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A Convenient Approach for Access to Both Carbapentofuranoses and Carbahexopyranoses. Stereocontrolled Synthesis of Enantiopure Carba-D-ribofuranoses, Carba-D-arabinofuranoses and Carba-L-gulopyranose

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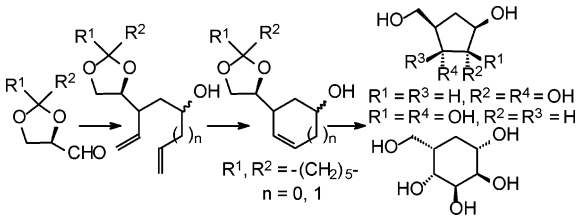

A new approach to carbasugars in enantiomerically pure form is reported. The key step involves ring-closing metathesis of dienols **6** derived from a (*R*)-(+)-glyceraldehyde derivative **4** to form the substituted cyclopentenol **9** and cyclohexenol **34a**. Stereocontrolled addition of hydroxyl groups followed by conversion of the ketal unit to hydroxymethyl group in these intermediates led to carbapentoses and -hexoses. Stereoselectivity during introduction of hydroxyl groups arises through the steric hindrance posed by the allylic substituents. A remarkable feature of the present approach is the accessibility of both D- and L-series of carbapentoses as illustrated by the synthesis of β-D- and β-L-carbaribofuranoses **17** and **20**, respectively. Carba-α-D-ribofuranose **25**, the biosynthetic intermediate to the antibiotic aristeromycin, has also been synthesized from the same cyclopentenol **9**. Functional group manipulation in the cyclopentenol **9a** also enabled access to carbaarabinofuranose **32**. The present synthetic strategy can be extended for the synthesis of carbahexopyranose, as illustrated by the synthesis of carba-β-L-gulopyranose **40b**.

Introduction

Carbocyclic analogues of pentoses and hexoses, often referred to as carbasugars,[1] are structural features present in many biologically interesting molecules. Because of improved acid and metabolic stability relative to their glycoside counterparts, compounds containing carbasugar moieties are potential therapeutic agents.[2] For example, a number of carbasugar-containing nucleoside analogues exhibits promising antiviral activities. Also oligosaccharide analogues containing carbasugar residues have been reported to be efficient glycosyltransferase inhibitors[3] which have considerable therapeutic potential in the management of cancer, diabetes, and viral infections. Thus, development of efficient routes for the synthesis of carbasugars continues to be at the forefront of organic synthesis.[4,5]

Apart from the construction of highly oxygenated carbocycles, stereocontrol in the synthesis of carbasugars is the major hurdle. Synthetic investigations made so far toward carbapentoses involve either transformation of carbohydrates[4a−j] with hydroxyl groups of predefined stereochemistry or fragmentation of norbornene derivatives.[4k−n] A few approaches involving construction of cyclopentene derivatives[5] followed by hydroxylation have also been reported. A novel substrate-dependent dihydroxylation of cyclopentene has been reported recently by Miller

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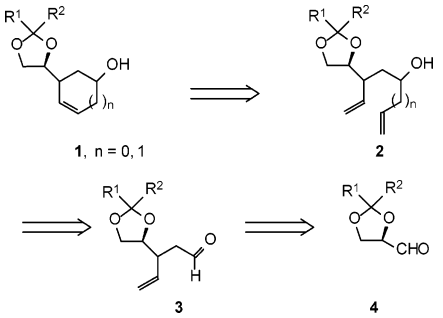
SCHEME 1



and co-workers.[6] All of these investigations were mainly aimed either at carbapentoses or at carbapyranoses, but there was no general approach that can lead access to both carbapentoses and carbahexoses.[7]

As part of our continued interest[8] in the synthesis of cyclopentane-containing molecules of biological interest, we initiated a program to design a general approach that would allow access to both carbapentofuranoses and carbahexopyranoses. We anticipated that carbaanalogues of pentoses and hexoses could be prepared from the carbocyclic enols of the general structure **1** (Scheme 1) on stereocontrolled introduction of the hydroxyl groups. The ketal moiety at the allylic center would be the source of chirality as well as the hydroxymethyl group. The cyclic alkenols **1** would be available by ring-closing metathesis[9,10] of the dienols **2**, which in turn would be available from the unsaturated aldehyde **3** on addition of alkenyl metal having the required number of methylenes for entry into either carbapentoses or carbahexoses. The unsaturated aldehyde **3** would be available from (*R*)-(+)-glyceraldehyde derivative **4**. We herein report the results of our investigation based on this concept.

Results and Discussion

For entry into carbapentoses, cyclopentenol **9a** (Scheme 2) is required. Toward this end the (*R*)-(+)-glyceraldehyde derivative **4** was converted to a chromatographically separable 1:1 mixture of the unsaturated esters **5a** and **5b** following the literature procedure.[10e] Conversion of the pure ester **5a** to the aldehyde **3a** and reaction of the latter with vinyl magnesium bromide gave a 1:1 mixture of the dienols **6a**. Ring-closing metathesis of the dienols **6a** with Grubbs I Ru-catalyst $(PCy_3)_2Cl_2Ru{=}CHPh$ afforded a mixture of the cyclopentenols **7a**.[10f] The desired cyclopentenol **9a** could however be obtained predominantly in the following way. We anticipated that reduction of the cyclopentenone, to be available from oxidation of this mixture of cyclopentenols, would proceed from the side opposite to the C-4 substituent to provide the desired cyclopentenol predominantly. The mixture of the cyclopentenols **7a** was oxidized to give the ketone **8a** in 96% yield. Reduction of the ketone **8a** with $LiAlH_4$ gave a mixture of the cyclopentenols **9a** along with its C-1 diastereomer in 16:1 ratio. The major cyclopentenol **9a** was obtained in 79% yield after column chromatography. The stereochemical assignment to **9a** was based on the NOE (1.8%) between C_1 and C_4 hydrogens. In a similar fashion the aldehyde **3b**, prepared from the diastereoisomeric ester **5b**, was converted to the cyclopentenol **9b**.

After successful synthesis of the cyclopentenols **9a** and **9b**, we focused on their transformation to both β-D- and β-L-carbaribofuranoses. The hydroxyl group in **9a** and **9b** was protected to provide the benzyl ethers **10a** and **10b**, respectively. Dihydroxylation of the cyclopentene derivative **10a** was achieved with OsO_4 to produce exclusively the diol **11** in 90% yield. Stereochemical assignment to the diol **11** was based on Kishi's principle,[11] according to which hydroxylation took place from the face of the double bond opposite to the alkoxy group. This stereochemical assignment was further confirmed through transformation of the diol **11** to carba-β-D-ribofuranose **17 (**vide infra**)**. For completion of the synthesis, the diol **11** was protected to afford the tribenzyl derivative **12**. Acid-induced deketalization of **12** afforded the diol **13**. Periodate cleavage of the diol **13** followed by reduction of the resulting aldehyde **15** afforded the polyoxygenated cyclopentane **16** in overall excellent yield. Finally, hydrogenolysis led to carba-β-D-ribofuranose **17**, $[\alpha]_D$ +8.5 (*c* 1.7, MeOH) [lit.[4k] $[\alpha]_D$ +8.0 (*c* 2.9, MeOH)]. ^1H and ^{13}C NMR spectra of the sample obtained in this way were closely comparable to those reported in literature.[4i] Following a similar protocol, dihydroxylation of the cyclopentene **10b**

