2960, 2929, 2850, 2350, 1420, 1237 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 5.64–5.52 (m, 2 H), 4.03 (app. d, J = 9.0 Hz, 1 H), 3.94–3.89 (m, 1 H), 3.77–3.75 (m, 2 H), 2.4–2.0 (m, 6 H), 1.7–1.5 (m, 2 H), 0.89 (s, 9 H), 0.87 (s, 9 H), 0.09 (s, 3 H), 0.088 (s, 3 H), 0.08 (s, 3 H), 0.06 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 131.1, 127.9, 88.0, 83.4, 81.1, 79.5, 29.4, 28.8 (2 C), 25.9, 25.7, 23.6, 18.0, 17.8, −4.4, −4.5, −4.7, −5.0. $C_{22}H_{44}O_3Si_2$: calcd. C 64.02, H 10.74; found C 63.64, H 10.75.

Acknowledgments

We gratefully acknowledge financial support by the Spanish Ministerio de Ciencia y Tecnología (PB98–0443-C02–02), the Canary Islands Consejería de Educación y Ciencia (COFI2000/03), and the FEDER (1SD97–0747-C4–01).

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Received June 8, 2001
[O01276]