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From Common Carbohydrates to Enantiopure Cyclooctane Polyols and Glycomimetics via Deoxygenative Zirconocene Ring Contraction

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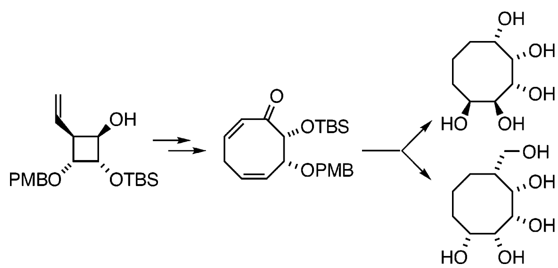

D-Arabinose and D-glucose are transformed into the identical vinyl furanoside, whose role is to serve as the precursor to enantiopure cyclooctadienone **6**. The key steps of this relay involve a zirconocene-promoted ring contraction and [3,3] sigmatropic rearrangement of an enynol. Subsequently defined are convenient synthetic routes to several cyclooctane-1,2,3-triols, 1,2,3,4,5-pentaols, and structurally related glycomimetics.

Introduction

In recent years, the search for new, therapeutically useful glycosidase inhibitors has turned to carbohydrate mimetics consisting of medium-sized carbocyclic cores. The potential advantages associated with this group of analogues include, but are not limited to, improved affinity for their cognate acceptors arising from greater degrees of conformational mobility, improved bioavailability, and enhanced stability toward degradative enzymes.[1−4] The probing of carbohydrate recognition events has consequently been extended beyond the realm of five- and six-membered cyclitols[1,2] to include polyhydroxylated cycloheptanes[5] and cyclooctanes.[6] From among the several approaches that have been developed to access these polyols, the most popular approaches have involved ring-closing metathesis, ring-expansion via Claisen rearrangement, and free radical mediated cyclization. Herein, we detail an entirely different approach that is based on use of the zirconocene-mediated ring contraction of a vinyl furanoside to generate an enantiopure cyclobutanol[7] and subsequent adaptation of a [3.3] sigmatropic rearrangement.[8] More extended functionalization provides the opportunity to generate stereodefined cyclooctane-1,2,3-triols and 1,2,3,4,5-pentaols[9] and to elaborate authentic carbasugar analogues as well.

Results and Discussion

Arrival at the first pivotal intermediate **3** was achieved from two directions as shown in Scheme 1. In the first approach, the

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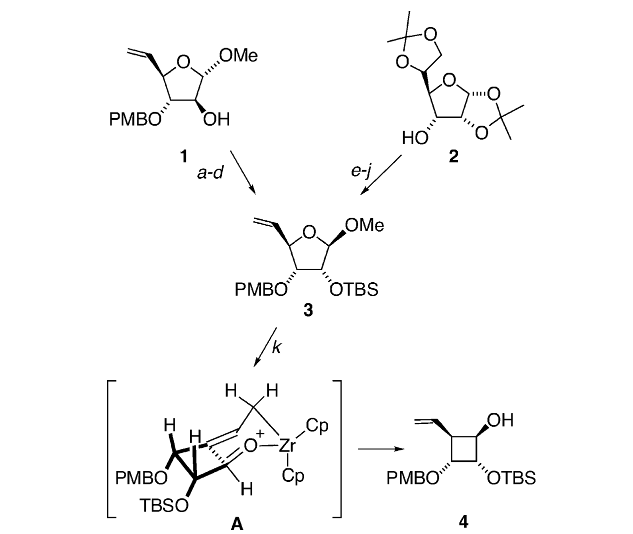
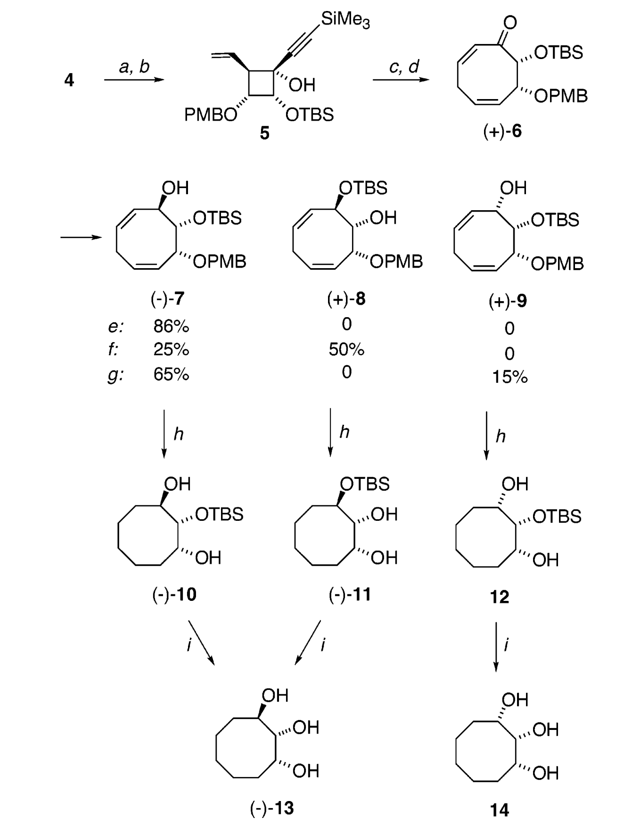
SCHEME 1[a]



[a] Key: (a) Dess−Martin periodinane, $NaHCO_3$, CH_2Cl_2; (b) $NaBH_4$, MeOH (88% for two steps); (c) TBSCl, imid, DMAP, CH_2Cl_2 (87%); (d) 1% HCl, MeOH; TBSCl, imid, DMAP, CH_2Cl_2 (67%); (e) PMBBr, (n-Bu)$_4$NI, NaH, THF (70%); (f) HCl, MeOH, H_2O, 0 °C → rt (59%); (g) TsCl, py (96%); (h) Zn, NaI, DMF, reflux overnight (87%); (i) 1% HCl, MeOH (79%); (j) TBSCl, imid, DMAP (88%); (k) Cp_2ZrCl_2, n-BuLi, toluene; $BF_3{\cdot}OEt_2$ (65%).

SCHEME 2[a]



[a] Key: (a) Dess-Martin periodinane, $NaHCO_3$, CH_2Cl_2. (b) BrMg−≡−$SiMe_3$, THF, 0 °C (65% over two steps); (c) K_2CO_3, CH_3OH, rt; (d) C_6H_6, Δ (98% for two steps); (e) $NaBH_4$, $CeCl_3$, CH_3OH; (f) $NaBH_4$, CH_3CH_2OH; (g) $NaBH_4$, CH_3OH; (h) H_2, Pd/C, CH_3OH (51−62%); (i) TBAF, THF (65−81%).

known alcohol **1**, readily available from D-arabinose,[8a,10] was subjected to Dess−Martin oxidation,[11] reduction with sodium borohydride,[12] silylation, and subsequent anomerization. The alternative route began with D-glucose diacetonide, whose conversion to **2** by the Horton protocol[12] was followed by formation of the PMB ether and controlled hydrolysis to the exocyclic vicinal diol. The targeted advancement to **3** was next realized by reductive elimination of the ditosylate with zinc dust and sodium iodide in hot DMF.[13−15] Acetalization and reprotection followed. The next transformation involved exposing **3** to the action of Cp_2Zr and boron trifluoride etherate in the expectation that **4** would result from adoption of the less sterically congested transition state **A**. Indeed, excellent forward progress was realized in that **4** was isolated as the only product in 65% yield.

Oxidation of **4** to the cyclobutanone level could be accomplished without the loss of stereochemical integrity by involvement of the Dess−Martin periodinane.[11] In addition, the vinylic double bond does not migrate into conjugation as long as chromatography on silica gel is avoided. The ability to preclude isomerization to the α,β-unsaturated four-membered ring ketone has been noted in other contexts.[15−17] The next tactical move involved 1,2-addition of the Grignard reagent generated from trimethylsilylacetylene. Not unexpectedly, carbinol **5** was formed with complete diastereocontrol (Scheme 2). Mild basic desilylation of **5** led to the tertiary carbinol, an advanced intermediate that proved notably responsive to its inherent ring strain. Thus, refluxing desilylated **5** in benzene led quantitatively to the enantiopure, dextrorotatory cyclooctadienone (+)-**6**.

The first experiments designed to extend the level of functionalization in (+)-**6** involved reduction with sodium borohydride under various conditions. With cerium(III) chloride as additive in methanol solution,[18] (−)-**7** was formed exclusively via α-hydride delivery. Omission of the lanthanide gave rise to **7** and its dextrorotatory epimer (+)-**9** in a 4.3:1 ratio. A similar

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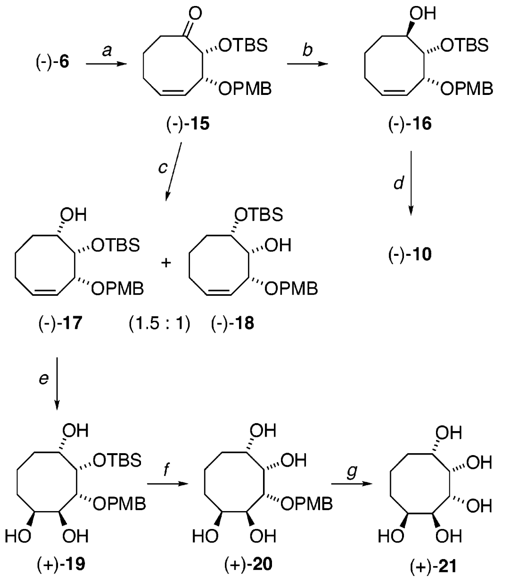
SCHEME 3[a]



[a] Key: (a) L-Selectride, THF, −78 °C (93%); (b) $NaBH_4$, MeOH (84%); (c) L-Selectride, THF, rt (95%); (d) H_2, Pd/C, CH_3OH (93%); (e) OsO_4, NMO, 8:1 acetone/water (62%); (f) TBAF, THF (87%); (g) H_2, Pd/C, CH_3OH (77%).

dropoff in stereoselectivity was not manifested in ethanol solution, but the silyl-migrated isomer (+)-**8** now emerged as the major product.[19]

Unequivocal definition of the stereochemical assignments to **7**−**9** was achieved in each case by a two-step sequence consisting of catalytic hydrogenation over 10% palladium on charcoal followed by desilylation with TBAF (Scheme 2). When processed in this manner, **7** and **8** were both converted to (−)-**13**, where the absence of symmetry was evidenced by its eight-line ^{13}C NMR spectrum and significant optical rotation. Alcohol **9** reacted with comparable efficiency. In contrast, triol **14** generated in this manner exhibited no optical rotation and was characterized by only five carbon signals. These properties are a direct consequence of its C_s symmetry.

When (+)-**6** was exposed at −78 °C to L-Selectride as the reducing agent, 1,4-addition operated smoothly with generation of the levorotatory cyclooctenone **15** (Scheme 3). This transformation allowed for subsequent conversion to the β-configured carbinol (−)-**16** with sodium borohydride in methanol. Without making a direct comparison of **6** and **15** because of their different connectivities, we point out that their MM3-derived minimum energy conformations (Figure 1) are quite disparate. The different spatial projections of their carbonyl double bond is especially pronounced and may be the root cause underlying the divergent stereochemical pathways associated with their 1,2-reductions.[20] More to the point are the essentially isoenergetic E_s values for **16** and **17**. This matchup precludes any key role assignable to thermodynamic control. The absolute configuration of the hydroxyl group in **16** was corroborated via its hydrogenation to give (−)-**10**.