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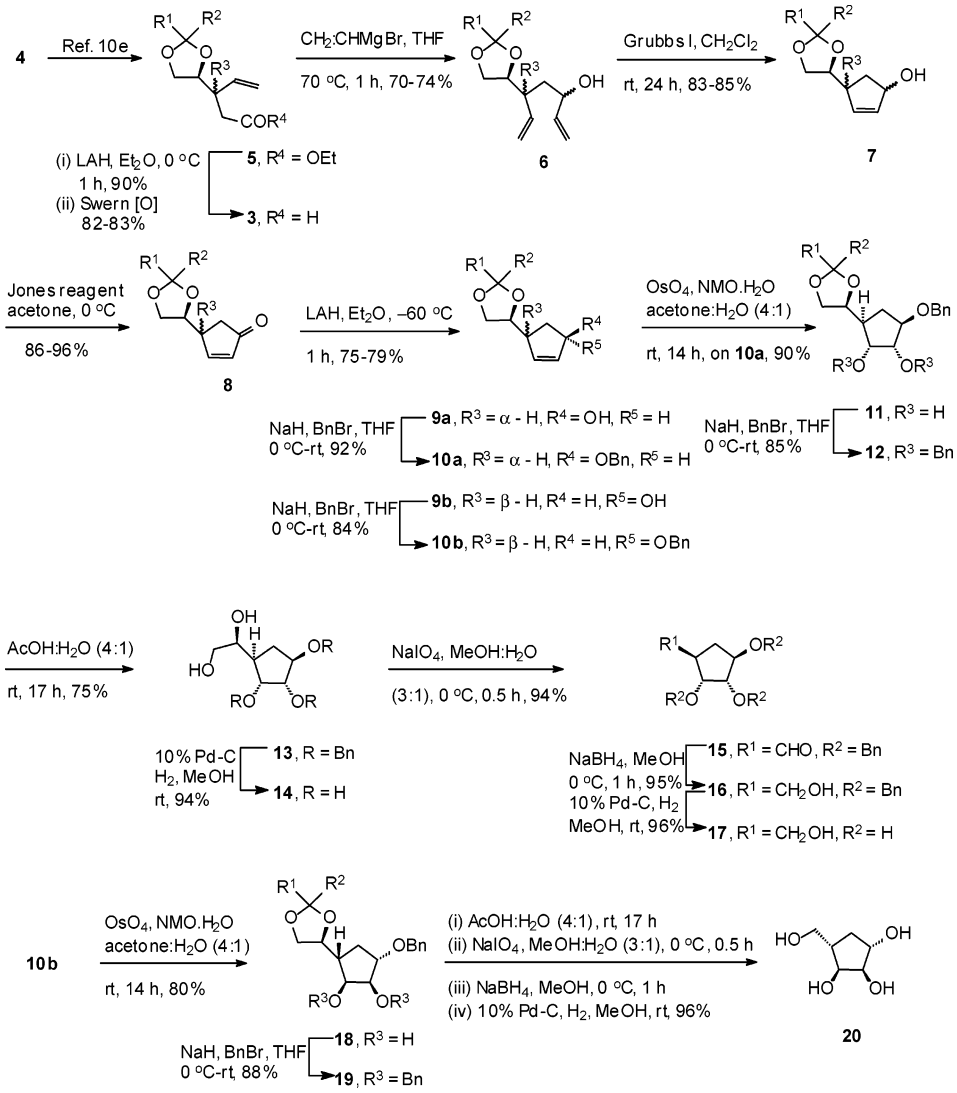
SCHEME 2[a]



[a] For structures **3**−**12**, **18**, and **19**: R^1, R^2 = -$(CH_2)_5$- and for structures **3** and **5**−**8**: **a**, R^3 = α-H; **b**, R^3 = β-H.

afforded the diol **18**, which on benzylation gave the tribenzyl derivative **19**. Carba-β-L-ribofuranose **20**, $[\alpha]_D$ −6.2 (*c* 1.5, MeOH), was then obtained from **19** following the protocol used for the synthesis of **17**. Thus, availability of the carbaribofuranoses of both the D- and L-series from a single enantiomer, (*R*)-(+)-glyceraldehyde derivative **4** is a remarkable advantage of this approach. Further, hydrogenolysis of the tribenzyl derivative **13** afforded the carbaaldohexofuranose **14**, a new class of carbasugars for synthesis of which there is only a single report.[4e]

The cyclopentenol **9a** can also be employed for synthesis of the carba-α-D-ribofuranose. For this purpose it is necessary to invert the configuration of the C-1 hydroxyl group. This was achieved as delineated in Scheme 3. The cyclopentenol **9a** was converted to the silyl ether **21**. Dihydroxylation of the cyclopentene **21** followed by benzylation of the diol **22a** gave the dibenzyl ether **22b**. The latter on desilylation gave the cyclopentanol **22c**. Oxidation of the cyclopentanol **22c** with Jones reagent afforded the ketone **23** in 87% yield. Reduction of the ketone **23** with $LiAlH_4$ took place from addition of the hydride predominantly from the side opposite to C-2, C-3 benzyloxy groups to afford the cyclopentanol **24** in 60% isolated yield with 9% yield of the diastereomeric cyclopentanol **22c**. The ketal group in **24** was then converted to a hydroxymethyl group using the four-step protocol for conversion of **12** to **17** as described in Scheme 2 to afford carba-α-D-ribofuranose **25**, $[\alpha]_D$ +42.4 (*c* 1.7, MeOH) [lit.[5b] $[\alpha]_D$ +46.1 (*c* 0.8, MeOH)]. ^{1}H NMR[4h] and ^{13}C NMR[5b] spectral data of the carbasugar **25** were closely comparable to those reported in literature. The importance of the carbasugar **25** as a biosynthetic intermediate to the antibiotic aristeromycin **26**[5b] has already been established.

The cyclopentanol **22c** can be used for entry into the arabino series. It is interesting to note that whereas Jones oxidation of the cyclopentanol **22c** gave the cyclopentanone **23**, Swern oxidation gave the cyclopentenone **27** in excellent yield (Scheme 4). Triethylamine used during Swern oxidation probably facilitated elimination of the benzyloxy group β to the carbonyl of the initially formed cyclopentanone **23**. Hydroboration of the enone **27** gave a mixture of the diols, which on chromatography afforded the pure diols **29a** (20%) and **30a** (54%). The moderate stereoselectivity observed during this reaction may be rationalized as follows. Reduction of carbonyl group in conjugated enone with diborane generally proceeds[12] at a faster rate to form

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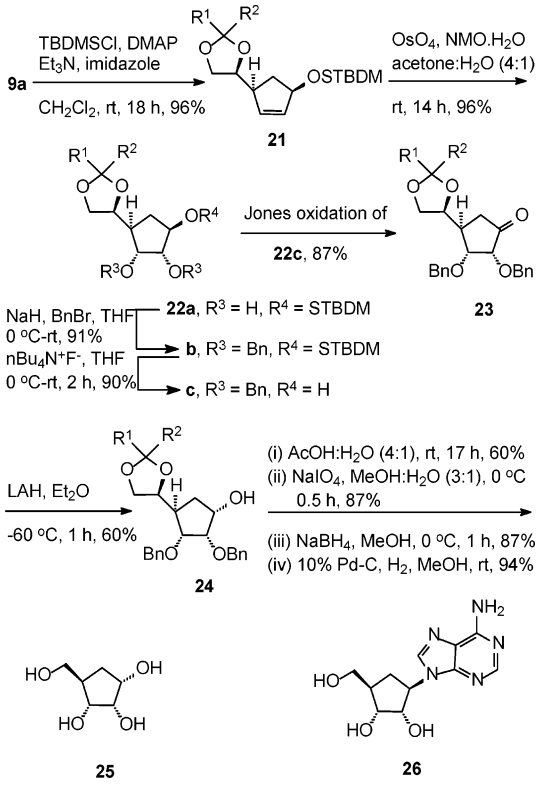
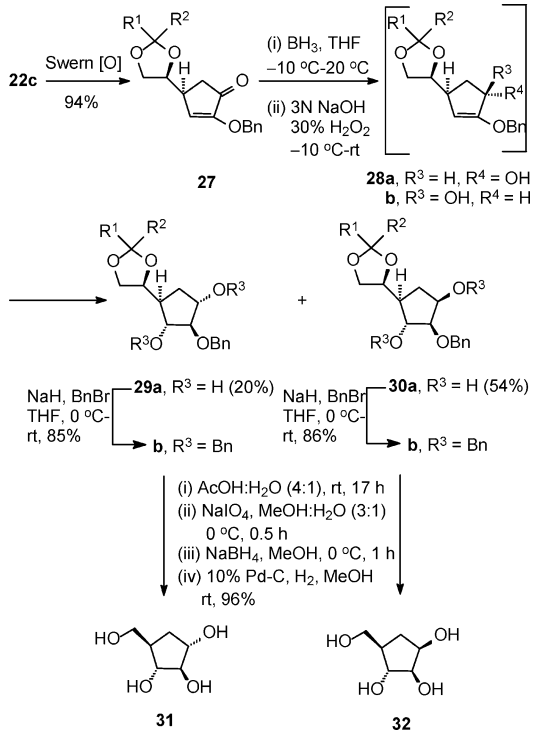
SCHEME 3[a]



[a] For structures **21**−**24**: R^1, R^2 = -$(CH_2)_5$-.

