Sequenced Reactions with Samarium(II) Iodide. Domino Epoxide Ring-Opening/Ketyl Olefin Coupling Reactions

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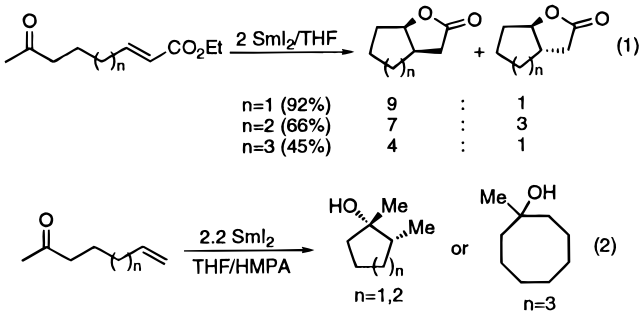
A new sequential reductive coupling process promoted by samarium(II) iodide is described. Cascade epoxide ring opening and ketyl radical olefin cyclization leads to a variety of *cis*-1,3-cyclopentanediols and *cis*-1,3-cyclohexanediols in good yields and with high diastereoselectivity.

Introduction

The development of novel synthetic methods for carbon−carbon bond formation is an important goal in organic synthesis. The significance of this goal is enhanced when the new methods lead to annulated products. It has been shown that samarium(II) iodide efficiently promotes a variety of regio- and stereoselective reductive coupling reactions, providing access to a wide range of carbocycles.[1] Here we report the synthetic utility of samarium(II) iodide in a novel sequential transformation resulting in the formation of stereodefined *cis*-1,3-cyclopentanediols and *cis*-1,3-cyclohexanediols.

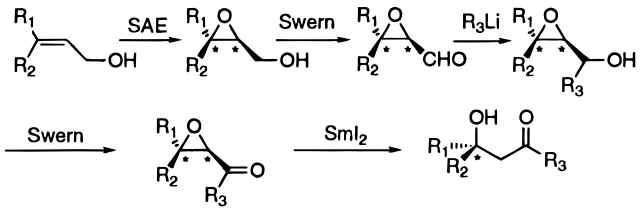
Previously, we reported a preparation of β-hydroxy ketones (aldols) that proceeded via reduction of α,β-epoxy ketones with samarium(II) iodide (Scheme 1). By employing the Sharpless asymmetric epoxidation for the preparation of the substrates, enantiomerically enriched, highly functionalized aldols could be obtained.[2]

Our earlier work[3] and results reported from other laboratories[4] have demonstrated that samarium(II) iodide also promotes intramolecular ketyl olefin cyclization processes (eqs 1 and 2). These reactions occur with high

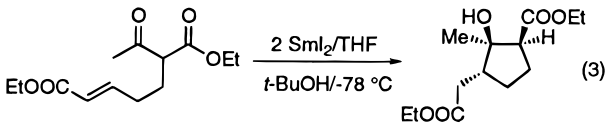


diastereoselectivity about the newly formed carbon−carbon bonds. The presence of HMPA (hexamethylphosphoramide) is necessary to effect these cyclizations when an unactivated olefin serves as the ketyl radical acceptor. In the reductive cyclization of substrates bearing unactivated (terminal) olefins, additives such as HMPA have been postulated to increase the steric bulk about the ketyl oxygen.[3] Under these conditions, higher diastereoselectivities are achieved at the newly formed stereocenters compared to other methods that create the ketyl radical (e.g., by electrochemical,[5] photochemical[6] or other chemical[7] methods).

Scheme 1



Further studies demonstrated that unsaturated β-dicarbonyl systems cyclize efficiently with complete diastereoselectivity (eq 3). Presumably, this process is controlled by chelation of the oxophilic Sm(III) species with the ketyl oxygen and the ester carbonyl of the substrate.[8]



Herein we describe a novel combination of these SmI_2-promoted processes; i.e., a sequential epoxide ring-opening linked to a ketyl olefin cyclization. This protocol utilizes α,β-epoxy ketones bearing remote olefins as

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(6) (a) Belotti, D.; Cossy, J.; Pete, J. P.; Portella, C. *Tetrahedron Lett.* **1985**, *26*, 4591. (b) Belotti, D.; Cossy, J.; Pete, J. P.; Portella, C. *J. Org. Chem.* **1986**, *51*, 4196. (c) Cossy, J.; Belotti, D. *Tetrahedron Lett.* **1988**, *29*, 6113.

(7) (a) Sowinski, A. F.; Whitesides, G. M. *J. Org. Chem.* **1979**, *44*, 2369. (b) Corey, E. J.; Pyne, S. G. *Tetrahedron Lett.* **1983**, *24*, 2821.

