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Synthesis and Biological Evaluation of Aromatic Analogues of Conduritol F, L-*chiro*-Inositol, and Dihydroconduritol F Structurally Related to the Amaryllidaceae Anticancer Constituents

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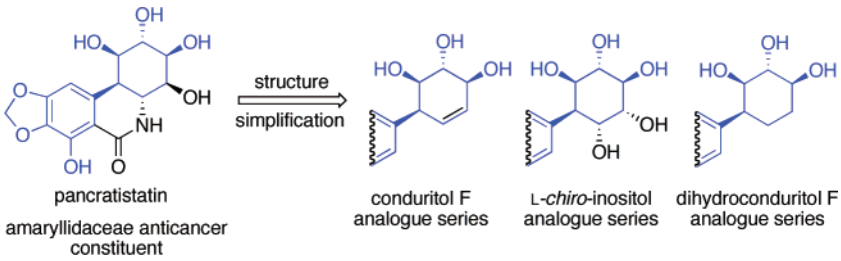

Pancratistatin is a potent anticancer natural product, whose clinical evaluation is hampered by the limited natural abundance and the stereochemically complex structure undermining practical chemical preparation. Fifteen aromatic analogues of conduritol F, L-*chiro*-inositol, and dihydroconduritol F that possess four of the six pancratistatin stereocenters have been synthesized and evaluated for anticancer activity. These compounds serve as truncated pancratistatin analogues lacking the lactam ring B, but retaining the crucial C10a−C10b bond with the correct stereochemistry. The lack of activity of these compounds provides further insight into pancratistatin's minimum structural requirements for cytotoxicity, particularly the criticality of the intact phenanthridone skeleton. Significantly, these series provide rare examples of simple aromatic conduritol and inositol analogues and, therefore, this study expands the chemistry and biology of these important classes of compounds.

Introduction

Inositols, conduritols, and their numerous derivatives continue to attract a great deal of attention due to their roles in living organisms[1] and, consequently, diverse biological activities.[2] In addition, synthetic chemists have utilized these classes of compounds as intermediates in the synthesis of natural products and other biologically relevant complex structures.[3] Cyclitol preparation is challenging due to the dense stereochemistry of the hydroxylated carbon cycles. Furthermore, analogues of these compounds possessing a carbon substituent in place of a hydroxyl group are even more difficult synthetic targets due to the challenge of creating a carbon−carbon bond with stereocontrol. Such compounds, however, are particularly desirable from the biological perspective. For example, fungal metabolite cyclophellitol (**1**) is a potent inactivator of β-glucosidase and a

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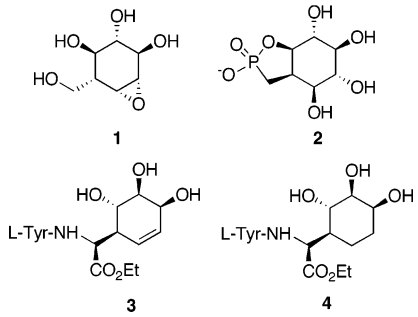

FIGURE 1. Cyclitol analogues with medicinal promise.

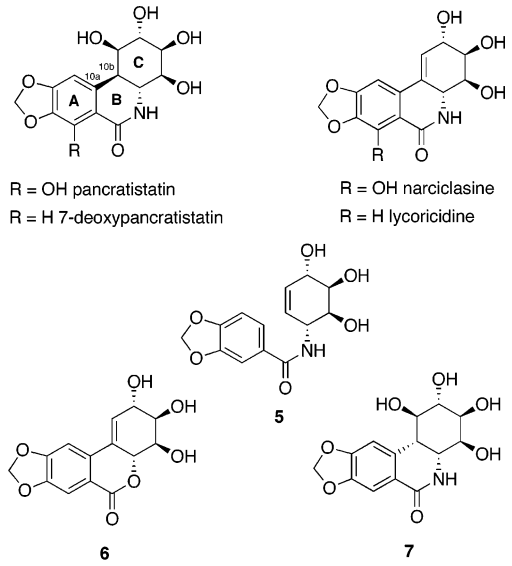

FIGURE 2. Amaryllidaceae constituents with anticancer activity and their ring B analogues.

promising anti-HIV agent (Figure 1).[4] *myo*-Inositol cyclic phosphonate analogue **2** is an inhibitor of phosphatidylinositol-specific phospholipase C.[5] Conduritol F analogues **3** and **4** are nanomolar inhibitors of *S.* aureus tyrosyl tRNA synthetase.[6]

Several amaryllidaceae constituents, including pancratistatin, narciclasine, and their 7-deoxy congeners, have attracted considerable interest due to their promising anticancer activities (Figure 2). These natural products incorporate an arylcyclitol structural motif and a significant body of synthetic work has shown that the creation of a C10b-stereocenter renders pancratistatin a more challenging synthetic target than narciclasine, which lacks this stereocenter.[7] Pancratistatin has been found to exhibit strong in vitro cancer cell growth inhibitory activities against the U.S. National Cancer Institute (NCI) panel of cancer cell lines as well as a number of in vivo experimental cancer systems.[8] Powerful antiviral[9] and antiparasitic[10] activities of pancratistatin constitute a related area of promise. Although less potent, 7-deoxypancratistatin exhibits a better therapeutic index in in vitro antiviral (RNA) assays due to reduced toxicity.[9] A number of recent reports demonstrate that pancratistatin is specifically toxic to cancer cells as opposed to normal ones, whereas the currently used anticancer drugs, such as taxol and etoposide, are equally toxic to both cell types.[11] Pancratistatin's clinical development has been hampered in part by its inadequate supply and this problem continues to be addressed with total synthesis[12] and biotechnological routes.[13]

The elucidation of the pancratistatin's cytotoxic pharmacophore and synthesis of structurally simplified analogues is an alternative strategy, which is currently pursued by a number of laboratories.[14] All three rings A, B, and C have been targeted to obtain SAR data. The importance of ring B has been addressed by Chapleur and co-workers, who showed that lycoricidine analogues with the open ring B (absent C10a−C10b bond in **5**)[14a] or the ester group in lieu of the amide (**6**)[14h] were both devoid of anticancer activity. Additionally, Hudlicky and co-workers synthesized the C10b-epimer of 7-deoxypancratistatin (**7**) and found that it was inactive.[14c,d] Thus, it appears that the configuration at the position C10b is critical for activity as well.

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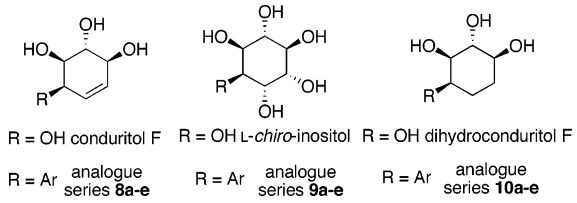


FIGURE 3. Structures of parent cyclitols and their proposed aromatic analogue series.

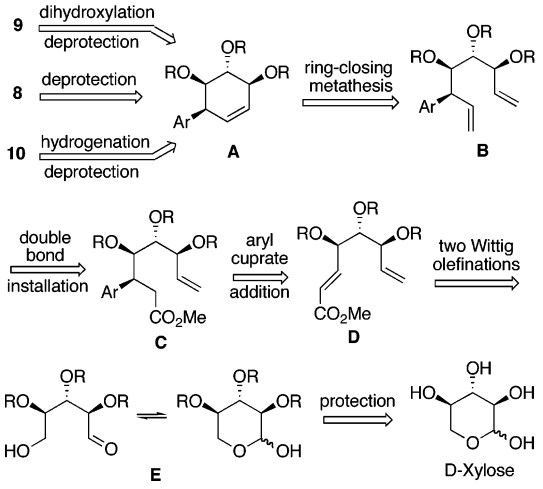


FIGURE 4. Retrosynthetic analysis of the target arylcyclitols.

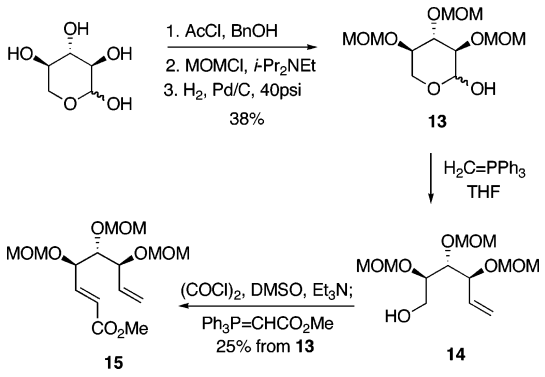
In our pursuit of a scalable synthesis of pancratistatin and its aromatic analogues we have identified a series of aromatic conduritols F (**8**, Figure 3) as key intermediates.

These compounds, along with the related L-*chiro*-inositol and dihydroconduritol F congeners (**9** and **10**), possess four of the six pancratistatin stereocenters and serve as truncated pancratistatin analogues lacking the lactam ring B, but retaining the crucial C10a−C10b bond with the correct stereochemistry. In this article we report the synthesis and anticancer evaluation of arylcyclitols **8**, **9**, and **10**, providing further insight into pancratistatin's minimum structural requirements for cytotoxicity. Significantly, these series provide rare examples of simple aromatic conduritol and inositol analogues[15] and, therefore, this study expands the chemistry and biology of these important classes of compounds.[16]

Results and Discussion

The penultimate key intermediates, protected arylconduritols **A** (Figure 4), would furnish the target series **8**, **9**, and **10** by way of the direct removal of the protecting groups R, olefin dihydroxylation followed by deprotection, and hydrogenation with the subsequent deprotection, respectively. Further retrosynthetic sequence includes ring-closing metathesis of dienes **B**, terminal double bond installation in esters **C**, and a diastereoselective arylcuprate conjugate addition to enoate **D**. The relative stereochemistry of the three oxy-stereocenters in enoate **D** points to the potential use of D-xylose as a readily

SCHEME 1



available starting material. The application of two Wittig olefination reactions to a D-xylose-derived intermediate **E** would be expected to provide **D**.

A crucial element in the proposed synthetic plan is the choice of a hydroxyl protecting group R. The identity of the group R is dictated in part by the deprotection conditions necessary to generate the target series from arylconduritols **A**. Of particular concern would be the synthesis of the series **8**, because an acidic milieu could potentially cause the double bond isomerization into conjugation with the aromatic moiety, while hydrogenolytic conditions would result in olefin hydrogenation. Additionally, in the transformation **D** to **C**, the hydroxyl protecting group is also a stereochemistry-controlling moiety facilitating an anti-selective addition. This process would need not only be highly diastereoselective to avoid potentially troublesome chromatographic separations of epimers, but also general for structurally diverse aromatic residues.

Due to these potential impediments, we selected two protecting groups MOM and Bn as suitable candidates for our proposed synthetic sequence and pursued two independent approaches with each one. Although prior to the initiation of this work there had been no examples of a highly anti-selective arylcuprate conjugate addition process to either γ-MOMO- or γ-BnO-α,β-enoates, various alkyl- and vinylcuprates had been used with success in these reactions.[17]

In the pursuit of the synthetic plan utilizing the MOM protection, we developed a five-step synthesis of enoate **15** from D-xylose (Scheme 1). Thus, the anomeric position of D-xylose was protected as benzyl ether following a method that was reported by Ireland and co-workers for L-arabinose.[18] The mixture of α- and β-benzyl xylopyranosides was treated with MOMCl in the presence of Hunig's base in CH_2Cl_2 and then hydrogenolyzed at 40 psi for 10 h over 10% Pd/C. Tri-*O*-methoxymethyl-D-xylopyranose (**13**) was obtained in 38% yield over the three-step sequence. Disappointingly, each of the three steps requires a chromatographic purification of the product, complicating the scale-up. Wittig methylenation at the free anomeric carbon of **13** was achieved by direct treatment with 2.5 equiv of $H_2C{=}PPh_3$ in THF at 50 °C. Both the product yield and purification are compromised by the side products,

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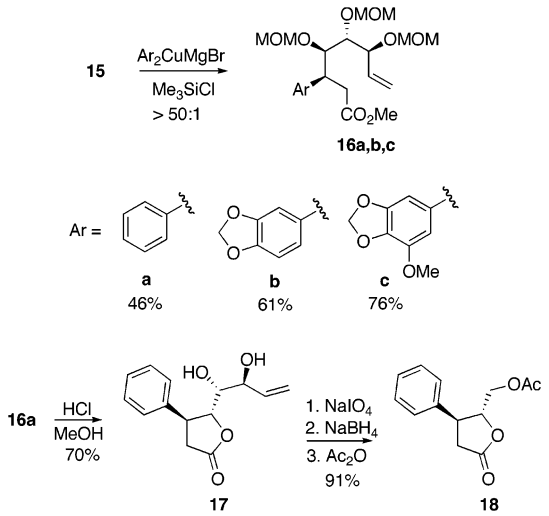
SCHEME 2



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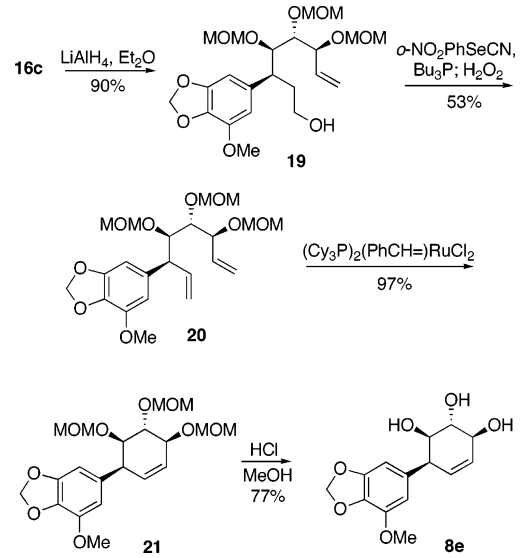
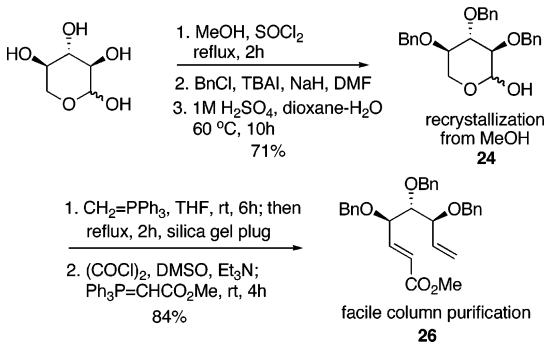


evidently resulting from the competing deprotonation of the α-position with the subsequent elimination of the *β*-methoxymethyloxy group. A one-pot Swern oxidation and olefination with the commercial $Ph_3P{=}CHCO_2Me$ reagent, performed according to a report by Ziegler and co-workers,[17a,b] gives the desired enoate **15** in 25% overall yield from **13**.

The addition of arylcuprates, derived from the corresponding aromatic Grignard reagents, to enoate **15** proceeds with exclusive anti-diastereoselectivities (based on the NMR analysis of crude and purified reaction mixtures) in acceptable yields (Scheme 2). To confirm the assigned anti-stereochemistry, the addition product **16a** was treated with methanolic HCl to remove the MOM protection. The resulting triol undergoes lactonization under the reaction conditions to form **17**. Cleavage of the vicinal diol functionality with $NaIO_4$ followed by treatment of the crude aldehyde with $NaBH_4$ and Ac_2O gives known lactone **18**, whose NMR data are identical with those reported in the literature.[19]

The completion of the synthetic sequence was investigated with the arylcuprate addition product **16c**. Ester reduction with

SCHEME 4



$LiAlH_4$ in ether gives primary alcohol **19**, whose subsequent conversion to arylselenide and selenoxide elimination affords diene **20**. Ring-closing metathesis, performed with the 1st generation Grubbs' catalyst in CH_2Cl_2 at room temperature, cleanly provides protected arylconduritol **21**. Finally, deprotection without an accompanying double bond migration was achieved with a dilute solution of HCl in MeOH at 60 °C with careful monitoring of the reaction mixture by TLC.

Thus, the synthetic pathway to the target arylcyclitols has been developed with use of MOM as a protecting group. However, we have been frustratingly unsuccessful in our attempts to scale-up the preparation of enoate **15**. In contrast, our parallel investigation of the synthetic plan based on the Bn protection had been showing a lot of promise and our initial concerns over the removal of Bn groups in the presence of the olefinic functionality in arylconduritols **A** (see the proposed synthesis of the series **8** from **A** in Figure 4) were completely dispelled after this deprotection had been successfully optimized with the dissolving metal reduction method. In the remaining portion of this article we describe the synthesis of the arylcyclitols **8**, **9**, and **10** using the Bn protection scheme and the biological evaluation of these compounds.

