Sequential Ketyl−Olefin Coupling/β-Elimination Reactions Mediated by Samarium(II) Iodide

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Samarium(II) iodide (SmI_2) has been employed in an intramolecular sequential ketyl−olefin coupling/β-elimination reaction. The overall process results in the net addition of an alkenyl species to a ketone carbonyl. This novel protocol for the intramolecular delivery of an alkenyl moiety avoids the basic reaction conditions typical of nucleophilic additions that are mediated by alkenylmagnesium halides and alkenyllithium reagents. A high degree of stereocontrol is imparted in the SmI_2-mediated process as a result of the excellent facial selectivity conveyed in the initial ketyl−olefin coupling reaction. The relative asymmetric induction engendered in these addition reactions is complementary to more traditional nucleophilic addition reactions in that the alkenyl group is directed to the carbonyl center by an attached tether.

Introduction

The nucleophilic addition of organometallics such as alkenylmagnesium halides and alkenyllithium reagents to carbonyl compounds represents a powerful tool in synthetic organic chemistry.[1] However, nucleophilic addition reactions of these unsaturated organometallics are at times problematic. For example, the preparation of these organometallic species often requires special reaction conditions.[2] Additionally, the diastereoselectivity in the nucleophilic addition reaction is often low. Furthermore, because of the ability of these organometallic agents to function both as nucleophiles and as bases, enolate formation often competes with the nucleophilic addition reaction.[3] Some improvement in the yield of carbonyl addition of these alkenylmetallics has been realized by the use of Lewis acids such as $CeCl_3$[3] or the use of ultrasound techniques.[4] Additional modifications of these reagents involving the use of covalent chiral reagents[1] and organocuprates[5] have been introduced to provide increased stereocontrol and enhanced yield in the carbonyl addition reactions.

Other organometallic reagents have also been developed that are quite successful.[6] Thus, anhydrous chromium(II) chloride, in the presence of catalytic Ni(II), is able to reduce alkenyl halides and alkenyl triflates to provide an alkenylchromium species that participates in carbonyl additions. Initially described by Nozaki and coworkers[7] and later expanded upon by Kishi and coworkers,[8] the alkenylchromium reagents are particularly useful for the addition of alkenyl units to carbonyl compounds, especially aldehydes.

During the course of a previous investigation a novel radical-based protocol was discovered that resulted in the net addition of an alkenyl moiety to a carbonyl group. As outlined in Scheme 1, the SmI_2-promoted cyclization of the keto enol ether was anticipated to afford the oxabicyclo[3.3.0]octane. Instead, the reaction provided 2-(hydroxymethyl)-1-ethenylcyclopentan-1-ol in high yield and high diastereoselectivity even in the presence of an added proton source. The overall conversion thus involved a ketyl−olefin coupling between the ketone and the enol ether (Scheme 1). The organosamarium that was generated after ketyl−olefin coupling and subsequent reduction suffered β-elimination (instead of undergoing protonation) to generate the observed 2-(hydroxymethyl)-1-ethenylcyclopentan-1-ol. The observed stereocontrol in these ring-forming reactions has been extensively investigated previously and results from a cis-fused stereochemistry generated at the ring junction upon radical cyclization onto a preexisting five-, six-, or seven-membered ring.[9]

Realizing that this novel protocol represented an alternative method to perform a net carbonyl addition reaction with an alkenyl unit, we sought to explore the scope and limitations of this internal alkenyl delivery process. There were several perceived advantages to pursuing this line of research. For example, the system developed would provide a novel pathway for the directed addition of an alkenyl group to a carbonyl moiety (eq 1). The SmI_2-mediated procedure was anticipated to allow excellent stereocontrol in the net delivery of the alkenyl species because the stereochemistry of the product would be established in a preliminary 5-exo or 6-exo ketyl−olefin coupling reaction.[9c] Notably, the introduction of the alkenyl species would be directed by a tether to the reaction center. This stereochemical outcome would be