SCHEME 4[a]



[a] For structures **27**−**30**: R^1, R^2 = -$(CH_2)_5$-.

allylic alcohol. Thus reaction of the enone **27** probably proceeded through preferential addition of diborane to an initially formed carbonyl-borane complex from the face opposite to the C-4 substituent leading to a mixture of the nonisolable allylic alcohols **28a** and **28b**, with the latter predominating. Subsequent addition of borane to the alkene units in these alcohols occurred exclusively from the opposite face of the C-4 substituent leading to the diols **29a** and **30a**. For completion of the synthesis of the carbaarabinofuranoses, the diols **29a** and **30a** were benzylated to afford **29b** and **30b**, respectively. Each of the benzyloxy cyclopentanes **29b** and **30b** were subjected to the four-step protocol already described for conversion of **12** to carba-β-D-ribofuranose **17**, to give carba-α-D-arabinofuranose **31**, $[\alpha]_D$ +44.5 (*c* 1.5, MeOH) [lit.[4i] (for *ent*-**31**) $[\alpha]_D$ −40.5 (*c* 0.84, MeOH)] and carba-β-D-arabinofuranose **32**, $[\alpha]_D$ +9.2 (*c* 1.5, MeOH) [lit.[4g] $[\alpha]_D$ +9.7 (*c* 0.7, MeOH)]. ^{1}H and ^{13}C NMR spectral data of the carbasugars **31** and **32** were also comparable to those reported in literature.[4i,n]

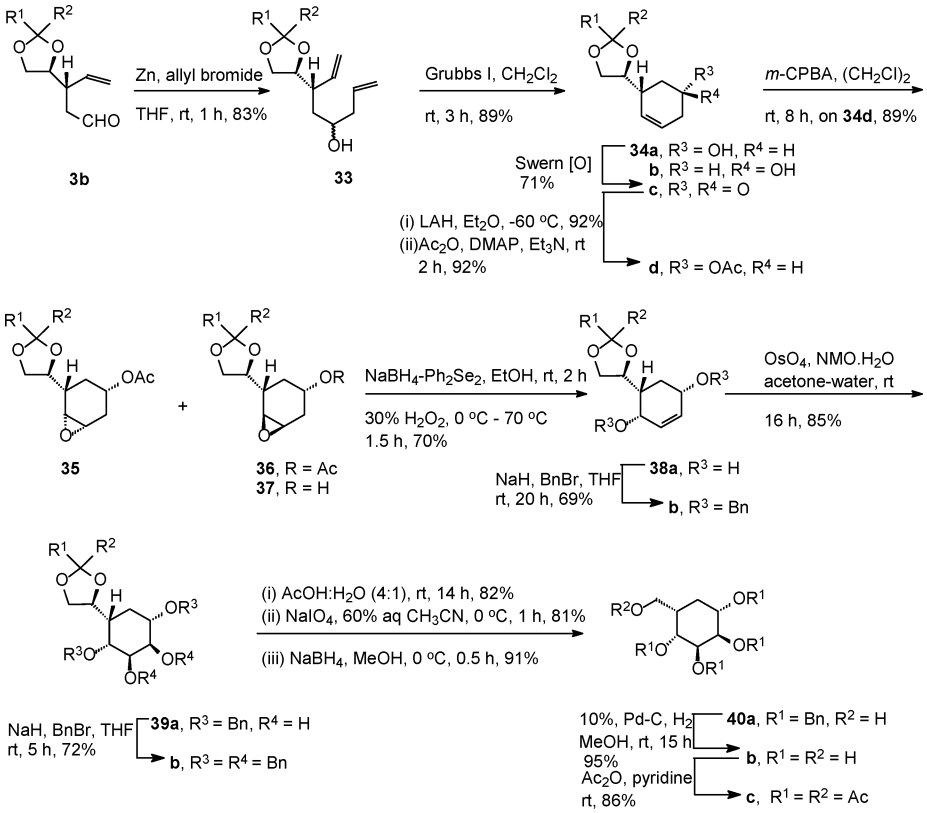
The above protocol can be extended for access to carbahexopyranoses as illustrated by the synthesis of 5a-carba-β-L-gulopyranose. Toward this end, the aldehyde **3b** was allowed to react with allyl zinc to afford a diastereoisomeric mixture of the alcohols **33** (Scheme 5). Ring-closing metathesis of this dienol mixture with Grubbs' first generation catalyst afforded the cyclohexenols **34a** and **34b** in excellent yield. The cyclohexenol **34a** could be exclusively obtained by oxidation of the mixture of the cyclohexenols **34a** and **34b** to the cyclohexenone **34c** followed by its reduction with $LiAlH_4$. NOE (1.8%) between C-1 and C-5 hydrogens in the acetate **34d** derived from **34a** confirmed the syn stereochemical assignment. For introduction of the hydroxyl groups, the cyclohexenol **34a** was subjected to epoxidation with *m*-CPBA. A mixture of products was obtained from which no desired epoxide could be isolated. However, epoxidation of the acetate **34d** with *m*-CPBA proceeded smoothly to produce in 89% yield an inseparable mixture of the oxiranes **35** and the diastereoisomer **36**. An attempt to convert these oxiranes to the corresponding allylic alcohols using the procedure (Ph_2Se_2/$NaBH_4$/30% H_2O_2) of Sharpless and Lauer[13] led to isolation of the ene-diol **38a** in 41% yield. During this reaction, the oxirane ring in **36** remained unchanged and produced only the deacetylated epoxide **37** in 29% yield. The inertness of the oxirane ring in **36** toward nucleophilic opening may be explained as follows. Opening of the oxirane ring in **36** requires the nucleophile to approach from the opposite face of the epoxide ring, which is hindered by the bulky ketal substituent. The hydroxyl groups in the cyclohexenediol **38a** were protected to provide the benzyl ether **38b**. Dihydroxylation with OsO_4 led exclusively the *cis*-diol **39a**. The stereochemical assignment to the diol **39a** follows from its conversion to the known gulopyranose **40b** as stated below. The diol **39a** was benzylated, and the ketal unit in tetrabenzylated derivative **39b** was converted to the hydroxymethyl group using the four-step protocol used in the synthesis of carbafuranoses to afford carba-β-L-gulopyranose **40b**. The pentaacetate **40c**, $[\alpha]_D^{25}$ +21.5 (*c* 2.0, $CHCl_3$) [lit.[7f] $[\alpha]^{20}_D$ +20.5 (*c* 1.0, $CHCl_3$)] obtained from acetylation of **40b** displayed ^{1}H NMR spectral data comparable to those reported in literature.[7f]

Conclusion

We have developed a new synthetic approach that provided access to both carbapentoses and carbahexoses in enantiomerically pure form. A ring-closing metathesis of dienols derived from (*R*)-(+)-glyceraldehyde derivative afforded the basic carbocyclic units, which on stereoselective hydroxylation gave

(13) Sharpless, K. B.; Lauer, R. F. *J. Am. Chem. Soc.* **1973**, *95*, 2697.

SCHEME 5[a]



[a] For structures **3b** and **33**−**39**: R^1, R^2 = -$(CH_2)_5$-.

the carbasugars. The synthesis of both the D- and L-series of carbaribofuranoses from a single enantiomer of glyceraldehyde derivative is the most remarkable feature of the present approach.

Experimental Section

(4*S*)-4-[(2*S*)-1,4-Dioxaspiro[4.5]dec-2-yl]cyclopent-2-en-1-one 8a. To a magnetically stirred solution of the mixture of the cyclopentenol derivatives **7a**, prepared by ring-closing metathesis of the dienol mixture **6a** according to the previously published procedure,[10f] (350 mg, 1.56 mmol) in acetone (10 mL) was added dropwise Jones reagent (1.2 mL) at 0 °C till the color of the reagent persisted. After stirring at that temperature for an additional 30 min, the reaction mixture was diluted with water (2 mL) and extracted with diethyl ether (2 × 15 mL). The combined organic layer was washed sequentially with aqueous NaOH solution (20%, 5 × 1 mL) and water (5 × 1 mL) and dried. Removal of the solvent in vacuo followed by column chromatography using ether/petroleum ether (1:6) as eluent afforded the cyclopentenone derivative **8a** (333 mg, 96%): IR 1715.0 cm^{-1}; ^1H NMR δ 1.41 (2H, br s, CH_2), 1.53−1.64 (8H, m, CH_2), 2.04 (1H, dd, J = 2.4, 18.6 Hz, CH_2), 2.45 (1H, dd, J = 6.6, 18.9 Hz, CH_2), 3.08−3.14 (1H, m, CH), 3.67−3.73 (1H, m), 3.98−4.09 (2H, m), 6.26 (1H, dd, J = 1.8, 5.4 Hz, =CH), 7.77 (1H, dd, J = 2.4, 5.4 Hz, =CH); ^{13}C NMR δ 23.7 (CH_2), 23.9 (CH_2), 25.0 (CH_2), 34.6 (CH_2), 36.4 (CH_2), 36.9 (CH_2), 45.4 (CH), 67.2 (OCH_2), 77.3 (OCH), 110.3 (C), 135.3 (CH), 165.1 (CH), 208.5 (CO); HRMS (ESI) calcd for $C_{13}H_{18}O_3Na$ $(M + Na)^+$, 245.1154; found, 245.1112.