Enoate **26** had been utilized previously in a total synthesis of (+)-cyclophellitol and is available from D-xylose via a synthetic sequence involving eight steps and six chromatographic purifications.[17a,b] We sought a more practical route, which could be readily scaled-up. Thus, the mixture of α- and *β*-methyl xylosides, prepared by refluxing D-xylose and $SOCl_2$ in methanol, was directly benzylated with inexpensive BnCl/Bu_4NI and NaH (Scheme 4). Hydrolysis of the crude benzylated anomeric mixture yielded tri-*O*-benzyl-D-xylopyranose (**24**), which was purified by recrystallization from methanol in good overall yield. This procedure has a significant advantage over the previously reported methods,[20] as it requires neither the separation of the intermediate xylose anomers nor purification of the synthetic intermediates. The sequence of Wittig methylenation at the free anomeric carbon, one-pot Swern oxidation, and olefination with the commercial $Ph_3P{=}CHCO_2Me$ reagent was significantly higher yielding than the one performed on the MOM-protected material (Scheme 1). We attribute this difference in reactivity to the less acidic nature of the α-benzyloxy position in the aldehyde form of **24** compared to the α-methyloxymethyl one in the aldehyde form of **13**. This high throughput five-step synthesis involves only one chromatographic purification and it has allowed us to prepare ca. 100 g of **26**.

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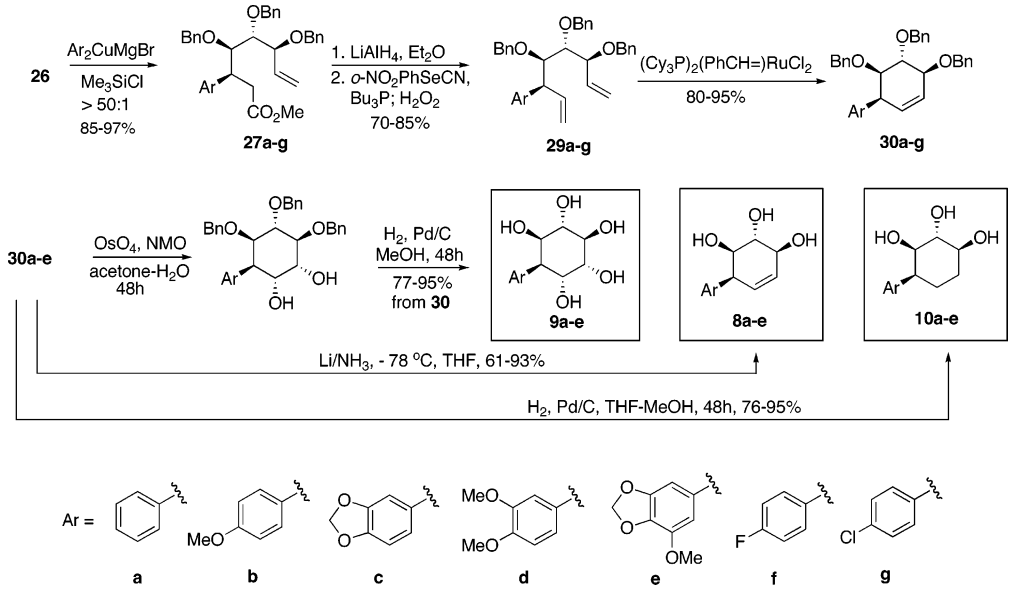
SCHEME 5

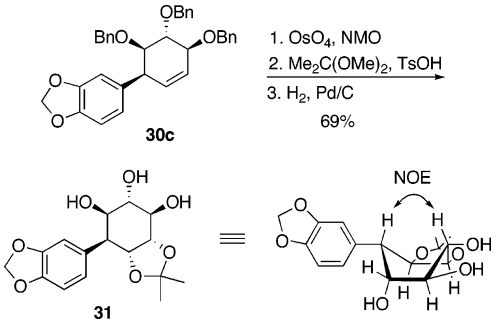


The reaction of enoate **26** with a broad range of aromatic organocopper reagents again affords exclusive anti-selectivities and gives addition products **27a**−**g** in excellent yields (Scheme 5). Similarly to the MOM-based chemistry the sequence involving ester reduction, selenide formation, selenoxide elimination, and ring-closing metathesis provides protected arylconduritols **30a**−**g** in good overall yields. Column purification of **30a**−**g** was made facile by preliminary oxidation of the ruthenium catalyst with DMSO.[21]

At this juncture the generation of the target series of arylcyclitols was attempted. Dihydroxylation of compounds **30a**−**e** with catalytic OsO_4 and NMO yields single stereoisomeric diols due to much greater steric accessibility of the α-face of the double bond. These compounds undergo facile hydrogenolytic cleavage of benzyl ethers when their solutions in MeOH are stirred under a hydrogen balloon in the presence of 10% Pd/C catalyst for 2 days, providing the aromatic *chiro*-inositol series **9**. To generate the series **8**, arylconduritols **30a**−**e** were subjected to the dissolving metal reduction method. To this end, compounds **30a**−**e** were dissolved in THF and the resulting mixtures were titrated with a blue solution generated by the dissolution of chopped Li in liquid ammonia at −78 °C. After the blue color persisted for 15 s the mixtures were immediately quenched with solid NH_4Cl. Since the benzyl ether cleavage is faster under these conditions than the reduction of the aromatic or olefinic moieties, the utilization of this technique allowed us to avoid overreduction and prepare the aromatic conduritol F series **8** in consistently good yields. Finally, the exhaustive hydrogenation of **30a**−**e** over 10% Pd/C removes the benzyl protection and reduces the olefinic functionality to afford the aromatic dihydroconduritol F series **10**. Unfortunately, we were unable to deprotect the halogen-containing arylconduritols **30f** and **30g** without a loss of the halogen atom. The unsubstituted phenyl group-containing arylcyclitols **8a**, **9a**, and **10a** were produced from these compounds under both hydrogenolytic and the Li/NH_3 deprotection conditions.

Although ^1H NMR analyses of the cyclized products supported our original anti-stereochemistry assignment in arylcuprate conjugate addition reactions, we searched for unambiguous proof of stereochemistry through NOE experiments. To this end arylconduritol **30c** was converted to arylinositol derivative **31** by dihydroxylating the double bond, isopropylidenating the newly introduced cis diol, and thereafter *O*-debenzylating (Scheme 6). The cis ring fusion forced the inositol ring into a boat conformation; the proximity of H_1 and H_4 could clearly be detected by NOE difference experiments. Additionally, the NMR spectra of arylconduritol **8e** obtained by using either MOM-based (Scheme 3) or Bn-based approaches (Scheme 5) are indistinguishable.

SCHEME 6



Due to unavailability of pancratistatin, biological evaluation of the synthesized arylcyclitols was performed with the use of anticancer amaryllidaceae metabolites lycorine and narciclasine as positive controls. This choice is justified by the similar activity profiles and potencies of narciclasine and pancratistatin.[8] Since lycorine is the most abundant amaryllidaceae alkaloid, its isolation from *Sternbergia lutea* Ker Gawl by using a procedure reported by Evidente and co-workers[22] was straightforward and provided 11.22 g/kg of dry bulbs. To obtain narciclasine various isolation methods and plant sources were investigated. The base extraction method reported by Evidente was found to be the most efficient and high yielding.[23] When applied to *Narcissus pseudonarcissus* King Alfred grown in New Mexico, it resulted in the isolation yield of 170.4 mg/kg of dry

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(22) Evidente, A.; Iasiello, I.; Randazzo, G. *Chem. Ind.* **1984**, 348−349.
(23) Evidente, A. *Planta Med.* **1991**, *57*, 293−295.

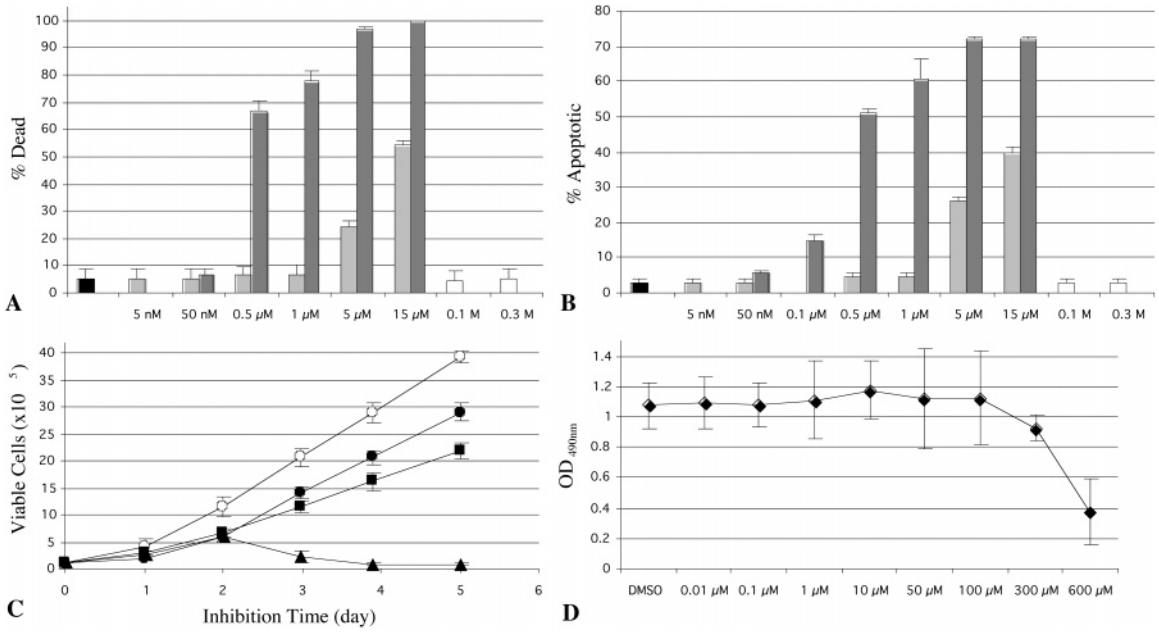


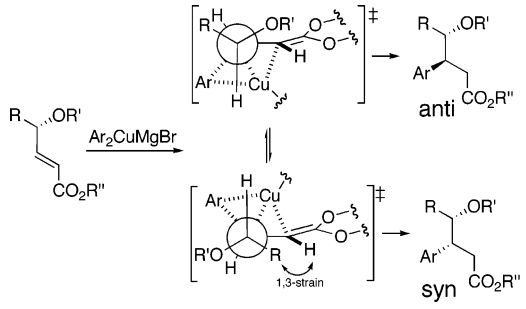
FIGURE 5. Biological evaluation of the arylcyclitol series. (A) Effect of lycorine (light gray, shaded columns), narciclasine (dark gray, shaded columns), solvent control (0.1% DMSO in RPMI-1640 10% FBS medium, black column), and any compound from the series **8**, **9**, or **10** (open columns) on the survival of Jurkat cells in Trypan Blue dye exclusion assay. (B) Induction of apoptosis in Jurkat cells treated for 20 h with lycorine (light gray, shaded columns), narciclasine (dark gray, shaded columns), solvent control (0.1% DMSO in RPMI-1640 10% FBS medium, black column), and any compound from the series **8**, **9**, or **10** (open columns) in flow cytometric annexin-V/propidium iodide assay. (C) Effect of lycorine (1 μM, black circle marker), narciclasine (0.05 μM, triangle marker), **8a** (300 μM, square marker), and any other compound from the series **8**, **9**, or **10** (300 μM, open circle marker) on the growth of Jurkat cells estimated by the Trypan Blue dye exclusion method. Untreated Jurkat cells and a solution of 0.1% DMSO in RPMI-1640 10% FBS medium were used as controls (open circle marker). (D) Growth inhibitory properties of **8a** toward Jurkat cells in Sulforhodamine B (SRB) assay.

bulbs. To our knowledge, this is the second highest yield reported for the isolation of this natural product and represents a 2-fold increase relative to other isolation methods that had been previously used with this Narcissus species.[24]

Arylcyclitol series **8a**−**e**, **9a**−**e**, and **10a**−**e**, along with lycorine and narciclasine, were assayed for cytotoxic, apoptosis-inducing, and growth inhibitory properties with use of Jurkat and HeLa cell lines as models for human T-cell leukemia and adenocarcinoma, respectively. The results with Jurkat cells are given in Figure 5. While both lycorine and narciclasine showed consistent dose-dependent activities in all three assays, almost all of the synthesized arylcyclitols were inactive in up to 300 μM concentrations. The only exception is weak cell growth inhibitory activity of phenylconduritol F analogue **8a** ($GI_{50} \sim$ 300 μM, Figure 5C,D). Since none of the oxygenated aromatic conduritol F analogues, whose structures more closely resemble those of the potent natural products (especially **8c**, **8d**, and **8e**), exhibit any growth inhibitory properties, this activity is likely due to a different mode of action. Notably, narciclasine, which is considerably more potent than lycorine, induces apoptosis in Jurkat cells in submicromolar concentrations. Although it is generally accepted that narciclasine is a potent cytotoxic natural product and a promising anticancer drug,[25] its mechanism of action is still poorly understood.[26] On the basis of these findings, further studies are underway in our laboratories to elucidate the origin of narciclasine's anticancer properties.

Conclusions

The lack of activity of aromatic analogues of conduritol F, L-*chiro*-inositol, and dihydroconduritol F that possess four of the six pancratistatin stereocenters provides further insight into pancratistatin's minimum structural requirements for cytotoxicity, particularly the criticality of the intact phenantridone skeleton. Significantly, these compounds provide rare examples of simple aromatic conduritol and inositol analogues and, therefore, this study expands the chemistry and biology of these important classes of compounds. Another notable finding of this study involves high anti-selectivities in arylcuprate conjugate addition reactions to both tri-γ,δ,ϵ-OMOM-enoate **15** and tri-γ,δ,ϵ-OBn-enoate **26**. We have studied the origin of these high diastereoselectivities in detail[27] and recently proposed a new reductive elimination-based stereochemical model[27b] for this process.



(24) Piozzi, F.; Marino. M. L.; Fuganti, C.; Di Martino, A. *Phytochemistry* **1969**, *8*, 1745−1748.

(25) See: Pettit, G. R.; Melody, N.; Simpson, M.; Thompson, M.; Herald, D. L.; Knight, J. C. *J. Nat. Prod.* **2003**, *66*, 92−96 and references therein.

(26) (a) Carrasco, L.; Fresno, M.; Vazquez, D. *FEBS Lett.* **1975**, *52*, 236−239. (b) Jimenez, A.; Sanchez, L.; Vazquez, D. *FEBS Lett.* **1975**, *55*, 53−56. (c) Jimenez, A.; Santos, A.; Alonso, G.; Vasquez, D. *Biochim. Biophys. Acta* **1976**, *425*, 342−348.

Thus, we showed that a single γ-alkoxy stereocenter is sufficient to attain very high anti-selectivities, and that if a group R is sterically demanding then the transition state leading to the anti-product is favored on the basis of both stereoelectronic and steric considerations. In this study we found that the identity of the γ-alkoxy group (MOMO vs BnO) is inconsequential and the δ- and ϵ-alkoxy groups are unlikely to contribute to the control of stereochemistry. These observations are fully consistent with our proposed model.

Finally, we provided a recommendation for a convenient isolation of narciclasine and reported its potent apoptosis inducing properties. This work is expected to encourage further efforts to understand the mechanism of action of these natural products and develop their active structurally simplified analogues for clinical investigations.

Experimental Section

Mixture of α- and β-Benzyl D-Xylopyranosides (11). To stirring benzyl alcohol (50 mL) was added acetyl chloride (2 mL) followed by D-xylose (10 g, 66.7 mmol) and the resulting mixture was stirred for 24 h at 50 °C. The cold reaction mixture was then dissolved in 500 mL of CH_2Cl_2, and the solution was run through a silica gel pad. After the solution was washed with CH_2Cl_2 (500 mL), α- and β-benzyl D-xylopyranosides were eluted with 10% MeOH/CH_2Cl_2 solution (500 mL). The solvent was removed under reduced pressure to give virtually pure residue (11.8 g, yield 73.8%), which was used in the next step without additional purification.