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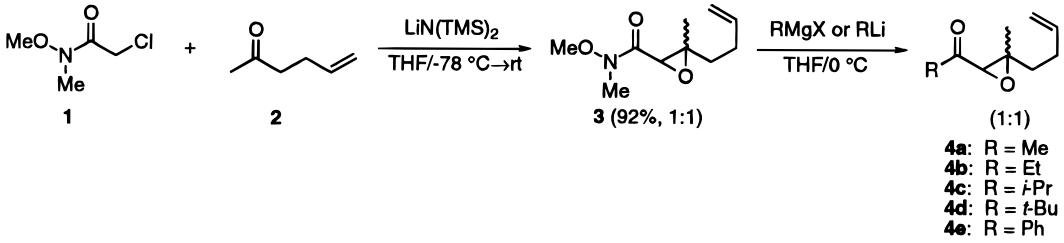
Scheme 2

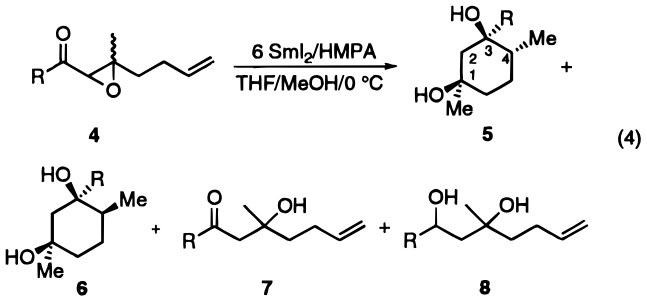


substrates, with the stereochemistry of the process being controlled by chelation effects.[9]

Results and Discussion

In order to probe the scope of the samarium(II) iodide-promoted epoxide ring-opening/ketyl olefin cyclization, a series of olefinic α,β-epoxy ketones was prepared. Compounds **4a**−**e** were assembled through Darzens condensation[10] of Weinreb amide **1** with ketone **2** to afford the epoxy amide **3** as a mixture of diastereomers at the methyl-bearing stereocenter. This was followed by treatment with an organomagnesium or organolithium reagent[11] to afford compounds **4a**−**e** in good yields (Scheme 2).[12]

Optimal reaction conditions for the epoxide ring-opening/ketyl olefin cyclization of compounds **4a**−**e** were found to involve the slow addition of a methanol/THF (1:30) solution of the α,β-epoxy ketones **4** to a THF/HMPA (1:4) solution of SmI_2 (6 equiv)[13] at 0 °C (eq 4). These reactions generally required 15 min to 1 h to proceed to completion, after which the reaction mixtures were quenched with Rochelle's salt.[14] An extractive workup and flash chromatography provided the desired *cis*-1,3-cyclohexanediols (Table 1).



(4)

For substrates **4a**, **4b**, and **4c** (R = Me, Et, *i*-Pr), reductive cyclization proceeded smoothly to afford *cis*-1,3-cyclohexanediols **5a**−**c** and **6a**−**c**, respectively. Reductive opening of the α,β-epoxy ketones and subsequent ketyl olefin cyclization provided the respective diols as a mixture of two diastereomers. The mixture results from imperfect diastereoselectivity at the stereocenter formed in the ketyl olefin cyclization step. The diastereomeric ratios were 10:1 or greater in all of these cases. The yield of cyclization products drops off dramatically in the reductive cyclization of substrate **4d** (R = *t*-Bu) with only a modest yield of the diol product (10%) being formed. Presumably, the increase in steric congestion adjacent to the reacting center supresses the efficiency of the cyclization. The initial aldol product is simply further reduced to the acyclic diol **8d**. For the phenyl ketone **4e**, reduction with samarium(II) iodide leads only to the hydroxy ketone **7e** in low yield and the corresponding acyclic diol **8e**. In this case, the stable ketyl−radical anion intermediate is simply protonated and reduced to afford the major product.

Table 1. Sequential Cyclizations of α,β-Epoxy Ketones 4 To Yield Cyclohexanediols 5 and 6, Aldols 7, and Open-Chain 1,3-Diols 8

entry	substrate	R	% yield **5** + **6** (ratio **5**:**6**)[a]	% yield **7**	% yield **8**	reaction times (min)
1	**4a**	Me	88 (12:1)			15
2	**4b**	Et	86 (10:1)			20
3	**4c**	*i*-Pr	72 (10:1)			20
4	**4d**	*t*-Bu	10 (7:1)		47	60
5	**4e**	Ph		16[b]	45[b]	20

[a] The ratios of diastereomers were determined by fused silica capillary GC analysis of crude reaction mixtures. [b] This reaction was carried out at −78 °C. At 0 °C the reaction afforded a mixture of products.

The exclusive formation of *cis*-diols (**5a**−**d**, **6a**−**d**) is believed to be the direct result of a samarium(III) chelate in the carbon−carbon bond-forming process (Scheme 3).[3c] Chelation of the ketyl oxygen and the β-hydroxy group with samarium(III) in the cyclization step enforces the *cis*-1,3-diol stereochemistry. The second stereocenter formed in the ketyl olefin cyclization, the methyl-bearing stereocenter, is also formed with high diastereoselectivity. Stereochemical control at this center has been ascribed to favorable secondary orbital overlap interactions between the developing methylene radical and the adjacent alkyl substituent in the transition state.[5d,6a,15] Electrostatic interactions may also contribute to the formation of this product. Both the ketyl oxygen and the developing methylene radical centers carry partial negative charge. As a consequence, the trans relationship is adopted to avoid unfavorable electronic interactions.