Reduction of Ketone 8a. (1*R*,4*S*)-4-[(2*S*)-1,4-Dioxaspiro[4.5]-dec-2-yl]cyclopent-2-en-1-ol 9a and its C-1 Diastereoisomer. To a stirred suspension of $LiAlH_4$ (260 mg, 6.84 mmol) in diethyl ether (15 mL) at −60 °C was added dropwise a solution of the cyclopentenone derivative **8a** (1.38 g, 6.22 mmol) in diethyl ether (20 mL). After stirring at that temperature for 1 h, the reaction mixture was quenched by sequential addition of water (0.26 mL), aqueous NaOH solution (15%, 0.26 mL), and water (0.78 mL) and allowed to attain room temperature. After stirring at room temperature for 15 min, the white solid formed was filtered off. The solid was washed thoroughly with diethyl ether. The combined ether layer was dried. Removal of solvent in vacuo followed by column chromatography of the residual mass with silica gel (100−200 mesh) using ether/petroleum ether (1:3) as eluent afforded the cyclopentenol derivatives **9a** (1.1 g, 79%) and its C-1 diastereomer (70 mg, 5%) as viscous liquid.

9a. R_f = 0.54 (EtOAc/petroleum ether 1:1); $[\alpha]^{22}_D$ −90.5 (*c* 5.1, $CHCl_3$); ^1H NMR δ 1.37 (2H, br s, CH_2), 1.56−1.57 (8H, m, CH_2), 2.26−2.36 (2H, m, CH_2), 2.73−2.77 (2H, m), 3.70 (1H, dd, J = 6.5, 8.0 Hz, OCH_2), 4.04 (1H, dd, J = 6.3, 7.7 Hz, OCH_2), 4.10−4.15 (1H, m, OCH), 4.62−4.64 (1H, m, C_1−H), 5.88 (1H, dd, J = 2.2, 5.5 Hz, =CH), 6.01−6.02 (1H, m, =CH); ^{13}C NMR δ 24.1 (CH_2), 24.3 (CH_2), 25.4 (CH_2), 35.1 (CH_2), 36.2 (CH_2), 37.5 (CH_2), 47.0 (CH), 67.4 (OCH_2), 75.8 (OCH), 77.8 (OCH), 110.2 (C), 133.1 (CH), 136.8 (CH); HRMS (ESI) calcd for $C_{13}H_{20}O_3Na$ $(M + Na)^+$, 247.1310; found, 247.1343.

C-1 Diastereomer of 9a. R_f = 0.49 (EtOAc/petroleum ether 1:1); $[\alpha]^{22}_D$ −161.7 (*c* 2.9, $CHCl_3$); ^1H NMR δ 1.40 (2H, br s, CH_2), 1.52−1.68 (8H, m, CH_2), 1.75−1.93 (2H, m, CH_2), 3.03−3.09 (2H, m), 3.58 (1H, t, J = 6.9 Hz), 3.87 (1H, dd, J = 6.4, 13.0 Hz), 3.97−4.02 (1H, m), 4.87−4.90 (1H, m, C_1−H), 5.92−5.94 (1H, m, =CH), 6.05−6.08 (1H, m, =CH); ^{13}C NMR δ 23.8 (CH_2), 24.0 (CH_2), 25.1 (CH_2), 34.9 (CH_2), 36.1 (CH_2), 36.4 (CH_2), 48.3 (CH), 67.5 (OCH_2), 76.9 (OCH), 78.9 (OCH), 109.7 (C), 134.6 (CH), 136.5 (CH); HRMS (ESI) calcd for $C_{13}H_{20}O_3Na$ $(M + Na)^+$, 247.1310; found, 247.1313.

(2*S*)-2-[(1*S*,4*R*)-4-(Benzyloxy)cyclopent-2-en-1-yl]-1,4-dioxaspiro[4.5]decane 10a. To a magnetically stirred suspension of NaH (60 mg, 1.25 mmol, 50% in oil), freed from adhering oil

by repeated washing with petroleum, in dry THF (3 mL) at 0 °C was added dropwise a solution of the alcohol **9a** (140 mg, 0.63 mmol) in dry THF (3 mL) under N_2 atmosphere. The mixture was allowed to stir at room temperature for 2 h, and then to it was added HMPA (0.3 mL) dropwise followed by benzyl bromide (0.15 mL, 1.25 mmol). After stirring for an additional 12 h at room temperature, the reaction mixture was cooled to 0 °C and quenched by adding cold water (1 mL). Usual workup of the reaction mixture followed by column chromatography using ether/petroleum ether (1:4) as eluent afforded the benzyl ether **10a** (180 mg, 92%) as a colorless viscous liquid: $[\alpha]^{23}_D$ −23.9 (*c* 1.5, $CHCl_3$); ^{1}H NMR δ 1.39−1.49 (2H, m, CH_2), 1.56−1.63 (8H, m, CH_2), 2.27 (2H, td, J = 7.7, 13.7 Hz, CH_2), 2.74−2.77 (1H, m, CH), 3.66 (1H, ddd, J = 3.4, 5.9, 9.3 Hz), 3.94−4.04 (3H, m), 4.51 (1H, d, J = 11.9 Hz, $PhCH_2$), 4.56 (1H, d, J = 12.0 Hz, $PhCH_2$), 5.94 (1H, td, J = 2.0, 5.7 Hz, =CH), 6.03 (1H, td, J = 1.7, 5.8 Hz, =CH), 7.25−7.34 (5H, m, ArH); ^{13}C NMR δ 23.8 (CH_2), 24.0 (CH_2), 25.1 (CH_2), 32.2 (CH_2), 34.9 (CH_2), 36.5 (CH_2), 48.0 (CH), 67.3 (OCH_2), 70.9 (OCH_2) 78.8 (OCH), 83.7 (OCH), 109.5 (C), 127.5 (CH), 127.7 (CH), 128.3 (CH), 132.4 (CH), 135.9 (CH), 138.5 (C); HRMS (ESI) calcd for $C_{20}H_{26}O_3Na$ $(M + Na)^+$, 337.1780; found, 337.1784.

(1*R*,2*R*,3*R*,5*S*)-3-(Benzyloxy)-5-[(2*S*)-1,4-dioxaspiro[4.5]dec-2-yl]cyclopentane-1,2-diol 11. To a magnetically stirred solution of the cyclopentene derivative **10a** (160 mg, 0.51 mmol) in acetone/water (4:1, 7.5 mL) at room temperature was added *N*-methylmorpholine *N*-oxide monohydrate (207 mg, 1.53 mmol) followed by a catalytic amount of OsO_4. After the reaction mixture stirred at room temperature for 14 h, acetone was removed under reduced pressure. The residual mass was extracted with chloroform (2 × 10 mL), washed with brine (2 × 2 mL), and dried. Removal of solvent in vacuo followed by column chromatography using ethyl acetate/petroleum ether (2:3) afforded the *cis*-diol **11** (159 mg, 90%): $[\alpha]^{23}_D$ +1.2 (*c* 1.5, $CHCl_3$); ^{1}H NMR δ 1.26 (1H, ddd, J = 5.6, 9.6, 13.1 Hz, CH_2), 1.39 (2H, br s, CH_2), 1.57−1.61 (8H, m, CH_2), 1.98−2.09 (1H, m, CH), 2.17 (1H, td, J = 8.3, 13.3 Hz, CH_2), 3.13 (1H, br s, OH), 3.32 (1H, br s, OH), 3.60 (1H, dd, J = 6.0, 7.0 Hz), 3.86 (1H, dt, J = 2.0, 7.4 Hz), 4.0−4.12 (4H, m), 4.51 (1H, d, J = 11.8 Hz, $PhCH_2$), 4.57 (1H, d, J = 11.8 Hz, $PhCH_2$), 7.24−7.38 (5H, m, ArH); ^{13}C NMR δ 23.7 (CH_2), 23.9 (CH_2), 24.9 (CH_2), 30.4 (CH_2), 34.8 (CH_2), 36.2 (CH_2), 45.1 (CH), 67.9 (OCH_2), 71.5 (OCH_2), 75.4 (OCH), 75.8 (OCH), 78.9 (OCH), 82.7 (OCH), 109.7 (C), 127.5 (CH), 128.2 (CH), 138.0 (C); HRMS (ESI) calcd for $C_{20}H_{28}O_5Na$ $(M + Na)^+$, 371.1834; found, 371.1840.