Mixture of α- and β-Benzyl 2,3,4-Tri-*O*-methoxymethyl-D-xylopyranosides (12). To a stirred solution of α- and β-benzyl D-xylopyranosides (15 g, 62.5 mmol) in dichloromethane (250 mL) at room temperature were added diisopropylethylamine (97.8 mL, 0.56 mol) and methoxymethyl chloride (28.5 mL, 0.38 mol) over a 10 min period. The reaction mixture was stirred for 12 h. Saturated aqueous NH_4Cl solution (100 mL) was then added. The organic layer was separated, washed with 0.2 M HCl (2 × 200 mL), water (200 mL), and brine (100 mL), dried with anhydrous $MgSO_4$, and concentrated under reduced pressure. The residue was adsorbed on silica gel and eluted with gradients: 10%, 30% EtOAc/hexanes (500 mL) to obtain 19 g (82%) of **12**; R_f 0.70 (50% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 7.39−7.23 (m, 5H), 4.92 (d, J = 3.6 Hz, 1H), 4.84 (d, J = 6.6 Hz, 1H), 4.77 (d, J = 6.3 Hz, 1H), 4.76 (d, J = 6.9 Hz, 1H), 4.74 (d, J = 12.1 Hz, 1H), 4.72 (d, J = 6.9 Hz, 1H), 4.64 (d, J = 6.9 Hz, 1H), 4.61 (d, J = 6.6 Hz, 1H), 4.51 (d, J = 12.1 Hz, 1H), 3.91 (app t, J = 9.1 Hz, 1H), 3.75 (dd, J = 16.5, 11.8 Hz, 1H), 3.62−3.56 (m, 2H), 3.75 (dd, J = 9.6, 3.6 Hz, 1H), 3.39 (s, 3H), 3.34 (s, 3H), 3.23 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 137.1, 128.4, 128.3, 127.9, 98.0, 97.4, 96.7, 78.6, 77.2, 77.1, 76.7, 69.1, 60.7, 55.9, 55.6, 55.4; HRMS *m/z* (ESI) calcd for $C_{18}H_{28}O_8Na$ (M + Na)$^+$ 395.1676, found 395.1690.

2,3,4-Tri-*O*-methoxymethyl-D-xylopyranose (13). A solution of **12** (6.5 g, 17.5 mmol) in THF (100 mL) underwent hydrogenolysis (40 psi) in the presence of 10% Pd/C catalyst (10 mol %) for 12 h. The resulting solution was filtered from the catalyst, concentrated under reduced pressure, presorbed on silica gel, and purified by chromatography with gradients: 30% EtOAc/hexanes, 50% EtOAc/hexanes to recover unreacted **12** followed by 5% and 10% MeOH/CH_2Cl_2 to obtain **13** (3.02 g, 61.3%); R_f 0.28 (50% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 5.21 (m, 1H), 4.89−4.71 (m, 5H), 4.65 (d, J = 6.6 Hz, 1H), 4.55 (app t, J = 3.4 Hz, 1H), 4.41 (m, 1H), 4.19 (dd, J = 9.6, 3.6 Hz, 1H), 3.89 (app t, J = 7.2 Hz, 1H), 3.79 (m, 1H), 3.70−3.49 (m, 2H), 3.47 (s, 3H), 3.41 (s, 3H), 3.36 (s, 3H), 3.27 (m, 1H), 3.09 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 98.4, 97.8, 97.7, 97.6, 97.2, 97.1, 96.6, 92.4, 82.6, 78.9, 78.4, 76.6, 76.3, 76.2, 64.5, 61.1, 56.2, 56.0, 55.9, 55.7, 55.6; HRMS *m/z* (ESI) calcd for $C_{11}H_{22}O_8Na$ (M + Na)$^+$ 305.1207, found 305.1216.

(2*R*,3*R*,4*S*)-2,3,4-Tri(methoxymethyloxy)-5-hexene-1-ol (14). To a stirred suspension of methyltriphenylphosphonium bromide (15.8 g, 44.3 mmol) in THF (50 mL) was added BuLi (17.7 mL of 2.5 M solution in hexanes, 44.3 mmol) dropwise at 0 °C. The mixture was stirred for 2 h at room temperature. To the above red solution was added **13** (5.0 g, 17.7 mmol) in THF (50 mL) dropwise at 45−50 °C with continued stirring overnight at this temperature. NH_4Cl (1 M, 50 mL) was added at room temperature to the reaction mixture and the latter was extracted with ether (3 × 100 mL). The organic extracts were combined, washed with brine, and dried ($MgSO_4$). After removal of the solvent under reduced pressure, the residue was adsorbed on silica gel and purified by chromatography with gradients: 40%, 50%, 60% EtOAc/hexanes, to obtain 3.02 g (60.8%) of **14**; R_f 0.23 (50% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 5.70 (ddd, J = 17.9, 10.2, 8.0 Hz, 1H), 5.31−5.25 (m, 2H), 4.85 (d, J = 6.6 Hz, 1H), 4.69 (d, J = 6.6 Hz, 1H), 4.65 (d, J = 6.9 Hz, 1H), 4.64 (d, J = 6.6 Hz, 1H), 4.57 (d, J = 6.9 Hz, 1H), 4.51 (d, J = 6.6 Hz, 1H), 4.27 (app t, J = 7.2 Hz, 1H), 3.75−3.65 (m, 3H), 3.38 (s, 3H), 3.36 (s, 3H), 3.31 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 134.4, 119.8, 98.9, 98.1, 94.1, 81.4, 79.9, 77.9, 62.8, 56.5, 56.1, 55.8; HRMS *m/z* (ESI) calcd for $C_{12}H_{24}O_7Na$ (M + Na)$^+$ 303.1444, found 303.1419.

Methyl (2*E*,4*R*,5*R*,6*S*)-4,5,6-Tri(methoxymethyloxy)-2,7-octadienoate (15). To oxalyl chloride (11.9 mL of 2 M in CH_2Cl_2, 23.7 mmol) in dry CH_2Cl_2 (50 mL) at −78 °C was added DMSO (3.5 mL, 49.6 mmol) in CH_2Cl_2 (20 mL) over 10 min and the mixture was stirred for 20 min. Alcohol **14** (3.02 g, 10.8 mmol) in CH_2Cl_2 (20 mL) was added over 10 min and the mixture was stirred for an additional 10 min period. Triethylamine (14.5 mL, 96 mmol) in CH_2Cl_2 (20 mL) was added over 10 min and the white slurry was stirred for 20 min at −78 °C. To the cold reaction mixture was added methyl (triphenylphosphoranylidene)acetate (7.2 g, 21.6 mmol) in one portion, and the resulting mixture was stirred for 10 h while it was allowed to warm to room temperature. Water (200 mL) was added to the reaction mixture, the two layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were dried ($MgSO_4$) and evaporated under reduced pressure. The residual oil was presorbed on silica gel and purified by chromatography with gradients: 25%, 30%, 35% EtOAc/hexanes to afford enoate **15** (1.48 g, 41.1%) as a colorless oil; R_f 0.50 (50% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 7.02 (dd, J = 18.7, 6.1 Hz, 1H), 6.08 (dd, J = 15.7, 1.4 Hz, 1H), 5.84 (ddd, J = 17.6, 10.5, 7.4 Hz, 1H), 5.38−5.32 (m, 2H), 4.84 (d, J = 6.9 Hz, 1H), 4.78 (d, J = 6.9 Hz, 1H), 4.69 (d, J = 6.9 Hz, 1H), 4.64 (s, 2H), 4.57 (d, J = 6.9 Hz, 1H), 4.45 (m, 1H), 4.27 (m, 1H), 3.74 (s, 3H), 3.65 (app t, J = 5.0 Hz, 1H), 3.38 (s, 3H), 3.36 (s, 3H), 3.31 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 166.5, 145.5, 134.7, 122.7, 119.5, 98.4, 95.7, 94.4, 81.3, 77.1, 75.9, 56.5, 56.3, 56.1, 51.8; HRMS *m/z* (ESI) calcd for $C_{15}H_{26}O_8Na$ (M + Na)$^+$ 357.1520, found 357.1516.

General Procedure for Arylcuprate Addition (16). A 1 mL aryl bromide (15 mmol) solution in THF (30 mL) was added to magnesium turnings (0.36 g, 15 mmol). Magnesium was crushed in the flask with a glass rod and the solution started to turn yellowish and warm. The rest of the aryl bromide solution was added dropwise to maintain gentle boiling of the stirred reaction mixture. After the solution was cooled to room temperature Grignard reagent was transferred to a slurry of CuI (1.43 g, 7.5 mmol) in THF (10 mL) at −20 °C via cannula. The resulting mixture was stirred at −20 °C for 30 min, then treated with TMSCl (1.63 g, 15 mmol) at −78 °C, followed by the addition of enoate **6** (0.50 g, 15 mmol) in THF (20 mL). Stirring was continued overnight, while the mixture was allowed to warm to room temperature. The reaction mixture was quenched with a mixture of concentrated NH_4OH−saturated NH_4Cl (1:9, 50 mL), diluted with ether, and separated. The aqueous layer was extracted with ether (3 × 100 mL) and the combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated

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under reduced pressure. The residue was presorbed on silica gel and purified by column chromatography (25%, 30%, 35%, 40% EtOAc/hexanes) to afford exclusively anti-addition products **16a**−**c**.

Methyl (3*S*,4*R*,5*R*,6*S*)-3-Phenyl-4,5,6-tri(methoxymethoxy)-7-octaenoate (16a). 46.0%; R_f 0.51 (50% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 7.31−7.17 (m, 5H), 5.56 (ddd, J = 18.2, 10.7, 7.4 Hz, 1H), 5.27−5.32 (m, 2H), 5.26 (br d, J = 4.1 Hz, 1H), 5.22 (br d, J = 10.5 Hz, 1H), 4.78 (d, J = 6.9 Hz, 1H), 4.73 (d, J = 6.9 Hz, 1H), 4.72 (d, J = 6.9 Hz, 1H), 4.63 (d, J = 6.9 Hz, 1H), 4.60 (d, J = 6.6 Hz, 1H), 4.49 (d, J = 6.6 Hz, 1H), 4.10 (app t, J = 7.0 Hz, 1H), 3.85 (dd, J = 8.8, 3.0 Hz, 1H), 3.59 (m, 1H), 3.52 (s, 3H), 3.50 (s, 3H), 3.43 (dd, J = 6.9, 3.0 Hz, 1H), 3.38 (s, 3H), 3.30 (s, 3H), 2.98 (dd, J = 15.7, 5.0 Hz, 1H), 2.65 (dd, J = 15.7, 10.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 172.9, 141.3, 134.7, 128.6, 127.0, 119.5, 98.7, 98.6, 94.1, 80.9, 79.2, 77.7, 56.4, 56.4, 55.7, 51.4, 44.4, 37.5; HRMS *m*/*z* (ESI) calcd for $C_{21}H_{32}O_8Na$ (M + Na)$^+$ 435.1989, found 435.1986.

Methyl (3*S*,4*R*,5*R*,6*S*)-3-(Benzo[*d*][1,3]dioxol-6-yl)-4,5,6-tri-(methoxymethoxy)-7-octaenoate (16b). 61.4%; R_f 0.43 (50% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 6.75 (s, 1H), 6.71 (s, 2H), 5.92 (s, 2H), 5.58 (ddd, J = 18.4, 11.0, 7.4 Hz, 1H), 5.29 (br s, 2H), 5.24 (br d, J = 8.5 Hz, 1H), 4.80 (d, J = 6.9 Hz, 1H), 4.73 (d, J = 6.9 Hz, 1H), 4.71 (d, J = 6.9 Hz, 1H), 4.62 (d, J = 6.9 Hz, 2H), 4.51 (d, J = 6.9 Hz, 1H), 4.14 (app t, J = 7.2 Hz, 1H), 3.76 (dd, J = 8.8, 3.0 Hz, 1H), 3.53 (m, 1H), 3.54 (s, 3H), 3.49 (s, 3H), 3.44 (dd, J = 6.9, 3.0 Hz, 1H), 3.39 (s, 3H), 3.32 (s, 3H), 2.94 (dd, J = 15.4, 4.7 Hz, 1H), 2.57 (dd, J = 15.4, 10.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 172.9, 147.8, 146.5, 135.1, 134.7, 121.8, 119.7, 108.9, 108.4, 101.0, 98.8, 98.7, 94.2, 81.1, 79.3, 77.9, 56.5, 56.4, 55.7, 51.5, 44.1, 37.6; HRMS *m*/*z* (ESI) calcd for $C_{22}H_{32}O_{10}Na$ (M + Na)$^+$ 479.1887, found 479.1865.

Methyl (3*S*,4*R*,5*R*,6*S*)-3-(4-Methoxybenzo[*d*][1,3]dioxol-6-yl)-4,5,6-tri(methoxymethoxy)-7-octaenoate (16c). 76.0%; R_f 0.39 (50% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 6.47 (d, J = 1.1 Hz, 1H), 6.42 (d, J = 1.1 Hz, 1H), 5.91 (s, 2H), 5.56 (m, 1H), 5.29 (br s, 1H), 5.23 (br d, J = 6.9 Hz, 1H), 4.81 (d, J = 6.9 Hz, 1H), 4.74 (d, J = 6.9 Hz, 1H), 4.70 (d, J = 6.9 Hz, 1H), 4.62 (d, J = 6.9 Hz, 1H), 4.61 (d, J = 6.6 Hz, 1H), 4.50 (d, J = 6.6 Hz, 1H), 4.13 (app t, J = 7.3 Hz, 1H), 3.85 (s, 3H), 3.73 (dd, J = 8.8, 2.8 Hz, 1H), 3.54 (s, 3H), 3.53 (m, 1H), 3.49 (s, 3H), 3.43 (dd, J = 6.9, 2.8 Hz, 1H), 3.38 (s, 3H), 3.31 (s, 3H), 2.94 (dd, J = 15.7, 5.0 Hz, 1H), 2.58 (dd, J = 15.7, 10.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 172.9, 148.9, 143.5, 135.8, 134.7, 134.1, 119.8, 108.3, 102.2, 101.4, 98.8, 98.7, 94.1, 81.1, 79.3, 77.9, 56.5, 56.5, 56.4, 55.7, 51.5, 44.4, 37.6; HRMS *m*/*z* (ESI) calcd for $C_{23}H_{34}O_{11}Na$ (M + Na)$^+$ 509.1993, found 509.1996.

(4*S*,5*R*)-4,5-Dihydro-5-((1*R*,2*S*)-1,2-dihydroxybut-3-enyl)-4-phenyl-2(3*H*)-furanone (17). To the solution of the addition product **16a** (0.158 g, 0.34 mmol) in MeOH (26 mL) were added 4−6 drops of concentrated HCl. The reaction mixture was stirred for 3 h at 60 °C, cooled to room temperature, quenched with 7 drops of concentrated NH_4OH, and evaporated under reduced pressure. The residue was dried by coevaporating with acetone (20 mL) and purified by column chromatography (40%, 45%, 50% EtOAc/hexanes) to afford lactone **17** (60 mg, 70%); R_f 0.41 (50% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 7.39−7.23 (m, 5H), 5.77 (ddd, J = 17.3, 10.5, 6.9 Hz, 1H), 5.39 (d, J = 17.3 Hz, 1H), 5.24 (d, J = 10.2 Hz, 1H), 4.50 (d, J = 6.3 Hz, 1H), 4.28 (app t, J = 7.0 Hz, 1H), 3.85 (dd, J = 16.0, 7.2 Hz, 1H), 3.52 (d, J = 6.3 Hz, 1H), 3.08 (dd, J = 17.9, 9.4 Hz, 1H), 2.67 (dd, J = 17.9, 8.5 Hz, 1H), 1.25 (br s, 2H); ^{13}C NMR ($CDCl_3$) δ 176.7, 140.0, 136.1, 129.3, 127.8, 127.2, 119.0, 86.1, 74.1, 73.5, 42.8, 36.9, 29.8; HRMS *m*/*z* (ESI) calcd for $C_{14}H_{16}O_4Na$ (M + Na)$^+$ 271.0940, found 271.0951.

(4*R*,5*S*)-5-Acetoxymethyl-4-phenyl-4,5-dihydro-2(3*H*)-furanone (18).[19] To a solution of lactone **17** (0.05 g, 0.2 mmol) in ether (2 mL) at 0 °C was added $NaIO_4$ (53 mg, 0.25 mmol). To the resulting suspension was added water (1 mL). The resulting mixture was stirred for 28 h. The organic layer was separated, and the aqueous fraction was extracted with ether (3 × 5 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), and evaporated under reduced pressure. The residue was dissolved in absolute EtOH (2 mL). To this solution at 0 °C was added $NaBH_4$ (0.15 g, 3.9 mmol) in one portion and glacial acetic acid (0.3 mL). Stirring was continued for 12 h, and then the reaction mixture was quenched with a mixture of concentrated NH_4OH−saturated NH_4Cl (1:8, 90 mL). The aqueous phase was extracted with EtOAc (5 × 100 mL). The combined organic layers were washed with saturated. NH_4Cl (2 × 100 mL) and brine, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was dried by coevaporating with toluene (5 × 1 mL) and dissolved in anhydrous pyridine (3 mL). To this solution at 0 °C was added acetic anhydride (0.196 g, 1.92 mmol). The resulting mixture was allowed to warm to room temperature and the reaction mixture was stirred for 5 h. The mixture was extracted with ether (3 × 12 mL). The combined organic layers were washed with water (10 mL), dried ($MgSO_4$), and evaporated. The residue was presorbed on silica gel and purified by column chromatography (5−10% EtOAc/hexanes) to afford lactone **18**[19] (42 mg, 91%).