Compound **5c** formed crystals suitable for single-crystal X-ray analysis, and the three-dimensional structure of this compound was confirmed by this technique. Cyclic diols **5a**, **5b**, **6a**, and **6b** required structural assignment using spectroscopic techniques. The high-dilution (0.02 M in CCl_4) IR spectra of compounds **5a**, **5b**, **6a**, and **6b** revealed two hydroxyl resonances. This is indicative of a structure possessing intramolecular

(9) Several different examples of samarium(II) iodide-promoted sequential reactions have recently been described: (a) Molander, G. A.; Kenny, C. *J. Org. Chem.* **1991**, *56*, 1439. (b) Molander, G. A.; Harris, C. R. *J. Am. Chem. Soc.* **1995**, *117*, 3705. (c) Molander, G. A.; Harris, C. R. *J. Am. Chem. Soc.* **1996**, *118*, 4059.

(10) Borch, R. F. *Tetrahedron Lett.* **1972**, *13*, 3761.

(11) Nahm, S.; Weinreb, S. M. *Tetrahedron Lett.* **1981**, *22*, 3815.

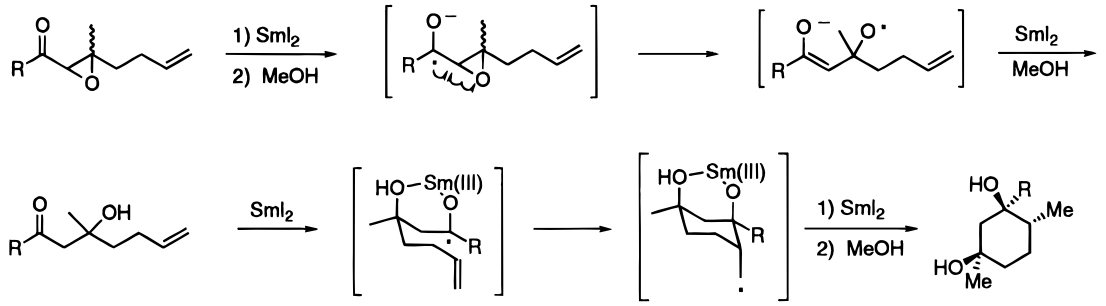
(12) RLi was used only when R = *t*-Bu. The reaction performed with the corresponding Grignard reagent failed.

(13) The use of less than 6 equiv of samarium(II) iodide in this process resulted in the recovery of some starting material.

(14) Rochelle's salt is a 10% solution of sodium potassium tartrate tetrahydrate in water. The use of this solution in the workup of samarium(II) iodide-promoted reactions was first described by: Schwaebe, M.; Little, R. D. *J. Org. Chem.* **1996**, *61*, 3240.

(15) (a) Beckwith, A. L. J. *Tetrahedron* **1981**, *37*, 3073. (b) Giese, B. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 253.

Scheme 3



hydrogen bonding between two hydroxyls and was taken as evidence for the *cis*-1,3-diol stereochemistry. Another experiment that provided useful stereochemical information was pyridine-d_5/$CDCl_3$ difference ^{1}H NMR.[16] On the basis of the magnitude of pyridine-d_5 deshielding (compared to $CDCl_3$ frequencies), the stereochemistry of the C-4 methyl group relative to the C-3 hydroxyl functionality could be determined. For example, the pyridine-d_5 ^{1}H NMR resonance frequency for the C-4 methyl in **5b** is downfield 0.05 ppm with respect to its resonance frequency in $CDCl_3$. For **6b** the deshielding is 0.18 ppm. These results suggest a trans relationship between the C-3 hydroxyl and the C-4 methyl in **5b** and a cis relationship in **6b**.

A straightforward mechanism for these sequential reactions can be envisioned to occur through a series of electron-transfer reactions. Single-electron reduction of the ketone by SmI_2 first generates a ketyl intermediate, inducing epoxide ring opening. Protonation and further reduction in the protic media affords the aldol intermediate. Subsequently, the ketone of the aldol is reduced by a third equivalent of SmI_2, providing the corresponding ketyl intermediate. Irreversible addition of the Sm(III)-chelated hydroxy-ketyl to the olefin and reduction/protonation of the resulting primary radical afford the carbocyclic products (Scheme 3).