Advancement to the pentahydroxy cyclooctane (+)-**21** was conveniently initiated by L-Selectride reduction of (−)-**15** at room temperature, a process that gave rise to the α-oriented carbinol (−)-**17** and its silyl migrated isomer (−)-**18** in a ratio of 1.5:1. After chromatographic separation, (−)-**17** was dihy-

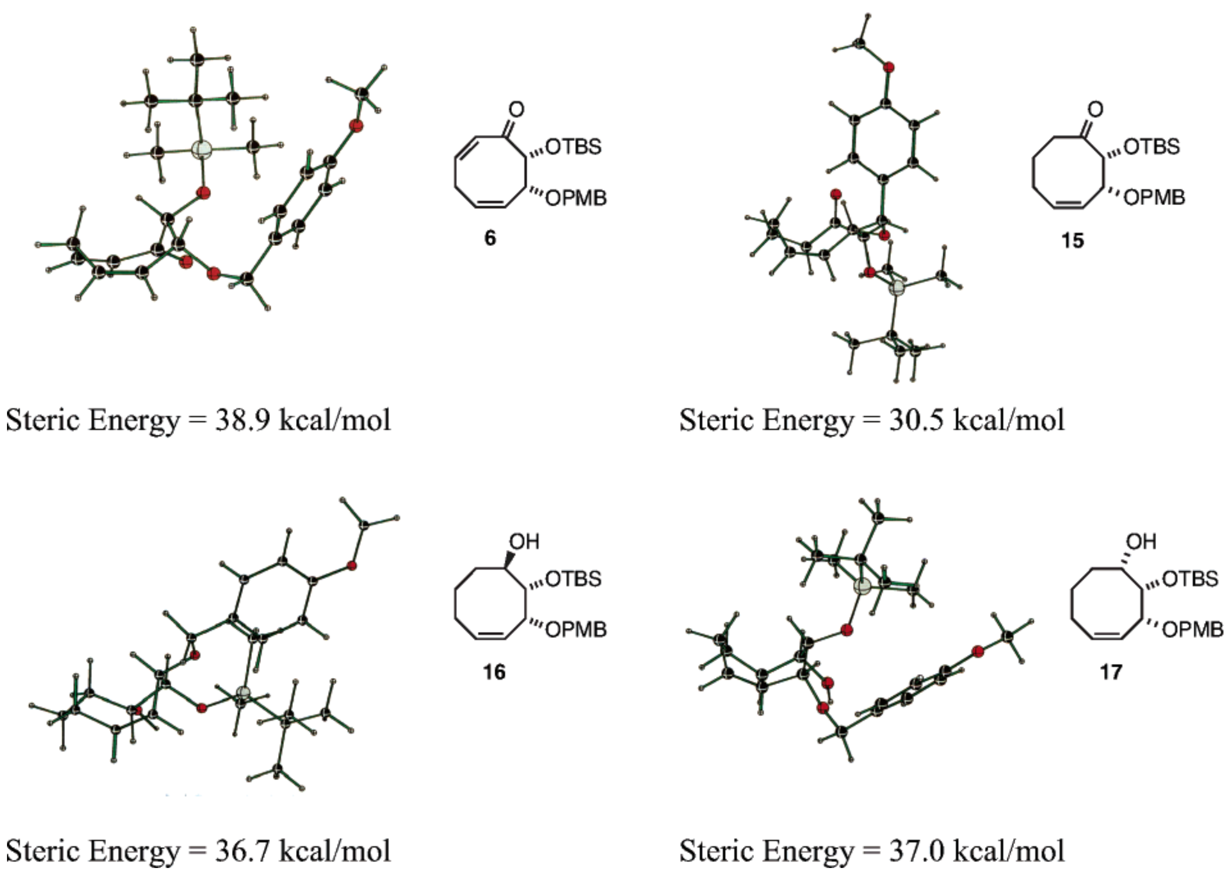
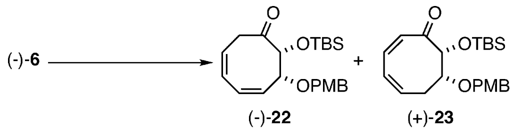


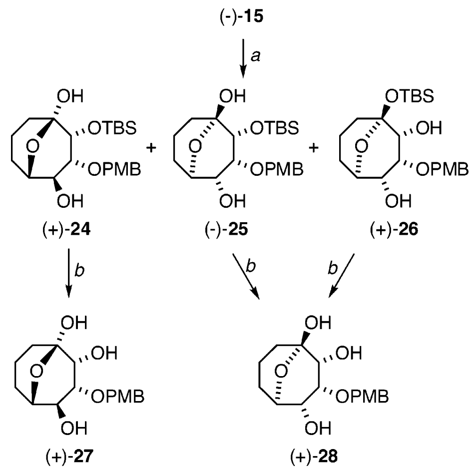
FIGURE 1. MM3-based global low energy conformations for **6** and **15**−**17** and their associated steric energy (E_s) values.

SCHEME 4



	(-)-22	(+)-23
toluene, reflux, 4-5 h	50%	50%
Et_3N, THF, rt, 2 days	90%	----
Al(O*i*-Pr)$_3$, 94 °C, 1 h	34%	50%

SCHEME 5[a]



[a] Key: (a) OsO_4·NMO, acetone−H_2O (1:1) (56% of **24**, 38% of **25**, 4% of **36**); (b) THF, rt (41% of **27**, 80% of **28** from **25**, 65% of **28** from **26**).

droxylated with osmium tetraoxide in the presence of NMO to produce (+)-**19**, thereby setting the stage for stepwise deprotection. The display by **21** of a positive optical rotation and eight distinct ^{13}C NMR signals indicated it not to be the meso isomer. Consequently, the osmylation step had necessarily proceeded by approach to the β-face of the π-bond as shown.

Heating solutions of (+)-**6** in toluene at the reflux temperature led to double bond migration and generation of a 1:1 mixture of (−)-**22** and (+)-**23** (^{1}H NMR analysis). As seen in Scheme 4, this equilibration could also be brought about under varying basic conditions. The further chemical transformations of these thermodynamically more favored isomers will be reported at a later date.

Access to cyclooctane glycomimetics was achieved by early dihydroxylation of the double bond in (−)-**15**. This particular unsaturated ketone was transformed in the presence of OsO_4 and NMO into three bicyclic products, the chromatographic separation of which could be readily achieved (Scheme 5). The major constituent proved to be a colorless solid amenable to X-ray crystallographic analysis. These data identified the substance to be (+)-**24**, whose formation arises as the consequence of expected β-attack by the oxidant followed by transannular hemiketal formation. The next most prevalent product was shown to be (−)-**25** by direct NMR comparison with its stereoisomer and on the basis of several chemical transformations. Similar interconversions made possible the identification of (+)-**26** as the silyl-migrated isomer of **25**. The centrally important transformations involved those TBAF-promoted desilylations that demonstrated triol **27** to arise uniquely from **24** and **28** to be the common end product from both **25** and **26**.

(19) For other examples of related silyl transfers, consult: (a) Paquette, L. A.; Hartung, R. E.; Hofferberth, J. E.; Vilotijevic, I.; Yang, J. *J. Org. Chem.* **2004**, *69*, 2454. (b) Hartung, R. E.; Hilmey, D. G.; Paquette, L. A. *Adv. Synth. Catal.* **2004**, *346*, 713.

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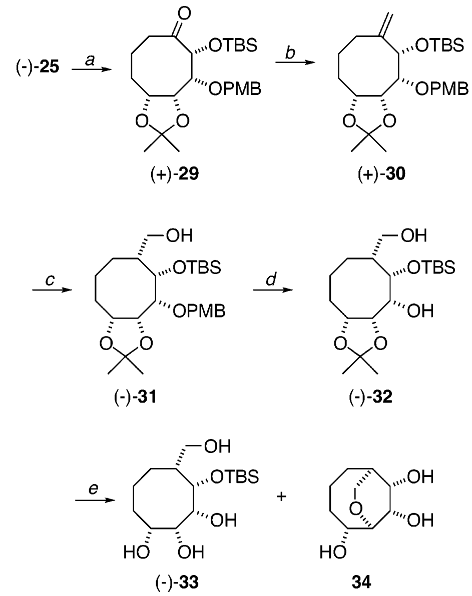
SCHEME 6[a]

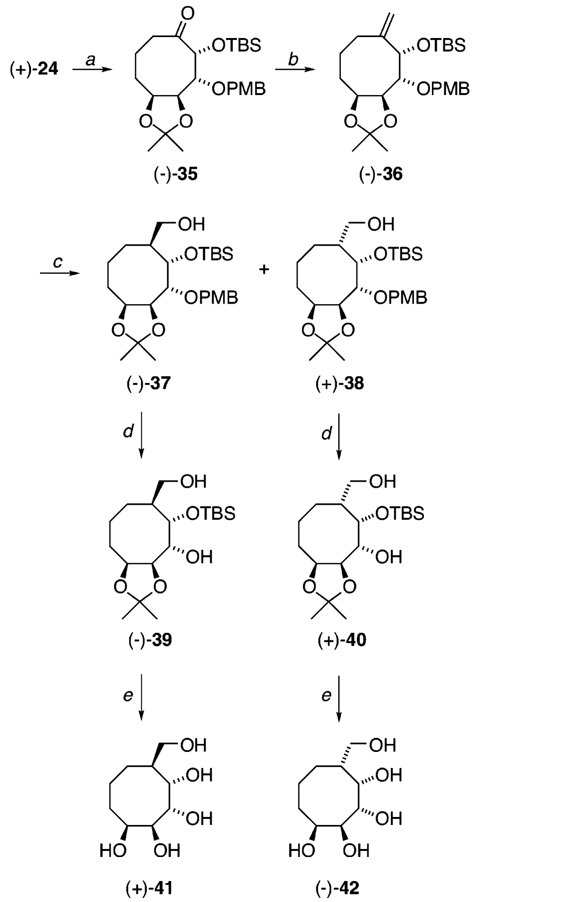


[a] Key: (a) $Me_2C(OMe)_2$, PPTS (83%); (b) $Ph_3P{=}CH_2$, THF (50%); (c) BH_3·THF; H_2O_2, NaOH (65%); (d) DDQ, CH_2Cl_2, H_2O, rt, 2 h (81%); (e) 1 M HCl, CH_3OH (37% of **33**; 28% of **34**).

The experiments reported below involve disassembly of the hemiacetal bridge in **24** and **25** by acetonide generation on the periphery of the cyclooctane ring. In the case of **25**, acid-catalyzed reaction with 2,2-dimethoxypropane furnished ketone (+)-**29** efficiently (Scheme 6). Unmasking of a carbonyl group in this fashion allowed for homologation to the dextrorotatory exomethylene derivative **30**. In line with our expectation that the stereochemical course of the hydroboration of **30** would be largely controlled by steric considerations, its exposure to the borane tetrahydrofuran complex led uniquely to (−)-**31**. Evidently, the α-orientation of all four vicinal protected oxygen atoms in **30** is conducive to attack entirely from the β-face. Arrival at carbasugar (−)-**33** was most expediently accomplished by dismantling of the *p*-methoxybenzyl ether with DDQ in wet dichloromethane in advance of acid-catalyzed hydrolysis. The pentahydroxy product (−)-**33** formed in this manner was amenable to chromatographic separation from an oxygen-bridged triol tentatively assigned as **34** on the basis of ^{1}H and ^{13}C NMR spectroscopy.

The same protocol was successfully applied to (+)-**24** (Scheme 7). In this stereoisomeric series, the β-configured acetonide has the consequence of eroding the level to which β-approach of the borane reagent operates in (−)-**36**. Although this stereochemical channel continues to be dominant (76% of **38**), modest amounts (9%) of **37** are now formed competitively. The two-step sequences leading to (+)-**41** and (+)-**42** proceeded smoothly, efficiently, and without evidence of dehydrative transannular cyclization as seen with **34**. For confirmatory purposes, (−)-**42** was subjected to X-ray crystallographic analysis. The ORTEP diagram of this pentaol (see the Supporting Information) addresses the engaging question of the solid state conformation of its medium-sized ring, information that

SCHEME 7[a]



[a] Key: (a) $Me_2C(OMe)_2$, PPTS (91%); (b) $Ph_3P{=}CH_2$, THF (81%); (c) $BH_3{\cdot}THF$; H_2O_2, NaOH (76% of **38**; 9% of **37**); (d) DDQ, CH_2Cl_2, H_2O, rt (81% of **39**; 93% of **40**); (e) 1 M HCl, CH_3OH (83% of **41**; 87% of **42**).

has otherwise proven difficult to secure by ^{1}H NMR spectrosopy (e.g., NOE effects and coupling constants). Thus, the quasiequatorial nature of the $-CH_2OH$ substituent is quite apparent, as are the comparable projections of the $-OH$ groups bonded to C-3, C-4, and C-5. In this context, the quasiaxial orientation of the C-2 hydroxyl is not unexpected.

Summary

To recapitulate, readily available D-arabinose and D-glucose have been transformed enantioselectively into the pivotal cyclooctadienone (+)-**6** via a relatively short series of transformations. Zirconocene-promoted ring contraction and [3.3] sigmatropic rearrangement proved to be the notably productive steps that allowed for convenient elaboration of the functionalized eight-membered ring. The platform provided by **6** proved to be highly utilitarian in paving the way to stereoisomeric cyclooctane-1,2,3-triols (controlled hydride reduction, hydrogenation, and desilylation) and the pentahydroxy derivative (+)-**21** (an added dihydroxylation step). Also defined experimentally was the feasibility of migrating the double bonds in **6** so as to generate (−)-**22** and/or (+)-**23**. In addition, the dihydroxylation of (−)-**15**, which leads to hemiketals **24**−**26**, makes possible straightforward homologation in a manner that ultimately provides the glycomimetics (−)-**33**, (+)-**41**, and (−)-**42**. The chemistry undertaken here provides a unique illustration of the manner in which differing levels of hydroxylation can be incorporated into a cyclooctane ring in enantiocontrolled fashion.

Experimental Section

Periodinane Oxidation/Sodium Borohydride Reduction of 1. A magnetically stirred mixture of **1** (107 mg, 0.38 mmol) and sodium bicarbonate (638 mg, 7.6 mmol) in CH_2Cl_2 (20 mL) was treated with the Dess−Martin periodinane (486 mg, 1.14 mmol). After 3 h at rt, the resulting white suspension was filtered through a pad of Celite (hexanes/ethyl acetate 8:1 rinse) and the filtrate was evaporated to leave a residue that was dissolved in methanol (10 mL). After the addition of sodium borohydride (43 mg, 1.14 mmol) at 0 °C, the reaction mixture was stirred for 30 min at this temperature, quenched with saturated NH_4Cl solution, and freed of methanol under reduced pressure. After extraction of the product into ethyl acetate, the combined organic layers were dried, filtered, and evaporated. Purification of the residue by chromatography on silica gel (elution with hexanes/ethyl acetate 2:1) gave the α-alcohol as a colorless oil (94 mg, 88%): IR (neat, cm^{-1}) 3552, 1612, 1586; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (d, J = 8.5 Hz, 2H), 6.88 (d, J = 8.6 Hz, 2H), 5.71 (ddd, J = 17.0, 10.4, 6.5 Hz, 1H), 5.26 (d, J = 17.1 Hz, 1H), 5.13 (d, J = 10.4 Hz, 1H), 4.90 (d, J = 4.6 Hz, 1H), 4.68 (d, J = 11.9 Hz, 1H), 4.56 (d, J = 11.9 Hz, 1H), 4.52−4.41 (m, 1H), 4.10 (ddd, J = 11.1, 7.0, 4.7 Hz, 1H), 3.80 (s, 3H), 3.60 (dd, J = 7.0, 3.8 Hz, 1H), 3.48 (s, 3H), 2.93 (d, J = 10.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.4, 135.8, 129.6, 129.5 (2C), 116.6, 113.8 (2C), 102.6, 82.9, 79.0, 72.7, 71.3, 55.6, 55.2; ES HRMS m/z (M + Na)$^+$ calcd 303.1203, obsd 303.1215; $[\alpha]^{22}_D$ +109.7 (c 0.4, $CHCl_3$).