(3*S*,4*R*,5*R*,6*S*)-3-(4-Methoxybenzo[*d*][1,3]dioxol-6-yl)-4,5,6-tri-(methoxymethoxy)-7-octaen-1-ol (19). To a solution of ester **16c** (0.153 g, 0.32 mmol) in ether (15 mL) cooled to 0 °C was added $LiAlH_4$ (0.024 g, 0.63 mmol) in one portion. The reaction mixture was stirred for 3 h while it was allowed to warm to room temperature. Careful quenching with saturated NH_4Cl (10 mL) was followed by extraction with ether (3 × 50 mL). Organic layers were combined, dried ($MgSO_4$), and concentrated under reduced pressure to afford primary alcohol **19** (0.130 g, 90.2%) as a colorless oil; R_f 0.05 (50% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 6.43 (d, J = 1.4 Hz, 1H), 6.40 (d, J = 1.4 Hz, 1H), 5.91 (s, 2H), 5.58 (m, 1H), 5.26 (m, 2H), 4.76 (d, J = 6.9 Hz, 1H), 4.73 (d, J = 6.9 Hz, 1H), 4.72 (d, J = 6.9 Hz, 1H), 4.65 (d, J = 6.9 Hz, 1H), 4.61 (d, J = 6.6 Hz, 1H), 4.50 (d, J = 6.6 Hz, 1H), 4.14 (app t, J = 7.2 Hz, 1H), 3.85 (s, 3H), 3.73 (dd, J = 8.5, 3.0 Hz, 1H), 3.49 (m, 1H), 3.43 (s, 3H), 3.40 (s, 3H), 3.31 (s, 3H), 3.06 (m, 1H), 2.16 (m, 1H), 1.76 (m, 1H), 1.22 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 149.0, 143.6, 136.5, 134.8, 133.9, 119.5, 108.4, 102.3, 101.4, 98.8, 94.2, 81.7, 79.8, 77.9, 61.2, 56.6, 56.5, 56.2, 55.7, 44.7, 34.6, 29.7; HRMS *m*/*z* (ESI) calcd for $C_{22}H_{34}O_{10}Na$ (M + Na)$^+$ 481.2044, found 481.2033.

6-((3*S*,4*R*,5*R*,6*S*)-4,5,6-Tri(methoxymethoxy)octa-1,7-dien-3-yl)-4-methoxybenzo[*d*][1,3]dioxole (20). To a solution of alcohol **19** (0.130 g, 0.28 mmol) and *o*-nitrophenylselenocyanate (0.097 g, 0.43 mmol) in THF (10 mL) was added tributylphosphine (0.086 g, 0.43 mmol) at room temperature. The reaction mixture immediately turned deep brown and TLC showed complete disappearance of the starting material. The mixture was quenched with 1 M NaOH (5 mL) and stirred for 30 min. The mixture was diluted with water (20 mL) and extracted with ether (3 × 50 mL). Organic layers were combined, dried ($MgSO_4$), and concentrated under reduced pressure. The yellow residue was dissolved in THF (10 mL) and cooled to 0 °C, and 30% H_2O_2 (0.48 g, 4.3 mmol) was added to the solution. After an overnight stirring at room temperature the reaction mixture was quenched with $NaHSO_3$ and extracted with ether (3 × 50 mL). Organic layers were combined, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was presorbed on silica gel and purified by column chromatography (20%, 25%, 30% EtOAc/hexanes) to afford pure diene **20** (0.066 g, 52.8%) as a colorless oil; R_f 0.54 (50% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 6.44 (s, 1H), 6.43 (s, 1H), 6.10 (m, 1H), 5.91 (s, 2H), 5.71 (m, 1H), 5.31 (m, 2H), 5.12 (m, 2H), 4.76 (s, 2H), 4.66 (d, J = 6.9 Hz, 1H), 4.65 (d, J = 6.9 Hz, 1H), 4.56 (d, J = 6.9 Hz, 1H), 4.55 (d, J = 6.9 Hz, 1H), 4.14 (app t, J = 6.7 Hz, 1H), 3.91 (dd, J = 7.2, 4.1 Hz, 1H), 3.86 (s, 3H), 4.62 (app t, J = 8.3 Hz, 1H), 3.48 (dd, J = 6.3, 1.9 Hz, 1H), 3.45 (s, 3H), 3.36 (s, 3H), 3.27 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 149.0, 143.6, 138.2, 136.4, 135.0, 133.8, 119.3, 117.4, 107.9, 102.4, 101.4, 98.8, 98.5, 94.2, 80.4, 80.0, 77.4,

56.6, 56.4, 56.3, 55.8, 52.2; HRMS *m*/*z* (ESI) calcd for $C_{22}H_{32}O_9Na$ $(M + Na)^+$ 463.1944, found 463.1963.

6-((1*S*,4*S*,5*R*,6*R*)-4,5,6-Tri(methoxymethoxy)cyclohex-2-enyl)-4-methoxybenzo[*d*][1,3]dioxole (21). To a solution of diene **20** (0.066 g, 0.15 mmol) in dry CH_2Cl_2 (10 mL) was added $(Cy_3P)_2$-(PhCH=)$RuCl_2$ (0.012 g, 0.015 mmol). After the solution was stirred overnight DMSO (0.059 g, 0.75 mmol) was added and the reaction mixture was stirred for an additional 6 h. The mixture was concentrated under reduced pressure and the residue was presorbed on silica gel and purified by column chromatography (30%, 35%, 40% EtOAc/hexanes) to afford pure olefin **21** (0.060 g, 97.1%) as a colorless oil; R_f 0.73 (50% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 6.47 (d, J = 1.4 Hz, 1H), 6.43 (d, J = 1.4 Hz, 1H), 5.93 (s, 2H), 5.90 (ddd, J = 10.2, 3.0, 1.7 Hz, 1H), 5.31 (ddd, J = 10.2, 3.9, 1.7 Hz, 1H), 4.84 (d, J = 6.9 Hz, 1H), 4.77 (d, J = 6.9 Hz, 1H), 4.72 (br s, 2H), 4.66 (d, J = 6.9 Hz, 1H), 4.49 (d, J = 6.9 Hz, 1H), 4.15 (m, 1H), 3.90 (app t, J = 4.7 Hz, 1H), 3.69 (m, 1H), 3.43 (s, 3H), 3.38 (s, 3H), 3.28 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 148.7, 143.2, 134.2, 133.8, 129.3, 127.6, 109.5, 104.1, 101.4, 97.2, 96.7, 96.4, 76.5, 76.3, 75.8, 56.7, 56.0, 55.8, 55.6, 44.6; HRMS *m*/*z* (ESI) calcd for $C_{20}H_{28}O_9Na$ $(M + Na)^+$ 435.1625, found 435.1615.

(1*R*,2*R*,3*S*,6*R*)-6-(4-Methoxybenzo[*d*][1,3]dioxol-6-yl)-4-cyclohexene-1,2,3-triol (8e). To a solution of **21** (0.025 g, 0.06 mmol) in MeOH (10 mL) was added 1−2 drops of concentrated HCl. After the reaction mixture was stirred for 3 h at 60 °C it was cooled to room temperature, quenched with 3 drops of concentrated NH_4OH, and evaporated under reduced pressure. Acetone (20 mL) was added and evaporated again to remove traces of water. The residue was adsorbed on a preparative TLC plate and separated chromatographically with 5% MeOH/CH_2Cl_2 to obtain 13 mg of **8e** (76%); R_f 0.04 (50% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 6.43 (s, 1H), 6.39 (s, 1H), 5.92 (s, 1H), 5.91 (s, 1H), 5.77 (d, J = 9.9 Hz, 1H), 5.67 (dd, J = 9.9, 3.6 Hz, 1H), 4.02 (br s, 1H), 3.88 (s, 3H), 3.60−3.48 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 148.9, 143.3, 134.6, 131.7, 130.0, 128.0, 110.3, 104.4, 101.6, 73.5, 72.8, 70.6, 56.9, 47.2; HRMS *m*/*z* (ESI) calcd for $C_{14}H_{16}O_6Na$ $(M + Na)^+$ 303.0839, found 303.0829.

Mixture of α- and β-Methyl D-Xylopyranosides (22). A methanolic solution of 1% HCl was prepared by a careful addition of $SOCl_2$ (5 mL, 0.069 mol) to stirred dry MeOH (250 mL) at 0 °C. d-Xylose (25 g, 0.17 mol) was added in one portion and the resulting solution was refluxed for 4 h. The reaction mixture was allowed to cool to room temperature, neutralized by the addition of solid $NaHCO_3$ (17.5 g, 0.21 mol), and concentrated under reduced pressure. The residue was dissolved in EtOH (200 mL), the solution was concentrated to one-half of the original volume, toluene (100 mL) was added, and the mixture was concentrated to dryness. The residual viscous oil was used without purification in the next step.

Mixture of α- and β-Methyl 2,3,4-Tri-*O*-benzyl-D-xylopyranosides (23). To NaH 60% suspension in mineral oil (34 g, 0.85 mol) in a 1 L flask was added a solution of methyl xylosides from the previous step in DMF (500 mL) in 100 mL portions at 0 °C with vigorous stirring. After the hydrogen evolution was complete the mixture was treated with Bu_4NI (11 g, 0.03 mol) and BnCl (70 mL, 0.61 mol) and stirred for 30 min at 0 °C and then overnight at room temperature. The reaction mixture was carefully quenched with a cold aqueous solution of 10% NH_4Cl (130 g). Water (400 mL) was added to the mixture and the aqueous layer was extracted with ether (3 × 200 mL). The combined organic extracts were washed with water (2 × 300 mL), then dried ($MgSO_4$) and concentrated under reduced pressure. The residual oil (about 250 mL) was subjected to the next step without purification.

2,3,4-Tri-*O*-benzyl-D-xylopyranose (24).[20a,b] The crude mixture of xylosides from the previous step was heated under reflux for 10 h with 1 M H_2SO_4 (210 mL), AcOH (240 mL), and dioxane (220 mL). After allowing the mixture to cool to room temperature, hexane (100 mL) and water (800 mL) were added with intense stirring. The separated precipitate was collected by filtration, washed with hexane (2 × 250 mL), and air-dried. Recrystallization from methanol gave 2,3,4-tri-*O*-benzyl-D-xylose as white needles (50.7 g, 71%); mp 137−138 °C (lit.[20] mp 139−142 °C); R_f 0.45 (33% EtOAc/hexanes).

(2*R*,3*R*,4*S*)-2,3,4-Tri(benzyloxy)-5-hexene-1-ol (25).[17b,28] To a stirred suspension of methyltriphenylphosphonium bromide (42 g, 0.1 mol) in THF (150 mL) was added BuLi (50 mL of 2 M solution in pentane, 0.1 mol) dropwise at 0 °C. The mixture was stirred for 2 h at room temperature. To the above red solution was added tri-*O*-benzylxylopyranose (20 g, 0.048 mol) in THF (150 mL) dropwise at 0 °C. The reaction mixture was stirred overnight at room temperature and then at reflux for 2 h. NH_4Cl (1 M, 200 mL) was added at room temperature to the reaction mixture and the latter was extracted with ether (3 × 200 mL). The organic extracts were combined, washed with brine, and dried ($MgSO_4$). After the removal of the solvent, the residue was passed through a short column of silica gel with gradients: 15%, 35% EtOAc/hexanes, to obtain 16 g (80%) of the enol product; R_f 0.38 (33% EtOAc/hexanes).

Methyl (2*E*,4*R*,5*R*,6*S*)-4,5,6-Tri(benzyloxy)-2,7-octadienoate (26).[17b] To oxalyl chloride (27 mL of 2M in CH_2Cl_2, 54 mmol) in dry CH_2Cl_2 (100 mL) at −78 °C was added DMSO (7.8 mL, 110 mmol) in CH_2Cl_2 (40 mL) over 20 min and the mixture was stirred for 40 min. The above alcohol (10 g, 24 mmol) in CH_2Cl_2 (40 mL) was added over 30 min and the mixture was stirred for an additional 1 h. Triethylamine (20 mL, 133 mmol) in CH_2Cl_2 (40 mL) was added over 20 min and the white slurry was stirred for 30 min at −78 °C. To the cold reaction mixture was added methyl (triphenylphosphoranylidene)acetate (18 g, 54 mmol) in one portion, and the resulting mixture was stirred for 10 h while it was allowed to warm to room temperature. Water (300 mL) was added to the reaction mixture, the two layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 200 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), and evaporated under reduced pressure. The residual oil was split into two fractions, which were presorbed on silica gel and purified by chromatography with gradients: 5%, 15% EtOAc/hexanes to afford enoate **26** (9.7 g, 84%) as a colorless oil; R_f 0.55 (25% EtOAc/hexanes).

General Procedure for the Arylcuprate Addition. One milliliter of a required aryl bromide (7.03 mmol) solution in THF was added to crushed Mg turnings (0.17 g, 7.03 mmol) in THF (10 mL) under nitrogen atmosphere. Once the reaction started the solution warmed and slightly darkened. The rest of the aryl bromide was added dropwise to allow a gentle reaction. The reaction mixture was allowed to cool to room temperature and then cannulated to a slurry of CuI (0.67 g, 3.52 mmol) in THF (10 mL) at −78 °C. The mixture was stirred at −78 °C for 40 min. Me_3SiCl (0.76 g, 7.03 mmol) and the enoate (0.703 mmol in 10 mL of THF) were added sequentially at −78 °C. The yellow-brown suspension was stirred overnight while slowly warming up to room temperature. The reaction mixture was quenched with a mixture of concentrated NH_4OH and saturated NH_4Cl (1:9, 30 mL) and extracted with ether (3 × 30 mL). The combined organic layers were washed with brine, dried with $MgSO_4$, and concentrated under reduced pressure. The residue was absorbed on silica gel and purified by column chromatography (5−30% EtOAc/hexanes) to yield corresponding addition products **27a**−**g** as an oil.

Methyl (3*S*,4*R*,5*R*,6*S*)-3-Phenyl-4,5,6-tri(benzyloxy)-7-octaenoate (27a). 97%; R_f 0.66 (25% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 7.46−7.23 (m, 20H), 6.01 (m, 1H), 5.44 (br d, J = 9.4 Hz, 1H), 5.39 (br d, J = 17.1 Hz, 1H), 4.90 (d, J = 11.6 Hz, 1H), 4.89 (d, J = 11.3 Hz, 1H), 4.74 (d, J = 11.8 Hz, 1H), 4.67 (d, J = 11.6 Hz, 1H), 4.57 (d, J = 11.3 Hz, 1H), 4.44 (d, J = 11.8 Hz, 1H), 4.11 (app t, J = 5.8 Hz, 1H), 4.04 (dd, J = 6.9, 5.2 Hz, 1H), 3.80 (m, 1H), 3.55 (m, 1H), 3.54 (s, 3H), 3.09 (dd, J = 15.7, 4.4 Hz, 1H), 2.86 (dd, J = 15.7, 10.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 173.1, 141.9, 139.1, 139.0, 138.4, 135.6, 128.7, 128.6, 128.5, 128.3,

(28) Kornienko, A.; d'Alarcao, M. *Tetrahedron Lett.* **1997**, *38*, 6497−6500.

128.0, 127.9, 127.8, 127.6, 127.6, 127.0, 119.2, 82.4, 82.3, 81.5, 75.0, 73.4, 70.9, 51.6, 43.6, 36.7; HRMS *m*/*z* (ESI) calcd for $C_{36}H_{39}O_5$ $(M + H)^+$ 551.2798, found 551.2795.

Methyl (3*S*,4*R*,5*R*,6*S*)-3-(4-Methoxyphenyl)-4,5,6-Tri(benzyloxy)-7-octaenoate (27b). 95%; R_f 0.54 (25% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 7.41−7.36 (m, 15H), 7.09 (d, J = 8.5 Hz, 2H), 6.83 (d, J = 8.5 Hz, 2H), 5.95 (m, 1H), 5.39 (br d, J = 9.5 Hz, 1H), 5.34 (br d, J = 17.9 Hz, 1H), 4.85 (d, J = 11.6 Hz, 1H), 4.83 (d, J = 11.3 Hz, 1H), 4.68 (d, J = 11.8 Hz, 1H), 4.61 (d, J = 11.6 Hz, 1H), 4.54 (d, J = 11.3 Hz, 1H), 4.39 (d, J = 11.8 Hz, 1H), 4.06 (app t, J = 6.1 Hz, 1H), 3.93 (dd, J = 7.4, 5.2 Hz, 1H), 3.82 (s, 3H), 3.68 (m, 1H), 3.51 (s, 3H), 3.49 (m, 1H), 3.00 (dd, J = 15.4, 4.4 Hz, 1H), 2.75 (dd, J = 15.4, 10.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 173.2, 158.5, 139.1, 139.0, 138.4, 135.6, 133.7, 129.4, 128.5, 128.4, 128.2, 127.9, 127.8, 127.7, 127.5, 119.1, 114.0, 82.4, 81.6, 75.0, 73.2, 70.8, 55.3, 51.5, 42.8, 36.9; HRMS *m*/*z* (ESI) calcd for $C_{37}H_{41}O_6$ $(M + H)^+$ 581.2903, found 581.2910.