(1) O'Neill, B. T. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: New York, 1991; Vol. 1, pp 397−458.
(2) (a) Newman, H. *Tetrahedron Lett.* **1971**, 4571. (b) Jacob P., III.; Brown, H. C. *J. Org. Chem.* **1977**, *42*, 579.
(3) (a) Thies, R. W.; Daruwala, K. P. *J. Org. Chem.* **1987**, *52*, 3798. (b) Cowan, D. O.; Mosher, H. S. *J. Org. Chem.* **1962**, *27*, 1.
(4) Luche, J.-L.; Damianco, J.-C. *J. Am. Chem. Soc.* **1980**, *102*, 7926.
(5) (a) Grootaert, W. M.; De Clercq, P. J. *Tetrahedron Lett.* **1982**, *23*, 3291. (b) Whitesides, G. M.; Casey, C. P.; Krieger, J. K. *J. Am. Chem. Soc.* **1971**, *93*, 1379. (c) Patterson, J. W., Jr.; Fried, J. H. *J. Org. Chem.* **1974**, *39*, 2506.
(6) Saccomano, N. A. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: New York, 1991; Vol. 1, pp 193−201 and references therein.
(7) Takai, K.; Kimura, K.; Kuroda, T.; Hiyama, T.; Nozaki, H. *Tetrahedron Lett.* **1983**, *24*, 5281. (b) Takai, K.; Tagashira, M.; Kurada, T.; Shima, K. O.; Utimoto, K.; Nozaki, H. *J. Am. Chem. Soc.* **1986**, *108*, 6048.
(8) (a) Jin, H.; Uenishi, J.-i.; Christ, W. J.; Kishi, Y. *J. Am. Chem. Soc.* **1986**, *108*, 5644.
(9) (a) Molander, G. A.; Shakya, S. R. *J. Org. Chem.* **1996**, *61*, 5885. (b) Molander, G. A.; McKie, J. A. *J. Org. Chem.* **1995**, *60*, 872. (c) Molander, G. A.; McKie, J. A. *J. Org. Chem.* **1992**, *57*, 3132.

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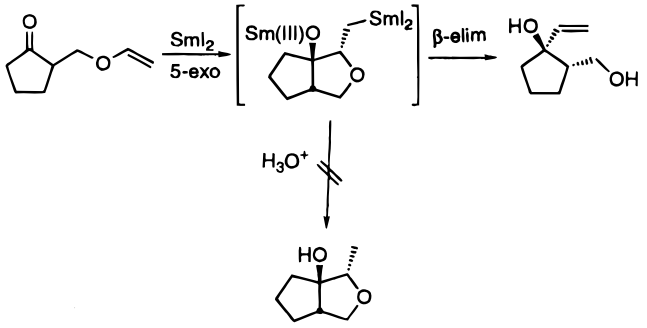
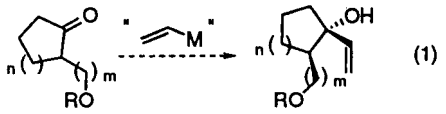
Scheme 1



complementary to alkenylmetallic carbonyl addition reactions.[10] Additionally, the SmI_2-mediated protocol would not suffer the consequences of a strongly basic reaction mixture and hence substrate enolization would not be problematic as with magnesium- and lithium-based organometallics.



(1)

Results and Discussion

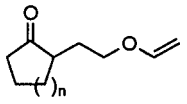
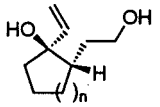
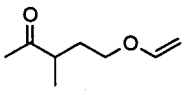
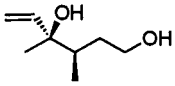
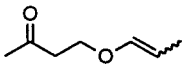
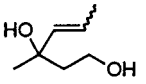
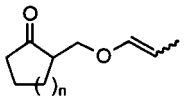
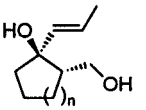
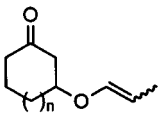
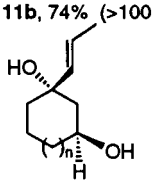
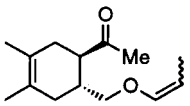
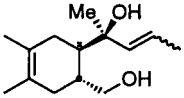
Initially, a series of keto−enol ether substrates was prepared to investigate the potential of this novel alkenyl addition protocol. Substrates **3a**−**c** (entries 1 and 2, Table 1) were prepared in two steps from commercially available starting materials by alkylation of the appropriate β-keto ester **1** with 2-chloroethyl vinyl ether and catalytic NaI in DMF solvent.[11] Subsequent decarboxylation of the β-keto ester **2** with LiI afforded the desired vinyl ether **3** in good yield (Scheme 2).[12]

The keto enol ether **6** (entry 3, Table 1) was prepared by acid-catalyzed conjugate addition of allyl alcohol to methyl vinyl ketone to afford allyl ether **5**. Isomerization of **5** to the enol ether **6** was accomplished with Wilkinson's catalyst, $ClRh(PPh_3)_3$ (Scheme 3).[13] The isomerization with Wilkinson's catalyst generally afforded a 1−2:1 mixture of *E* and *Z* olefins, respectively.

Attempts to prepare the remainder of the desired substrates (entries 4−6, Table 1) via this short protocol were thwarted because the acid-catalyzed conjugate addition reaction of allyl alcohol would proceed only with monosubstituted enones. The requisite substrates **10a**−**c** in entry 4, Table 1, were thus prepared from the readily available keto esters **1a**−**c** as outlined in Scheme 4. In each instance the keto ester **1** was protected as the ethylene glycol acetal[14] and subsequently ester **7** was reduced with $LiAlH_4$ in THF.[15] The alcohol **8** was *O*-alkylated with allyl bromide under standard reaction conditions[16] and then subjected to an acidic aqueous workup which afforded allyl ether **9** directly. The resultant allyl ether **9** was isomerized to the enol ether **10** with Wilkinson's catalyst, as above, to afford the desired substrates **10a**−**c**, entry 4.