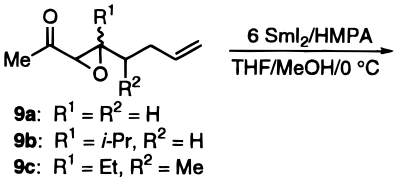
To explore more thoroughly the effects of substrate substitution on the diastereomeric ratio of products, the α,β-epoxy ketones **9** were synthesized. Substrate **9a** was prepared by Darzens condensation of 4-pentenal and acetamide **1** with subsequent treatment with methylmagnesium bromide. The preparation of **9b** was carried out by reaction of *N*,*O*-dimethylhydroxylamine hydrochloride, 4-pentenoic acid, and trimethylamine−borane complex in boiling xylenes.[17] This afforded the unsaturated Weinreb amide. Addition of isopropylmagnesium bromide, followed by Darzens condensation with acetamide **1** and exposure to methylmagnesium bromide, provided the desired product. The last compound in this series, compound **9c**, was obtained by alkylation of 3-pentanone with allyl bromide. Subsequent Darzens condensation with **1** and reaction with methylmagnesium bromide afforded **9c**.

Exposure of substrates **9a**−**c** to samarium(II) iodide led once again to a mixture of diastereomeric 1,3-cyclohexanediols (Table 2) and the acyclic diols from reduction of the ketyl (except in the case of the α,β-epoxy ketone **9a**). As with the previously observed cyclization adducts, *cis*-1,3-cyclohexanediols were obtained. However, diastereoselectivity at the C-4 methyl-bearing stereocenter decreased markedly. Cyclization of **9a** provided **10a** and **11a** in a 3:1 ratio, respectively. Cyclization of **9b** also afforded a 3:1 ratio of products **10b** and **11b**. Cyclization of **9c** led to a mixture of six products, including both cyclized and uncyclized diols.

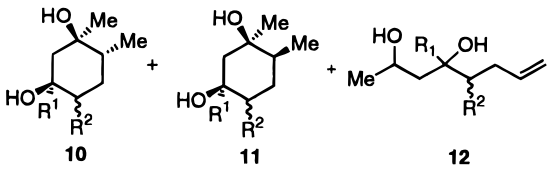
Table 2. Sequential Cyclizations of α,β-Epoxy Ketones 9 To Yield Cyclohexanediols 10 and 11 and Open-Chain 1,3-Diols 12

entry	substrate	R^1	R^2	% yield **10** + **11** (ratio **10**:**11**)[a]	% yield **12**
1	**9a**	H	H	74 (3:1)	
2	**9b**	*i*-Pr	H	40 (3:1)	26
3	**9c**	Et	Me	mixture[b]	[b]

[a] Ratios of diastereomers were determined by fused silica capillary GC analysis of crude reaction mixtures. [b] This reaction led to an inseparable mixture.



9a: $R^1 = R^2 = H$
9b: R^1 = *i*-Pr, R^2 = H
9c: R^1 = Et, R^2 = Me



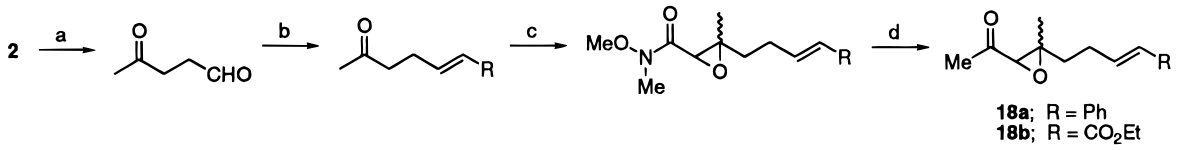
(5)

With these data hand, it became apparent that, in general, an increase in the steric requirements of the starting materials resulted in lower diastereoselectivities in the final products. For such substrates, side reactions producing uncyclized reduction products also became more important. More difficult to explain is the case of **9a**, wherein steric hindrance is seemingly less, but only a 3:1 mixture of diastereomers was obtained.

The extension of this protocol to the synthesis of 5-membered rings was examined next. Substrates **13a**−**e** were prepared once again through Darzens condensation of the Weinreb amide **1**, this time using 4-penten-2-one. Subsequent treatment with the appropriate organolithium or Grignard reagent provided the desired products. Exposure of the substrates **13a**−**e** to the samarium(II)-promoted epoxide ring-opening/ketyl olefin cyclization conditions resulted in smooth conversion to the corresponding *cis*-1,3-cyclopentanediols (eq 6, Table 3). Interestingly, cyclization of compounds **13a**−**c** proceeded with very high diastereoselection, producing essentially a single diastereomer in each case (compounds **14a**−**c**, respectively). The cyclization of **13d** proceeded in good

(16) Trapani, G.; Reho, A.; Latrofa, A. *Synthesis* **1983**, 1013.
(17) Demarco, P. V.; Farkas, E.; Doddrell, D.; Mylari, B. L.; Wenkert, E. *J. Am. Chem. Soc.* **1968**, *90*, 5480.

Scheme 4[a]



[a] Key: (a) $O_3/Me_2S/NaHCO_3$, MeOH/CH_2Cl_2/−78 °C; (b) $(EtO)_2P(O)CH_2R$, base/THF/0 °C; (c) $LiN(SiMe_3)_2$, THF/0 °C → rt, **1**; (d) MeMgBr/THF, 0 °C/30 min.