Methyl (3*S*,4*R*,5*R*,6*S*)-3-(Benzo[*d*][1,3]dioxol-6-yl)-4,5,6-tri(benzyloxy)-7-octaenoate (27c). 95%; ^{1}H NMR ($CDCl_3$) δ 7.38−7.33 (m, 15H), 6.70 (d, J = 8.0 Hz, 1H), 6.64 (br s, 1H), 6.59 (br d, J = 8.0 Hz, 1H), 5.93 (s, 2H), 5.92 (m, 1H), 5.38 (br d, J = 5.2 Hz, 1H), 5.34 (br d, J = 13.7 Hz, 1H), 4.83 (d, J = 11.8 Hz, 1H), 4.78 (d, J = 11.3 Hz, 1H), 4.65 (d, J = 11.6 Hz, 1H), 4.59 (d, J = 11.6 Hz, 1H), 4.50 (d, J = 11.3 Hz, 1H), 4.37 (d, J = 11.8 Hz, 1H), 4.07 (app t, J = 6.1 Hz, 1H), 3.86 (dd, J = 6.9, 5.2 Hz, 1H), 3.60 (m, 1H), 3.51 (s, 3H), 3.47 (app t, J = 5.2 Hz, 1H), 2.93 (dd, J = 15.7, 4.4 Hz, 1H), 2.69 (dd, J = 15.7, 10.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 173.0, 147.7, 146.4, 138.9, 138.8, 138.2, 135.5, 135.4, 128.5, 128.4, 128.2, 127.9, 127.8, 127.7, 127.5, 121.6, 119.2, 108.6, 108.3, 101.0, 82.3, 82.2, 81.5, 74.9, 73.2, 70.8, 51.5, 43.0, 36.7; HRMS *m*/*z* (ESI) calcd for $C_{37}H_{38}O_7$ $(M)^+$ 594.2618, found 594.2612.

Methyl (3*S*,4*R*,5*R*,6*S*)-3-(3,4-Dimethoxyphenyl)-4,5,6-tri(benzyloxy)-7-octaenoate (27d). 78%; R_f 0.59 (25% EtOAc/hexanes); $[\alpha]^{22}_D$ 37.7 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.48−7.21 (m, 15H), 6.70 (d, J = 8.8 Hz, 1H), 6.62 (br d, J = 6.8 Hz, 2H), 5.95−5.83 (m, 1H), 5.32 (d, J = 3.0 Hz, 1H), 5.28 (br d, J = 9.6 Hz, 1H), 4.76 (dd, J = 11.8, 4.4 Hz, 2H), 4.60 (d, J = 11.8 Hz, 1H), 4.51 (d, J = 11.8 Hz, 1H), 4.40 (d, J = 11.8 Hz, 1H), 4.32 (d, J = 11.8 Hz, 1H), 4.00 (t, J = 6.0 Hz, 1H), 3.86 (dd, J = 12.1, 7.4 Hz, 1H), 3.83 (s, 3H), 3.58 (s, 3H), 3.46 (s, 3H), 3.44 (m, 1H), 2.90 (dd, J = 15.7, 4.4 Hz, 1H), 2.71 (dd, J = 15.7, 10.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 173.1, 148.8, 147.8, 138.9, 138.3, 135.5, 134.3, 128.4, 128.3, 128.0, 127.6, 127.5, 127.4, 120.1, 118.9, 111.6, 111.2, 82.5, 82.4, 81.5, 74.8, 73.1, 70.8, 55.8, 55.6, 51.5, 42.8, 36.5; HRMS *m*/*z* (ESI) calcd for $C_{38}H_{42}O_7Na$ $(M + Na)^+$ 633.2822, found 633.2831.

Methyl (3*S*,4*R*,5*R*,6*S*)-3-(4-Methoxybenzo[*d*][1,3]dioxol-6-yl)-4,5,6-tri(benzyloxy)-7-octaenoate (27e). 97%; R_f 0.42 (25% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 7.36−7.28 (m, 15H), 6.33 (s, 1H), 6.32 (s, 1H), 5.94 (br s, 2H), 5.93 (m, 1H), 5.38 (s, 1H), 5.34 (br d, J = 6.6 Hz, 1H), 4.84 (d, J = 11.8 Hz, 1H), 4.78 (d, J = 11.3 Hz, 1H), 4.65 (d, J = 11.6 Hz, 1H), 4.56 (d, J = 11.6 Hz, 1H), 4.46 (d, J = 11.3 Hz, 1H), 4.37 (d, J = 11.8 Hz, 1H), 4.08 (app t, J = 5.8 Hz, 1H), 3.86 (dd, J = 6.3, 5.5 Hz, 1H), 3.65 (s, 3H), 3.59 (m, 1H), 3.51 (s, 3H), 3.48 (app t, J = 5.5 Hz, 1H), 2.90 (dd, J = 15.7, 4.7 Hz, 1H), 2.70 (dd, J = 15.7, 10.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 173.0, 148.9, 143.5, 139.0, 138.9, 138.2, 136.4, 135.4, 134.0, 128.5, 128.4, 128.1, 127.7, 127.6, 127.5, 119.1, 107.8, 102.1, 101.4, 82.5, 82.4, 81.5, 74.9, 73.2, 70.9, 56.4, 51.6, 43.2, 36.4; HRMS *m*/*z* (ESI) calcd for $C_{38}H_{40}O_8$ $(M)^+$ 624.2723, found 624.2715.

Methyl (3*S*,4*R*,5*R*,6*S*)-3-(4-Fluorophenyl)-4,5,6-tri(benzyloxy)-7-octaenoate (27f). 88%; R_f 0.78 (25% EtOAc/hexanes); $[\alpha]^{22}_D$ 53.1 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.42−7.23 (m, 15H), 7.01 (dd, J = 8.5, 5.5 Hz, 2H), 6.88 (app t, J = 8.8 Hz, 2H), 5.94−5.82 (m, 1H), 5.33 (br d, J = 8.8 Hz 1H), 5.27 (br d, J = 8.8 Hz, 1H), 4.74 (d, J = 11.8 Hz, 2H), 4.62 (d, J = 11.8 Hz, 1H), 4.53 (d, J = 11.8 Hz, 1H), 4.33 (t, J = 12.1 Hz, 2H), 3.98 (app t, J = 6.0 Hz, 1H), 3.81 (app t, J = 6.0 Hz, 1H), 3.60−3.51 (m, 1H), 3.45 (s, 3H), 3.39 (m, 1H), 2.89 (dd, J = 15.7, 4.4 Hz, 1H), 2.68 (dd, J = 15.7, 10.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 172.9, 138.7, 137.5, 137.4, 135.4, 129.8, 129.7, 128.4, 128.3, 128.2, 127.9, 127.7, 127.5, 127.4, 115.4, 115.2, 82.3, 82.2, 81.0, 74.7, 73.4, 70.8, 51.4, 42.6, 35.9; HRMS *m*/*z* (ESI) calcd for $C_{36}H_{37}O_5FNa$ $(M + Na)^+$ 591.2523, found 591.2507.

Methyl (3*S*,4*R*,5*R*,6*S*)-3-(4-Chlorophenyl)-4,5,6-tri(benzyloxy)-7-octaenoate (27g). 91%; R_f 0.46 (25% EtOAc/hexanes); $[\alpha]^{22}_D$ 43.3 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.48−7.04 (m, 15H), 6.98 (d, J = 8.2 Hz, 2H), 6.74 (d, J = 8.8 Hz, 2H), 5.94−5.82 (m, 1H), 5.35−5.20 (m, 2H), 4.73 (dd, J = 11.8, 3.8 Hz, 2H), 4.62 (d, J = 11.8 Hz, 1H), 4.52 (d, J = 11.8 Hz, 1H), 4.32 (dd, J = 11.8, 7.7 Hz, 2H), 4.00 (app t, J = 6.0 Hz, 1H), 3.80 (app t, J = 6.0 Hz, 1H), 3.60−3.51 (m, 1H), 3.45 (s, 3H), 3.39 (m, 1H), 2.89 (dd, J = 15.7, 4.4 Hz, 1H), 2.72 (dd, J = 15.7, 10.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 173.1, 140.5, 138.6, 138.5, 135.2, 132.6, 129.7, 129.5, 128.6, 128.4, 128.2, 127.5, 127.9, 127.7, 127.6, 127.5, 119.1, 116.7, 82.2, 80.9, 74.8, 73.6, 70.8, 51.6, 42.7, 36.3; HRMS *m*/*z* (ESI) calcd for $C_{36}H_{37}O_5ClNa$ $(M + Na)^+$ 607.2227, found 607.2222.

General Procedure for Ester Reduction. A solution of a desired ester **27** (1.5 mmol) in ether (25 mL) was cooled to 0 °C, and $LiAlH_4$ was added (0.23 g, 6 mmol) in one portion. The reaction mixture was stirred for 3 h while slowly warming up to room temperature. Careful quenching with saturated NH_4Cl (10 mL) was followed by extraction with ether (3 × 25 mL). Organic layers were combined, dried with $MgSO_4$, and concentrated under reduced pressure to afford the corresponding primary alcohols as viscous colorless oils. Reduction products **28a**−**g** were used without purification in the next step. A small portion of each crude alcohol was purified (35% EtOAc/hexanes) for characterization.

(3*S*,4*R*,5*R*,6*S*)-3-Phenyl-4,5,6-tri(benzyloxy)-7-octaen-1-ol (28a). R_f 0.30 (25% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 7.35−7.12 (m, 20H), 5.91 (m, 1H), 5.36 (br d, J = 8.8 Hz, 1H), 5.31 (br d, J = 16.5 Hz, 1H), 4.78 (d, J = 11.4 Hz, 1H), 4.77 (d, J = 11.2 Hz, 1H), 4.64 (d, J = 11.8 Hz, 1H), 4.54 (d, J = 11.4 Hz, 1H), 4.47 (d, J = 11.2 Hz, 1H), 4.36 (d, J = 11.8 Hz, 1H), 4.05 (app t, J = 5.5 Hz, 1H), 3.88 (dd, J = 6.6, 5.4 Hz, 1H), 3.49 (app t, J = 6.2 Hz, 1H), 3.46 (m, 1H), 3.22 (m, 1H), 3.20 (m, 1H), 2.18 (m, 1H), 2.00 (m, 1H), 1.35 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 142.4, 139.1, 138.2, 135.5, 128.7, 128.5, 128.4, 128.4, 127.9, 127.8, 127.5, 127.4, 126.7, 119.0, 83.2, 82.7, 81.3, 74.9, 73.4, 70.8, 61.2, 43.4, 33.7; HRMS *m*/*z* (ESI) calcd for $C_{35}H_{39}O_4$ $(M + H)^+$ 523.2848, found 523.2848.

(3*S*,4*R*,5*R*,6*S*)-3-(4-Methoxyphenyl)-4,5,6-tri(benzyloxy)-7-octaen-1-ol (28b). R_f 0.33 (25% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 7.38−7.29 (m, 15H), 7.04 (d, J = 8.5 Hz, 2H), 6.81 (d, J = 8.5 Hz, 2H), 5.91 (m, 1H), 5.36 (br d, J = 8.8 Hz, 1H), 5.32 (br d, J = 16.0 Hz, 1H), 4.80 (d, J = 11.6 Hz, 1H), 4.77 (d, J = 11.0 Hz, 1H), 4.65 (d, J = 11.8 Hz, 1H), 4.55 (d, J = 11.6 Hz, 1H), 4.50 (d, J = 11.0 Hz, 1H), 4.37 (d, J = 11.8 Hz, 1H), 4.06 (app t, J = 5.8 Hz, 1H), 3.84 (dd, J = 6.6, 5.2 Hz, 1H), 3.80 (s, 3H), 3.49 (app t, J = 5.2 Hz, 1H), 3.46 (m, 1H), 3.32 (m, 1H), 3.16 (m, 1H), 2.16 (m, 1H), 1.95 (m, 1H), 1.58 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 158.4, 139.1, 138.2, 135.5, 134.3, 129.6, 128.5, 128.4, 128.4, 127.9, 127.8, 127.7, 127.5, 127.4, 119.0, 114.0, 83.3, 82.7, 81.3, 74.9, 73.4, 70.8, 61.2, 55.3, 42.6, 33.9; HRMS *m*/*z* (ESI) calcd for $C_{36}H_{41}O_5$ $(M + H)^+$ 553.2954, found 553.2947.

(3*S*,4*R*,5*R*,6*S*)-3-(Benzo[*d*][1,3]dioxol-6-yl)-4,5,6-tri(benzyloxy)-7-octaen-1-ol (28c). R_f 0.12 (25% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 7.38−7.29 (m, 15H), 6.71 (d, J = 7.9 Hz, 1H), 6.65 (d, J = 1.5 Hz, 1H), 6.56 (dd, J = 8.0, 1.5 Hz, 1H), 5.93 (s, 2H), 5.92 (m, 1H), 5.39 (br d, J = 3.2 Hz, 1H), 5.34 (br d, J = 10.5 Hz, 1H), 4.81 (d, J = 11.6 Hz, 1H), 4.77 (d, J = 11.0 Hz, 1H), 4.65 (d, J = 11.8 Hz, 1H), 4.56 (d, J = 11.6 Hz, 1H), 4.51 (d, J = 11.0 Hz, 1H), 4.38 (d, J = 11.8 Hz, 1H), 4.09 (app t, J = 5.8 Hz, 1H), 3.81 (app t, J = 5.4 Hz, 1H), 3.52 (app t, J = 5.4 Hz, 1H), 3.48 (m, 1H), 3.32 (m, 1H), 3.12 (m, 1H), 2.13 (m, 1H), 1.90 (m, 1H), 1.40 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 147.9, 146.3, 139.1, 139.0, 138.2,

136.2, 135.4, 128.5, 128.4, 127.8, 127.5, 127.4, 121.8, 119.0, 108.7, 108.3, 101.0, 83.3, 82.6, 81.3, 74.9, 73.5, 70.8, 61.1, 43.0, 33.8; HRMS *m*/*z* (ESI) calcd for $C_{36}H_{38}O_6$ $(M)^+$ 566.2668, found 566.2663.

(3*S*,4*R*,5*R*,6*S*)-3-(3,4-Dimethoxyphenyl)-4,5,6-tri(benzyloxy)-7-octaen-1-ol (28d). R_f 0.32 (25% EtOAc/hexanes); $[\alpha]^{22}_D$ 26.6 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.50−7.21 (m, 15H), 6.73 (br d, *J* = 7.9 Hz, 1H), 6.66 (br d, *J* = 9.0 Hz, 1H), 6.63 (br d, *J* = 8.2 Hz, 1H), 5.97−5.85 (m, 1H), 5.33 (br d, *J* = 11.2 Hz, 1H), 5.31 (br d, *J* = 5.5 Hz, 1H), 4.77 (dd, *J* = 11.5, 4.9 Hz, 2H), 4.62 (d, *J* = 11.8 Hz, 1H), 4.51 (d, *J* = 11.5 Hz, 1H), 4.42 (d, *J* = 11.8 Hz, 1H), 4.35 (d, *J* = 11.5 Hz, 1H), 4.06 (app t, *J* = 6.6 Hz, 1H), 3.84 (s, 3H), 3.57 (s, 3H), 3.52 (m, 2H), 3.37−3.26 (m, 1H), 3.15−3.08 (m, 1H), 2.17−2.03 (m, 1H), 2.01−1.91 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 149.0, 147.7, 139.2, 139.0, 138.2, 135.5, 135.0, 128.4, 128.3, 128.2, 127.7, 127.6, 127.4, 127.3, 120.5, 118.8, 111.5, 111.2, 83.5, 82.8, 81.2, 74.8, 73.4, 70.8, 61.2, 55.9, 55.6, 42.8, 33.5; HRMS *m*/*z* (ESI) calcd for $C_{37}H_{42}O_6Na$ $(M + Na)^+$ 605.2873, found 605.2860.