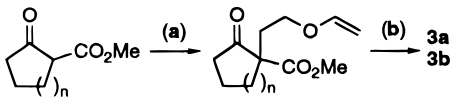
Substrates **14** in entry 5 were prepared similarly from the allyl ether generated in two steps from the cycloalkane-1,3-diol as outlined in Scheme 5. The cycloalkane-1,3-diol was monoalkylated with allyl bromide, and the resultant alcohol **12** was subjected to a Swern oxidation,[17]

Table 1. Sequential Ketyl-Olefin Coupling/β-Elimination Reactions Mediated by SmI_2

entry	substrate	product % yield (ds)
1	 **3a**, n = 1 **3b**, n = 3	 **4a**, 50% (50 : 1)[d,e] **4b**, 71% (4 : 1)[d,e]
2	 **3c**	 **4c**, 77% (2.7 : 1)[d,e]
3[a]	 **6**	 **7**, 85% (6 : 1)[b,e]
4[a]	 **10a**, n = 1 **10c**, n = 2 **10b**, n = 3	 **11a**, 92% (>100 : 1)[c,d,f] **11c**, 93% (>100 : 1)[c,d,f] **11b**, 74% (>100 : 1)[c,d,f]
5[a]	 **14a**, n = 1 **14b**, n = 0	 **15a**, 74% (>100 : 1)[c,d,f] complex
6[a]	 **19**	 **20**, 83% (5 : 1 : 1 : 1)[f]

[a] The reaction was performed on a 1−2:1 mixture of diastereomeric olefin isomers. [b] The ratios refer to olefin diastereoselectivity. [c] A >20:1 mixture of diastereomeric olefins (^1H NMR) was obtained. [d] The ratios refer to diastereoselectivity at the newly created stereogenic center. [e] The reaction was performed at rt. [f] The reaction was performed at 60 °C.

Scheme 2

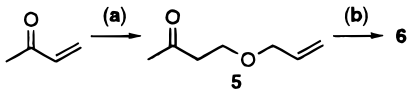


1a, n = 1 **1b**, n = 3 **2a** **2b**

(a) $Cl(CH_2)_2OCH{=}CH_2$, NaH, DMF, cat. NaI, 60 °C
(b) LiI, HMPA, 120 °C

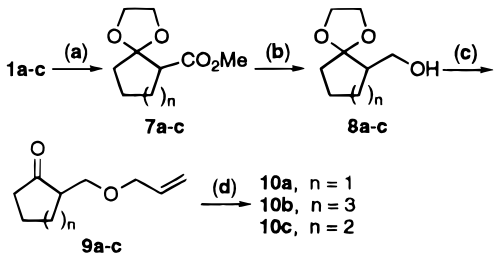
(10) Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307.
(11) Molander, G. A.; Harris, C. R. *J. Am. Chem. Soc.* **1995**, *117*, 3705.
(12) Bunce, R. A.; Dowdy, E. D.; Jones, P. B.; Holt, E. M. *J. Org. Chem.* **1993**, *58*, 7143.
(13) (a) Gent, P. A.; Gigg, R. *J. Chem. Soc., Chem. Commun.* **1974**, 277. (b) Corey, E. J.; Suggs, J. W. *J. Org. Chem.* **1973**, *38*, 3224.
(14) Molander, G. A.; Harris, C. R. *J. Am. Chem. Soc.* **1996**, *118*, 4059−4071.
(15) Brown, W. G. *Org. React.* **1951**, *6*, 469.
(16) Hart, D. J.; Hong, W.-P.; Hsu, L.-Y. *J. Org. Chem.* **1987**, *52*, 4665.

Scheme 3



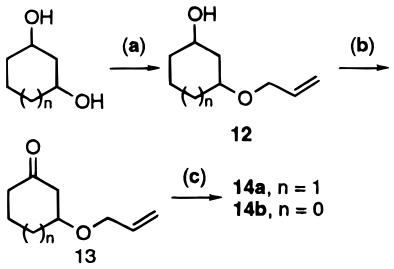
(a) CH_2=$CHCH_2OH$, cat. H_2SO_4, 18 h
(b) $ClRh(PPh_3)_3$, EtOH-H_2O (9:1)

Scheme 4



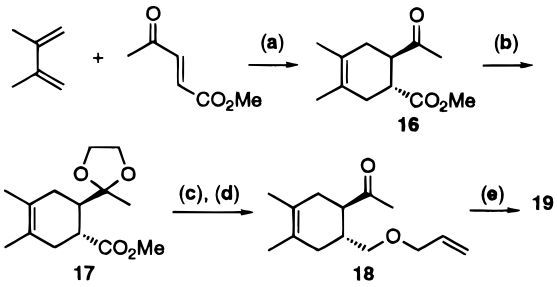
(a) $HO(CH_2)_2OH$, cat. *p*-TsOH (b) $LiAlH_4$, THF, rt
(c) allyl bromide, NaH, THF; then 10% HCl, 5 min
(d) $ClRh(PPh_3)_3$, EtOH-H_2O (9:1)