(2*S*)-2-[(1*R*,2*R*,3*S*,4*R*)-2,3,4-tris(Benzyloxy)cyclopent-1-yl]-1,4-dioxaspiro[4.5]decane 12. Following the procedure for the benzylation of the alcohol **9a**, the *cis*-diol **11** (140 mg, 0.40 mmol) was benzylated with benzyl bromide (0.19 mL, 1.61 mmol) to afford the benzyl ether **12** (180 mg, 85%) as a colorless viscous liquid: $[\alpha]^{23}_D$ −16.8 (*c* 1.5, $CHCl_3$); ^{1}H NMR δ 1.22−1.30 (1H, m, CH_2), 1.39 (2H, br s, CH_2), 1.49−1.61 (8H, m, CH_2), 2.17−2.33 (2H, m, CH_2, CH), 3.62 (1H, dd, J = 6.6, 6.9 Hz), 3.81 (1H, *t*, J = 5.4 Hz), 3.92−4.02 (3H, m), 4.13 (1H, dd, J = 6.6, 13.2 Hz), 4.52−4.66 (6H, m, $PhCH_2$), 7.23−7.39 (15H, m, ArH); ^{13}C NMR δ 23.7 (CH_2), 23.9 (CH_2), 25.1 (CH_2), 29.5 (CH_2), 34.8 (CH_2), 36.4 (CH_2), 43.7 (CH), 67.2 (OCH_2), 71.2 (OCH_2), 71.6 (OCH_2), 71.7 (OCH_2), 77.1 (OCH), 78.3 (OCH), 81.0 (OCH), 82.9 (OCH), 109.5 (C), 127.36 (CH), 127.40 (CH), 127.43 (CH), 127.5 (CH), 127.6 (CH), 128.0 (CH), 128.12 (CH), 128.14 (CH), 128.2 (CH), 138.3 (C), 138.4 (C); HRMS (ESI) calcd for $C_{34}H_{41}O_5$ $(M + H)^+$, 529.2954; found, 529.2917.

(1*S*)-1-[(1*R*,2*R*,3*S*,4*R*)-2,3-4-Tris(benzyloxy)cyclopent-1-yl]ethane-1,2-diol 13. A mixture of the cyclopentane derivative **12** (160 mg, 0.30 mmol) and aqueous acetic acid (80%, 2.5 mL) was stirred at room temperature for 17 h. The resulting solution was diluted with ethyl acetate (10 mL) and washed repeatedly with aqueous NaOH solution (20%, 5 × 1.5 mL) to make it just alkaline (pH paper). The organic layer was washed with brine (2 × 1 mL), dried, and concentrated, and the residual mass was column chromatographed using ethyl acetate/petroleum ether (2:3) to afford the diol **13** (96 mg, 71%): $[\alpha]^{24}_D$ +44.7 (*c* 1.5, $CHCl_3$); ^{1}H NMR δ 1.33 (1H, ddd, J = 4.2, 8.5, 13.0 Hz, CH_2), 2.21−2.31 (1H, m, CH), 2.37 (1H, t, J = 8.3 Hz, CH_2), 2.75 (2H, br s, OH), 3.45 (1H, dd, J = 5.7, 11.7 Hz, OCH_2), 3.59 (2H, dd, J = 3.0, 11.7 Hz, OCH_2, OCH), 3.88 (1H, dd, J = 1.9, 4.5 Hz), 3.95 (2H, dd, J = 4.7, 7.7 Hz), 4.39−4.60 (6H, m, $PhCH_2$), 7.29−7.34 (15H, m, ArH); ^{13}C NMR δ 30.5 (CH_2), 42.1 (CH), 65.1 (OCH_2), 71.25 (OCH_2), 71.27 (OCH_2), 71.7 (OCH_2), 75.0 (OCH), 80.0 (OCH), 80.1 (OCH), 81.3 (OCH), 127.5 (CH), 127.70 (CH), 127.72 (CH), 127.8 (CH), 127.9 (CH), 128.0 (CH), 128.3 (CH), 128.37 (CH), 128.38 (CH), 137.3 (C), 137.9 (C), 137.9 (C); HRMS (ESI) calcd for $C_{28}H_{33}O_5$ $(M + H)^+$, 449.2328; found, 449.2328.

(1*R*,2*S*,3*R*,4*R*)-4-[(1*S*)-1,2-Dihydroxyethyl]cyclopentane-1,2,3-triol (Carba-β-D-allofuranose) 14. A solution of the diol **13** (16 mg, 0.03 mmol) in dry methanol (2 mL) containing Pd−C (10%) was stirred under hydrogen atmosphere at room temperature for 20 h. The catalyst was filtered off, and removal of solvent in vacuo afforded the alcohol **14** (6 mg, 94%): $[\alpha]^{24}_D$ −7.5 (*c* 0.5, CH_3OH); ^{1}H NMR (CD_3OD) δ 1.25−1.33 (1H, m), 2.03 (1H, m), 2.12−2.22 (1H, m), 3.54−3.70 (4H, m), 3.96−3.98 (1H, m), 4.10 (1H, m); ^{13}C NMR (CD_3OD) δ 33.7 (CH_2), 45.9 (CH), 66.0 (OCH_2), 73.7 (OCH), 75.5 (OCH), 76.5 (OCH), 79.6 (OCH); HRMS (ESI) calcd for $C_7H_{14}O_5Na$ $(M + Na)^+$, 201.0739; found, 201.0723.

(1*S*,2*R*,3*S*,4*R*)-2,3,4-Tris(benzyloxy)cyclopentanecarbaldehyde 15. To a magnetically stirred ice-cold solution of the diol **13** (80 mg, 0.18 mmol) in methanol/water (3:1, 1.6 mL) was added $NaIO_4$ (76 mg, 0.36 mmol) in multiple portions. The reaction mixture was allowed to stir at 0 °C for 30 min. The precipitated white solid was filtered off after washing it thoroughly with diethyl ether. Usual workup of the filtrate afforded the aldehyde **15** (70 mg, 94%): IR 1722.3 cm^{-1}; ^{1}H NMR δ 1.91−1.99 (1H, m, CH_2), 2.34 (1H, ddd, J = 6.6, 10.6, 14.3 Hz, CH_2), 3.05−3.12 (1H, m, CH), 3.89 (1H, t, J = 3.3 Hz), 4.03−4.06 (1H, m), 4.27 (1H, dd, J = 4.6, 6.4 Hz), 4.45−4.87 (6H, m, $PhCH_2$), 7.28−7.35 (15H, m, ArH), 9.72 (1H, s, CHO); ^{13}C NMR δ 27.5 (CH_2), 53.3 (CH), 71.2 (OCH_2), 72.0 (OCH_2), 72.1 (OCH_2), 79.0 (OCH), 80.3 (OCH), 81.1 (OCH), 127.5 (CH), 127.61 (CH), 127.65 (CH), 127.70 (CH), 127.73 (CH), 128.28(CH), 128.31 (CH), 137.7 (C), 137.9 (C), 138.0 (C), 201.7 (CHO); HRMS (ESI) calcd for $C_{27}H_{28}O_4Na$ $(M + Na)^+$, 439.1885; found 439.1832.

[(1*R*,2*R*,3*S*,4*R*)-2,3,4-Tris(benzyloxy)cyclopent-1-yl]methanol 16. To a magnetically stirred ice-cold solution of the aldehyde **15** (70 mg, 0.17 mmol) in methanol (1.8 mL) under argon atmosphere was added $NaBH_4$ (13 mg, 0.34 mmol) in small portions, and the mixture was allowed to stir for 30 min at 0 °C. The reaction mixture was quenched with water. Usual workup of the residual mass obtained after evaporation of methanol under reduced pressure followed by column chromatography using ethyl acetate/petroleum ether (1:3) as eluent afforded the alcohol **16** (67 mg, 95%): $[\alpha]^{20}_D$ +33.0 (*c*1.5, $CHCl_3$); ^{1}H NMR δ 1.30 (1H, ddd, J = 4.9, 7.9, 13.1 Hz, CH_2), 2.21−2.31 (1H, m), 2.35−2.43 (2H, m), 3.56−3.63 (2H, m, OCH_2), 3.80 (1H, dd, J = 4.9, 7.1 Hz), 3.86 (1H, dd, J = 3.1, 4.7 Hz), 4.00 (1H, ddd, J = 3.1, 4.9, 7.6 Hz), 4.43−4.61 (6H, m, $PhCH_2$), 7.23−7.35 (15H, m, ArH); ^{13}C NMR δ 30.1 (CH_2), 42.5 (CH), 65.1 (OCH_2), 71.3 (OCH_2), 71.5 (OCH_2), 71.7 (OCH_2), 80.8 (OCH), 81.07 (OCH), 81.09 (OCH), 127.5 (CH), 127.56 (CH), 127.58 (CH), 127.59 (CH), 127.78 (CH), 127.80 (CH), 128.2 (CH), 128.27 (CH), 128.31 (CH), 138.06 (C), 138.09 (C), 138.2 (C); HRMS (ESI) calcd for $C_{27}H_{30}O_4Na$ $(M + Na)^+$, 441.2042; found, 441.2041.