TBS Protection and Anomerization of the α-Alcohol. A mixture of the above product (64 mg, 0.23 mmol), imidazole (63 mg, 0.92 mmol), DMAP (3 mg, 0.02 mmol), and *tert*-butyldimethylsilyl chloride (69 mg, 0.46 mmol) in CH_2Cl_2 (5 mL) was stirred for 2 days at rt, filtered through a short column of silica gel (hexanes/ethyl acetate 10:1 rinse), and evaporated. Chromatography of the residue on silica gel (elution with hexanes/ethyl acetate 10:1) afforded the silyl ether as a colorless oil (78 mg, 87%): IR (neat, cm^{-1}) 1613, 1514, 1249; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (d, J = 8.5 Hz, 2H), 6.85 (d, J = 8.6 Hz, 2H), 5.72 (ddd, J = 17.0, 10.3, 6.5 Hz, 1H), 5.25 (d, J = 17.1 Hz, 1H), 5.10 (d, J = 10.4 Hz, 1H), 4.80 (d, J = 4.4 Hz, 1H), 4.73 (d, J = 12.6 Hz, 1H), 4.54 (d, J = 12.6 Hz, 1H), 4.50−4.47 (m, 1H), 4.06 (dd, J = 6.6, 4.4 Hz, 1H), 3.80 (s, 3H), 3.54 (dd, J = 6.6, 4.0 Hz, 1H), 3.46 (s, 3H), 0.94 (s, 9 H), 0.12 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 136.4, 130.3, 129.3 (2C), 116.3, 113.6 (2C), 103.3, 82.9, 78.9, 72.8, 71.9, 55.5, 55.2, 25.9 (3C), 18.4, −4.7, −4.9; ES HRMS m/z (M + Na)$^+$ calcd 417.2068, obsd 417.2070; $[\alpha]^{22}_D$ +108.7 (c 1.32, $CHCl_3$).

A sample of the preceding product (512 mg, 1.29 mmol) in 1% methanolic HCl (130 mL) was stirred overnight at rt, cooled to 0 °C, and neutralized with saturated $NaHCO_3$ solution. After methanol removal under reduced pressure, the remaining oil was triturated with ethyl acetate, the combined organic layers were dried and evaporated, and the residue was taken up in CH_2Cl_2 (10 mL), mixed with imidazole (263 mg, 3.86 mmol), DMAP (32 mg, 0.31 mmol), and *tert*-butyldimethylsilyl chloride (292 mg, 1.94 mmol), and stirred for 2 days at rt. The resulting white heterogeneous mixture was filtered through a short pad of silica gel (CH_2Cl_2 rinse), evaporated, and chromatographed on silica gel (elution with hexanes/ethyl acetate 10:1) to give **3** as a colorless oil (345 mg, 67%) and return unreacted starting material (44 mg, 9%): IR (neat, cm^{-1}) 1613, 1514, 1250; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24 (d, J = 8.7 Hz, 2H), 6.86 (d, J = 8.6 Hz, 2H), 5.83 (ddd, J = 17.2, 10.3, 6.4 Hz, 1H), 5.36 (d, J = 17.1 Hz, 1H), 5.16 (d, J = 10.3 Hz, 1H), 4.73 (s, 1H), 4.58 (d, J = 11.5 Hz, 1H), 4.48 (t, J = 7.2 Hz, 1H), 4.42 (d, J = 11.5 Hz, 1H), 4.11 (d, J = 4.0 Hz, 1H), 3.80 (s, 3H), 3.80−3.77 (m, 1H), 3.37 (s, 3H), 0.92 (s, 9 H), 0.10 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 138.0, 130.1, 129.2 (2C), 116.9, 113.7 (2C), 108.6, 82.1, 81.7, 74.7, 72.0, 55.2, 55.1, 25.8 (3C), 18.2, −4.7, −4.8; ES HRMS *m*/*z* (M + Na)$^+$ calcd 417.2068, obsd 417.2099; $[\alpha]^{22}_D$ +12.0 (*c* 1.22, $CHCl_3$).

Conversion of 2 to 3. A cold (0 °C) suspension of sodium hydride (1.59 g, 40 mmol) in dry THF (20 mL) was treated with **2** (6.9 g, 26.5 mmol) dissolved in dry THF (60 mL) and stirred for 20 min at 0 °C and for 10 min at rt. Following a return to 0 °C, *p*-methoxybenzyl bromide (6.9 g, 34 mmol) in THF (20 mL) containing tetra-*n*-butylammonium iodide (1.0 g, 2.7 mmol) was introduced. The reaction mixture was stirred at rt for 3 h, quenched with saturated NH_4Cl solution (100 mL) at 0 °C, and extracted with ethyl acetate. The combined organic layers were dried and evaporated, leaving a residue that was chromatographed on silica gel (elution with hexanes/ethyl acetate 2:1) to furnish 7.0 g (70%) of the ether as a white solid: mp 75−77 °C; IR (neat, cm^{-1}) 1614, 1514, 1462; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.7 Hz, 2 H), 6.89 (d, *J* = 8.7 Hz, 2H), 5.74 (d, *J* = 3.8 Hz, 1H), 4.70 (d, *J* = 11.9 Hz, 1H), 4.56−4.51 (m, 1H), 4.53 (d, *J* = 11.5 Hz, 1H), 4.35 (dt, *J* = 7.1, 3.1 Hz, 1H), 4.12 (dd, *J* = 8.7, 3.1 Hz, 1H), 4.02−3.92 (m, 2H), 3.86 (dd, *J* = 8.7, 4.5 Hz, 1H), 3.80 (s, 3H), 1.58 (s, 3H), 1.39 (s, 3H), 1.37 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 129.5 (2C), 129.3, 113.5 (2C), 112.5, 109.2, 103.6, 77.7, 77.5, 76.9, 74.5, 71.4, 64.7, 54.9, 26.5, 26.3, 25.9, 24.8; ES HRMS *m*/*z* (M + Na)$^+$ calcd 403.1727, obsd 403.1717; $[\alpha]^{20}_D$ +95.5 (*c* 1.0, $CHCl_3$).

To a cold (0 °C) solution of the OPMB derivative (54.8 g, 144 mmol) in methanol (600 mL) were added concentrated HCl (0.6 mL) and water (6 mL). The reaction mixture was stirred for 2 h in the cold, maintained at rt for 3 h, returned to 0 °C, neutralized with saturated $NaHCO_3$ solution, and evaporated. The product was extracted into ethyl acetate, the combined organic layers were dried and evaporated, and the residue was chromatographed on silica gel (elution with hexanes/ethyl acetate 1:5) to give the diol as a colorless oil (28.7 g, 59%): IR (neat, cm^{-1}) 3444, 1613, 1514; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.6 Hz, 2H), 6.89 (d, *J* = 8.6 Hz, 2H), 5.76 (d, *J* = 3.7 Hz, 1H), 4.72 (d, *J* = 11.1 Hz, 1H), 4.59 (t, *J* = 4.0 Hz, 1H), 4.49 (d, *J* = 11.0 Hz, 1H), 4.09 (dd, *J* = 8.9, 3.2 Hz, 1H), 4.01−3.97 (m, 1H), 3.90 (dd, *J* = 8.9, 4.3 Hz, 1H), 3.80 (s, 3H), 3.77−3.61 (m, 2H), 2.46 (br s, 2H), 1.59 (s, 3H), 1.36 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 129.6 (2C), 128.8, 113.6 (2C), 112.7, 103.8, 78.7, 77.1, 76.2, 71.5, 70.8, 62.8, 54.9, 26.5, 26.3; ES HRMS *m*/*z* (M + Na)$^+$ calcd 363.1414, obsd 363.1418; $[\alpha]^{22}_D$ +96.4 (*c* 1.32, $CHCl_3$).

A solution of the above diol (24.0 g, 70.5 mmol) and *p*-toluenesulfonyl chloride (54.1 g, 282 mmol) in pyridine (150 mL) was stirred at rt for 2 days, diluted with ethyl acetate, and washed sequentially with 1 N HCl, saturated $NaHCO_3$ solution, and brine prior to drying and solvent evaporation. The residue was purified by chromatography on silica gel (elution with hexanes/ethyl acetate 1:1) to afford the ditosylate as a colorless oil (43.9 g, 96%): IR (neat, cm^{-1}) 1612, 1514, 1458; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.3 Hz, 2H), 7.65 (d, *J* = 8.4 Hz, 2H), 7.28 (br d, *J* = 8.0 Hz, 4H), 7.24 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 5.44 (d, *J* = 3.5 Hz, 1H), 4.99−4.94 (m, 1H), 4.59 (d, *J* = 11.2 Hz, 1H), 4.42 (d, *J* = 11.2 Hz, 1H), 4.43−4.40 (m, 1H), 4.13−4.01 (m, 3H), 3.82 (s, 3H), 3.82−3.75 (m, 1H), 2.44 (s, 6 H), 1.48 (s, 3H), 1.30 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.6, 145.2, 144.9, 133.8, 132.2, 129.9 (2C), 129.7 (6C), 129.1, 127.9 (2C), 113.9 (2C), 113.3, 104.2, 77.8, 77.7 (2C), 77.3, 71.7, 66.9, 55.2, 26.8, 26.5, 21.6 (2C); ES HRMS *m*/*z* (M + Na)$^+$ calcd 671.1591, obsd 671.1562; $[\alpha]^{22}_D$ +42.8 (*c* 1.16, $CHCl_3$).

A heterogeneous mixture of the ditosylate from above (46.6 g, 71.8 mmol), sodium iodide (108 g, 720 mmol), and zinc dust (47 g, 719 mmol) in DMF (500 mL) was refluxed overnight, diluted with water, filtered, diluted with ethyl acetate, and washed with brine. After drying and evaporation of the organic phase, the residue was chromatographed on silica gel (elution with hexanes/ethyl acetate 5:1) to furnish the deprotected vinyl furanoside as a colorless oil (19.2 g, 87%): IR (neat, cm^{-1}) 1613, 1514, 1374; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8.8 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 5.79 (ddd, *J* = 17.2, 10.4, 6.7 Hz, 1H), 5.73 (d, *J* = 3.8 Hz, 1H), 5.44 (d, *J* = 17.0 Hz, 1H), 5.25 (d, *J* = 10.3 Hz, 1H), 4.67 (d, *J* = 11.9 Hz, 1H), 4.56 (d, *J* = 11.9 Hz, 1H), 4.54−4.52 (m, 1H), 4.48−4.43 (m, 1H), 3.81 (s, 3H), 3.48 (dd, *J* = 9.0, 4.3 Hz, 1H), 1.61 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.0, 134.6, 129.1 (3C), 118.1, 113.4 (2C), 112.3, 103.3, 81.1, 78.6, 77.1, 71.4, 54.8, 26.3, 26.1; ES HRMS *m*/*z* (M + Na)$^+$ calcd 329.1359, obsd 329.1379; $[\alpha]^{22}_D$ +59.9 (*c* 1.61, $CHCl_3$).

A solution of the above intermediate (21.2 g, 69.2 mmol) in methanolic 1% HCl (1300 mL) was stirred overnight, cooled to 0 °C, neutralized with saturated $NaHCO_3$ solution, and evaporated. The residue was extracted with ethyl acetate, the combined organic layers were dried and evaporated, and the residue was chromatographed on silica gel (elution with hexanes/ethyl acetate 3:2) to give the hydroxy methyl acetal as a colorless oil (15.4 g, 79%) consisting of an inseparable 8:1 mixture of β- and α-anomers. This mixture was subsequently dissolved in CH_2Cl_2 (200 mL), treated sequentially with imidazole (11.2 g, 165 mmol), DMAP (672 mg, 0.55 mmol),and *tert*-butyldimethylsilyl chloride (10.8 g, 71.7 mmol), and stirred at rt for 2 days prior to dilution with ethyl acetate and washing with water and brine. The organic solution was dried and evaporated to leave a residue that was chromatographed on silica gel (elution with hexanes/ethyl acetate 10:1). There was isolated 19.2 g (88%) of **3** and 2.4 g (11%) of the α-anomer.