Scheme 5



(a) allyl bromide, NaH, THF (b) Swern oxidation
(c) $ClRh(PPh_3)_3$, (9:1) EtOH-H_2O

Scheme 6



(a) $AlCl_3$, -78 °C to rt (b) $HO(CH_2)_2OH$, *p*-TsOH
(c) $LiAlH_4$, THF, rt (d) allyl bromide, NaH, THF; 10% HCl
(e) $ClRh(PPh_3)_3$, (9:1) EtOH-H_2O

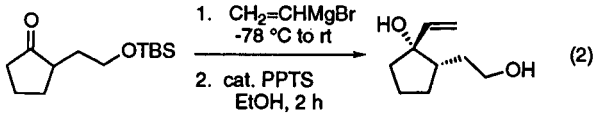
affording the requisite allyl ether **13**. The latter isomerized readily upon treatment with Wilkinson's catalyst to provide the requisite enol ethers **14a,b**, entry 5.

Finally, substrate **19** in entry 6 was prepared in several steps beginning with the Diels–Alder adduct **16** derived from the reaction of 2,3-dimethyl-1,3-butadiene and methyl 4-oxo-2(*E*)-pentenoate and catalytic $AlCl_3$ (Scheme 6).[18] The resultant ketone **16** was protected as the ethylene glycol acetal, and the ester **17** was reduced to the alcohol with $LiAlH_4$. The alcohol was *O*-alkylated with allyl bromide, and the resultant allyl ether **18** was isomerized to the requisite enol ether **19**, entry 6, upon treatment with Wilkinson's catalyst.

Thus prepared, these substrates were employed to examine the intramolecular alkenyl transfer reactions promoted by SmI_2. The results of this study are presented in Table 1. Optimized reaction conditions for this cyclization–elimination protocol were determined to involve the dropwise addition of the enol ether substrate (0.03–0.05 M in THF) to a solution of SmI_2 (5 equiv, 0.12 M in THF) containing 5 equiv of HMPA. In substrates where the alkenyl group did not contain a substituent at the terminal position, performing the reaction at ambient temperature met with success. However, for substrates in which the alkenyl group was terminally substituted, optimum yields of the alkenyl transfer product could be obtained only if the substrate was added to a solution of SmI_2–HMPA in THF heated at 60 °C. Performing transfer reactions with more highly substituted alkenyl units at ambient temperatures resulted in the isolation of products resulting from β-hydride elimination instead of elimination of the primary alcohol. In either case, the transfer reactions were found to be complete immediately upon addition of the starting enol ether substrates to the SmI_2 solution.

Substrates **3a,b** (entry 1) were converted in fair yield to afford the desired alkenyl transfer products **4a,b** with excellent diastereoselectivity when the radical cyclization event took place upon the preexisting five-membered cyclopentanone **3a**. Cyclization onto the preexisting seven-membered ring **3b** afforded only a 4:1 mixture of diastereomeric products. The stereochemistry in these transformations was assigned on the basis of previous cyclizations employing the all-carbon cyclization analogues.[9] The major diastereomers observed in the 5-exo and 6-exo ketyl–olefin cyclization reactions were those with the developing radical center trans to the alkoxy group. The formation of this isomer avoids unfavorable stereoelectronic interactions in the radical cyclization.[19]

The anticipated relative asymmetric induction was further confirmed by independent synthesis of the diastereomer of **4a**, (1*R**,2*R**)-1-ethenyl-2-(2-hydroxyethyl)-cyclopentan-1-ol, by addition of vinylmagnesium bromide[10] to the requisite ketone and subsequent deprotection as outlined in eq 2.



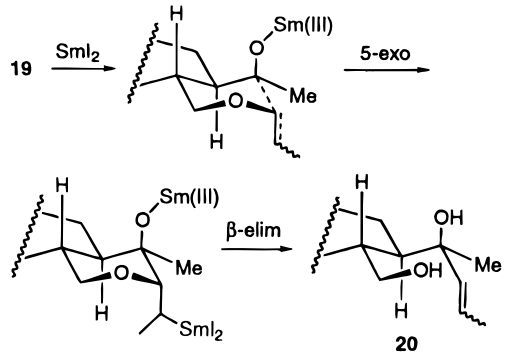
Cyclization of substrate **3c** in entry 2 likewise proceeded in good yield to afford the alkenyl transfer product **4c**, albeit with fairly low diastereoselectivity. The stereochemistry of the major diastereomer in this cyclization/elimination event was not proven rigorously, but was assigned on the basis of comparison with the all-carbon cyclization analogue. It was anticipated that a moderate level of asymmetric induction would be evident in the alkenyl group transfer as the previously investigated all-carbon substrate had afforded a 6:1 mixture of diastereomeric products.[9b]

In general, the yields and diastereoselectivities of these alkenyl transfer reactions were higher in instances where the ketyl–olefin reaction transpired via a 5-exo-trig process. This is clearly evident in entries 3–5, where the desired alkenyl transfer products (**7**, **11a–c**, **15a**)

(17) (a) Omura, K.; Swern, D. *Tetrahedron* **1978**, *34*, 1651. (b) Mancuso, A. J.; Huang, S.-L.; Swern, D. J. *J. Org. Chem.* **1978**, *43*, 2480.