Synthesis of Dienols 6b. To a magnetically stirred solution of vinyl magnesium bromide [prepared by addition of vinyl bromide (3.3 g, 31 mmol) in THF (40 mL) to magnesium turnings (370 mg, 15.5 mmol)] was added a solution of the aldehyde **3b** (690 mg, 3.1 mmol) in THF (8 mL) and refluxed gently for 1 h. The reaction mixture was allowed to attain room temperature, then cooled to 0 °C, quenched by water (4 mL), and filtered. Organic phase was washed with brine (3 × 4 mL) and dried. Removal of solvent in vacuo followed by column chromatography using ether/

petroleum ether (1:4) as eluent afforded the alcohol **6b** (550 mg, 70%) as a mixture of two diastereoisomers: IR 3445.0 cm^{-1}; ^1H NMR (of the diastereoisomeric mixture) δ 1.33 (4H, br s), 1.42−1.55 (18H, m), 1.74−1.87 (2H, m), 2.18−2.30 (1H, m), 2.33−2.46 (1H, m), 2.82 (2H, br s), 3.52−3.60 (2H, m), 3.84−3.91 (4H, m), 4.11−4.21 (2H, m), 4.99−5.20 (8H, m), 5.47−5.56 (2H, m), 5.77−5.85 (2H, m); ^{13}C NMR (for one isomer from the mixture) δ 24.2 (CH_2), 24.2 (CH_2), 25.4 (CH_2), 35.5 (CH_2), 36.7 (CH_2), 39.8 (CH_2), 45.4 (CH), 68.2 (OCH_2), 71.4 (OCH), 78.3 (OCH), 110.3 (C), 115.4 (CH_2), 117.5 (CH_2), 138.3 (CH), 140.9 (CH) and (for the other isomer) δ 24.2 (CH_2), 24.2 (CH_2), 25.4 (CH_2), 35.5 (CH_2), 36.7 (CH_2), 40.1 (CH_2), 46.1 (CH), 68.4 (OCH_2), 70.9 (OCH), 78.4 (OCH), 110.3 (C), 114.1 (CH_2), 117.7 (CH_2), 138.2 (CH), 141.9 (CH); HRMS (ESI) calcd for $C_{15}H_{24}O_3Na$ $(M + Na)^+$, 275.1623; found, 275.1627.

(1*S*,4*R*)-4-[(2*S*)-1,4-Dioxaspiro[4.5]dec-2-yl]cyclopent-2-en-1-ol 9b and Its C-1 Diastereoisomer. A solution of the above diene mixture **6b** (370 mg, 1.47 mmol) in dry dichloromethane(12 mL) was degassed by bubbling argon through it. To it was added Grubbs' first generation catalyst (44 mg, 0.05 mmol) in one portion. The resulting pink solution was stirred at room temperature under argon atmosphere for 24 h. The residual mass obtained after removal of solvent was chromatographed using ether/petroleum ether (1:3) as eluent to afford the pure cyclopentenol derivative **7b** (280 mg, 85%) as a 1:1 diastereoisomeric mixture.

The mixture of the cyclopentenol derivatives **7b** (362 mg, 1.62 mmol) was oxidized with Jones reagent, as described for oxidation of **7a**, to the cyclopentenone derivative **8b** (310 mg, 86%): IR 1716.5 cm^{-1}; ^1H NMR δ 1.26−1.33 (2H, m, CH_2), 1.47−1.55 (8H, m, CH_2), 2.19 (1H, dd, J = 2.3, 18.8 Hz, CH_2), 2.39 (1H, dd, J = 6.5, 18.8 Hz, CH_2), 3.10−3.15 (1H, m, CH), 3.55 (1H, dd, J = 6.5, 8.2 Hz, OCH_2), 4.01 (1H, dd, J = 6.6, 8.2 Hz, OCH_2), 4.17 (1H, dd, J = 6.3, 11.6 Hz, OCH), 6.21 (1H, dd, J = 2.0, 5.6 Hz, =CH), 7.51 (1H, dd, J = 2.5, 5.7 Hz, =CH); ^{13}C NMR δ 23.5 (CH_2), 23.7 (CH_2), 24.9 (CH_2), 34.3 (CH_2), 35.8 (CH_2), 36.3 (CH_2), 44.4 (CH), 66.4 (OCH_2), 75.7 (OCH), 109.9 (C), 135.7 (CH), 163.5 (CH), 208.7 (CO); HRMS (ESI) calcd for $C_{13}H_{18}O_3Na$ $(M + Na)^+$, 245.1154; found, 245.1179.

Following the procedure for the reduction of the cyclopentenone derivative **8a**, the cyclopentenone derivative **8b** (310 mg, 1.40 mmol) was reduced with $LiAlH_4$ (58 mg, 1.54 mmol) at −60 °C to the cyclopentenol derivative **9b** (272 mg, 75%) and its C-1 diastereoisomer (18 mg, 5%) as viscous liquid.

9b. R_f = 0.55 (EtOAc/petroleum ether 1:1); $[\alpha]^{24}_D$ +33.0 (*c* 1.7, $CHCl_3$); ^1H NMR δ 1.32−1.38 (2H, m, CH_2), 1.48−1.66 (8H, m, CH_2), 2.21 (2H, ddd, J = 7.2, 8.2, 14.1 Hz, CH_2), 2.40−2.42 (1H, m, OH), 2.78−2.82 (1H, m, CH), 3.57 (1H, t, J = 7.9 Hz, OCH_2), 4.03 (1H, dd, J = 6.5, 7.9 Hz, OCH_2), 4.12−4.18 (1H, m, OCH), 4.61−4.63 (1H, m, C_1−H), 5.80 (1H, dd, J = 2.2, 5.6 Hz, =CH), 5.95−5.98 (1H, m, =CH); ^{13}C NMR δ 23.6 (CH_2), 23.9 (CH_2), 25.1 (CH_2), 33.9 (CH_2), 34.6 (CH_2), 35.8 (CH_2), 46.2 (CH), 67.7 (OCH_2), 75.3 (OCH), 75.5 (OCH), 109.8 (C), 134.4 (CH), 135.5 (CH); HRMS (ESI) calcd for $C_{13}H_{20}O_3Na$ $(M + Na)^+$, 247.1310; found, 247.1299.

C-1 Diastereomer of 9b. R_f = 0.50 (EtOAc/petroleum ether 1:1); $[\alpha]^{24}_D$ +131.8 (*c* 2.3, $CHCl_3$); ^1H NMR δ 1.33−1.40 (2H, m, CH_2), 1.48−1.60 (8H, m, CH_2), 1.84 (1H, ddd, J = 3.2, 8.0, 11.2 Hz, CH_2), 2.08 (1H, ddd, J = 4.7, 7.2, 12.0 Hz, CH_2), 3.06−3.12 (2H, m), 3.51−3.58 (1H, m), 3.94−4.01 (2H, m), 4.87−4.90 (1H, m, C_1−H), 5.81 (1H, dd, J = 1.9, 5.5 Hz, =CH), 5.92−5.95 (1H, m, =CH); ^{13}C NMR δ 23.7 (CH_2), 23.9 (CH_2), 25.1 (CH_2), 34.8 (CH_2), 36.2 (CH_2), 36.4 (CH_2), 47.9 (CH), 67.0 (OCH_2), 76.9 (OCH), 77.9 (OCH), 109.5 (C), 134.9 (=CH) 135.7 (=CH); HRMS (ESI) calcd for $C_{13}H_{20}O_3Na$ $(M + Na)^+$, 247.1310; found, 247.1333.

(1*S*,2*R*,3*R*,4*S*)-2-(Benzyloxy)-4-[(2*S*)-1,4-dioxaspiro[4.5]dec-2-yl]cyclopentane-1,3-diol 29a and (1*R*,2*R*,3*R*,4*S*)-2-(Benzyloxy)-4-[(2*S*)-1,4-dioxaspiro[4.5]dec-2-yl]cyclopentane-1,3-diol 30a. To a magnetically stirred solution of $BF_3{\cdot}OEt_2$ (5 mL) in diglyme (20 mL) at 45 °C was added $NaBH_4$ (1.0 g) in small portion, and the BH_3 gas thus liberated was subsequently bubbled through a solution of the cyclopentenone derivative **27** (330 mg, 1.01 mmol) in THF (20 mL) at −10 °C till complete disappearance of the starting cyclopentenone derivative. The reaction mixture was then warmed to 20 °C and was diluted with THF (10 mL). To the magnetically stirred reaction mixture, cooled to −10 °C was added dropwise aqueous NaOH solution (3 N, 7 mL) to make it alkaline (pH paper) followed by H_2O_2 (30%, 7 mL). The reaction mixture was allowed to attain room temperature very slowly when the two layers separated. The organic layer was separated, and the aqueous layer was extracted with ether (2 × 10 mL). The two organic layers were combined and washed with water (4 × 2 mL) and brine (2 × 2 mL) and dried, and the solvent was removed in vacuo. The residual mass was column chromatographed using ethyl acetate/petroleum ether (3:7) as eluent to afford the alcohols **29a** (70 mg, 20%) and **30a** (190 mg, 54%).