Table 3. Sequential Cyclizations of α,β-Epoxy Ketones 13 To Yield Cyclopentanediols 14 and 15, Aldols 16, and Open-Chain 1,3-Diols 17

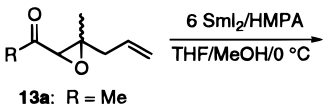
entry	substrate	R	% yield **14** + **15** (ratio **14**:**15**)[a]	% yield **16**	% yield **17**	reaction times (min)
1	**13a**	Me	61 (>100:1)			10
2	**13b**	Et	65 (100:1)			15
3	**13c**	*i*-Pr	66 (50:1)			20
4	**13d**	*t*-Bu	81 (2:1)			30
5	**13e**	Ph		53[b]	24[b]	15

[a] Ratios of diastereomers were determined by fused silica capillary GC analysis of crude reaction mixtures. [b] This reaction was carried out at −78 °C. At 0 °C the reaction afforded a mixture of products.

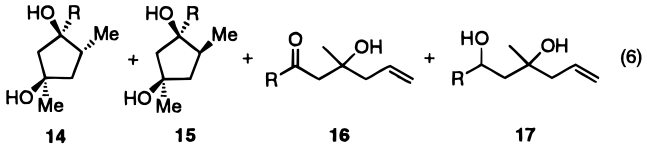
Table 4. Sequential Cyclizations of α,β-Epoxy Ketones 18 To Yield Cyclohexanediols 19 and 20

entry	substrate	R_1	R_2	*T* (°C)	*n*	% yield **19** + **20** (ratio **19**:**20**)[a]
1	**18a**	Ph	Me	−78	1	82 (2.55:1)
2	**18b**	CO_2Et	Me	−78	1	85 (>50:1)
3	**18c**	CO_2Et	*i*-Pr	−78	0	81 (>50:1)
4	**18a**	Ph	Me	rt	1	79 (1:1.6)
5	**18a**	Ph	Me	0	1	76 (1:1)
6	**18a**	Ph	Me	−20	1	78 (1.5:1)

[a] Ratios of diastereomers were determined by fused silica capillary GC analysis of crude reaction mixtures.



13a: R = Me
13b: R = Et
13c: R = *i*-Pr
13d: R = *t*-Bu
13e: R = Ph

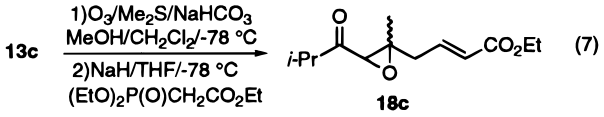


14 **15** **16** **17** (6)

yield but suffered from low diastereoselectivity. As in the previous case (i.e., compound **4e**), the phenyl ketone-containing substrate **13e** did not cyclize, instead providing the aldol product **16e** and acyclic diol **17e**.

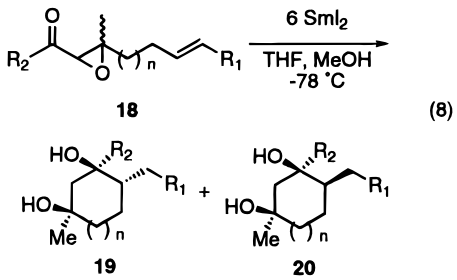
The stereochemistry of the compounds **14d** and **15d** was confirmed by use of the previously described techniques. High-dilution IR spectra (0.02 M in CCl_4) of the products **14d** and **15d** showed two hydroxyl absorbances, indicating a cis diol configuration. The pyridine-d_5/$CDCl_3$ difference proton NMR study revealed a 0.09 ppm shift for **14d** and a 0.245 ppm change for **15d**, indicative of a trans and cis relationship, respectively. The stereochemistry of the other cyclization products was assigned by comparison of their proton NMR's to compounds **14d** and **15d**.

The third phase of our study was to investigate the reductive cyclization of α,β-epoxy ketones possessing activated olefins. Substrates **18a** and **18b** ($n = 1$) were readily prepared through ozonolysis of 5-penten-2-one, followed by a Horner−Emmons reaction[18] with the appropriate phosphonate. Darzens condensation with the amide **1** and treatment with methylmagnesium bromide afforded **18a** and **18b** (Scheme 4). This method failed to provide **18c**. However, **18c** could be obtained via ozonolysis of **13a** and subsequent Horner−Emmons condensation with triethyl phosphonoacetate (eq 7).