(18) Angelli, E. C.; Fringnelli, F.; Guo, M.; Minuti, L.; Taticchi, A.; Wenkert, E. *J. Org. Chem.* **1988**, *53*, 859.

Scheme 7



were obtained with excellent diastereoselectivity and in high yield. The diastereomers in entry 3, performed at ambient temperature, were a mixture of cis and trans olefin isomers resulting from incomplete stereocontrol in the β-elimination step. Entries 4 and 5 depict substrates exhibiting excellent stereocontrol created by the initial ketyl−olefin coupling sequence (>100:1 diastereoselectivity at the newly created stereogenic center as determined by fused silica capillary GC). The diastereoselectivity in the β-elimination step for terminally substituted olefins in this sequential process was determined to be temperature dependent. For example, the alkenyl transfer reactions for entries 4 and 5, performed at 60 °C, showed enhanced diastereoselectivity in the β-elimination step (>20:1 by ^{1}H NMR) as compared to diastereomeric ratios of 5−6:1 for the trans olefin isomer in reactions performed at ambient temperature. The cyclization product resulting from the cyclohexanone derivative **14a** in entry 5 afforded excellent 1,3-asymmetric induction in the alkenyl delivery. Such diastereoselectivities cannot be readily achieved through traditional carbonyl addition methods. The sequential cyclization event failed for the cyclopentanone **14b** in entry 5. In this example, the 5-exo ketyl−olefin cyclization did not proceed and, instead, the reaction provided an intractable mixture of products. The major diastereomeric product depicted in each entry assumes that the ketyl−olefin coupling reactions proceed through transition structures similar to those previously reported.[9]

Finally, the level of asymmetric induction for substrate **19** (entry 6) was investigated. The keto−enol ether **19** in this example cyclized in excellent yield but only fair diastereoselectivity to afford a 5:1:1:1 mixture of diastereomers inseparable by flash column chromatography. The derived products in this cyclization−elimination sequence appear to result from incomplete stereocontrol in both the 6-exo ketyl−olefin coupling reaction and the β-elimination reaction. By comparison with the previously investigated all-carbon analogue,[9c] the major diastereomer **20** is expected to be that depicted in Table 1, entry 6. The asymmetric induction anticipated in the sequential cyclization-elimination process in entry 6 is likely to proceed as outlined in Scheme 7.[9b]

Conclusion

The ketyl−olefin cyclization/β-elimination reaction described herein provides a novel method for the introduction of an alkenyl moiety to a carbonyl species in high yield while maintaining an excellent degree of stereocontrol. The method is complementary in many ways to the more familiar methods of nucleophilic alkenyl addition to carbonyl compounds. For example, stereochemical complementarity is observed because of the directed addition of the alkenyl group to the carbonyl through a tethered unit. Higher diastereoselectivities often result. Additionally, more traditional methods often suffer from enolization of the substrate carbonyl species. The SmI_2-mediated net alkenyl addition protocol developed herein avoids the strongly basic, nucleophilic reaction conditions typical of the traditional organometallic alkenyl addition reactions. Finally, this protocol permits the introduction of trans-substituted alkenyl groups to carbonyl species by use of substituted enol ethers in the initial ketyl−olefin coupling reaction.

We are currently investigating this novel method for the construction of more elaborate ring systems in another SmI_2-mediated sequential process.

Experimental Section

Reagents. Tetrahydrofuran (THF) was distilled immediately prior to use from benzophenone ketyl under Ar. Samarium metal was purchased from Cerac Inc., Milwaukee, WI, and was stored under an inert atmosphere. CH_2I_2 was purchased from Aldrich Chemicals and was distilled prior to use and stored over copper turnings under an inert atmosphere. Standard benchtop techniques were employed for handling air-sensitive reagents,[20] and all reactions were carried out under argon.