29a. $[\alpha]^{23}_D$ −5.1 (*c* 0.3, $CHCl_3$); ^1H NMR δ 1.39−1.40 (2H, m, CH_2), 1.48−1.71 (8H, m, CH_2), 2.06−2.22 (3H, m, CH_2, CH), 2.98 (2H, br s, OH), 3.61 (1H, dd, J = 4.9, 6.5 Hz), 3.75 (1H, dd, J = 4.4, 6.3 Hz), 3.97−4.07 (3H, m), 4.11 (1H, dd, J = 4.4, 10.5 Hz), 4.65 (1H, d, J = 11.8 Hz, $PhCH_2$), 4.82 (1H, d, J = 11.8 Hz, $PhCH_2$), 7.26−7.39 (5H, m, ArH); ^{13}C NMR δ 23.8 (CH_2), 24.1 (CH_2), 25.0 (CH_2), 32.2 (CH_2), 35.0 (CH_2), 36.3 (CH_2), 45.8 (CH), 68.0 (OCH_2), 72.1 (OCH_2), 74.4 (OCH), 79.4 (OCH), 80.1 (OCH), 91.3 (OCH), 109.9 (C), 127.7 (CH), 127.8 (CH), 128.4 (CH), 138.4 (C); HRMS (ESI) calcd for $C_{20}H_{28}O_5Na$ $(M + Na)^+$, 371.1834; found, 371.1846.

30a. $[\alpha]^{23}_D$ −1.9 (*c* 0.8, $CHCl_3$); ^1H NMR δ 1.30−1.40 (2H, m, CH_2), 1.53−1.64 (8H, m, CH_2), 1.80−1.86 (2H, m, CH_2), 2.01−2.11 (1H, m, CH), 2.68 (1H, br s, OH), 2.78 (1H, br s, OH), 3.61 (1H, dd, J = 6.2, 7.8 Hz), 3.70 (1H, dd, J = 5.5, 7.2 Hz), 4.02−4.15 (3H, m), 4.25 (1H, t, J = 7.7 Hz), 4.68 (1H, d, J = 11.8 Hz, $PhCH_2$), 4.81 (1H, d, J = 11.7 Hz, $PhCH_2$), 7.26−7.38 (5H, m, ArH); ^{13}C NMR δ 23.8 (CH_2), 24.1 (CH_2), 25.0 (CH_2), 31.7 (CH_2), 34.9 (CH_2), 36.4 (CH_2), 44.8 (CH), 67.9 (OCH_2), 68.9 (OCH), 72.2 (OCH_2), 79.3 (OCH), 79.9 (OCH), 85.0 (OCH), 109.9 (C), 127.9 (CH), 128.5 (CH), 137.9 (C); HRMS (ESI) calcd for $C_{20}H_{29}O_5$ $(M + H)^+$, 349.2015; found, 349.2029.

(4*R*,6*S*)-6-[(2*S*)-1,4-Dioxa-spiro[4.5]dec-2-yl]octa-1,7-dien-4-ol and Its C-4 Diastereoisomer 33. A solution of allyl bromide (1.0 g, 8.37 mmol) in THF (10 mL) was added dropwise to a stirred suspension of commercial zinc dust (0.4 g, 6.69 mmol) in THF (5 mL) at room temperature, and the mixture was stirred for 1 h to produce a clear solution. A solution of the aldehyde **3b** (1.25 g, 5.58 mmol) in THF (15 mL) was added dropwise to this solution at room temperature and stirred for 1 h. The reaction mixture was then cooled to 0 °C and quenched with a few drops of water. Usual workup of the reaction mixture followed by column chromatography using ether/petroleum ether (1:6) as eluent afforded an inseparable mixtures of dienols **33** (1.23 g, 83%) in a ca. 1:1 ratio: ^1H NMR δ (for both diastereoisomers) 1.35 (2H, br s), 1.47−1.53 (1H, m), 1.58 (4H, br s), 1.62 (4H, br s), 1.72−1.82 (1H, m), 2.23−2.29 (2H, m), 2.33−2.40 (1H, m), 2.60 (1H, br s), 3.62−3.73 (2H, m), 3.85−3.97 (2H, m), 5.05−5.10 (4H, m), 5.52−5.59 (1H, m), 5.80−5.87 (1H, m); ^{13}C NMR δ (for both isomers) 23.9 (CH_2), 24.0 (CH_2), 24.1 (CH_2), 25.10 (CH_2), 25.15 (CH_2), 35.2 (CH_2), 35.3 (CH_2), 36.4 (CH_2), 36.5 (CH_2), 39.7 (CH_2), 39.8 (CH_2), 41.4 (CH_2), 42.68 (CH_2), 42.70 (CH_2), 45.6 (CH), 46.3 (CH), 68.1 (CH_2), 68.2 (CH_2), 68.9 (CH), 69.1 (CH), 78.0 (CH), 78.3 (CH), 109.9 (C), 110.0 (C), 117.0 (CH_2), 117.2 (CH_2), 117.5 (CH_2), 117.6 (CH_2), 135.0 (CH), 135.1 (CH), 138.0 (CH), 138.2 (CH); HRMS (ESI) calcd for $C_{16}H_{26}O_3Na$ $(M + Na)^+$, 289.1780; found, 289.1779.

(5*R*)-5-[(2*S*)-1,4-Dioxa-spiro[4.5]dec-2-yl]-cyclohex-3-enone 34c. A solution of diastereoisomeric dienols **33** (1.1 g, 4.14 mmol) in dichloromethane (50 mL) was treated with Grubbs' first generation catalyst (90 mg, 0.11 mmol) under argon atmosphere and stirred at room temperature for 3 h. The residual mass obtained after removal of solvent was chromatographed using ether/petroleum

ether (1:4) to afford an inseparable mixture of cyclohexenols **34a** and **34b** (0.88 g, 89%) in a ca. 1:1 ratio.

A solution of cyclohexenols **34a** and **34b** (0.4 g, 1.68 mmol) was oxidized through Swern oxidation following the procedure for the synthesis of the aldehyde **3b** with oxalyl chloride (0.23 mL, 2.69 mmol), DMSO (0.36 mL, 5.04 mmol), and triethylamine (1.4 mL, 10.08 mmol) to afford the cyclohexenone **34c** (280 mg, 71%) as a colorless oil: IR (neat) ν_{max} 1718 cm^{-1}; ^{1}H NMR δ 1.36 (2H, br s), 1.51 (4H, br s), 1.54−1.59 (4H, m), 2.44−2.61 (2H, m), 2.74−2.78 (1H, m), 2.85−2.90 (2H, m), 3.62−3.69 (1H, m), 3.98−4.05 (2H, m), 5.74−5.79 (1H, m), 5.84−5.91 (1H, m); ^{13}C NMR δ 23.7 (CH_2), 23.9 (CH_2), 25.1 (CH_2), 34.6 (CH_2), 35.9 (CH_2), 39.8 (CH_2), 40.4 (CH), 40.9 (CH_2), 66.6 (CH_2), 77.5 (CH), 110.0 (C), 126.4 (CH), 127.4 (CH), 209.0 (CO); HRMS (ESI) calcd for $C_{14}H_{21}O_3$ $(M + H)^+$, 237.1491; found, 237.1470.

Acetic Acid (1*R*,5*R*)-5-[(2*S*)-1,4-dioxa-spiro[4.5]dec-2-yl]-cyclohex-3-enyl Ester 34d. The cyclohexenone **34c** (280 mg, 1.19 mmol) was reduced with $LiAlH_4$ (50 mg, 1.30 mmol) at −60 °C, following the procedure for the reduction of **8a**, to afford exclusively the cyclohexenol **34a** (260 mg, 92%) as a colorless viscous liquid: $[\alpha]^{25}_D$ +47.9 (*c* 0.9, $CHCl_3$); ^{1}H NMR δ 1.22−1.37 (3H, m), 1.51 (4H, br s), 1.55−1.60 (4H, m), 1.97−2.00 (1H, m), 2.05−2.09 (1H, m), 2.33−2.38 (2H, m), 2.51 (1H, br s), 3.60−3.66 (1H, m), 3.88−3.91 (1H, m), 3.94−4.05 (2H, m), 5.45−5.51 (1H, m), 5.66−5.73 (1H, m); ^{13}C NMR δ 23.7 (CH_2), 23.9 (CH_2), 25.1 (CH_2), 34.7 (CH_2), 34.8 (CH_2), 34.9 (CH_2), 36.0 (CH_2), 39.3 (CH), 66.4 (CH_2), 66.8 (CH), 78.1 (CH), 109.4 (C), 126.3 (CH), 126.8 (CH); HRMS (ESI) calcd for $C_{14}H_{22}O_3Na$ $(M + Na)^+$, 261.1467; found, 261.1487.