(3*S*,4*R*,5*R*,6*S*)-3-(4-Methoxybenzo[*d*][1,3]dioxol-6-yl)-4,5,6-tri(benzyloxy)-7-octaen-1-ol (28e). R_f 0.30 (25% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 7.35−7.28 (m, 15H), 6.33 (s, 1H), 6.32 (s, 1H), 5.94 (s, 2H), 5.93 (m, 1H), 5.39 (m, 1H), 5.35 (br d, *J* = 5.2 Hz, 1H), 4.83 (d, *J* = 11.6 Hz, 1H), 4.79 (d, *J* = 11.3 Hz, 1H), 4.65 (d, *J* = 11.8 Hz, 1H), 4.55 (d, *J* = 11.6 Hz, 1H), 4.48 (d, *J* = 11.3 Hz, 1H), 4.38 (d, *J* = 11.8 Hz, 1H), 4.11 (app t, *J* = 5.5 Hz, 1H), 3.82 (app t, *J* = 5.8 Hz, 1H), 3.65 (s, 3H), 3.54 (app t, *J* = 5.5 Hz, 1H), 3.49 (m, 1H), 3.34 (m, 1H), 3.12 (m, 1H), 2.11 (m, 1H), 1.92 (m, 1H), 1.38 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 149.0, 143.6, 139.1, 138.2, 137.1, 135.4, 133.9, 128.5, 128.4, 128.3, 127.8, 127.6, 127.5, 127.4, 119.0, 107.9, 102.3, 101.4, 83.4, 82.8, 81.3, 74.9, 73.4, 70.8, 61.1, 56.4, 43.2, 33.7; HRMS *m*/*z* (ESI) calcd for $C_{37}H_{40}O_7$ $(M)^+$ 596.2774, found 596.2775.

(3*S*,4*R*,5*R*,6*S*)-3-(4-Fluorophenyl)-4,5,6-Tri(benzyloxy)-7-octaen-1-ol (28f). R_f 0.66 (25% EtOAc/hexanes); $[\alpha]^{22}_D$ 55.9 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.48−7.16 (m, 15H), 7.03 (app t, *J* = 5.8 Hz, 2H), 6.91 (app t, *J* = 6.6 Hz, 2H), 6.01−5.85 (m, 1H), 5.33 (br d, *J* = 9.6 Hz, 1H), 5.29 (br d, *J* = 8.5 Hz, 1H), 4.74 (d, *J* = 11.6 Hz, 2H), 4.63 (d, *J* = 11.6 Hz, 1H), 4.53 (d, *J* = 11.6 Hz, 1H), 4.35 (dd, *J* = 11.8, 3.3 Hz, 2H), 4.02 (app t, *J* = 6.3 Hz, 1H), 3.78 (app t, *J* = 5.8 Hz, 1H), 3.55−3.39 (m, 2H), 3.32−3.15 (m, 1H), 3.14−3.08 (m, 1H), 2.20−2.03 (m, 1H), 2.02−1.89 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 138.9, 138.8, 138.0, 135.3, 130.0, 129.9, 128.5, 128.4, 128.3, 127.8, 127.7, 127.5, 127.4, 118.9, 115.4, 115.2, 83.3, 82.6, 80.9, 74.8, 73.7, 70.8, 60.9, 42.4, 33.3; HRMS *m*/*z* (ESI) calcd for $C_{35}H_{38}O_4F$ $(M)^+$ 541.2754, found 541.2750.

(3*S*,4*R*,5*R*,6*S*)-3-(4-Chlorophenyl)-4,5,6-tri(benzyloxy)-7-octaen-1-ol (28g). R_f 0.16 (25% EtOAc/hexanes); $[\alpha]^{22}_D$ 45.3 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.48−7.23 (m, 15H), 7.19 (d, *J* = 8.0 Hz, 2H), 7.0 (d, *J* = 8.2 Hz, 2H), 5.99−5.83 (m, 1H), 5.35 (br d, *J* = 9.6 Hz, 1H), 5.32 (br d, *J* = 8.5 Hz, 1H), 4.74 (d, *J* = 11.6 Hz, 2H), 4.63 (d, *J* = 11.6 Hz, 1H), 4.53 (d, *J* = 11.6 Hz, 1H), 4.35 (dd, *J* = 11.8, 3.3 Hz, 2H), 4.04 (app t, *J* = 6.3 Hz, 1H), 3.78 (app t, *J* = 5.8 Hz, 1H), 3.55−3.39 (m, 2H), 3.35−3.18 (m, 1H), 3.15−3.08 (m, 1H), 2.18−2.03 (m, 1H), 2.02−1.89 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 140.9, 138.8, 138.7, 135.2, 132.3, 129.9, 128.6, 128.5, 128.4, 128.3, 127.9, 127.7, 127.5, 127.4, 118.9, 83.1, 82.5, 80.8, 74.8, 73.8, 70.8, 67.1, 60.8, 42.4, 33.0; HRMS *m*/*z* (ESI) calcd for $C_{35}H_{38}O_4Cl$ $(M)^+$ 557.2459, found 557.2463.

General Procedure for the Terminal Double Bond Installation by Selenoxide Elimination. Tributylphosphine (0.51 g, 2.5 mmol) was added to the solution of an appropriate alcohol **28** (0.5 mmol) and *o*-nitrophenylselenocyanate (0.56 g, 2.5 mmol) in THF (30 mL). The reaction went to completion immediately and was quenched with 1 M NaOH solution (15 mL) for 30 min. The resulting mixture was diluted with water (100 mL) and extracted with ether (3 × 100 mL). Organic layers were combined, dried with $MgSO_4$, and concentrated under reduced pressure. The yellow residue was dissolved in THF (30 mL) and cooled to 0 °C, and an aqueous solution (wt 35%) of hydrogen peroxide (0.56 g, 5 mmol) was added. After overnight stirring at room temperature, the reaction mixture was quenched with dry $NaHSO_3$ and extracted with ether (3 × 100 mL). Organic layers were combined, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was presorbed on silica gel and purified by column chromatography (1−2%, EtOAc/hexanes) to afford pure dienes **29a**−**g** as a colorless oil.

1-((3*S*,4*R*,5*R*,6*S*)-4,5,6-Tri(benzyloxy)octa-1,7-dien-3-yl)benzene (29a). 75% (3 steps); R_f 0.73 (25% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 7.44−7.21 (m, 20H), 6.40 (m, 1H), 6.01 (m, 1H), 5.39 (br d, *J* = 8.5 Hz, 1H), 5.36 (br d, *J* = 17.3 Hz, 1H), 5.20 (br d, *J* = 10.5 Hz, 1H), 5.00 (br d, *J* = 17.1 Hz, 1H), 4.77 (d, *J* = 11.3 Hz, 1H), 4.74 (d, *J* = 11.8 Hz, 1H), 4.68 (d, *J* = 10.7 Hz, 1H), 4.67 (d, *J* = 11.3 Hz, 1H), 4.44 (d, *J* = 11.8 Hz, 1H), 4.27 (d, *J* = 10.7 Hz, 1H), 4.11 (m, 2H), 3.59 (dd, *J* = 9.4, 5.2 Hz, 1H), 3.52 (app t, *J* = 5.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 142.6, 139.1, 138.1, 137.8, 136.1, 128.8, 128.5, 128.4, 128.3, 128.2, 128.0, 127.9, 127.5, 127.4, 126.5, 119.0, 117.4, 83.5, 83.1, 80.0, 75.4, 74.2, 70.4, 51.2; HRMS *m*/*z* (ESI) calcd for $C_{35}H_{37}O_3$ $(M + H)^+$ 505.2743, found 505.2757.

1-((3*S*,4*R*,5*R*,6*S*)-4,5,6-Tri(benzyloxy)octa-1,7-dien-3-yl)-4-methoxybenzene (29b). 84% (3 steps); R_f 0.69 (25% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 7.36−7.18 (m, 15H), 7.07 (d, *J* = 8.5 Hz, 2H), 6.82 (d, *J* = 8.5 Hz, 2H), 6.31 (m, 1H), 5.95 (m, 1H), 5.34 (br d, *J* = 8.5 Hz, 1H), 5.30 (br d, *J* = 15.4 Hz, 1H), 5.13 (dd, *J* = 10.5, 1.7 Hz, 1H), 4.93 (dd, *J* = 17.1, 1.7 Hz, 1H), 4.72 (d, *J* = 11.3 Hz, 1H), 4.68 (d, *J* = 11.8 Hz, 1H), 4.63 (d, *J* = 11.0 Hz, 1H), 4.60 (d, *J* = 11.3 Hz, 1H), 4.38 (d, *J* = 11.8 Hz, 1H), 4.27 (d, *J* = 11.0 Hz, 1H), 4.06 (dd, *J* = 7.2, 4.7 Hz, 1H), 3.98 (app t, *J* = 5.8 Hz, 1H), 3.80 (s, 3H), 3.50 (dd, *J* = 9.4, 5.5 Hz, 1H), 3.45 (app t, *J* = 6.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 158.2, 139.1, 138.1, 136.1, 134.7, 129.3, 128.7, 128.5, 128.3, 128.2, 128.0, 127.9, 127.4, 127.3, 118.9, 117.0, 113.9, 83.4, 83.0, 80.2, 75.4, 74.1, 70.4, 55.3, 50.3; HRMS *m*/*z* (ESI) calcd for $C_{36}H_{38}O_4$ $(M)^+$ 534.2770, found 534.2757.

5-((3*S*,4*R*,5*R*,6*S*)-4,5,6-Tri(benzyloxy)octa-1,7-dien-3-yl)benzo[*d*][1,3]dioxole (29c). 77% (3 steps); R_f 0.69 (25% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 7.35−7.17 (m, 15H), 6.70 (d, *J* = 7.9 Hz, 1H), 6.64 (d, *J* = 1.5 Hz, 1H), 6.57 (dd, *J* = 7.9, 1.5 Hz, 1H), 6.25 (m, 1H), 5.93 (m, 1H), 5.92 (s, 2H), 5.33 (dd, *J* = 8.4, 1.9 Hz, 1H), 5.29 (br d, *J* = 13.5 Hz, 1H), 5.11 (dd, *J* = 10.3, 1.9 Hz, 1H), 4.92 (dd, *J* = 17.2, 1.9 Hz, 1H), 4.71 (d, *J* = 11.4 Hz, 1H), 4.66 (d, *J* = 11.8 Hz, 1H), 4.62 (d, *J* = 10.9 Hz, 1H), 4.60 (d, *J* = 11.4 Hz, 1H), 4.36 (d, *J* = 11.8 Hz, 1H), 4.29 (d, *J* = 10.9 Hz, 1H), 4.04 (dd, *J* = 7.5, 4.7 Hz, 1H), 3.94 (app t, *J* = 5.8 Hz, 1H), 3.44 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 147.6, 146.0, 139.0, 138.1, 137.9, 136.5, 136.0, 128.7, 128.5, 128.3, 128.2, 128.0, 127.9, 127.5, 127.4, 121.3, 118.9, 117.2, 108.8, 108.3, 100.9, 83.3, 83.0, 80.1, 75.4, 74.2, 70.4, 50.7; HRMS *m*/*z* (ESI) calcd for $C_{36}H_{36}O_5$ $(M)^+$ 548.2563, found 548.2562.

4-((3*S*,4*R*,5*R*,6*S*)-4,5,6-Tri(benzyloxy)-1,7-octadien-3-yl)-1,2-dimethoxybenzene (29d). 83%; R_f 0.66 (25% EtOAc/hexanes); $[\alpha]^{22}_D$ 20.8 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.50−7.13 (m,15H), 6.75 (br d, *J* = 8.0 Hz, 1H), 6.66 (br d, *J* = 7.7 Hz, 2H), 6.36−6.24 (m, 1H), 6.01−5.89 (m, 1H), 5.32 (br d, *J* = 10.2 Hz, 1H), 5.30 (br d, *J* = 17.3 Hz, 1H), 5.13 (dd, *J* = 10.2, 1.7 Hz, 1H), 4.94 (dd, *J* = 17.3, 1.1 Hz, 1H), 4.68 (br t, *J* = 11.3 Hz, 2H), 4.63 (dd, *J* = 11.0, 4.1 Hz, 2H), 4.35 (d, *J* = 11.8 Hz, 1H), 4.20 (d, *J* = 11.0 Hz, 1H), 4.05 (dd, *J* = 7.4, 4.4 Hz, 1H), 3.98 (dd, *J* = 6.6, 5.0 Hz, 1H), 3.84 (s, 3H), 3.62 (s, 3H), 3.50−3.43 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 148.8, 147.5, 139.0, 138.9, 138.1, 137.8, 136.0, 135.3, 128.5, 128.4, 128.2, 128.1, 127.8, 127.7, 127.4, 127.3, 120.1, 118.8, 117.1, 111.5, 111.2, 83.5, 83.2, 80.1, 75.4, 74.1, 70.4, 55.9, 55.6, 50.6; HRMS *m*/*z* (ESI) calcd for $C_{37}H_{40}O_5Na$ $(M + Na)^+$ 587.2767, found 587.2786.

6-((3*S*,4*R*,5*R*,6*S*)-4,5,6-Tri(benzyloxy)octa-1,7-dien-3-yl)-4-methoxybenzo[*d*][1,3]dioxole (29e). 84% (3 steps); R_f 0.65 (25% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 7.39−7.19 (m, 15H), 6.36 (d, *J* = 1.4 Hz, 1H), 6.34 (d, *J* = 1.4 Hz, 1H), 6.28 (m, 1H), 5.98

(m, 1H), 5.94 (s, 2H), 5.37 (br d, J = 3.3 Hz, 1H), 5.32 (br d, J = 10.5 Hz, 1H), 5.16 (dd, J = 10.2, 1.9 Hz, 1H), 4.97 (dd, J = 17.3, 1.9 Hz, 1H), 4.75 (d, J = 11.6 Hz, 1H), 4.69 (d, J = 11.8 Hz, 1H), 4.67 (d, J = 10.7 Hz, 1H), 4.63 (d, J = 11.6 Hz, 1H), 4.39 (d, J = 11.8 Hz, 1H), 4.30 (d, J = 10.7 Hz, 1H), 4.08 (dd, J = 7.4, 4.4 Hz, 1H), 3.97 (dd, J = 6.6, 5.0 Hz, 1H), 3.69 (s, 3H), 3.49 (dd, J = 6.6, 4.4 Hz, 1H), 3.45 (dd, 1H); ^{13}C NMR ($CDCl_3$) δ 148.8, 143.5, 139.0, 138.1, 137.6, 137.3, 136.0, 133.7, 128.6, 128.5, 128.3, 128.2, 127.9, 127.8, 127.4, 127.3, 118.9, 117.4, 107.6, 102.4, 101.3, 83.5, 83.1, 80.1, 75.4, 74.2, 70.4, 56.4, 51.0; HRMS *m*/*z* (ESI) calcd for $C_{37}H_{38}O_6$ $(M)^+$ 578.2668, found 578.2677.

1-((3*S*,4*R*,5*R*,6*S*)-4,5,6-Tri(benzyloxy)-1,7-octadien-3-yl)-4-chlorobenzene (29f). 79%; R_f 0.59 (25% EtOAc/hexanes); $[\alpha]^{22}_D$ 106.0 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.53−7.15 (m,15H), 7.09 (dd, J = 8.8, 5.5 Hz, 2H), 6.95 (t, J = 8.8 Hz, 2H), 6.44−6.26 (m, 1H), 6.11−5.86 (m, 1H), 5.36 (br d, J = 10.4 Hz, 1H), 5.33 (br d, J = 17.9 Hz, 1H), 5.17 (d, J = 10.1 Hz, 1H), 4.92 (d, J = 17.3 Hz, 1H), 4.71 (d, J = 11.0 Hz, 2H), 4.64 (dd, J = 10.7, 5.0 Hz, 2H), 4.39 (d, J = 12.1 Hz, 1H), 4.19 (d, J = 10.7 Hz, 1H), 4.06 (dd, J = 7.4, 4.4 Hz, 1H), 3.97 (dd, J = 6.9, 4.6 Hz, 1H), 3.56−3.42 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 138.8, 138.4, 138.0, 137.3, 135.9, 129.7, 129.6, 128.7, 128.5, 128.3, 128.2, 128.0, 127.9, 127.8, 127.5, 127.3, 118.9, 117.5, 115.2, 114.9, 83.4, 83.0, 79.7, 75.3, 74.4, 70.3, 50.2; HRMS *m*/*z* (ESI) calcd for $C_{35}H_{35}O_3FNa$ $(M + Na)^+$ 545.2468, found 545.2469.