1-Ethenyl-2-(2-hydroxyethyl)cycloheptan-1-ol (4b). General Procedure for the Alkenyl Transfer Reactions. Samarium metal (0.15 g, 1.00 mmol) and CH_2I_2 (0.24 g, 0.90 mmol) in 15 mL of dry THF were stirred together vigorously for 2 h. HMPA (1.34 g, 7.50 mmol) was added to the deep blue-green SmI_2 solution to afford a deep violet reaction mixture. **3b** (0.116 g, 0.64 mmol) was added dropwise via cannula over 1.0 h as a 0.03 M solution in THF to the SmI_2−HMPA−THF solution. TLC analysis of the reaction mixture after the substrate addition was finished revealed the complete consumption of the starting keto olefin and formation of a major, lower R_f product. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ and subjected to an aqueous workup. The desired diols **4b** (39.2 mg, 0.21 mmol, a 4:1 mixture of diastereomers) were isolated in 71% combined yield after flash column chromatography with 50% EtOAc/hexanes: (low R_f, minor) ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.95 (dd, J = 10.9, 17.2 Hz, 1H), 5.25 (dd, J = 0.4, 17.2 Hz, 1H), 5.09 (dd, J = 1.29, 10.9 Hz, 1H), 3.73 (m, 1H), 3.58 (m, 1H), 2.02 (bs, 2H), 1.81 (m, 2H), 1.70 (m, 1H), 1.69−1.57 (m, 4H), 1.56 (m, 1H), 1.43−1.22 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.44, 112.19, 78.21, 61.64, 45.84, 43.40, 36.35, 30.70, 29.95, 29.83, 21.62; IR (neat) 3353.4, 1681.7 cm^{-1}; HRMS calcd for $C_{11}H_{20}O_2$ 184.1463, found 184.1471; LRMS (EI$^+$) m/z 184 (10), 167 (53), 149 (100), 137 (62), 123 (22), 109 (41), 97 (40), 83 (98), 70 (62), 55 (83); (high R_f, major) ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.92 (dd, J = 17.4, 10.8 Hz, 1H), 5.21 (dd, J = 17.37, 1.19 Hz, 1H), 5.04 (dd, J = 10.8, 1.19 Hz, 1H), 3.71 (m, 1H), 3.59 (m, 1H), 1.85 (m, 2H), 1.78 (m, 2H), 1.71−1.62 (m, 5H), 1.57 (m, 1H), 1.48−1.42 (m, 3H), 1.34 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.45, 110.89, 77.13, 60.74, 44.49, 41.82, 34.08, 28.83, 28.33, 26.89, 21.35; IR (neat) 3389.9, 1651.7 cm^{-1}; HRMS calcd for $C_{11}H_{20}O_2$ 184.1463, found 184.1466; LRMS (EI$^+$) m/z 184 (13), 167 (49), 149 (72), 139 (100), 109 (42), 97 (30), 83 (98), 70 (61), 55 (72).

(1*R,2*S**)-1-Ethenyl-2-(2-hydroxyethyl)cyclopentan-1-ol (4a)** was prepared from **3a** according to the general procedure outlined for the preparation of **4b** to afford the desired diol as a single diastereomeric product (TLC and ^{1}H

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NMR) in 50% yield after flash column chromatography with 50% EtOAc/hexanes: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.98 (dd, J = 10.9, 17.3 Hz, 1H), 5.26 (dd, J = 1.49, 17.3 Hz, 1H), 5.14 (dd, J = 1.39, 10.92 Hz, 1H), 3.77 (m, 1H), 3.59 (ddd, J = 10.7, 9.23, 4.37 Hz, 1H), 2.24 (bs, 2H), 1.99 (m, 1H), 1.91 (m, 1H), 1.87−1.75 (m, 3H), 1.62 (m, 2H), 1.44 (m, 1H), 1.35 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.39, 112.50, 82.03, 62.76, 49.31, 39.61, 32.76, 30.33, 20.38; IR (neat) 3389.8, 1643.6 cm^{-1}; HRMS calcd for $C_9H_{16}O_2$ 156.1150, found 156.1128; LRMS (EI$^+$) m/z 156 (10), 138 (100), 111 (42), 83 (43), 70 (49), 55 (98), 41 (39), 27 (61), 18 (71).

(3*R,4*R**)/(3*R**,4*S**)-3,4-Dimethyl-5-hexene-1,4-diol (4c) (major/minor)** was prepared from **3c** according to the general procedure outlined for the preparation of **4b** to afford the desired 1,4-diol as a 2.7:1 mixture of diastereomers inseparable by chromatography in 77% combined yield after an aqueous workup and flash column chromatography with 45% EtOAc/hexanes: (major diastereomer) ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.91 (dd, J = 10.8, 17.3 Hz, 1H), 5.22 (d, J = 17.3 Hz, 1H), 5.10 (dd, J = 10.8, 1.29 Hz, 1H), 3.75 (m, 1H), 3.60 (m, 1H), 2.03 (bs, 2H), 1.79 (m, 1H), 1.70 (m, 1H), 1.37 (m, 1H), 1.28 (s, 3H), 0.91 (d, J = 6.95 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.38, 112.95, 75.38, 61.30, 40.74, 34.57, 26.49, 15.65; HRMS calcd for $C_7H_{13}O_2$ [M − CH_3]$^+$ 129.0916, found 129.0900; LRMS (EI$^+$) m/z 129 (10), 111 (100), 71 (95), 55 (32), 43 (98); (minor diastereomer) ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.91 (dd, J = 10.8, 17.4 Hz, 1H), 5.22 (d, J = 17.4 Hz, 1H), 5.08 (dd, J = 10.8, 1.29 Hz, 1H), 3.75 (m, 1H), 3.60 (m, 1H), 2.03 (bs, 2H), 1.79 (m, 1H), 1.70 (m, 1H), 1.42 (m, 1H), 1.23 (s, 3H), 0.91 (d, J = 6.95 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.05, 112.31, 75.28, 61.10, 34.95, 34.54, 23.78, 14.78; IR (neat) 3353.9, 1643.8 cm^{-1}.