(1*R*,2*S*,3*R*,4*S*)-3-(4-Methoxybenzyloxy)-2-(*tert*-butyldimethylsilyloxy)-4-vinylcyclobutanol (4). A cold (−78 °C) solution of zirconocene dichloride (4.6 g, 15.7 mmol) in toluene (30 mL) was treated with *n*-butyllithium (18.2 mL of 1.67 M, 30.4 mmol) and stirred for 1 h at this temperature. After the introduction of **3** (2.0 g, 5.1 mmol) as a solution in toluene (120 mL), the reaction mixture was stirred at rt for 3 h, cooled to 0 °C, and exposed to boron trifluoride etherate (3 mL, 24 mmol). After 30 min, 1 N HCl was added, and the product was extracted into ethyl acetate. The combined organic layers were washed with saturated $NaHCO_3$ solution, dried, and evaporated. The residue was chromatographed on silica gel (elution with hexanes/ethyl acetate 7:1) to give **4** as a colorless oil (1.2 g, 65%): IR (neat, cm^{-1}) 3454, 1613, 1514; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (d, *J* = 8.3 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 5.79 (ddd, *J* = 17.3, 10.5, 8.4 Hz, 1H), 5.25 (d, *J* = 10.5 Hz, 2H), 5.14 (d, *J* = 17.3 Hz, 1H), 4.66 (d, *J* = 11.3 Hz, 1H), 4.45 (d, *J* = 11.4 Hz, 1H), 4.41−4.36 (m, 1H), 4.09 (td, *J* = 6.2, 1.0 Hz, 1H), 3.94 (dd, *J* = 6.0, 1.9 Hz, 1H), 3.80 (s, 3H), 2.99 (br t, *J* = 8.4 Hz, 1H), 1.80 (br s, 1H), 0.93 (s, 9H), 0.13 (s, 3H), 0.12 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 133.9 (2C), 130.4, 129.4 (2C), 118.5, 113.7, 76.2, 76.0, 75.1, 71.3, 55.2, 45.8, 25.8 (3C), 18.2, −4.7, −5.0; ES HRMS *m*/*z* (M + Na)$^+$ calcd 387.1962, obsd 387.1955; $[\alpha]^{22}_D$ +10.6 (*c* 1.44, $CHCl_3$).

(1*R*,2*R*,3*R*,4*R*)-3-(4-Methoxybenzyloxy)-2-(*tert*-butyldimethylsilyloxy)-1-(2-trimethylsilyl)ethynyl)-4-vinylcyclobutanol (5). A mixture of **4** (144 mg, 0.39 mmol) and sodium bicarbonate (655 mg, 7.8 mmol) in CH_2Cl_2 (40 mL) was treated with the Dess−Martin periodinane (496 mg, 1.17 mmol), stirred at rt for 3 h, filtered through a pad of Celite (hexanes rinse), and evaporated. The residue was taken up in THF (2 mL) and added at 0 °C to the Grignard of trimethylsilylacetylene. This reagent was prepared by treating a solution of the alkyne (0.18 mL, 1.3 mmol) in THF (1.5 mL) with *n*-butyllithium (0.7 mL of 1.67 M, 1.17 mmol) at −78 °C, gradual warming to 0 °C, and treatment with an excess of magnesium bromide etherate. The white suspension was stirred at 0 °C for 30 min prior to use.

The original reaction mixture was stirred for 3 h at 0 °C, quenched with saturated NH_4Cl solution (5 mL), and extracted with ethyl acetate. The combined organic layers were dried and evaporated to leave a residue that was purified chromatographically on silica gel (elution with hexanes/ethyl acetate 10:1). There was isolated 118 mg (65%) of **5** as a colorless oil: IR (neat, cm^{-1}) 3511, 2169, 1613; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.6 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 6.01−5.89 (m, 1H), 5.14 (d, *J*

= 16.0 Hz, 1H), 5.13 (d, J = 11.4 Hz, 1H), 4.48 (d, J = 11.4 Hz, 1H), 4.43 (d, J = 11.4 Hz, 1H), 4.36 (d, J = 4.8 Hz, 1H), 3.81 (s, 3H), 3.81−3.74 (m, 1H), 3.31 (s, 1H), 2.99 (t, J = 8.2 Hz, 1H), 0.94 (s, 9H), 0.17 (s, 9 H), 0.15 (s, 3H), 0.14 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 135.3, 130.1, 129.2 (2C), 116.9, 113.6 (2C), 103.8, 92.7, 76.2, 73.6, 71.0, 68.2, 59.1, 55.2, 25.8 (3C), 18.4, −0.1 (3C), −4.6, −4.9; ES HRMS m/z (M + Na)$^+$ calcd 483.2357, obsd 483.2375; $[\alpha]^{22}_D$ +3.0 (c 1.0, $CHCl_3$).

(2*Z*,5*Z*,7*R*,8*R*)-7-(4-Methoxybenzyloxy)-8-(*tert*-butyldimethylsilyloxy)cycloocta-2,5-dienone (6). A mixture of **5** (118 mg, 0.26 mmol) and K_2CO_3 (54 mg, 0.39 mmol) in methanol (5 mL) was stirred for 1 h at rt, cooled to 0 °C, and quenched with saturated NH_4Cl solution. The methanol was carefully removed under reduced pressure, and the aqueous phase was extracted with CH_2Cl_2. The combined organic phases were dried and evaporated. The residue was purified by chromatography on silica gel (elution with hexanes−ethyl acetate 10:1) to give the unsubstituted alkyne as a colorless oil that was used directly.

The above material in benzene (5 mL) was refluxed for 2 h, cooled to rt, and evaporated. The residue was chromatographed on silica gel (elution with hexane−ethyl acetate 10:1) to provide **6** as a colorless oil (84 mg, 98%): IR (neat, cm^{-1}) 1703, 1612, 1514; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (d, J = 8.4 Hz, 1H), 6.87 (d, J = 8.6 Hz, 2H), 6.11−6.03 (m, 1H), 5.88−5.75 (m, 3H), 4.79 (d, J = 2.7 Hz, 1H), 4.62 (dd, J = 6.8, 2.8 Hz, 1H), 4.56 (d, J = 11.6 Hz, 1H), 4.49 (d, J = 11.6 Hz, 1H), 3.81 (s, 3H), 2.93−2.80 (m, 2H), 0.93 (s, 9H), 0.13 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.2, 159.1, 137.3 (2C), 133.8, 130.2, 129.4, 129.1, 127.2, 113.6 (2C), 81.8, 74.5, 70.7, 55.2, 29.0, 25.8, 18.6 (3C), −4.7, −5.2; ES HRMS m/z (M + Na)$^+$ calcd 411.1962, obsd 411.1968; $[\alpha]^{20}_D$ +0.17 (c 1.0 $CHCl_3$).

(1*R*,2*Z*,5*Z*,7*R*,8*S*)-7-(4-Methoxybenzyloxy)-8-(*tert*-butyldimethylsilyloxy)cycloocta-2,5-dienol (7). A solution of (+)-**6** (125 mg, 0.32 mmol) in methanol (3 mL) was cooled to 0 °C, treated with cerium trichloride heptahydrate (120 mg, 0.32 mmol), and stirred for 5 min. After the careful introduction of sodium borohydride (12 mg, 0.32 mmol), the reaction mixture was stirred in the cold for 10 min, quenched with saturated NH_4Cl solution, and freed of methanol under reduced pressure. The residue was extracted into ethyl acetate, and the combined organic layers were dried and evaporated. Purification of the product by chromatography on silica gel (elution with hexanes/ethyl acetate 30:1) afforded **7** as a colorless oil (107 mg, 86%): IR (neat, cm^{-1}) 3434, 1645, 1248; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (d, J = 8.6 Hz, 2H), 6.86 (d, J = 8.6 Hz, 2H), 5.79−5.73 (m, 1H), 5.60−5.52 (m, 2H), 5.41−5.33 (m, 1H), 4.66−4.61 (m, 1H), 4.53−4.50 (m, 1H), 4.52 (d, J = 11.4 Hz, 1H), 4.29 (d, J = 11.5 Hz, 1H), 3.81 (s, 3H), 3.69 (dd, J = 8.1, 3.3 Hz, 1H), 2.87 (br s, 2H), 2.25 (br s, 1H), 0.87 (s, 9H), 0.08 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.0, 132.0, 130.6, 130.4, 129.7, 129.6 (2C), 128.8, 113.5 (2C), 76.3, 75.5, 73.1, 70.1, 55.2, 30.2, 26.1 (3C), 18.5, −3.8, −4.8; ES HRMS m/z for $C_{22}H_{34}O_4SiNa^+$ calcd 413.2119, obsd 413.2144; $[\alpha]^{25}_D$ −44.9 (c 1.11, $CHCl_3$).

(1*R*,2*R*,3*Z*,6*Z*,8*R*)-2-(4-Methoxybenzyloxy)-8-(*tert*-butyldimethylsilyloxy)cycloocta-3,6-dienol (8). A solution of (+)-**6** (99 mg, 0.25 mmol) in 95% ethanol (3 mL) was treated with sodium borohydride (38.5 mg, 1.02 mmol) at 0 °C, stirred at this temperature for 1 h, and quenched with saturated NH_4Cl solution. The ethanol was removed under reduced pressure and the residue was extracted with ethyl acetate. The combined organic solutions were dried and concentrated. Subsequent chromatography on silica gel (elution with hexanes/ethyl acetate 80:1) afforded the less polar **7** (25 mg, 25%) followed by the more polar **8** (50 mg, 50%) as a colorless oil; IR (neat, cm^{-1}) 3473, 1613, 1249; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, J = 8.7 Hz, 2H), 6.86 (d, J = 8.7 Hz, 2H), 5.75−5.69 (m, 1H), 5.59−5.53 (m, 2H), 5.40−5.33 (m, 1H), 4.63−4.57 (m, 2H), 4.55 (d, J = 11.5 Hz, 1H), 4.42 (d, J = 11.5 Hz, 1H), 3.80 (s, 3H), 3.78−3.75 (m, 1H), 2.86 (br s, 2H), 2.45 (d, J = 1.5 Hz, 1H), 0.89 (s, 9H), 0.08 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 133.6, 130.9, 130.2, 129.3 (2C), 128.9, 128.0, 113.7 (2C), 75.1, 73.9, 73.4, 70.0, 55.3, 30.0, 25.8 (3C), 18.2, −4.6, −4.7; ES HRMS m/z for $C_{22}H_{34}O_4SiNa^+$ calcd 413.2119, obsd 413.2131; $[\alpha]^{25}_D$ + 42.0 (c 1.11, $CHCl_3$).

(1*S*,2*Z*,5*Z*,7*R*,8*S*)-7-(4-Methoxybenzyloxy)-8-(*tert*-butyldimethylsilyloxy)cycloocta-2,5-dienol (9). A solution of (+)-**6** (121 mg, 0.31 mmol) in methanol (3 mL) was treated with sodium borohydride (47.1 mg, 1.24 mmol) at 0 °C and processed as in part B. There was isolated 79 mg (65%) of **7** alongside 18 mg (15%) of **9** as a colorless oil: IR (neat, cm^{-1}) 3439, 1613; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, J = 8.7 Hz, 2H), 6.87 (d, J = 8.7 Hz, 2H), 5.81−5.71 (m, 2H), 5.38−5.32 (m, 1H), 5.25−5.19 (m, 1H), 4.56−4.52 (m, 1H), 4.54 (d, J = 11.6 Hz, 1H), 4.41 (d, J = 4.6 Hz, 1H), 4.36 (d, J = 11.6 Hz, 1H), 4.18 (br s, 1H), 3.81 (s, 3H), 2.74−2.66 (m, 1H), 2.53 (dd, J = 13.8, 6.9 Hz, 1H), 2.00 (d, J = 6.9 Hz, 1H), 0.87 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.0, 132.0, 130.5 (2C), 129.3, 129.0 (2C), 128.8, 113.6 (2C), 78.4, 76.3, 73.0, 69.8, 55.3, 28.5, 25.9 (3C), 18.3, −4.2, −5.2; ES HRMS m/z for $C_{22}H_{34}O_4SiNa^+$ calcd 413.2119, obsd 413.2128; $[\alpha]^{25}_D$ +18.7 (c 0.72, $CHCl_3$).

Catalytic Hydrogenation of the Cyclooctadienols. A. Involving (−)-7. A solution of (−)-**7** (51 mg, 0.13 mmol) in methanol (3 mL) was mixed with 5 mg of 10% Pd/C and stirred overnight under 55 psi of hydrogen. After catalyst removal by filtration and subsequent solvent evaporation, the residue was chromatographed on silica gel. Elution with hexanes/ethyl acetate 2:1 afforded 22 mg (61%) of **10** as a white solid: mp 84−86 °C; IR (neat, cm^{-1}) 3365, 1064; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.93−3.79 (m, 3H), 2.43 (d, J = 1.9 Hz, 1H), 2.35 (s, 1H), 1.91−1.86 (m, 2H), 1.75−1.51 (m, 7H), 1.42−1.31 (m, 1H), 0.94 (s, 9H), 0.17 (s, 3H), 0.15 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 77.4, 72.7, 68.5, 33.5, 29.2, 28.3, 25.8 (3C), 21.9, 21.7, 18.1, −4.4, −4.6; ES HRMS m/z for $C_{14}H_{30}O_3SiNa^+$ calcd 297.1856, obsd 297.1853; $[\alpha]^{25}_D$ −35.7 (c 0.35, $CHCl_3$).