18c (7)

With an ethyl ester activating the radical acceptor, substrates **18b** and **18c** underwent the epoxide ring-opening/ketyl olefin cyclization with samarium(II) iodide at −78 °C to provide essentially one diastereomer (eq 8, Table 4). However, when a phenyl substituent was used

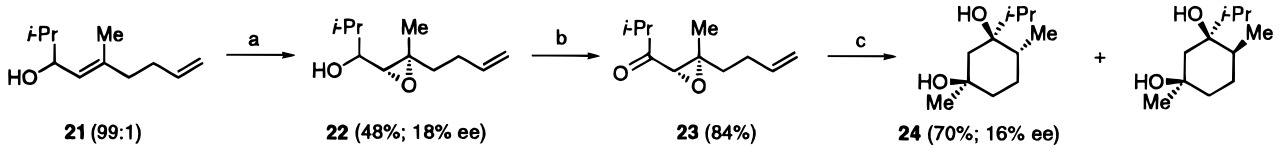


as the activating group (**18a**), control over the methyl-bearing stereocenter was lost. It is known that the rate of addition of free radicals to alkenes is greatly affected by substituents on the alkene,[15d] increasing up to 4 orders of magnitude when an electron-withdrawing group is positioned β to the carbon of the olefin undergoing radical attack. These electron-withdrawing substituents decrease the SOMO energy of the radical and thereby favor interactions between the SOMO of the radical and the HOMO of the olefin.[19] Esters are better activating groups than the phenyl group, and the lower temperatures that can be used with the former substituent could explain why the ester functionality showed higher stereochemical control. In fact, when the reaction of **18c** was performed at 0 °C (or at rt) in the absence of HMPA, four different products were detected by TLC.

Kinetic resolution of a racemic allylic alcohol using the Sharpless asymmetric epoxidation reaction could provide enantiomerically enriched α,β-epoxy ketones for an asymmetric preparation of *cis*-1,3-cyclohexanediols and *cis*-1,3-cyclopentanediols. Compound **21** was prepared by a route involving initial condensation of diethyl (cyanom-

(18) March, J. *Advanced Organic Chemistry*, 3rd ed.; Wiley-Interscience: New York, 1985 and references therein.
(19) Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*; Wiley-Interscience: New York, 1976.

Scheme 5[a]



21 (99:1) **22** (48%; 18% ee) **23** (84%) **24** (70%; 16% ee)

[a] Key: (a) *t*-BuOOH/Ti(O*i*-Pr)$_4$, L-(+)-DIPT, CH_2Cl_2/−20 °C/12 h; (b) Swern oxidation; (c) 6 SmI_2/HMPA, THF/MeOH/0 °C.

ethyl)phosphonate with 5-hexen-2-one (Scheme 5). The Wittig adduct was reduced with DIBAH, and subsequent addition of methylmagnesium bromide afforded **21**. The resulting allylic alcohol was subjected to Sharpless epoxidation conditions,[20] affording the nonracemic chiral epoxide **22**. Unfortunately, the kinetic resolution of *rac*-**21** afforded epoxide **22** in low enantiomeric excess (ee = 18%). Swern oxidation of **22** provided access to nonracemic **23**. Reaction with samarium(II) iodide resulted in a mixture of diastereomeric 1,3-cyclohexanediols **24**. The enantiomeric excess of each isomer of **24** was determined to be 16% based on chiral-GC analysis. This result indicates that, as expected, the overall process transpires with retention of the configuration at the position β to the ketone carbonyl.

Conclusions

The samarium(II) iodide-promoted epoxide ring-opening/ketyl olefin cyclization sequence efficiently converts a variety of α,β-epoxy ketones to *cis*-1,3-cyclopentanediols and *cis*-1,3-cyclohexanediols. In addition, the relative stereochemistry can be controlled at three stereocenters in the cyclization product. In all cases, complete selectivity for *cis*-1,3-diols was achieved. As expected, the diastereoselectivity at the second newly formed stereocenter was substrate dependent.

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 weighed and stored under an inert atmosphere. CH_2I_2 was purchased from Aldrich Chemicals and was distilled prior to use and stored under argon over copper turnings. HMPA was purchased from either Aldrich or Sigma Chemicals and was distilled from either Na(0) or CaH_2 at 0.04 mmHg and stored over 4 Å molecular sieves under Ar. Standard benchtop techniques were employed for handling air-sensitive reagents, and all reactions were carried out under argon.