(*E*)-3-Methyl-4-hexene-1,3-diol (7) was prepared from **6** according to the general procedure outlined for the preparation of **4b** to afford the desired 1,3-diol as a 6:1 mixture of *E* and *Z* olefin isomers (*E* isomer major) in 85% combined yield after an aqueous workup and flash column chromatography with 45% EtOAc/hexanes: (major diastereomer, lower R_f) ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.69 (dq, J = 15.5, 6.45 Hz, 1H), 5.52 (m, 1H), 3.81 (m, 2H), 2.40 (bs, 2H), 1.82 (m, 2H), 1.70 (d, J = 6.45 Hz, 3H), 1.29 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.26, 123.18, 73.94, 60.11, 42.48, 28.99, 17.63; IR (neat) 3344.1 cm^{-1}; HRMS calcd for $C_7H_{13}O_2$ (M − H)$^+$ 129.0916, found 129.0905; LRMS (EI$^+$) m/z 129 (100), 113 (21), 95 (65), 85 (71), 69 (82), 55 (42), 43 (92), 18 (98).

(1′*E*,1*R,2*S**)-2-(Hydroxymethyl)-1-(1′-propenyl)cyclopentan-1-ol (11a)** was prepared from **10a** according to the general procedure outlined for the preparation of **4b**, except the SmI_2−HMPA solution in THF was heated to 60 °C for the dropwise substrate addition, to afford the desired 1,3-diol, as a >20:1 mixture of *E* and *Z* olefin isomers (*E* isomer major) and >100:1 at the newly created stereogenic center, in 92% combined yield after an aqueous workup and flash column chromatography with 45% EtOAc/hexanes: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.78 (dq, J = 15.5, 6.16, 1H), 5.65 (m, 1H), 3.56 (d, J = 7.23 Hz, 2H), 2.11 (m, 1H), 1.90 (m, 1H), 1.87−1.73 (m, 7H), 1.64 (m, 2H), 1.25 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.93, 124.21, 82.55, 64.15, 51.88, 39.67, 25.78, 20.88, 17.96; IR (neat) 3353.8, 1671.8 cm^{-1}; HRMS calcd for $C_9H_{14}O$ (M − H_2O)$^+$ 138.1045, found 138.1095; LRMS (EI$^+$) m/z 156 (10), 138 (95), 123 (100), 84 (43), 69 (98), 41 (48).

(1′*E*,1*R,2*S**)-2-(Hydroxymethyl)-1-(1′-propenyl)cyclohexan-1-ol (11c)** was prepared from **10c** according to the general procedure outlined for the preparation of **11a** to afford the desired 1,3-diol as a >20:1 mixture of *E* and *Z* olefin isomers (*E* isomer major) and >100:1 at the newly created stereogenic center, in 93% combined yield after an aqueous workup and flash column chromatography with 45% EtOAc/hexanes: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.89 (dq, J = 15.5, 5.89 Hz, 1H), 5.83 (m, 1H), 3.63 (t, J = 10.4 Hz, 1H), 3.46 (dd, J = 10.7, 3.97 Hz, 1H), 2.64 (bs, 2H), 1.78 (m, 1H), 1.75 (d, J = 5.16 Hz, 3H), 1.73 (m, 1H), 1.71 (m, 1H), 1.66 (m, 1H), 1.51 (dt, J = 3.97, 13.0 Hz, 1H), 1.44 (m, 1H), 1.38 (dt, J = 3.57, 13.0 Hz, 1H), 1.34−1.23 (m, 1H), 0.97 (dq, J = 16.9, 3.87 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 131.11, 125.28, 75.83, 66.20, 48.32, 41.29, 25.76, 25.37, 23.07, 18.17; IR (neat) 3354.8, 1681.8 cm^{-1}; HRMS calcd for $C_{10}H_{18}O_2$ 170.1307, found 170.1293; LRMS (EI$^+$) m/z 170 (20), 152 (59), 137 (92), 97 (30), 84 (41), 69 (100), 41 (82), 27 (49).