B. Involving (+)-8. Comparable reduction of **8** (48 mg, 0.12 mmol) resulted in the isolation of **11** (21 mg, 62%) as a colorless oil: IR (neat, cm^{-1}) 3428; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.02−3.96 (m, 2H), 3.68 (dd, J = 2.4, 8.2 Hz, 1H), 3.23 (d, J = 0.8 Hz, 1H), 2.68 (d, J = 2.6 Hz, 1H), 1.83−1.51 (m, 10H), 0.91 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 74.8, 70.8, 70.1, 35.9, 28.6, 27.4, 25.8 (3C), 21.6, 21.4, 18.0, −4.3, −4.9; ES HRMS m/z for $C_{14}H_{30}O_3SiNa^+$ calcd 297.1856, obsd 297.1862; $[\alpha]^{25}_D$ −31.1 (c 0.71, $CHCl_3$).

C. Involving (+)-9. Analogous processing of (+)-**9** (20 mg, 0.051 mmol) furnished 7.2 mg (51%) of **12** as colorless needles: mp 109−110 °C; IR (neat, cm^{-1}) 3386, 1250; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.00−3.99 (m, 1H), 3.86 (br s, 2H), 2.71 (d, J = 4.2 Hz, 2H), 1.91−1.77 (m, 6H), 1.58−1.52 (m, 2H), 1.36−1.25 (m, 2H), 0.94 (s, 9H), 0.12 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 75.8 (2C), 75.3, 31.6 (2C), 28.3 (2C), 25.9 (3C), 22.3, 18.2, −4.6 (2C); ES HRMS m/z for $C_{14}H_{30}O_3SiNa^+$ calcd 297.1856, obsd 297.1853; $[\alpha]^{25}_D$ 0 (c 0.57, $CHCl_3$).

(1*R*,3*R*)-Cyclooctane-1,2,3-triol. A. From (−)-10. Compound (−)-**10** (6.4 mg, 0.023 mmol) dissolved in THF (2 mL) was treated with tetra-*n*-butylammonium fluoride (0.027 mL of 1 M in THF, 0.027 mmol) and stirred at rt for 1 h prior to solvent evaporation. Chromatography on silica gel (elution with hexanes/ethyl acetate 1:3) afforded **13** (2.4 mg, 65%) as a white solid: mp 69−71 °C; IR (neat, cm^{-1}) 3443, 1460; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.05−3.99 (m, 1H), 3.93−3.87 (m, 1H), 3.73−3.71 (m, 1H), 3.12 (br s, 1H), 2.44 (br s, 2H), 1.93−1.41 (series of m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 76.3, 71.3, 70.3, 33.5, 30.3, 27.4, 23.1, 22.7; ES HRMS m/z for $C_8H_{16}O_3Na^+$ calcd 183.0992, obsd 183.0993; $[\alpha]^{25}_D$ −61.8 (c 0.55, $CHCl_3$).

B. From (−)-11. Comparable treatment of (−)-**11** (15 mg, 0.055 mmol) delivered 6.7 mg (76%) of **13**, spectroscopically identical to the material obtained above.

(1*R*,3*S*)-Cyclooctane-1,2,3-triol (14). Entirely analogous processing of ***meso*-12** (7.9 mg, 0.03 mmol) yielded 3.9 mg (81%) of

14 as a white solid: mp 93−95 °C; IR (neat, cm^{-1}) 3428, 1450; ^1H NMR (300 MHz, $CDCl_3$) δ 3.97−3.93 (m, 3H), 3.39 (d, J = 5.5 Hz, 1H), 3.00−2.98 (m, 2H), 2.09−1.98 (m, 2H), 1.89−1.60 (m, 6H), 1.51−1.26 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 75.5 (2C), 72.2, 32.1 (2C), 28.8, 22.7 (2C); ES HRMS m/z for $C_8H_{16}O_3$-Na^+ calcd 183.0992, obsd 183.0996; $[\alpha]^{25}_D$ 0 (c 0.43, $CHCl_3$).

(2*R*,3*R*,4*Z*)-3-(4-Methoxybenzyloxy)-2-(*tert*-butyldimethylsilyloxy)cyclooct-4-enone (15). A solution of (+)-**6** (100 mg, 0.26 mmol) in 10 mL of THF was treated with L-Selectride (1 M in THF, 0.39 mL, 0.39 mmol) at −78 °C, stirred at this temperature for 1 h, quenched with saturated NH_4Cl solution, and extracted with ethyl acetate. The combined organic layers were dried and evaporated. Purification of the residue by chromatography on silica gel (elution with hexanes/ethyl acetate 30:1) afforded **15** (95 mg, 94%) as a colorless oil: IR (neat, cm^{-1}) 1612; ^1H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 5.78−5.69 (m, 2H), 4.51 (d, J = 11.5 Hz, 1H), 4.44 (br s, 1H), 4.41 (d, J = 11.5 Hz, 1H), 4.22 (d, J = 5.2 Hz, 1H), 3.81 (s, 3H), 3.06−2.97 (m, 1H), 2.10−2.03 (m, 1H), 1.99−1.82 (m, 3H), 1.59−1.51 (m, 1H), 0.89 (s, 9H), 0.07 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.9, 159.0, 132.7 (2C), 130.2, 129.1 (2C), 113.6 (2C), 84.4, 75.5, 70.1, 55.2, 33.5, 25.8, 25.7 (3C), 23.8, 18.3, −4.8, −5.2; ES HRMS m/z for $C_{22}H_{34}O_4SiNa^+$ calcd 413.2119, obsd 413.2099; $[\alpha]^{21}_D$ −56.8 (c 0.71, $CHCl_3$).

(1*R*,2*S*,3*R*,*Z*)-2-(*tert*-Butyldimethylsilanyloxy)-3-(4-methoxybenzyloxy)cyclooct-4-enol (16). A solution of (−)-**15** (24 mg, 0.061 mmol) in methanol (4 mL) was treated with sodium borohydride (3.4 mg, 0.09 mmol) at rt, stirred for 10 min, and worked up in the predescribed manner. Chromatographic purification on silica gel (elution with hexanes/ethyl acetate 30:1) afforded 20.1 mg (83%) of **16** as a colorless oil: IR (neat, cm^{-1}) 3435, 1248; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, J = 8.8 Hz, 2H), 6.89 (d, J = 8.8 Hz, 2H), 5.87 (dd, J = 18.8, 8.0 Hz, 1H), 5.64 (dt, J = 9.6, 1.1 Hz, 1H), 4.56 (d, J = 11.6 Hz, 1H), 4.34−4.32 (m, 1H), 4.31 (d, J = 11.6 Hz, 1H), 3.84 (s, 3H), 3.72 (dd, J = 7.6, 2.8 Hz, 1H), 3.54 (t, J = 7.6 Hz, 1H), 2.20 (s, 1H), 2.20−2.14 (m, 1H), 2.04−1.96 (m, 1H), 1.80−1.37 (m, 4H), 0.87 (s, 9H), 0.09 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.0, 132.0, 131.4, 130.4, 129.7 (2C), 113.6 (2C), 80.9, 75.8, 73.2, 69.5, 55.2, 32.0, 27.5, 26.8, 26.1 (3C), 18.4, −3.8, −4.9; ES HRMS m/z for $C_{22}H_{36}O_4SiNa^+$ calcd 415.2275, obsd 415.2279; $[\alpha]^{22}_D$ −23.8 (c 2.59, $CHCl_3$).

Catalytic Hydrogenation of (−)-16. Hydrogenation of (−)-**16** (20 mg, 0.051 mmol) over 10% Pd−C (2 mg) in methanol (3 mL) in the predescribed manner gave 13 mg (93%) of (−)-**10**, identical in all respects to the material isolated earlier.

L-Selectride Reduction of (−)-15. Ketone **15** (19 mg, 0.049 mmol) dissolved in THF (2 mL) was treated with L-Selectride (0.12 mL of 1 M in THF, 0.12 mmol) at rt, stirred for 3 h, quenched with saturated NH_4Cl solution, and extracted with ethyl acetate. After the usual workup and chromatography on silica gel (elution with hexanes/ethyl acetate 30:1), there was isolated 11 mg (58%) of **17** and 7.1 mg (37%) of **18**, both as colorless oils.

For **17**: IR (neat, cm^{-1}) 3400, 1642; ^1H NMR (300 MHz, $CDCl_3$) δ 7.24 (d, J = 8.6 Hz, 2H), 6.86 (d, J = 8.6 Hz, 2H), 5.66−5.58 (m, 2H), 4.52 (d, J = 11.6 Hz, 1H), 4.31 (d, J = 11.6 Hz, 1H), 4.20 (br s, 1H), 4.10 (d, J = 4.8 Hz, 1H), 3.81 (s, 3H), 3.49 (dt, J = 9.1, 1.9 Hz, 1H), 2.35−2.30 (m, 1H), 2.06−1.94 (m, 2H), 1.89 (d, J = 9.6 Hz, 1H), 1.76−1.71 (m, 1H), 1.50−1.47 (m, 1H), 1.24−1.17 (m, 1H), 0.90 (s, 9H), 0.12 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.9, 131.8, 130.5, 129.4, 129.2 (2C), 113.6 (2C), 79.4, 76.0, 73.4, 69.7, 55.2, 27.8, 26.0 (3C), 25.5, 24.7, 18.5, −3.9, −5.3; ES HRMS m/z for $C_{22}H_{36}O_4SiNa^+$ calcd 415.2275, obsd 415.2284; $[\alpha]^{21}_D$ −73 (c 0.1, $CHCl_3$).

For **18**: IR (neat, cm^{-1}) 3649, 1613; ^1H NMR (300 MHz, $CDCl_3$) δ 7.26 (d, J = 8.5 Hz, 2H), 6.87 (d, J = 8.5 Hz, 2H), 5.81−5.63 (m, 2H), 4.62 (d, J = 11.8 Hz, 1H), 4.35 (d, J = 11.8 Hz, 1H), 4.13 (d, J = 6.3 Hz, 1H), 4.07 (s, 1H), 3.80 (s, 3H), 3.56 (dd, J = 8.7, 2.1 Hz, 1H), 2.32−2.24 (m, 1H), 2.32 (s, 1H), 2.09−1.87 (m, 2H), 1.69−1.58 (m, 1H), 1.54−1.44 (m, 1H), 1.21−1.14 (m, 1H), 0.87 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 131.3, 130.2, 129.9, 129.5 (2C), 113.7 (2C), 78.6, 74.6, 73.9, 69.8, 55.2, 27.2, 25.8 (3C), 25.4, 24.4, 18.0, −4.7, −4.9; ES HRMS m/z for $C_{22}H_{36}O_4SiNa^+$ calcd 415.2275, obsd 415.2279; $[\alpha]^{21}_D$ −30.5 (c 0.55, $CHCl_3$).

(1*S*,2*S*,3*R*,4*S*,5*S*)-3-(4-Methoxybenzyloxy)-4-(*tert*-Butyldimethylsilyloxy)cyclooctane-1,2,5-triol (19). A solution of (−)-**17** (11 mg, 0.028 mmol) in 8:1 acetone/water (2 mL) was treated with *N*-methylmorpholine *N*-oxide (8.2 mg, 0.07 mmol) followed by osmium tetraoxide (0.7 mg, 0.0028 mmol). The reaction mixture was stirred at rt for 4 days, freed of acetone under reduced pressure, and extracted with ethyl acetate. The combined organic layers were dried and evaporated to leave a residue that was chromatographed on silica gel (elution with hexanes/ethyl acetate 1:1) to provide 7.4 mg (62%) of **19** as a colorless oil: IR (neat, cm^{-1}) 3435, 1513; ^1H NMR (300 MHz, $CDCl_3$) δ 7.26 (d, J = 8.6 Hz, 2H), 6.89 (d, J = 8.6 Hz, 2H), 4.64 (d, J = 11.1 Hz, 1H), 4.44 (d, J = 11.1 Hz, 1H), 4.25 (s, 1H), 4.12 (br s, 1H), 4.05−4.02 (m, 1H), 3.81 (s, 3H), 3.59−3.52 (m, 2H), 2.96 (s, 1H), 2.52 (br s, 1H), 1.90−1.47 (m, 7H), 0.92 (s, 9H), 0.12 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.5, 129.8 (2C), 129.4, 114.0 (2C), 78.5, 76.1, 73.9, 72.7, 71.1, 69.4, 55.3, 29.3, 29.1, 26.0 (3C), 18.8, 18.4, −4.1, −5.0; ES HRMS m/z for $C_{22}H_{38}O_6SiNa^+$ calcd 449.2330, obsd 449.2344; $[\alpha]^{21}_D$ +38.9 (c 0.54, $CHCl_3$).

(1*S*,2*S*,4*S*,5*S*)-3-(4-Methoxybenzyloxy)cyclooctane-1,2,4,5-tetraol (20). A solution of (+)-**19** (10.1 mg, 0.024 mmol) in THF (2 mL) was treated with tetra-*n*-butylammonium fluoride (0.04 mL of 1 M in THF, 0.04 mmol), stirred at rt for 2 h, and freed of solvent prior to the usual workup. Following chromatography on silica gel (elution with ethyl acetate/methanol 15:1), **20** was isolated as a colorless oil (6.4 mg, 87%): IR (neat, cm^{-1}) 3503, 1514, 1248; ^1H NMR (300 MHz, $CDCl_3$) δ 7.27 (d, J = 8.7 Hz, 2H), 6.89 (d, J = 8.7 Hz, 2H), 4.61 (d, J = 10.9 Hz, 1H), 4.55 (d, J = 10.9 Hz, 1H), 4.23 (s, 1H), 4.15−4.12 (m, 1H), 4.06−4.02 (m, 1H), 3.81 (s, 3H), 3.71 (dd, J = 7.6, 1.5 Hz, 1H), 3.69−3.65 (m, 1H), 3.19 (s, 1H), 2.87 (d, J = 3.2 Hz, 1H), 2.76 (d, J = 2.3 Hz, 1H), 2.51 (d, J = 8.2 Hz, 1H), 1.97−1.48 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.7, 129.9 (2C), 129.1, 114.1 (2C), 78.0, 77.2, 73.2, 71.9, 70.3, 69.3, 55.3, 28.7, 28.4, 19.2; ES HRMS m/z for $C_{16}H_{24}O_6$-Na^+ calcd 335.1465, obsd 335.1447; $[\alpha]^{21}_D$ +16.8 (c 0.31, $CHCl_3$).