1-((3*S*,4*R*,5*R*,6*S*)-4,5,6-Tri(benzyloxy)-1,7-octadien-3-yl)-4-fluorobenzene (29g). 71%; R_f 0.78 (25% EtOAc/hexanes); $[\alpha]^{22}_D$ 109.1 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.53−7.12 (m, 15H), 7.25 (d, J = 8.0 Hz, 2H), 7.05 (d, J = 8.5 Hz, 2H), 6.36−6.24 (m, 1H), 6.09−5.94 (m, 1H), 5.35 (br d, J = 8.5 Hz, 1H), 5.33 (br d, J = 17.9 Hz, 1H), 5.16 (d, J = 12.1 Hz, 1H), 4.91 (d, J = 17.3 Hz, 1H), 4.70 (d, J = 12.6 Hz, 2H), 4.64 (dd, J = 10.7, 3.8 Hz, 2H), 4.38 (d, J = 11.8 Hz, 1H), 4.18 (d, J = 10.7 Hz, 1H), 4.04 (dd, J = 7.1, 3.8 Hz, 1H), 3.96 (dd, J = 6.9, 4.6 Hz, 1H), 3.56−3.38 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 141.2, 138.8, 138.0, 137.0, 135.9, 132.1, 129.7, 128.7, 128.5, 128.4, 128.3, 128.2, 128.0, 127.9, 127.8, 127.5, 127.4, 118.9, 117.8, 83.4, 82.9, 79.6, 75.4, 74.5, 70.3, 50.4; HRMS *m*/*z* (ESI) calcd for $C_{35}H_{35}O_3ClNa$ $(M + Na)^+$ 561.2172, found 561.2167.

General Procedure for Ring-Closing Metathesis. An appropriate diene **29** (0.3 mmol) was dissolved in dry CH_2Cl_2 (16 mL) followed by the addition of the Grubbs' catalyst $(Cy_3P)_2(PhCH{=})$-$RuCl_2$ (11 mg, 11.4 μmol). After 12 h, DMSO (0.11 g, 1.4 mmol) was added, and the reaction mixture was stirred for an additional 6 h. The mixture was then concentrated under reduced pressure. The residue was presorbed on silica gel and purified by column chromatography (1−4% EtOAc/hexanes) to afford pure conduritol analogues **30a**−**g** as an oil.

((1*S*,4*S*,5*R*,6*R*)-4,5,6-Tri(benzyloxy)cyclohex-2-enyl)benzene (30a). 92%; R_f 0.66 (25% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 7.48−7.30 (m, 20H), 5.99 (dd, J = 10.1, 2.0 Hz, 1H), 5.85 (ddd, J = 10.1, 4.3, 1.9 Hz, 1H), 4.86−4.68 (m, 6H), 4.25 (br s, 1H), 3.91 (br s, 3H); ^{13}C NMR ($CDCl_3$) δ 138.9, 138.8, 138.7, 130.4, 129.0, 128.5, 128.3, 128.3, 128.0, 127.8, 127.7, 127.5, 127.4, 127.0, 79.9, 79.8, 79.1, 74.6, 72.8, 72.4, 45.8; HRMS *m*/*z* (ESI) calcd for $C_{33}H_{33}O_3$ $(M + H)^+$ 477.2430, found 477.2423.

1-((1*S*,4*S*,5*R*,6*R*)-4,5,6-Tri(benzyloxy)cyclohex-2-enyl)-4-methoxybenzene (30b). 89%; R_f 0.63 (25% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 7.42−7.28 (m, 15H), 7.24 (d, J = 8.7 Hz, 2H), 6.90 (d, J = 8.7 Hz, 2H), 5.97 (ddd, J = 9.9, 2.4, 0.9 Hz, 1H), 5.78 (ddd, J = 9.9, 4.5, 1.7 Hz, 1H), 4.81−4.64 (m, 6H), 4.19 (m, 1H), 3.83 (s, 3H), 3.80 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 158.7, 139.0, 138.9, 138.8, 131.3, 130.6, 129.3, 128.5, 128.4, 128.0, 127.9, 127.8, 127.5, 113.5, 80.2, 80.0, 79.3, 74.7, 72.9, 72.4, 55.3, 45.1; HRMS *m*/*z* (EI) calcd for $C_{34}H_{34}O_4$ $(M)^+$ 506.2457, found 506.2446.

5-((1*S*,4*S*,5*R*,6*R*)-4,5,6-Tri(benzyloxy)cyclohex-2-enyl)benzo-[*d*][1,3]dioxole (30c). 94%; R_f 0.59 (25% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 7.41−7.28 (m, 15H), 6.81 (m, 1H), 6.78 (br s, 1H), 6.75 (dd, J = 8.1, 1.5 Hz, 1H), 5.96 (s, 2H), 5.88 (ddd, J = 10.1, 2.4, 1.3 Hz, 1H), 5.73 (ddd, J = 10.1, 4.7, 1.9 Hz, 1H), 4.79−4.64 (m, 6H), 4.16 (m, 1H), 3.81 (m, 2H), 3.73 (app t, J = 4.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 147.6, 146.7, 139.0, 138.8, 132.5, 129.1, 128.6, 128.4, 128.1, 128.0, 127.8, 127.7, 127.6, 123.5, 110.9, 107.9, 101.1, 80.1, 80.0, 79.2, 74.8, 73.1, 72.5, 45.6; HRMS *m*/*z* (ESI) calcd for $C_{34}H_{32}O_5$ $(M)^+$ 520.2250, found 520.2265.

4-((1*S*,4*S*,5*R*,6*R*)-4,5,6-Tri(benzyloxy)cyclohex-2-enyl)-1,2-dimethoxybenzene (30d). 81%; R_f 0.58 (25% EtOAc/hexanes); $[\alpha]^{22}_D$ −93.7 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.60−7.19 (m, 15H), 6.81 (d, J = 11.8 Hz, 3H), 5.91 (dd, J = 9.9, 2.5 Hz, 1H), 5.79 (ddd, J = 9.9, 4.7, 1.6 Hz, 1H), 4.90−4.61 (m, 6H), 4.17 (m, 1H), 3.88 (s, 3H), 3.82 (m, 3H), 3.75 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 148.4, 148.0, 138.9, 138.8, 138.7, 131.0, 129.3, 128.4, 128.3, 128.0, 127.9, 127.7, 127.5, 122.1, 113.9, 110.7, 79.9, 79.8, 79.5, 74.5, 73.0, 72.1, 55.9, 55.8, 45.2; HRMS *m*/*z* (ESI) calcd for $C_{36}H_{36}O_5Na$ $(M + Na)^+$ 559.2454, found 559.2459.

6-((1*S*,4*S*,5*R*,6*R*)-4,5,6-Tri(benzyloxy)cyclohex-2-enyl)-4-methoxybenzo[*d*][1,3]dioxole (30e). 96%; R_f 0.57 (25% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 7.42−7.31 (m, 15H), 6.54 (d, J = 1.4 Hz, 1H), 6.47 (d, J = 1.4 Hz, 1H), 5.98 (s, 2H), 5.93 (ddd, J = 9.9, 2.8, 1.1 Hz, 1H), 5.78 (ddd, J = 9.9, 4.7, 1.7 Hz, 1H), 4.80−4.68 (m, 6H), 4.18 (m, 1H), 3.85 (m, 2H), 3.83 (s, 3H), 3.73 (app t, J = 4.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 148.6, 143.1, 138.9, 138.8, 134.3, 133.2, 129.1, 128.5, 128.4, 128.0, 127.9, 127.7, 127.6, 127.5, 110.0, 104.4, 101.5, 79.9, 79.8, 79.3, 74.6, 73.2, 72.2, 56.6, 45.7; HRMS *m*/*z* (ESI) calcd for $C_{35}H_{34}O_6$ $(M)^+$ 550.2355, found 550.2356.

1-((1*S*,4*S*,5*R*,6*R*)-4,5,6-Tri(benzyloxy)cyclohex-2-enyl)-4-fluorobenzene (30f). 73%; R_f 0.68 (25% EtOAc/hexanes); $[\alpha]^{22}_D$ −53.0 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.61−7.25 (m, 15H), 7.07 (t, J = 8.5 Hz, 4H), 5.97 (dd, J = 10.1, 2.5 Hz, 1H), 5.79 (ddd, J = 10.1, 4.7, 1.6 Hz, 1H), 4.90−4.65 (m, 6H), 4.23 (m, 1H), 4.06−3.78 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 138.7, 131.8, 131.7, 128.8, 128.6, 128.4, 128.1, 128.0, 127.8, 127.6, 115.0, 114.7, 79.8, 79.7, 79.0, 74.6, 73.0, 72.5, 45.0; HRMS *m*/*z* (ESI) calcd for $C_{33}H_{31}O_3FNa$ $(M + Na)^+$ 517.2155, found 517.2147.

1-((1*S*,4*S*,5*R*,6*R*)-4,5,6-Tri(benzyloxy)cyclohex-2-enyl)-4-chlorobenzene (30g). 77%; R_f 0.51 (25% EtOAc/hexanes); $[\alpha]^{22}_D$ −130.8 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.56−7.05 (m, 19H), 5.92 (dd, J = 9.9, 2.5 Hz, 1H), 5.73 (ddd, J = 9.9, 4.7, 1.6 Hz, 1H), 4.98−4.56 (m, 6H), 4.15 (m, 1H), 3.90−3.71 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 138.8, 138.6, 138.5, 137.2, 132.8, 131.6, 128.7, 128.5, 128.4, 128.1, 127.9, 127.8, 79.7, 79.6, 78.8, 74.6, 73.0, 72.5, 45.1; HRMS *m*/*z* (ESI) calcd for $C_{33}H_{31}O_3ClNa$ $(M + Na)^+$ 533.1859, found 533.1860.

Compound 31. To a solution of **30c** (0.114 g, 0.22 mmol) in 5 mL of a mixture of acetone−H_2O (9:1) was added NMO (0.036 g, 0.26 mmol) and 2.5% OsO_4 in *tert*-butyl alcohol (0.224 g solution, 0.022 mmol). The mixture was stirred overnight, then quenched with 10% $NaHSO_3$ (1 g), diluted with water (20 mL), extracted with ether (3 × 20 mL), and dried ($MgSO_4$). After the removal of the solvent the crude diol was dissolved in DMF (5 mL). 2,2-Dimethoxypropane (0.046 g, 0.44 mmol) and TsOH (0.0023 g, 0.022 mmol) were added and the reaction mixture was stirred for 3 h at room temperature. The mixture was diluted with water (30 mL), extracted with ether (3 × 30 mL), and dried ($MgSO_4$). After the removal of the solvent the residue was chromatographed (25% EtOAc/hexanes). The pure acetonide (0.090 g) was dissolved in MeOH (10 mL) and hydrogenolyzed overnight (50 psi H_2, 10% Pd/C). The resulting solution was filtered through a layer of Celite and the solvent was removed to give pure **31** (0.049 g, 69% from **30c**); ^{1}H NMR ($CDCl_3$) δ 6.82 (d, J = 1.4 Hz, 1H), 6.79 (d, J = 8.0 Hz, 1H), 6.73 (dd, J = 8.0, 1.4 Hz, 1H), 5.93 (s, 2H), 4.58 (dd, J = 6.6, 6.1 Hz, 1H), 4.31 (dd, J = 6.9, 6.1 Hz, 1H), 3.94 (dd, J = 5.5, 3.9 Hz, 1H), 3.81 (dd, J = 8.0, 6.9 Hz, 1H), 3.66 (dd, J = 8.0, 5.5 Hz, 1H), 3.30 (dd, J = 6.6, 3.9 Hz, 1H), 1.48 (s, 3H), 1.34 (s, 3H); ^{1}H NMR (D_2O, 45 °C) δ 7.17 (d, J = 1.7 Hz, 1H), 7.15 (d, J = 8.0 Hz, 1H), 7.09 (dd, J = 8.0, 1.7 Hz, 1H), 6.21 (s, 2H), 5.02 (dd, J = 8.5, 7.2 Hz, 1H), 4.58 (dd, J = 8.5, 7.2 Hz, 1H),

4.14 (dd, J = 4.4, 4.1 Hz, 1H), 4.00 (dd, J = 9.1, 8.8 Hz, 1H), 3.82 (dd, J = 9.1, 4.1 Hz, 1H), 3.44 (dd, J = 8.8, 4.4 Hz, 1H), 1.72 (s, 3H), 1.62 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 148.1, 147.0, 131.4, 122.3, 109.6, 109.1, 108.5, 101.2, 78.7, 75.9, 75.1, 74.3, 74.0, 46.5, 28.0, 25.5; HRMS *m*/*z* (ESI) calcd for $C_{16}H_{20}O_7$ $(M)^+$ 324.1209, found 324.1215.

General Procedure for the Preparation of the (1*R*,2*R*,3*S*,6*R*)-6-Aryl-4-cyclohexene-1,2,3-triol (8a−e). NH_3 gas was liquefied at −78 °C in two 50 mL flasks. The first flask was charged with chopped Li (0.2 g, 28 mmol), while compound **30a**−**e** (0.1 mmol) in THF (5 mL) was added to the second one. After the complete dissolution of Li, the deep blue solution was added dropwise via cannula to the compound **30a**−**e** until the blue color persisted for 15 s. The reaction mixture was quenched with dry NH_4Cl (0.2 g, 3.7 mmol) and allowed to stand at room temperature until the complete evaporation of NH_3. The residue was diluted with water (20 mL) and extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with brine and dried with $MgSO_4$. The solvent was removed, and residue was dissolved in dry methanol. Activated carbon was added to the solution. After the solution was stirred for 5 min, the carbon was filtered off with a Celite pad and solution was concentrated under reduced pressure. Lyophilization of its aqueous solution affords pure compounds **8a**−**e** as powders.

(1*R*,2*R*,3*S*,6*R*)-6-Phenyl-4-cyclohexene-1,2,3-triol (8a). 85%; R_f 0.36 (20% MeOH/EtOAc); $[\alpha]^{28}_D$ −304.0 (*c* 1, MeOH); ^{1}H NMR (D_2O) δ 7.47−7.24 (m, 5H), 5.89−5.73 (m, 2H), 4.21 (dd, J = 7.4, 1.6 Hz 1H), 3.95 (dd, J = 10.7, 6.6 Hz, 1H), 3.84 (app t, J = 6.0 Hz, 1H), 3.55 (dd, J = 10.7, 7.7 Hz, 1H); ^{13}C NMR (D_2O) δ 138.0, 130.6, 129.1, 128.6, 128.5, 127.5, 72.8, 72.7, 70.7, 47.5; HRMS *m*/*z* (ESI) calcd for $C_{12}H_{14}O_3Na$ $(M + Na)^+$ 229.0835, found 229.0834.

(1*R*,2*R*,3*S*,6*R*)-6-Methoxyphenyl-4-cyclohexene-1,2,3-triol (8b). 85%; R_f 0.27 (20% MeOH/EtOAc); $[\alpha]^{23}_D$ −220.0 (*c* 1, MeOH); ^{1}H NMR (D_2O) δ 7.25 (d, J = 8.0 Hz, 2H), 7.02 (d, J = 8.0 Hz, 2H), 5.89−5.73 (m, 2H), 4.23 (d, J = 7.2, Hz 1H), 3.93 (m, 2H), 3.85 (s, 3H), 3.78−3.53 (m, 1H); ^{13}C NMR (D_2O) δ 158.2, 131.7, 130.5, 128.9, 113.9, 72.9, 72.7, 70.8, 55.6, 46.7; HRMS *m*/*z* (ESI) calcd for $C_{13}H_{16}O_4Na$ $(M + Na)^+$ 259.0940, found 259.0936.

(1*R*,2*R*,3*S*,6*R*)-6-(Benzo[*d*][1,3]dioxol-5-yl)-4-cyclohexene-1,2,3-triol (8c). 61%; R_f 0.39 (10% MeOH/CH_2Cl_2); $[\alpha]^{23}_D$ −274.3 (*c* 1, MeOH); ^{1}H NMR (D_2O) δ 6.90 (d, J = 8.0 Hz, 1H), 6.83 (br s, 1H), 6.79 (br d, J = 8.0 Hz, 1H), 5.98 (s, 2H), 5.85−5.75 (m, 2H), 4.20 (br d, J = 7.4 Hz, 1H), 3.92 (app t, J = 8.8 Hz, 1H), 3.78 (m, 1H), 3.57 (app t, J = 8.8, Hz, 1H); ^{13}C NMR (D_2O) δ 147.2, 146.4, 131.9, 129.1, 128.8, 123.9, 110.9, 108.3, 101.2, 72.9, 72.7, 70.7, 47.2; HRMS *m*/*z* (ESI) calcd for $C_{13}H_{14}O_5Na$ $(M + Na)^+$ 273.0733, found 273.0735.

(1*R*,2*R*,3*S*,6*R*)-6-(3,4-Dimethoxyphenyl)-4-cyclohexene-1,2,3-triol (8d). 72%; R_f 0.45 (10% MeOH/CH_2Cl_2); $[\alpha]^{23}_D$ −221.2 (*c* 1, MeOH); ^{1}H NMR (D_2O) δ 7.03 (d, J = 8.2 Hz, 1H), 6.90 (br s, 1H), 6.87 (br d, J = 8.5, Hz 1H), 5.90−5.71 (m, 2H), 4.22 (d, J = 6.3 Hz, 1H), 4.03−3.73 (m, 2H), 3.86 (s, 6H), 3.65−3.52 (m, 1H); ^{13}C NMR (D_2O) δ 147.8, 147.5, 131.1, 129.1, 128.7, 123.1, 114.4, 111.7, 72.7, 70.7, 55.9, 47.0; HRMS *m*/*z* (ESI) calcd for $C_{14}H_{18}O_5Na$ $(M + Na)^+$ 289.1046, found 289.1052.