(1′*E*,1*R,2*S**)-2-(Hydroxymethyl)-1-(1′-propenyl)cycloheptan-1-ol (11b)** was prepared from **10b** according to the general procedure outlined for the preparation of **11a** to afford the desired 1,3-diol as a >20:1 mixture of *E* and *Z* olefin isomers (diastereomeric olefins, *E* isomer major) and >100:1 at the newly created stereogenic center, in 74% combined yield after an aqueous workup and flash column chromatography with 45% EtOAc/hexanes: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.78 (dq, J = 6.43, 15.3 Hz, 1H), 5.61 (m, 1H), 3.61 (dd, J = 10.57, 10.71 Hz, 1H), 3.47 (dd, J = 10.44, 4.81 Hz, 1H), 2.79 (bs, 1H), 2.41 (bs, 1H), 1.96 (m, 1H), 1.81 (m, 3H), 1.72 (dd, J = 1.34, 6.43 Hz, 3H), 1.64 (m, 2H), 1.56 (m, 2H), 1.39 (m, 1H), 1.25 (m, 1H), 1.12 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.45, 123.50, 78.46, 66.34, 49.98, 43.66, 30.18, 29.59, 26.10, 21.81, 17.86; IR (neat) 3356.0, 1684.0, 1455.5 cm^{-1}; HRMS calcd for $C_{11}H_{18}O$ (M − H_2O)$^+$ 166.1358, found 166.1346; LRMS (EI$^+$) m/z 166 (72), 137 (100), 128 (30), 109 (54), 91 (33), 79 (48), 67 (40), 55 (98), 41 (81), 27 (60).

(1*R,3*R**)-1-(1-Propenyl)cyclohexane-1,3-diol (15a)** was prepared from **14a** according to the general procedure outlined for the preparation of **11a** to afford the desired 1,3-diol as a >20:1 mixture of *E* and *Z* olefin isomers (diastereomeric olefins, *E* isomer major) and >100:1 at the newly created stereogenic center, in 74% combined yield after an aqueous workup and flash column chromatography with 45% EtOAc/hexanes: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.65 (dq, J = 15.5, 6.16 Hz, 1H), 5.56 (m, 1H), 3.95 (tt, J = 10.9, 4.37 Hz, 1H), 1.97 (m, 1H), 1.92 (m, 1H), 1.70 (m, 1H), 1.68 (d, J = 6.15 Hz, 3H), 1.64 (m, 1H), 1.52 (m, 1H), 1.41−1.22 (m, 4H), 1.14 (dq, J = 12.31, 4.47 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.12, 122.45, 73.10, 67.50, 46.26, 36.76, 35.04, 19.82, 17.68; IR (neat) 3389.9, 1651.5 cm^{-1}; LRMS (EI$^+$) m/z 156 (31), 138 (23), 84 (18), 69 (42), 39 (100), 27 (62). Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 69.00; H, 10.57.

(2′*R,4*R**,5*R**)-1,2-Dimethyl-4-(hydroxymethyl)-5-(2′-hydroxy-3′-pentenyl)cyclohexene (20)** was prepared from **19** according to the general procedure outlined for the preparation of **11a** to afford the desired 1,4-diol as a 5:1:1:1 mixture of diastereomers (at C2′ and C5, each diastereomer a mixture of cis and trans olefin isomers, trans olefin major) in 74% combined yield after an aqueous workup and flash column chromatography with 25% EtOAc/hexanes: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.68 (m, 0.20H), 5.63 (dq, J = 15.6, 6.25 Hz, 1H), 5.76−5.54 (m, 0.80H), 3.94 (dd, J = 11.4, 3.47 Hz, 0.20H), 3.90 (dd, J = 11.3, 2.68 Hz, 0.80H), 3.42 (dd, J = 11.4, 3.77 Hz, 0.80H), 3.37 (m, 0.20H), 2.38 (bs, 2H), 2.09 (m, 1H), 1.80 (m, 2H), 1.70 (d, J = 4.96 Hz, 3H), 1.67−1.59 (m, 3H), 1.57 (s, 3H), 1.55 (s, 3H), 1.29 (s, 3H); (major diastereomer) ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.24, 125.17, 124.40, 123.19, 75.67, 65.80, 45.95, 38.64, 36.87, 35.41, 21.19, 18.66, 18.48, 17.75; IR (neat) 3331.6, 1665.7, 1442.8 cm^{-1}; HRMS calcd for $C_{14}H_{22}O_2$ (M − H_2O)$^+$: 206.1671, found 206.1672; LRMS (EI$^+$) m/z 206 (8), 175 (12), 121 (19), 107 (59), 85 (100), 69 (38), 43 (37).

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Supporting Information Available: Complete experimental details for the preparation of substrates described herein and ^{1}H and ^{13}C NMR spectral data for all of the compounds prepared (13 pages). This material is contained in libraries on microfiche, immediately follows this article in the microform version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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