(1*S*,2*S*,4*S*,5*S*)-Cyclooctane-1,2,3,4,5-pentaol (21). Hydrogenation of (+)-**20** (16.1 mg, 0.052 mmol) over 10% Pd/C (2 mg) in methanol (3 mL) at 60 psi overnight returned 7.6 mg (77%) of **21** as a colorless oil: IR (neat, cm^{-1}) 3436; ^1H NMR (300 MHz, D_2O) δ 4.32−4.26 (m, 1H), 4.10 (d, J = 2.9 Hz, 1H), 3.92−3.83 (m, 2H), 3.78−3.72 (m, 1H), 1.77−1.56 (m, 5H), 1.34−1.20 (m, 1H); ^{13}C NMR (75 MHz, D_2O) δ 79.7, 78.2, 76.1, 75.0, 71.2, 31.1, 29.7, 20.5; ES HRMS m/z for $C_8H_{16}O_5Na^+$ calcd 215.0890, obsd 215.0891; $[\alpha]^{21}_D$ +8.7 (c 0.46, CH_3OH).

(3*Z*,5*Z*,7*R*,8*R*)-7-(4-Methoxybenzyloxy)-8-(*tert*-butyldimethylsilyloxy)cycloocta-3,5-dienone (22). A solution of (+)-**6** (21 mg, 0.054 mmol) in THF (2 mL) was treated with triethylamine (0.15 mL, 0.11 mmol) and stirred at rt for 2 days. Removal of the solvent and purification of the residue chromatographically on silica gel (elution with hexanes/ethyl acetate 30:1) gave **22** (19 mg, 90%) as a colorless oil: IR (neat, cm^{-1}) 3413, 1514; ^1H NMR (300 MHz, $CDCl_3$) δ 7.22 (d, J = 8.7 Hz, 2H), 6.86 (d, J = 8.7 Hz, 2H), 6.06−6.01 (m, 2H), 5.88−5.75 (m, 2H), 4.51 (d, J = 11.5 Hz, 1H), 4.43 (d, J = 11.5 Hz, 1H), 4.30 (s, 1H), 4.25 (d, J = 6.5 Hz, 1H), 3.80 (s, 3H), 3.56 (dd, J = 12.7, 7.8 Hz, 1H), 2.82 (dd, J = 12.7, 6.8 Hz, 1H), 0.90 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.6, 159.1, 134.2, 130.2, 129.5, 129.2 (2C), 127.5, 126.7, 113.7 (2C), 77.7, 77.3, 70.6, 55.2, 39.8, 25.7 (3C), 18.3, −5.0 (2C); ES HRMS m/z for $C_{22}H_{32}O_4Na^+$ calcd 411.1962, obsd 411.1959; $[\alpha]^{22}_D$ −196.8 (c 0.57, $CHCl_3$).

(2*Z*,4*Z*,7*R*,8*R*)-7-(4-Methoxybenzyloxy)-8-(*tert*-butyldimethylsilyloxy)cycloocta-2,4-dienone (23). A solution of (+)-**6** (24 mg, 0.062 mmol) in isopropyl alcohol (1 mL) was treated with aluminum isopropoxide (8.9 mg, 0.044 mmol). The mixture was refluxed for

6 h with provision for the slow evaporation of solvent. The residue was heated at 94 °C for 2 h prior to partitioning between ethyl acetate and water. The organic phase was dried and evaporated to leave a residue that was purified chromatographically on silica gel (elution with hexanes/ethyl acetate 30:1) to afford **22** (8.1 mg, 34%) and the more polar **23** (11.9 mg, 50%) as a colorless oil: IR (neat, cm^{-1}) 1670, 1124; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, $J = 8.7$ Hz, 2H), 6.87 (d, $J = 8.7$ Hz, 2H), 6.57−6.53 (m, 1H), 6.34−6.31 (m, 2H), 6.22 (d, $J = 12.8$ Hz, 1H), 4.98 (d, $J = 11.9$ Hz, 1H), 4.80 (d, $J = 3.3$ Hz, 1H), 4.66 (d, $J = 11.9$ Hz, 1H), 4.04 (ddd, $J = 11.3$, 6.0, 3.4 Hz, 1H), 3.82 (s, 3H), 2.50−2.44 (m, 1H), 2.26−2.18 (m, 1H), 0.90 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.7, 159.1, 135.9, 135.7, 132.2, 131.0, 130.3, 129.5 (2C), 113.6 (2C), 84.7, 79.0, 73.2, 55.3, 33.0, 25.9 (3C), 18.4, −4.7, −5.0; ES HRMS *m/z* for $C_{22}H_{32}O_4Si\ Na^+$ calcd 411.1962, obsd 411.1964; $[\alpha]^{22}_D$ +272.5 (*c* 0.63, $CHCl_3$).

(1*R*,2*R*,3*R*,4*R*,5*R*)-3-(4-Methoxybenzyloxy)-1-(*tert*-butyldimethylsilyloxy)-9-oxabicyclo[3.3.1]nonane-2,4-diol (26). To a solution of (−)-**15** (151 mg, 0.39 mmol) in acetone/water (8:1, 20 mL) were added NMO (91 mg, 0.78 mmol) and osmium tetraoxide (2 mg, 0.0078 mmol) at rt. Stirring for 3 days was followed by removal of the acetone. The residue was extracted with ethyl acetate, dried, and evaporated. The mixture was purified chromatographically on silica gel (elution with hexanes/ethyl acetate 4:1 to 1:1) to give the least polar product **26** (6 mg, 4%) as a colorless oil: IR (neat, cm^{-1}) 3456, 1514, 1178; ^{1}H NMR (300 MHz, C_6D_6) δ 7.28 (d, $J = 8.8$ Hz, 2H), 6.82 (d, $J = 8.8$ Hz, 2H), 4.53 (d, $J = 11.1$ Hz, 1H), 4.47 (d, $J = 11.1$ Hz, 1H), 4.27 (d, $J = 6.9$ Hz, 1H), 3.75−3.73 (m, 1H), 3.64−3.58 (m, 2H), 3.54−3.50 (m, 1H), 3.37 (s, 3H), 3.00 (d, $J = 4.8$ Hz, 1H), 1.63−1.59 (m, 1H), 1.44−1.34 (m, 2H), 1.19−1.13 (m, 1H), 1.07−0.98 (m, 1H), 1.06 (s, 9H), 0.81−0.73 (m, 1H), 0.38 (s, 3H), 0.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 129.9, 129.6 (2C), 113.9 (2C), 97.0, 76.5, 73.2, 72.1, 69.8, 69.2, 55.3, 32.9, 25.8 (3C), 23.2, 19.1, 18.0, −2.4, −2.8; ES HRMS *m/z* for $C_{22}H_{36}O_6SiNa^+$ calcd 447.2173, obsd 447.2188; $[\alpha]^{21}_D$ +9.7 (*c* 0.64, $CHCl_3$).

(1*S*,2*R*,3*R*,4*R*,5*R*)-3-(4-Methoxybenzyloxy)-2-(*tert*-butyldimethylsilyloxy)-9-oxabicyclo[3.3.1]nonane-1,4-diol (25). Further elution gave the more polar **25** (60 mg, 38%) as a colorless oil: IR (neat, cm^{-1}) 3540, 1514, 1122; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (d, $J = 8.6$ Hz, 2H), 6.89 (d, $J = 8.6$ Hz, 2H), 4.72 (d, $J = 11.2$ Hz, 1H), 4.48 (d, $J = 11.2$ Hz, 1H), 4.34 (d, $J = 7.4$ Hz, 1H), 3.87 (s, 1H), 3.83−3.80 (m, 1H), 3.82 (s, 3H), 3.76−3.73 (m, 2H), 3.37 (d, $J = 8.4$ Hz, 1H), 1.95−1.81 (m, 2H), 1.79−1.69 (m, 1H), 1.65−1.42 (m, 2H), 1.37−1.25 (m, 1H), 0.9 (s, 9H), 0.11 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.3, 130.0, 129.5 (2C), 113.7 (2C), 94.1, 76.2, 76.1, 72.6, 69.4, 69.0, 55.2, 29.9, 26.0 (3C), 22.8, 18.6, 18.4, −4.2, −5.1; ES HRMS *m/z* for $C_{22}H_{36}O_6SiNa^+$ calcd 447.2173, obsd 447.2173; $[\alpha]^{21}_D$ −16.3 (*c* 1.04, $CHCl_3$).

(1*R*,2*R*,3*R*,4*S*,5*S*)-3-(4-Methoxybenzyloxy)-2-(*tert*-butyldimethylsilyloxy)-9-oxabicyclo[3.3.1]nonane-1,4-diol (24). The most polar product **24** was obtained upon further elution as a white solid (88 mg, 56%): mp 107−109 °C; IR (neat, cm^{-1}) 3383, 1612, 1122; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 (d, $J = 8.9$ Hz, 2H), 6.88 (d, $J = 8.9$ Hz, 2H), 4.74 (d, $J = 11.2$ Hz, 1H), 4.44 (d, $J = 11.2$ Hz, 1H), 4.15−4.07 (m, 2H), 3.80 (s, 3H), 3.79−3.72 (m, 2H), 2.26−2.19 (m, 3H), 1.79−1.69 (m, 1H), 1.63−1.55 (m, 2H), 1.30−1.20 (m, 1H), 0.91 (s, 9H), 0.12 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 130.6, 129.2 (2C), 113.8 (2C), 98.9, 80.5, 77.6, 74.0, 73.1, 69.8, 55.3, 33.4, 25.9 (3C), 25.8, 18.3, 17.2, −4.5, −4.8; ES HRMS *m/z* for $C_{22}H_{36}O_6SiNa^+$ calcd 447.2173, obsd 447.2170; $[\alpha]^{19}_D$ +12.3 (*c* 0.6, $CHCl_3$).

(1*R*,2*R*,3*R*,4*S*,5*S*)-3-(4-Methoxybenzyloxy)-9-oxabicyclo[3.3.1]nonane-1,2,4-triol (27). A solution of **24** (37 mg, 0.087 mmol) in 2 mL of THF was treated with TBAF (1 M in THF, 0.1 mL, 0.1 mmol), stirred at rt for 6 h, and freed of solvent. The residue was purified chromatographically on silica gel (elution with hexanes/ethyl acetate 1:4) to give **27** (11.2 mg, 41%) as a white solid: mp 119−121 °C; IR (neat, cm^{-1}) 3378, 1612, 1094; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (d, $J = 8.7$ Hz, 2H), 6.90 (d, $J = 8.7$ Hz, 2H), 4.63 (d, $J = 11.1$ Hz, 1H), 4.55 (d, $J = 11.1$ Hz, 1H), 4.16 (d, $J = 9.3$ Hz, 1H), 3.97 (d, $J = 6.0$ Hz, 1H), 3.88 (t, $J = 4.8$ Hz, 1H), 3.81 (s, 3H), 3.73−3.70 (m, 1H), 2.83 (br s, 2H), 2.29−2.09 (m, 2H), 1.85−1.72 (m, 1H), 1.58−1.49 (m, 2H), 1.42−1.32 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.6, 129.7 (2C), 129.4, 114.1 (2C), 97.1, 79.4, 77.3, 72.9, 71.2, 70.0, 55.3, 30.8, 25.0, 16.8; ES HRMS *m/z* for $C_{16}H_{22}O_6Na^+$ calcd 333.1308, obsd 333.1307; $[\alpha]^{21}_D$ +3.7 (*c* 0.86, $CHCl_3$).

(1*S*,2*R*,3*R*,4*R*,5*R*)-3-(4-Methoxybenzyloxy)-9-oxabicyclo[3.3.1]nonane-1,2,4-triol (28). A solution of **25** (29 mg, 0.068 mmol) in 3 mL of THF was treated with TBAF (1 M in THF, 0.1 mL, 0.1 mmol), stirred at rt for 2 h, and freed of solvent. The residue was purified chromatographically on silica gel (elution with hexanes/ethyl acetate 1:4) to give **28** (17.1 mg, 80%) as a white solid: mp 104−105 °C; IR (neat, cm^{-1}) 3397, 1612, 1076; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, $J = 8.8$ Hz, 2H), 6.92 (d, $J = 8.7$ Hz, 2H), 4.71 (d, $J = 11.2$ Hz, 1H), 4.62 (d, $J = 11.1$ Hz, 1H), 4.51 (s, 1H), 4.33 (d, $J = 6.4$ Hz, 1H), 3.89 (t, $J = 4.0$ Hz, 1H), 3.82 (s, 3H), 3.74 (br s, 2H), 3.40−3.39 (m, 1H), 3.06 (br s, 1H), 1.98−1.87 (m, 2H), 1.81−1.74 (m, 1H), 1.68−1.64 (m, 1H), 1.53−1.36 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 129.7 (2C), 129.4, 114.1 (2C), 94.4, 74.9, 73.1, 72.5, 70.2, 69.7, 55.3, 30.1, 23.4, 18.9; ES HRMS *m/z* for $C_{16}H_{22}O_6Na^+$ calcd 333.1308, obsd 333.1300; $[\alpha]^{21}_D$ +13.2 (*c* 0.63, $CHCl_3$).