To a magnetically stirred solution of the cyclohexenol **34a** (260 mg, 1.09 mmol) in dichloromethane (10 mL) at 0 °C was added dropwise acetic anhydride (0.17 mL, 1.86 mmol), triethyl amine (0.34 mL, 2.40 mmol), and 4-(dimethylamino)pyridine (4-DMAP; 10 mg). The reaction mixture was then allowed to stir under argon atmosphere for 2 h at room temperature. Solvent was evaporated, and the residual mass was extracted with ether (30 mL). The ether layer was then washed with water (2 mL) followed by brine (2 mL) and dried. Removal of solvent under reduced pressure followed by column chromatography using ether/petroleum ether (1:9) afforded the corresponding acetate **34d** (280 mg, 92%) as a colorless oil: $[\alpha]^{25}_D$ +53.6 (*c* 1.8, $CHCl_3$); IR(neat): ν_{max} 1732 cm^{-1}; ^{1}H NMR δ 1.24−1.43 (3H, m), 1.56 (4H, br s), 1.68 (4H, br s), 2.02 (3H, s, $-OCOCH_3$), 2.03−2.15 (2H, m), 2.39−2.44 (1H, m), 2.52−2.58 (1H, m), 3.61−3.68 (1H, m), 3.92−4.03 (2H, m), 4.92−5.01 (1H, m), 5.46−5.49 (1H, m), 5.68−5.73 (1H, m); ^{13}C NMR δ 21.3 (CH_3), 23.8 (CH_2), 23.9 (CH_2), 25.1 (CH_2), 31.2 (CH_2), 31.3 (CH_2), 34.8 (CH_2), 36.1 (CH_2), 39.3 (CH), 66.6 (CH_2), 69.8 (CH), 78.1 (CH), 109.4 (C), 126.3 (CH), 126.5 (CH), 170.5 (CO); HRMS (ESI) calcd for $C_{16}H_{24}O_4Na$ $(M + Na)^+$, 303.1572; found, 303.1528.

Epoxidation of Acetate 34d. To a magnetically stirred cold (0 °C) solution of the acetate **34d** (170 mg, 0.61 mmol) in 1,2-dichloroethane (4.5 mL) was added *m*-CPBA (209 mg, 1.21 mmol) in one portion. After stirring at room temperature for 8 h, the reaction mixture was cooled to 0 °C and quenched by adding saturated Na_2SO_3 solution, extracted with ether (30 mL), and washed with ice-cold 2% NaOH solution (w/v) (3 × 2 mL) and dried. Evaporation of the solvent followed by column chromatography using ether/petroleum ether (1:6) afforded an inseparable mixture (2:3) of epoxides **35** and **36** (160 mg, 89%) as a colorless viscous liquid: IR(neat) ν_{max} 1728 cm^{-1}; ^{1}H NMR δ (for mixture of diastereomers) 1.23−1.42 (6H, m), 1.59 (8H, br s), 1.62 (8H, br s), 1.70−1.84 (4H, m), 2.02 (3H, s, CH_3 of one isomer), 2.03 (3H, s, CH_3 of other isomer), 2.23−2.54 (4H, m), 2.99−3.01 (1H, m), 3.07−3.08 (1H, m), 3.12−3.19 (1H, m), 3.29−3.31 (1H, m), 3.73 (1H, dd, J = 7.5, 7.2 Hz), 3.87−3.92 (1H, m), 4.06−4.14 (3H, m), 4.23 (1H, dd, J = 12.6, 6.6 Hz), 4.67−4.73 (1H, m), 4.83−4.91 (1H, m); ^{13}C NMR (for both isomers) δ 21.1 (CH_3), 21.2 (CH_3), 23.7 (CH_2), 23.8 (CH_2), 23.9 (CH_2), 25.1 (CH_2), 27.0 (CH_2), 28.8 (CH_2), 29.4 (CH_2), 30.6 (CH_2), 34.5 (CH_2), 35.1 (CH_2), 36.0 (CH_2), 36.2 (CH_2), 37.6 (CH), 38.2 (CH), 49.7 (CH), 51.8 (CH), 52.8 (CH), 53.8 (CH), 66.6 (CH_2), 66.7 (CH_2), 67.8 (CH), 68.6 (CH), 76.6 (CH), 77.2 (CH), 109.4 (C), 109.8 (C), 170.1 (CO), 170.4 (CO); HRMS (ESI) calcd for $C_{16}H_{24}O_5Na$ $(M + Na)^+$, 319.1521; found, 319.1528.

(1*R*,3*S*,5*S*,6*S*)-5-[(2*S*)-1,4-Dioxa-spiro[4.5]dec-2-yl]-7-oxa-bicyclo[4.1.0]heptan-3-ol 37 and (1*R*,4*S*,5*R*)-5-[(2*S*)-1,4-dioxa-spiro[4.5]dec-2-yl]-cyclohex-2-ene-1,4-diol 38a. To a magnetically stirred solution of diphenyl diselenide (125 mg, 0.4 mmol) in absolute ethanol (1.5 mL) was added sodium borohydride (26 mg, 0.69 mmol) in portions, and stirring was continued until the bright yellow solution turned colorless. A solution of epoxides **35** and **36** (170 mg, 0.57 mmol) in absolute ethanol (1.5 mL) was added dropwise to the reaction mixture, and the reaction mixture was stirred at room temperature for 2 h. The reaction mixture was cooled to 0 °C, and THF (2.5 mL) was added followed by addition of H_2O_2 (30%) (0.6 mL) over a period of 3 min. The reaction mixture was left to attain room temperature and then refluxed at 70 °C for 1.5 h. The resulting slurry was diluted with water (2 mL) and extracted with ether (3 × 5 mL). The organic phase was washed with aqueous Na_2CO_3 (10%, 2 × 2 mL), dried, and concentrated. Column chromatography of the residual mass using ethyl acetate/petroleum ether (3:5) afforded the epoxy alcohol **37** (42 mg, 29%) as a colorless viscous liquid: IR(neat) ν_{max} 3421 cm^{-1}; ^{1}H NMR δ 1.40 (2H, br s), 1.50−1.63 (9H, m), 1.77−1.81 (1H, m), 2.24−2.36 (2H, m), 2.37−2.48 (2H, m), 3.00−3.01 (1H, m), 3.29−3.30 (1H, m), 3.71−3.76 (1H, m), 3.95−4.02 (2H, m), 4.07−4.12 (1H, m); ^{13}C NMR δ 23.7 (CH_2), 23.9 (CH_2), 25.1 (CH_2), 34.2 (CH_2), 34.5 (CH_2), 36.0 (CH_2), 36.7 (CH_2), 37.5 (CH), 53.1 (CH), 54.4 (CH), 64.5 (CH), 66.6 (CH_2), 76.6 (CH), 109.9 (C); HRMS (ESI) calcd for $C_{14}H_{22}O_4Na$ $(M + Na)^+$, 277.1416; found, 277.1439. The cyclohexenediol **38a** (60 mg, 41%) was also produced as a white crystalline solid: mp 142 °C; $[\alpha]^{25}_D$ +32.1 (*c* 0.5, $CHCl_3$); IR (KBr) ν_{max} 3246.0 cm^{-1}; ^{1}H NMR δ 1.40 (2H, br s), 1.59 (4H, br s), 1.61 (4H, br s), 1.65−1.68 (2H, m), 2.11−2.17 (1H, m), 2.45 (1H, br s), 2.54 (1H, br s), 3.78 (1H, dd, J = 7.0, 6.8 Hz), 4.05−4.07 (1H, m), 4.10−4.30 (3H, m), 5.82−5.91 (2H, m); ^{13}C NMR δ 23.8 (CH_2), 24.0 (CH_2), 25.1 (CH_2), 29.0 (CH_2), 34.8 (CH_2), 36.3 (CH_2), 41.1 (CH), 64.9 (CH), 67.0 (CH_2), 67.5 (CH), 76.4 (CH), 109.5 (C), 129.1 (CH), 135.1 (CH); HRMS (ESI) calcd for $C_{14}H_{22}O_4Na$ $(M + Na)^+$, 277.1416; found, 277.1461.

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Supporting Information Available: General methods and procedures along with spectral data for compounds **3b**, **10b**, **17**−**25**, **27**, **29b**, **30b**, **31**, **32**, **38b**, **39a,b**, and **40a**−**c** and copies of ^{1}H, ^{13}C NMR and DEPT spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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