(1*R*,2*R*,3*S*,6*R*)-6-(4-Methoxybenzo[*d*][1,3]dioxol-6-yl)-4-cyclohexene-1,2,3-triol (8e). 93%; R_f 0.32 (10% MeOH/CH_2Cl_2); $[\alpha]^{23}_D$ −199.6 (*c* 1, MeOH); ^{1}H NMR (D_2O) δ 6.49 (s, 1H), 6.39 (s, 1H), 5.93 (s, 2H), 5.80 (d, J = 9.3 Hz, 1H), 5.75−5.65 (m, 1H), 4.18 (br d, J = 7.4 Hz, 1H), 3.86 (s, 3H), 3.77 (s, 1H), 3.73 (m, 1H), 3.55 (dd, J = 18.2, 8.2 Hz, 1H); ^{13}C NMR (D_2O) δ 160.0, 156.7, 148.3, 142.7, 141.0, 134.0, 132.7, 129.3, 128.5, 128.3, 110.4, 110.2, 108.6, 104.7, 101.7, 100.4, 72.7, 70.5, 56.7, 55.5, 47.5, 47.4; HRMS *m*/*z* (ESI) calcd for $C_{14}H_{16}O_6Na$ $(M + Na)^+$ 303.0839, found 303.0829.

General Procedure for the Preparation of the (1*R*,2*R*,3*R*,4*S*,5*R*,6*R*)-6-Arylcyclohexane-1,2,3,4,5-pentaol (9a−e). To a solution of olefin **30a**−**e** (0.22 mmol) in 5 mL of acetone−H_2O (9:1) was added NMO (0.036 g, 0.26 mmol) and a 2.5% solution of OsO_4 in *tert*-butyl alcohol (0.224 g solution, 0.022 mmol). The mixture was stirred at room temperature for 48 h, and then quenched with 10% $NaHSO_3$ (5 mL), diluted with water (20 mL), extracted with ether (3 × 20 mL), and dried ($MgSO_4$). After the solvent was removed, the crude diol was dissolved in MeOH (8 mL), and 10% Pd/C (75 mg, 0.06 mmol) was added. The suspension was stirred for 48 h with an H_2 balloon. The catalyst was filtered off with a Celite pad and solution was concentrated under reduced pressure. Redissolution of the material in H_2O followed by lyophilization gave pure compounds **9a**−**e** as powders.

(1*R*,2*R*,3*R*,4*S*,5*R*,6*R*)-6-Phenylcyclohexane-1,2,3,4,5-pentaol (9a). 77%; R_f 0.21 (2% MeOH/EtOAc); $[\alpha]^{25}_D$ 42.8 (*c* 1, MeOH); ^{1}H NMR (D_2O) δ 7.50−7.28 (m, 5H), 4.28−3.50 (m, 6H); ^{13}C NMR (D_2O) δ 137.7, 130.0, 128.8, 127.4, 74.0, 73.2, 72.2, 71.6, 71.2; HRMS *m*/*z* (ESI) calcd for $C_{12}H_{16}O_5Na$ $(M + Na)^+$ 263.0889, found 263.0891.

(1*R*,2*R*,3*R*,4*S*,5*R*,6*R*)-6-(4-Methoxyphenyl)cyclohexane-1,2,3,4,5-pentaol (9b). 95%; R_f 0.35 (10% MeOH/EtOAc); $[\alpha]^{28}_D$ 35.5 (*c* 1, MeOH); ^{1}H NMR (D_2O) δ 7.34 (d, J = 8.5 Hz, 2H), 7.00 (d, J = 8.5 Hz, 2H), 4.17 (m, 1H), 4.10 (d, J = 6.6 Hz, 1H), 3.98 (d, J = 8.0 Hz, 1H), 3.91 (d, J = 11.6 Hz, 1H), 3.89−3.76 (m, 1H), 3.84 (s, 3H), 3.53 (m, 1H); ^{13}C NMR (D_2O) δ 157.9, 131.3, 130.1, 114.2, 74.0, 73.2, 71.5, 71.2, 55.5; HRMS *m*/*z* (ESI) calcd for $C_{13}H_{18}O_6Na$ $(M + Na)^+$ 293.0995, found 293.1008.

(1*R*,2*R*,3*R*,4*S*,5*R*,6*R*)-6-(Benzo[*d*][1,3]dioxol-5-yl)cyclohexane-1,2,3,4,5-pentaol (9c). 95%; R_f 0.42 (10% MeOH/EtOAc); $[\alpha]^{28}_D$ 38.6 (*c* 1, MeOH); ^{1}H NMR (D_2O) δ 6.89 (s, 1H), 6.85 (s, 2H), 5.93 (s, 2H), 4.17 (m, 1H), 4.07 (app t, J = 8.0 Hz, 1H), 3.92 (m, 2H), 3.79 (app t, J = 8.0 Hz, 1H), 3.45 (dd, J = 10.5, 5.2 Hz, 1H); ^{13}C NMR (D_2O) δ 147.3, 146.0, 131.5, 123.3, 110.4, 108.6, 101.2, 73.8, 73.2, 71.8, 71.4; HRMS *m*/*z* (ESI) calcd for $C_{13}H_{16}O_7Na$ $(M + Na)^+$ 307.0788, found 307.0793.

(1*R*,2*R*,3*R*,4*S*,5*R*,6*R*)-6-(3,4-Dimethoxyphenyl)cyclohexane-1,2,3,4,5-pentaol (9d). 93%; R_f 0.46 (10% MeOH/EtOAc); $[\alpha]^{23}_D$ 44.7 (*c* 1, MeOH); ^{1}H NMR (D_2O) δ 7.04−6.96 (m, 3H), 4.22 (br s, 1H), 4.11 (app t, J = 6.6 Hz, 1H), 3.99−3.78 (m, 3H), 3.87 (s, 3H), 3.85 (s, 3H), 3.52 (m, 1H); ^{13}C NMR (D_2O) δ 148.0, 147.3, 130.8, 122.4, 114.3, 111.9, 73.9, 73.2, 71.6, 71.4, 55.9; HRMS *m*/*z* (ESI) calcd for $C_{14}H_{20}O_7Na$ $(M + Na)^+$ 323.1101, found 323.1095.

(1*R*,2*R*,3*R*,4*S*,5*R*,6*R*)-6-(4-Methoxybenzo[*d*][1,3]dioxol-5-yl)-cyclohexane-1,2,3,4,5-pentaol (9e). 95%; R_f 0.47 (10% MeOH/EtOAc); $[\alpha]^{28}_D$ 47.2 (*c* 1, MeOH); ^{1}H NMR (D_2O) δ 6.69 (s, 2H), 6.01 (s, 2H), 4.27 (s, 1H), 4.14 (m, 1H), 3.99−3.85 (m, 3H), 3.96 (s, 3H), 3.53 (m, 1H); ^{13}C NMR (D_2O) δ 148.6, 142.9, 133.9, 132.5, 110.1, 104.2, 101.8, 73.8, 73.2, 71.9, 71.6, 56.9; HRMS *m*/*z* (ESI) calcd for $C_{14}H_{18}O_8Na$ $(M + Na)^+$ 337.0893, found 337.0882.

General Procedure for the Preparation of the (1*S*,2*R*,3*R*,4*R*)-4-Arylcyclohexane-1,2,3-triol (10a−e). To a stirred solution of olefin **30a**−**e** (0.1 mmol) in THF−MeOH (9:1, 5 mL) was added 10% Pd/C (50 mg, 0.04 mmol). The suspension was stirred for 48 h with an H_2 balloon. The catalyst was filtered off with a Celite pad and solution was concentrated under reduced pressure. The residue was dissolved in ether (30 mL), washed with water (3 × 20 mL) and brine, dried ($MgSO_4$), and evaporated under reduced pressure. Redissolution of the material in H_2O followed by lyophilization gave pure compounds **10a**−**e** as powders.

(1*S*,2*R*,3*R*,4*R*)-4-Phenylcyclohexene-1,2,3-triol (10a). 90%; R_f 0.85 (20% MeOH/EtOAc); $[\alpha]^{26}_D$ 145.4 (*c* 1, MeOH); ^{1}H NMR (D_2O) δ 7.46−7.33 (d, J = 4.4 Hz, 4H), 5.32−5.23 (m, 1H), 3.84−3.92 (m, 2H), 3.79−3.71 (m, 1H), 3.28−3.21 (m, 1H), 2.18−1.64 (m, 4H); ^{13}C NMR (D_2O) δ 142.5, 129.1, 128.6, 126.7, 74.5, 73.2, 71.4, 43.4, 27.6, 22.3; HRMS *m*/*z* (ESI) calcd for $C_{12}H_{16}O_3Na$ $(M + Na)^+$ 231.0991, found 231.0990.

(1*S*,2*R*,3*R*,4*R*)-4-(4-Methoxyphenyl)cyclohexene-1,2,3-triol (10b). 95%; R_f 0.48 (10% MeOH/EtOAc); $[\alpha]^{28}_D$ 48.0 (*c* 1, MeOH); ^{1}H NMR (D_2O) δ 7.51 (d, J = 8.5 Hz, 2H), 7.15 (d, J = 8.8 Hz, 2H), 4.04 (m, 2H), 3.99 (s, 3H), 3.95 (m, 1H), 3.38 (m, 1H), 2.29−1.89 (m, 4H); ^{13}C NMR (D_2O) δ 157.7, 135.3, 130.4, 114.3, 74.7, 73.5,

71.7, 55.8, 42.7, 27.8, 22.7; HRMS *m*/*z* (ESI) calcd for $C_{13}H_{18}O_4Na$ $(M + Na)^+$ 261.1097, found 261.1093.

(1*S*,2*R*,3*R*,4*R*)-4-(Benzo[*d*][1,3]dioxol-5-yl)cyclohexene-1,2,3-triol (10c). 84%; R_f 0.55 (10% MeOH/EtOAc); $[\alpha]^{28}_D$ 41.9 (*c* 1, MeOH); ^{1}H NMR (D_2O) δ 6.98 (s, 1H), 6.92 (s, 2H), 5.99 (s, 2H), 4.12−4.75 (m, 3H), 3.21 (m, 1H), 2.21−1.62 (m, 4H); ^{13}C NMR (D_2O) δ 147.2, 145.6, 136.7, 122.1, 109.6, 108.4, 101.1, 74.6, 72.9, 71.2, 42.8, 27.7, 22.0; HRMS *m*/*z* (ESI) calcd for $C_{13}H_{16}O_5Na$ $(M + Na)^+$ 275.0889, found 275.0896.

(1*S*,2*R*,3*R*,4*R*)-4-(3.4-Dimethoxyphenyl)cyclohexene-1,2,3-triol (10d). 76%; R_f 0.46 (10% MeOH/EtOAc); $[\alpha]^{22}_D$ 29.7 (*c* 1, MeOH); ^{1}H NMR (D_2O) δ 6.96 (s, 3H), 4.20−3.73 (m, 3H), 3.85 (s, 3H), 3.83 (s, 3H), 3.19 (m, 1H), 2.22−1.62 (m, 4H); ^{13}C NMR (D_2O) δ 147.9, 146.8, 135.8, 121.4, 113.1, 111.9, 74.5, 73.1, 71.3, 55.9, 42.8, 27.7, 22.3; HRMS *m*/*z* (ESI) calcd for $C_{14}H_{20}O_5Na$ $(M + Na)^+$ 291.1203, found 291.1191.

(1*S*,2*R*,3*R*,4*R*)-4-(Methoxybenzo[*d*][1,3]dioxol-6-yl)cyclohexene-1,2,3-triol (10e). 95%; R_f 0.61 (10% MeOH/EtOAc); $[\alpha]^{28}_D$ 44.1 (*c* 1, MeOH); ^{1}H NMR (D_2O) δ 6.72 (s, 2H), 5.99 (s, 2H), 4.12−3.82 (m, 3H), 3.96 (s, 3H), 3.16 (m, 1H), 2.21−1.61 (m, 4H); ^{13}C NMR (D_2O) δ 148.4, 142.9, 137.8, 133.4, 108.5, 103.2, 101.6, 74.6, 72.6, 71.0, 56.8, 42.9, 27.8, 21.6; HRMS *m*/*z* (ESI) calcd for $C_{14}H_{18}O_6Na$ $(M + Na)^+$ 305.0995, found 305.0983.

Cell Culture. A human T cell leukemia cell line (Jurkat cells, Clone E6-1) was cultivated in RPMI-1640 medium supplemented with 10% (v/v) fetal bovine serum (FBS), 100 mg/L penicillin G, 100 mg/L streptomycin, 1.0 mM sodium pyruvate, 1.5 g/L sodium bicarbonate, and 4.5 g/L glucose at 37 °C in a humidified atmosphere with 10% CO_2. Cells were diluted at a ratio of 1:5 every 2−3 days.

Drugs. All compounds undergoing the drug screening were dissolved at 0.3 M dimethyl sulfoxide as a stock solution and diluted in DMSO just before use. The maximum final concentration of DMSO in medium was smaller than 0.1% (v/v).

Cell Counts. Jurkat control or drug treated cells were cultivated in a 24-well tissue culture plate. To examine the viability of treated Jurkat cells after appropriate culture for 20 h, 50 μL of 0.4% Trypan Blue stain was added to 50 μL of a sample cell suspension. Using a hemacytometer, both dead (Trypan Blue-positive) and live cells were counted four times. The results were then calculated and tabulated as percentage of dead cells. To examine the anti-proliferative effect of the tested compounds, growth curves were determined by a manual count method. After appropriate culture, viable cells were counted for up to 5 days by the Trypan Blue dye exclusion method.

Flow Cytometric Annexin-V/Propidium Iodide Assay. Flow cytometry was used to quantitatively measure apoptotic and necrotic rates. After being cultivated with medium alone (RPMI-1640 10%FBS) or medium containing 0.1% (v/v) DMSO, or one of the tested compounds at the indicated final concentration (0.5, 5, 15, 50, 100, and 300 μM) for 20 h, 3×10^5 Jurkat cells were centrifuged at 2200 rpm (400G) for 2 min. Supernatant was discarded and the remaining pellet was resuspended in 400 μL of Annexin Binding Buffer (ABB: Heinz-Hepes Buffer (HHB: 30 mM HEPES; 110 mM NaCl; 10 mM KCl; 10 mM glucose; 1 mM $MgCl_2$; pH 7.4) plus 9 mM $CaCl_2$) and centrifuged for 2 min at 2200 rpm. The supernatant was removed and the remaining pellet was resuspended in 200 μL of Annexin Binding Buffer (ABB). Then, cells in ABB were placed into an ice-cold bath and simultaneously fluorescently labeled with both 1 μL of propidium iodide (a 1 mg/mL stock solution in ABB was kept at −20 °C) and 2 μL of annexin-V FITC. After being incubated at 37 °C for 15 min, each labeled sample was transferred to a Falcon tube. Values of relative fluorescence intensity were measured and analyzed. The results were then calculated and tabulated as the percentage of apoptotic or necrotic cells.

Sulforhodamine B (SRB) Assay. A laboratory test measures cell growth inhibition. Jurkat cells in RPMI-1640 10% FBS were inoculated into 96 well plates in 100 μL and incubated for 24 h. Then, one plate was fixed in situ with 50 μL of 50% (w/v) trichloroacetic acid (TCA), to represent a measurement of the cell population at the time of drug addition. Jurkat cells in another plate were treated in triplicate with ether solvent (DMSO, 0.1% (v/v) final concentration) or with one of our compounds at the indicated final concentration (0.01, 0.1, 1, 10, 50, 100, 300, and 600 μM). Following drug addition, plates were incubated for an additional 48 h. After that, cells were fixed in situ by layering 50 μL of cold 50% (w/v) TCA directly on top of the incubation medium and incubated for an hour at 4 °C. The supernatant was discarded, and plates were washed five times with tap water and air-dried. Sulforhodamine B solution (200 μL) at 0.4% (w/v) in 1% acetic acid was added to each well, and plates were incubated for 30 min at room temperature. After staining, unbound dye was removed by washing five times with 1% acetic acid, and plates were air-dried. Bound stain was subsequently solubilized with 200 μL/well of 10 mM Tris buffer, pH 10.5, and absorbance was read on an automated plate reader at a wavelength of 490 nm.

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Supporting Information Available: General methods paragraph and copies of ^{1}H and ^{13}C NMR of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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