Comparable processing of (+)-**26** also returned exclusively (+)-**28** (65%).

(3a*R*,4*R*,5*R*,9a*R*)-4-(4-Methoxybenzyloxy)-5-(*tert*-butyldimethylsilyloxy)-2,2-dimethylhexahydrocycloocta[*d*][1,3]dioxol-6(3a*H*)-one (29). To a solution of **25** (265 mg, 0.62 mmol) in 2,2-dimethoxypropane (10 mL) was added PPTS (15 mg, 0.06 mmol). The mixture was refluxed for 4 h, and the solvent was removed. After the usual workup, the residue was purified chromatographically on silica gel (elution with hexanes/ethyl acetate 5:1) to give **29** (241 mg, 83%) as a colorless oil: IR (neat, cm^{-1}) 1728, 1248; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, $J = 8.5$ Hz, 2H), 6.84 (d, $J = 8.5$ Hz, 2H), 4.95 (d, $J = 10.8$ Hz, 1H), 4.64 (d, $J = 10.8$ Hz, 1H), 4.35−4.34 (m, 1H), 4.34 (s, 1H,), 4.18 (d, $J = 3.5$ Hz, 1H), 4.14−4.09 (m, 1H), 3.79 (s, 3H), 2.63−2.53 (m, 2H), 2.22−2.15 (m, 1H), 1.97−1.89 (m, 1H), 1.75−1.72 (m, 1H), 1.67−1.56 (m, 1H), 1.44 (s, 3H), 1.33 (s, 3H), 0.91 (s, 9H), 0.09 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.3, 158.8, 131.4, 128.8 (2C), 113.5 (2C), 106.0, 84.3, 82.0, 78.2, 77.4, 76.6, 55.2, 37.0, 27.7, 26.8, 25.7 (3C), 24.0, 23.2, 18.3, −4.7 (2C); ES HRMS *m/z* for $C_{25}H_{40}O_6SiNa^+$ calcd 487.2486, obsd 487.2474; $[\alpha]^{21}_D$ +13.1 (*c* 0.61, $CHCl_3$).

((3a*R*,4*R*,5*S*,9a*R*)-4-(4-Methoxybenzyloxy)-2,2-dimethyl-6-methyleneoctahydrocycloocta[*d*][1,3]dioxol-5-yloxy)(*tert*-butyl)-dimethylsilane (30). A suspension of $Ph_3P^+CH_3\ Br^-$ (428 mg, 1.2 mmol) in THF (5 mL) was treated with *n*-butyllithium (2.0 M, 0.45 mL, 0.9 mmol) at 0 °C and stirred for 30 min. The system was warmed to rt for 20 min and returned again to 0 °C. Ketone **29** (140 mg, 0.30 mmol) in THF (3 mL) was introduced at 0 °C. The reaction mixture was quenched with saturated NH_4Cl solution after 2 h and extracted with ethyl acetate. The combined organic layers were dried and evaporated. The residue was purified chromatographically on silica gel (elution with hexanes/ethyl acetate 40:1 to 20:1) to give **30** (69 mg, 50%) as a colorless oil: IR (neat, cm^{-1}) 1614, 1248; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, $J = 8.5$ Hz, 2H), 6.85 (d, $J = 8.5$ Hz, 2H), 5.29 (s, 1H), 4.98 (s, 1H), 4.97 (d, $J = 11.2$ Hz, 1H), 4.63 (d, $J = 11.1$ Hz, 1H), 4.18 (d, $J = 6.9$ Hz, 1H), 4.14 (d, $J = 2.6$ Hz, 1H), 4.13−4.08 (m, 1H), 4.06 (d, $J = 2.8$ Hz, 1H), 3.79 (s, 3H), 2.79−2.68 (m, 1H), 2.53−2.48 (m, 1H), 1.80−1.71 (m, 1H), 1.68−1.63 (m, 1H), 1.59−1.50 (m, 2H) 1.44 (s, 3H), 1.32 (s, 3H), 0.92 (s, 9H), 0.08 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6, 147.3, 132.2, 128.4 (2C), 114.1, 113.4 (2C), 105.5, 86.3, 78.8, 78.7, 78.3, 76.2, 55.2, 29.5, 27.7, 27.0, 26.9, 25.9 (3C), 24.2, 18.3, −4.8, −5.2; ES HRMS *m/z* for

$C_{26}H_{42}O_5SiNa^+$ calcd 485.2694, obsd 485.2684; $[\alpha]^{21}_D$ +15.5 (*c* 2.38, $CHCl_3$).

((3a*R*,4*R*,5*S*,6*R*,9a*R*)-4-(4-Methoxybenzyloxy)-5-(*tert*-butyldimethylsilyloxy)-2,2-dimethyloctahydrocycloocta[*d*][1,3]dioxol-6-yl)methanol (31). A solution of **30** (66 mg, 0.14 mmol) in THF (5 mL) was treated with BH_3·THF complex (1 M, 0.42 mL, 0.42 mmol) under N_2 at 0 °C. After 10 min of stirring, the temperature was raised to rt and the mixture was stirred for another 2 h. Ethanol (0.2 mL) was introduced, and stirring was maintained for 10 min prior to treatment with aqueous NaOH solution (2 M, 0.4 mL) and H_2O_2 (30%, 0.24 mL). After being stirred at rt for 2 h, the reaction mixture was quenched with saturated NH_4Cl solution and extracted with ethyl acetate. The organic layers were combined, dried, and evaporated. The residue was purified chromatographically on silica gel (elution with hexanes/ethyl acetate 5:1) to give **31** (45 mg, 65%) as a colorless oil: IR (neat, cm^{-1}) 3462, 1249; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.5 Hz, 2H), 6.85 (d, *J* = 8.5 Hz, 2H), 4.86 (d, *J* = 10.9 Hz, 1H), 4.64 (d, *J* = 10.9 Hz, 1H), 4.24 (ddd, *J* = 11.2, 7.1, 2.0 Hz, 1H), 4.19 (d, *J* = 4.0 Hz, 1H), 4.13 (d, *J* = 7.6 Hz, 1H), 3.96 (t, *J* = 3.8 Hz, 1H), 3.85−3.79 (m, 1H), 3.80 (s, 3H), 3.61−3.57 (m, 1H), 2.71−2.62 (m, 1H), 2.19−2.11 (m, 1H), 2.0 (br s, 1H), 1.81−1.75 (m, 1H), 1.73−1.68 (m, 1H), 1.61−1.56 (m, 1H), 1.51 (s, 3H), 1.41−1.37 (m, 1H), 1.33 (s, 3H), 1.07−0.99 (m, 1H), 0.91 (s, 9H), 0.11 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8, 131.6, 128.6 (2C), 113.5 (2C), 105.2, 85.2, 79.2, 77.6, 75.5, 73.8, 64.2, 55.2, 44.8, 29.7, 26.8, 26.0, 25.9 (3C), 23.9, 23.1, 18.1, −4.0, −5.1; ES HRMS *m*/*z* for $C_{26}H_{44}O_6SiNa^+$ calcd 503.2799, obsd 503.2803; $[\alpha]^{19}_D$ −6.5 (*c* 3.7, $CHCl_3$).

(3a*S*,4*R*,5*S*,6*R*,9a*R*)-5-(*tert*-Butyldimethylsilyloxy)-6-(hydroxymethyl)-2,2-dimethyloctahydrocycloocta[*d*][1,3]dioxol-4-ol (32). A solution of **31** (77 mg, 0.16 mol) in CH_2Cl_2/H_2O (20:1, 10 mL) was treated with DDQ (55 mg, 0.24 mmol) and stirred at rt for 2 h. The reaction mixture was quenched with saturated $NaHCO_3$ solution and extracted with CH_2Cl_2. The combined organic layers were combined, dried, and evaporated. The residue was purified chromatographically on silica gel (elution with hexanes/ethyl acetate 5:1) to give **32** (47 mg, 81%) as a colorless oil: IR (neat, cm^{-1}) 3471, 1172; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.42 (dd, *J* = 5.0, 1.0 Hz, 1H), 4.21 (ddd, *J* = 11.0, 7.0, 1.8 Hz, 1H), 4.04 (dd, *J* = 7.0, 1.0 Hz, 1H), 4.01 (dd, *J* = 5.0, 2.0 Hz, 1H), 3.53 (dd, *J* = 9.6, 9.4 Hz, 1H), 3.42 (dd, *J* = 9.9, 6.0 Hz, 1H), 2.71−2.60 (m, 1H), 2.55 (br s, 1H), 1.95−1.78 (m, 3H), 1.70−1.66 (m, 1H), 1.50 (s, 3H), 1.34−1.23 (m, 2H), 1.32 (s, 3H), 0.99−0.95 (m, 1H), 0.90 (s, 9H), 0.12 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 105.3, 79.7, 76.1, 75.1, 70.1, 64.9, 44.7, 31.6, 28.0, 27.2, 25.8 (3C), 23.8, 23.6, 18.1, −4.5, −5.0; ES HRMS *m*/*z* for $C_{18}H_{36}O_5SiNa^+$ calcd 383.2224, obsd 383.2238; $[\alpha]^{19}_D$ −1.9 (*c* 1.89, $CHCl_3$).

(1*R*,2*R*,3*S*,4*S*,5*R*)-5-(Hydroxymethyl)cyclooctane-1,2,3,4-tetraol (33). A solution of **32** (47 mg, 0.13 mmol) in methanol (2 mL) was treated with HCl (1 M, 2 mL), stirred for 24 h at rt, and freed of solvent under vacuum. The residue was purified chromatographically on silica gel (elution with ethyl acetate/methanol 5:1) to give the more polar **33** as a colorless oil (9.8 mg, 37%): IR (neat, cm^{-1}) 3354, 1250, 1078; ^{1}H NMR (400 MHz, D_2O) δ 4.17 (s, 2H), 3.96−3.93 (m, 1H), 3.80 (s, 1H), 3.50 (d, *J* = 6.6 Hz, 2H), 2.08−1.95 (m, 2H), 1.80−1.74 (m, 1H), 1.70−1.64 (m, 1H), 1.61−1.55 (m, 1H), 1.49−1.43 (m, 1H), 1.40−1.32 (m, 1H); ^{13}C NMR (75 MHz, D_2O) δ 81.6, 77.0, 76.7, 76.3, 67.8, 46.0, 33.5, 26.4, 26.2; ES HRMS *m*/*z* for $C_9H_{18}O_5Na^+$ calcd 229.1046, obsd 229.1052; $[\alpha]^{19}_D$ −3.9 (*c* 0.81, CH_3OH).

Also isolated was the less polar **34** (6.8 mg, 28%): IR (neat, cm^{-1}) 3393, 1096, 1020; ^{1}H NMR (400 MHz, D_2O) δ 4.20 (d, *J* = 2.0 Hz, 1H), 4.01 (s, 1H), 3.97−3.93 (m, 3H), 3.90 (dd, *J* = 4.0, 1.6 Hz, 1H), 2.21 (t, *J* = 5.2 Hz, 1H), 2.11−2.02 (m, 1H), 1.82−1.75 (m, 1H), 1.70−1.62 (m, 1H), 1.57−1.50 (m, 2H), 1.46−1.38 (m, 1H); ^{13}C NMR (75 MHz, D_2O) δ 94.7, 82.4, 76.2, 74.5, 73.7, 48.6, 33.7, 31.7, 18.2; ES HRMS *m*/*z* for $C_9H_{16}O_4Na^+$ calcd 211.0946, obsd 211.0946; $[\alpha]^{19}_D$ −4.4 (*c* 0.48, CH_3OH).

(3a*S*,4*R*,5*R*,9a*S*)-4-(4-Methoxybenzyloxy)-5-(*tert*-butyldimethylsilyloxy)-2,2-dimethylhexahydrocycloocta[*d*][1,3]dioxol-6(3a*H*)-one (35). To a solution of (+)-**24** (41 mg, 0.1 mmol) in 2, 2-dimethoxypropane (3 mL) was added PPTS (2.5 mg, 0.01 mmol). The mixture was refluxed overnight, and the solvent was removed. The residue was purified chromatographically on silica gel (elution with hexanes/ethyl acetate 5:1) to give **35** as a colorless oil (40.2 mg, 91%): IR (neat, cm^{-1}) 1612, 1167; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 4.70 (s, 2H), 4.47 (dd, *J* = 9.3, 5.4 Hz, 1H), 4.32 (d, *J* = 1.8 Hz, 1H), 3.92−3.86 (m, 2H), 3.81 (s, 3H), 2.54−2.48 (m, 1H), 2.16−2.09 (m, 1H), 1.88−1.78 (m, 1H), 1.76−1.56 (m, 3H), 1.38 (s, 3H), 1.33 (s, 3H), 0.91 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.6, 159.2, 130.0, 129.8 (2C), 113.7 (2C), 107.1, 80.0, 77.1, 76.5, 76.0, 72.1, 55.2, 36.1, 30.0, 28.1, 25.7 (3C), 25.5, 23.8, 18.4, −5.0 (2C); ES HRMS *m*/*z* for $C_{25}H_{40}O_6SiNa^+$ calcd 487.2486, obsd 487.2486; $[\alpha]^{19}_D$ −29.4 (*c* 0.68, $CHCl_3$).