3,4-Epoxy-4-methyl-7-octen-2-one (4a). General Procedure for the Preparation of α,β-Epoxy Ketones 4. To a stirred solution of *N*-chloro-*N*-methylacetamide (2.75 g, 20.0 mmol) in 20 mL of THF at −78 °C was added dropwise lithium bis(trimethylsilyl)amide (22 mL of a 1.0 M solution in THF, 22.0 mmol). After the addition, the reaction mixture was stirred for an additional 20 min at −78 °C. After this period of stirring, a solution of 5-hexen-2-one (**2**) (1.96 g, 20.0 mmol) in 30 mL of THF was added slowly dropwise, and when the addition was complete, the reaction mixture was warmed to room temperature with continued stirring overnight. The reaction mixture was then quenched with saturated aqueous NH_4Cl after TLC analysis revealed the complete comsumption of the starting material. Aqueous workup followed by flash chromatography (50% EtOAc/hexanes) afforded 3.66 g (18.4 mmol) of **3** in 92% yield. To a stirred solution of **3** (0.99 g, 5.0 mmol) in 20 mL of THF at 0 °C was added dropwise methylmagnesium bromide (4.28 mL of a 1.4 M solution in THF, 6.0 mmol), and the reaction mixture was stirred for an additional 30 min period at 0 °C. Then, TLC revealed the complete comsumption of the starting material, and the reaction mixture was quenched with saturated aqueous NH_4Cl. Aqueous workup followed by flash chromatography (20% ethyl ether/hexanes) afforded 0.75 g (4.85 mmol) of **4a** in 97% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.23 (s, 1.62H), 1.39 (s, 1.38H), 1.52−1.65 (m, 2H), 1.76−1.83 (m, 1H), 2.04−2.22 (m, 1H), 2.18 (s, 1.62H), 2.21 (s, 1.38H), 3.35 (s, 0.46H), 3.37 (s, 0.54H), 4.90−5.05 (m, 2H), 5.64−5.83 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.22, 22.06, 28.07, 28.39, 29.32, 29.64, 31.58, 37.41, 63.14, 63.72, 64.82, 65.79, 115.52, 137.18, 137.24, 204.30; IR (neat) 3077.9, 2976.2, 1721.5, 1453.2, 1406.6, 1185.1 cm^{-1}; HRMS calcd for $C_9H_{14}O_2$ (M + H)$^+$ 155.1072, found 155.1031; LRMS (EI) *m*/*z* 139 (14), 111 (32), 99 (82), 81 (31), 71 (74), 55 (59), 43 (100).

4,5-Epoxy-5-methyl-8-nonen-3-one (4b) was prepared from **3** according to the general procedure for the preparation of **4a** by reaction with ethylmagnesium bromide (3.0 mL of a 2.0 M solution in THF, 6.0 mmol) to afford **4b** in 78% yield after flash chromatography with 20% ethyl ether/hexanes: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.05 (t, J = 7.41 Hz, 3H), 1.20 (s, 1.68H), 1.39 (s, 1.32H), 1.49−1.81 (m, 2H), 1.98−2.23 (m, 2H), 2.49−2.60 (m, 2H), 3.37 (s, 0.44H), 3.39 (s, 0.56H), 4.90−5.07 (m, 2H), 5.62−5.83 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.18, 16.15, 22.00, 29.29, 29.66, 31.45, 34.12, 34.42, 37.37, 64.36, 65.32, 115.38, 115.44, 137.19, 137.27, 206.68; IR (neat) 3077.8, 2977.2, 2938.3, 1722.5, 1409.7, 1381.4 cm^{-1}; HRMS calcd for $C_{10}H_{16}O_2$ (M + H)$^+$ 169.1228, found 169.1183; LRMS (EI) *m*/*z* 153 (12), 113 (79), 97 (18), 81 (36), 71 (73), 57 (100), 43 (72).

4,5-Epoxy-2,5-dimethyl-8-nonen-3-one (4c) was prepared from **3** according to the general procedure for the preparation of **4a** by reaction with isopropylmagnesium bromide (3.0 mL of a 2.0 M solution in THF, 6.0 mmol) to afford **4c** in 81% yield after flash chromatography with 20% ethyl ether/hexanes: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01−1.06 (m, 6H), 1.13 (s, 1.56H), 1.35 (s, 1.44H), 1.44−1.48 (m, 1H), 1.57−1.76 (m, 1H), 1.96−2.16 (m, 2H), 2.70−2.80 (m, 1H), 3.40 (s, 0.48H), 3.43 (s, 0.52H), 4.85−5.00 (m, 2H), 5.60−5.77 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.92, 16.86, 17.02, 17.54, 17.60, 21.75, 29.06, 29.44, 31.11, 37.17, 38.62, 63.22, 63.42, 63.59, 64.42, 115.08, 115.22, 137.11, 208.88, 209.06; IR (neat) 2971.3, 2932.6, 1718.5, 1465.9, 1405.3, 1383.8 cm^{-1}; HRMS calcd for $C_{11}H_{18}O_2$ (M + H)$^+$ 183.1385, found 184.1423; LRMS (EI) *m*/*z* 127 (29), 111 (12), 85 (14), 71 (75), 55 (25), 43 (100).

4,5-Epoxy-2,2,5-trimethyl-8-nonen-3-one (4d) was prepared from **3** according to the general procedure for the preparation of **4a** by reaction with *tert*-butyllithium (3.53 mL of a 1.7 M solution in pentane, 6.0 mmol) to afford **4d** in 71% yield after flash chromatography with 20% ethyl ether/hexanes: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28 (s, 1.5H), 1.29 (s, 9H), 1.42 (s, 1.5H), 1.50−1.58 (m, 1H), 1.68−1.82 (m, 1H), 2.01−2.25 (m, 2H), 3.69 (s, 0.5H), 3.72 (s, 0.5H), 4.91−5.06 (m, 2H), 5.68-5.85 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.67, 21.61, 26.03, 28.95, 29.46, 30.49, 37.09, 43.38, 43.43, 61.68, 62.94, 63.46, 63.80, 115.05, 115.23, 137.28, 137.38, 208.90, 208.98; IR (neat) 2967.7, 2933.2, 1712.4, 1478.1, 1398.6 cm^{-1}; HRMS calcd for $C_{12}H_{20}O_2$ (M + H)$^+$ 197.1542, found 197.1539; LRMS (EI) *m*/*z* 141 (19), 111 (11), 99 (21), 85 (14), 71 (36), 57 (100).