((3a*S*,4*R*,5*S*,9a*S*)-4-(4-Methoxybenzyloxy)-2,2-dimethyl-6-methyleneoctahydrocycloocta[*d*][1,3]dioxol-5-yloxy)*(tert*-butyl)dimethylsilane (36). A suspension of $Ph_3P^+CH_3Br^-$ (600 mg, 1.68 mmol) in THF (5 mL) was treated with *n*-butyllithium (2.0 M, 0.63 mL, 1.26 mmol) at 0 °C and stirred for 30 min. The system was warmed to rt for 20 min and returned to 0 °C again when **35** (196 mg, 0.42 mmol) dissolved in THF (5 mL) was added. The reaction mixture was quenched after 2 h with saturated NH_4Cl solution. After extraction with ethyl acetate, the combined organic layers were dried and evaporated. The residue was purified chromatographically on silica gel (elution with hexanes/ethyl acetate 20:1) to afford **36** (157 mg, 81%) as a colorless oil: IR (neat, cm^{-1}) 1513, 1125; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 5.20 (s, 1H), 4.89 (s, 1H), 4.74 (d, *J* = 11.8 Hz, 1H), 4.67 (d, *J* = 11.8 Hz, 1H), 4.43 (dd, *J* = 9.8, 5.6 Hz, 1H), 4.25 (d, *J* = 1.4 Hz, 1H), 4.09−4.05 (m, 1H), 3.81 (s, 3H), 3.68 (dd, *J* = 9.7, 2.2 Hz, 1H), 2.19−2.13 (m, 1H), 1.77−1.68 (m, 1H), 1.65−1.49 (m, 4H), 1.41 (s, 3H), 1.34 (s, 3H), 0.9 (s, 9H), 0.09 (s, 3H), 0.0 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 148.2, 130.8, 130.0 (2C), 113.6 (2C), 113.2, 106.2, 77.9, 77.1, 76.1, 75.8, 72.5, 55.5, 30.3, 28.8, 28.6, 28.2, 26.0 (3C), 25.4, 18.4, −4.4, −5.0; ES HRMS *m*/*z* for $C_{26}H_{42}O_5SiNa^+$ calcd 485.2694, obsd 485.2699; $[\alpha]^{18}_D$ −24.5 (*c* 2.63, $CHCl_3$).

((3a*S*,4*R*,5*S*,6*S*,9a*S*)-4-(4-Methoxybenzyloxy)-5-(*tert*-butyldimethylsilyloxy)-2,2-dimethyloctahydrocycloocta[*d*][1,3]dioxol-6-yl)methanol (37). A solution of **36** (153 mg, 0.33 mol) in THF (5 mL) was treated with BH_3·THF complex (1 M, 0.99 mL, 0.99 mmol) under N_2 protection at 0 °C. After 10 min of stirring, the temperature was raised to rt, and stirring was continued for another 2 h. Ethanol (0.4 mL) was introduced, and stirring was maintained for 10 min, followed by addition of 2 M NaOH solution (0.85 mL) and H_2O_2 (30%, 0.5 mL). After a further 2 h of agitation, the reaction mixture was quenched with saturated NH_4Cl solution and extracted with ethyl acetate. The organic layers were combined, dried, and evaporated. The residue was purified chromatographically on silica gel (elution with hexanes/ethyl acetate 10:1) to afford **37** (15 mg, 9%) as a colorless oil: IR (neat, cm^{-1}) 3453, 1249; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 8.5 Hz, 2H), 4.77 (d, *J* = 11.6 Hz, 1H), 4.65 (d, *J* = 11.6 Hz, 1H), 4.50 (dd, *J* = 9.5, 5.3 Hz, 1H), 4.17 (dd, *J* = 9.7, 5.3 Hz, 1H,), 3.81 (s, 3H), 3.75 (d, *J* = 9.8 Hz, 1H), 3.70 (d, *J* = 9.6 Hz, 1H), 3.65 (dd, *J* = 9.8, 4.3 Hz, 1H), 3.49 (dd, *J* = 10.1, 5.4 Hz, 1H), 1.80−1.74 (m, 2H), 1.71−1.68 (m, 1H), 1.65−1.48 (m, 3H), 1.44 (s, 3H), 1.40−1.32 (m, 1H), 1.35 (s, 3H), 0.99−0.90 (m, 1H), 0.87 (s, 9H), 0.10 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 130.9, 130.0 (2C), 113.5 (2C), 106.3, 78.3, 77.2, 76.4, 74.2, 72.6, 66.0, 55.2, 45.8, 32.8, 28.4, 26.7, 26.2 (4C), 25.5, 18.5, −3.4, −5.0; ES HRMS *m*/*z* for $C_{26}H_{44}O_6SiNa^+$ calcd 503.2799, obsd 503.2814; $[\alpha]^{19}_D$ −18.9 (*c* 1.01, $CHCl_3$).

((3a*S*,4*R*,5*S*,6*R*,9a*S*)-4-(4-Methoxybenzyloxy)-5-(*tert*-butyldimethylsilyloxy)-2,2-dimethyloctahydrocycloocta[*d*][1,3]dioxol-6-yl)methanol (38). Continued elution gave **38** (121 mg, 76%) as a colorless oil: IR (neat, cm^{-1}) 3462, 1248; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, J = 8.5 Hz, 2H), 6.86 (d, J = 8.5 Hz, 2H), 4.69 (d, J = 11.2 Hz, 1H), 4.63−4.58 (m, 1H), 4.53 (dd, J = 9.1, 6.3 Hz, 1H), 4.30 (br s, 1H), 4.16−4.11 (m, 1H), 3.79 (s, 3H), 3.44 (d, J = 8.2 Hz, 2H), 3.33 (br s, 1H), 1.79−1.69 (m, 3H), 1.63−1.55 (m, 2H), 1.52−1.33 (m, 2H), 1.45 (s, 3H), 1.36 (s, 3H), 1.02−0.87 (m, 1H), 0.87 (s, 9H), 0.10 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 131.0, 129.5 (2C), 113.5 (2C), 105.9, 81.4, 76.4, 76.2, 72.9, 71.6, 65.7, 55.2, 43.3, 27.7, 26.5, 26.1 (3C), 24.9, 24.2, 20.6, 18.5, −3.4, −5.5; ES HRMS *m*/*z* for $C_{26}H_{44}O_6SiNa^+$ calcd 503.2799, obsd 503.2777; $[\alpha]^{19}_D$ +3.0 (*c* 3.11, $CHCl_3$).

(3a*R*,4*R*,5*S*,6*S*,9a*S*)-5-(*tert*-Butyldimethylsilyloxy)-6-(hydroxymethyl)-2,2-dimethyloctahydrocycloocta[*d*][1,3]dioxol-4-ol (39). A solution of (−)-**37** (33 mg, 0.069 mol) in CH_2Cl_2/H_2O (20:1, 6 mL) was treated with DDQ (23 mg, 0.1 mmol), stirred at rt for 2 h, quenched with saturated $NaHCO_3$ solution, and extracted with CH_2Cl_2. The organic layers were combined, dried, and evaporated. The residue was purified chromatographically on silica gel (elution with hexanes/ethyl acetate 3:1) to give **39** (20 mg, 81%) as a colorless oil: IR (neat, cm^{-1}) 3446, 1096; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.38 (dd, J = 9.6, 5.7 Hz, 1H), 4.21 (ddd, J = 10.5, 5.7, 1.8 Hz, 1H), 3.98 (dd, J = 9.6, 1.9 Hz, 1H), 3.84 (dd, J = 9.8, 2.0 Hz, 1H), 3.73 (dd, J = 9.8, 4.2 Hz, 1H), 3.56 (dd, J = 10.2, 5.6 Hz, 1H), 2.42 (br s, 1H), 1.89−1.78 (m, 2H), 1.76−1.64 (m, 1H), 1.62−1.58 (m, 2H), 1.42 (s, 3H), 1.33 (s, 3H), 1.30−1.23 (m, 2H), 1.22−1.15 (m, 1H), 0.90 (s, 9H), 0.15 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 106.6, 78.3, 75.1, 73.8, 70.3, 65.9, 45.5, 31.9, 28.1, 27.4, 26.4, 26.2 (3C), 25.3, 18.6, −3.4, −4.8; ES HRMS *m*/*z* for $C_{18}H_{36}O_5SiNa^+$ calcd 383.2224, obsd 383.2232; $[\alpha]^{21}_D$ −22.0 (*c* 1.82, $CHCl_3$).

(3a*R*,4*R*,5*S*,6*R*,9a*S*)-5-(*tert*-Butyldimethylsilyloxy)-6-(hydroxymethyl)-2,2-dimethyloctahydrocycloocta[*d*][1,3]dioxol-4-ol (40). A solution of (+)-**38** (30.1 mg, 0.063 mol) in CH_2Cl_2/H_2O (20:1, 5 mL) was treated with DDQ (21.4 mg, 0.094 mmol) and stirred at rt for 2 h. The reaction mixture was quenched with saturated $NaHCO_3$ aqueous solution and extracted with CH_2Cl_2. The organic layers were combined, dried, and evaporated. The residue was purified chromatographically on silica gel (elution with hexanes/ethyl acetate 5:1) to give **40** (21 mg, 93%) as a colorless oil: IR (neat, cm^{-1}) 3522, 1124; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.45 (dd, J = 9.3, 5.7 Hz, 1H), 4.28 (s, 1H), 4.15 (ddd, J = 11.5, 5.6, 3.5 Hz, 1H), 3.57−3.53 (m, 2H), 3.45 (dd, J = 10.0, 6.3 Hz, 1H), 3.10 (s, 1H), 1.98−1.94 (m, 1H), 1.79−1.69 (m, 1H), 1.65−1.49 (m, 5H), 1.44 (s, 3H), 1.38 (s, 3H), 1.04−1.03 (m, 1H), 0.89 (s, 9H), 0.14 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 106.6, 77.3, 74.1, 71.4, 71.0, 65.6, 41.6, 27.9, 26.2 (3C), 25.6, 25.1, 23.4, 20.9, 18.7, −3.2, −5.3; ES HRMS *m*/*z* for $C_{18}H_{36}O_5SiNa^+$ calcd 383.2224, obsd 383.2221; $[\alpha]^{18}_D$ +11.1 (*c* 2.07, $CHCl_3$).

(1*S*,2*S*,3*S*,4*S*,5*S*)-5-(Hydroxymethyl)cyclooctane-1,2,3,4-tetraol (41). A solution of (−)-**39** (20.1 mg, 0.056 mmol) in methanol (1 mL) was treated with HCl (1 M, 1 mL), stirred for 24 h at rt, and freed of solvent under vacuum. The residue was triturated with chloroform (3 × 5 mL) and dried under vacuum to give pure **41** (9.6 mg, 83%) as a colorless oil: IR (neat, cm^{-1}) 3381, 1360; ^{1}H NMR (400 MHz, D_2O) δ 3.99−3.97 (m, 1H), 3.83−3.80 (m, 1H), 3.72 (d, J = 8.4 Hz, 1H), 3.65−3.61 (m, 2H), 3.44−3.40 (m, 1H), 1.84−1.77 (m, 2H), 1.61−1.51 (m, 4H), 1.30−1.25 (m, 1H); ^{13}C NMR (75 MHz, D_2O) δ 76.0, 75.5, 75.4, 72.7, 67.7, 47.5, 33.1, 28.8, 28.5; ES HRMS *m*/*z* for $C_9H_{18}O_5Na^+$ calcd 229.1046, obsd 229.1050; $[\alpha]^{22}_D$ +3.7 (*c* 0.71, CH_3OH).

(1*S*,2*S*,3*S*,4*S*,5*R*)-5-(Hydroxymethyl)cyclooctane-1,2,3,4-tetraol (42). A solution of (+)-**40** (51 mg, 0.14 mmol) in methanol (2 mL) was treated with HCl (1 M, 2 mL), stirred for 24 h at rt, and freed of solvent under vacuum. The residue was triturated with chloroform (3 × 5 mL) and dried under vacuum to give pure **42** (25 mg, 87%) as a white solid: mp 137−139 °C; IR (neat, cm^{-1}) 3384, 1343; ^{1}H NMR (400 MHz, D_2O) δ 4.05 (br s, 1H), 4.04−4.0 (m, 1H), 3.84 (dd, J = 7.9, 2.7 Hz, 1H), 3.72 (d, J = 8 Hz, 1H), 3.42 (dd, J = 10.8, 7.6 Hz, 1H), 3.33 (dd, J = 10.9, 6.6 Hz, 1H), 1.65−1.54 (m, 4H), 1.34−1.25 (m, 3H); ^{13}C NMR (75 MHz, D_2O) δ 73.2, 73.1, 72.4, 70.1, 64.4, 43.4, 28.4, 21.0, 20.9; ES HRMS *m*/*z* for $C_9H_{18}O_5Na^+$ calcd 229.1046, obsd 229.1051; $[\alpha]^{22}_D$ −3.4 (*c* 1.0, CH_3OH).

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Supporting Information Available: High-field ^{1}H and ^{13}C NMR spectra for **3**−**42** and X-ray crystallographic data for (+)-**24** and (−)-**42** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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