1,2-Epoxy-2-methyl-5-hexenyl phenyl ketone (4e) was prepared from **3** according to the general procedure for the preparation of **4a** by reaction with phenylmagnesium bromide

(20) (a) Martin, S. V.; Woodard, S. S.; Katsuki, T.; Yamada, Y.; Ikeda, M.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 6237. (b) Woodard, S. S.; Finn, M. G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1991**, *113*, 106.

(2.0 mL of a 3.0 M solution in ethyl ether, 6.0 mmol) to afford **4e** in 99% yield after flash chromatography with 20% ethyl ether/hexanes: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22 (s, 1.5H), 1.51−1.60 (m, 1H), 1.55 (s, 1.5H), 1.85−1.91 (m, 1H), 1.97−2.07 (m, 0.5H), 2.10−2.19 (m, 0.5H), 2.20−2.29 (m, 1H), 4.04 (s, 0.5H), 4.06 (s, 0.5H), 4.80−4.91 (m, 1H), 5.00−5.10 (m, 1H), 5.54−5.65 (m, 0.5H), 5.80−5.90 (m, 0.5H), 7.19−7.60 (m, 3.5H), 7.93−7.98 (m, 1.5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.41, 21.76, 29.12, 29.60, 31.58, 37.09, 63.51, 63.58, 63.99, 64.65, 115.26, 115.55, 127.16, 127.26, 128.24, 128.76, 128.84, 133.85, 135.76, 137.29, 137.40, 193.98, 194.25; IR (neat) 3066.3, 2975.6, 2928.6, 1690.5, 1449.8, 1228.3 cm^{-1}; HRMS calcd for $C_{14}H_{16}O_2$ (M − H)$^+$ 215.1072, found 215.1084; LRMS (EI) *m*/*z* 201 (10), 154 (64), 105 (100), 89 (35), 77 (77).

3,4-Epoxy-7-octen-2-one (9a). A solution of 4-penten-1-ol (1.72 g, 20 mmol) in 60 mL of CH_2Cl_2 was treated with Et_3N (8.09 g, 80 mmol), cooled to 0 °C, treated with a solution of pyridine·SO_3 complex (9.55 g, 60 mmol) in 60 mL of DMSO, and stirred for 1 h at 0 °C. The reaction mixture was then quenched with aqueous saturated $NaHCO_3$. The aqueous layer was extracted with Et_2O (3 × 50 mL), and the combined organic extracts were washed with 1 M Na_2HPO_4 solution (100 mL), 5 M $CuSO_4{\cdot}5H_2O$ solution (100 mL), and brine (100 mL), respectively. The organic layer was dried ($MgSO_4$), concentrated in vacuo, and used without further purification (because the aldehyde formed was very volatile). **9a** was prepared from this aldehyde according to the general procedure for the preparation of **4a** in an 28% overall yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.48−1.73 (m, 2H), 2.01 (s, 0.78H), 2.21 (s, 2.22H), 2.10−2.25 (m, 2H), 3.02−3.08 (m, 0.26H), 3.14−3.21 (m, 0.74H), 3.52 (s, 0.26H), 3.54 (s, 0.74H), 4.94−5.04 (m, 2H), 5.68−5.82 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.75, 28.35, 29.26, 29.90, 30.38, 31.03, 57.55, 58.03, 58.82, 59.90, 115.84, 115.90, 136.80, 204.14, 205.87; IR (neat) 3078.0, 2978.8, 1722.2, 1421.4, 1356.0, 1180.4 cm^{-1}; HRMS calcd for $C_8H_{12}O_2$ (M − H)$^+$ 139.0759, found 139.0743; LRMS (EI) *m*/*z* 107 (11), 97 (62), 85 (70), 67 (63), 57 (65), 43 (100).

3,4-Epoxy-4-isopropyl-7-octen-2-one (9b). $Me_3N{\cdot}BH_3$ complex (1.46 g, 20 mmol) was added to a solution of 4-pentenoic acid (2.0 g, 20 mmol) and *N*,*O*-dimethylhydroxylamine hydrochloride (1.95 g, 20 mmol) in 100 mL of xylenes, and the resultant solution was heated at reflux at 137−144 °C for 8 h. The mixture was then cooled to room temperature and shaken with aqueous 10% $NaHCO_3$ (2 × 25 mL). Aqueous workup followed by flash chromatography (50% ethyl ether/hexanes) afforded 2.14 g (15.0 mmol) of *N*-methoxy-*N*-methyl-4-pentenamide in 75% yield. To a solution of this amide in 30 mL of THF was added isopropylmagnesium bromide (9 mL of a 2.0 M solution in THF, 18 mmol), and the reaction mixture was stirred for 30 min at 0 °C. After this period of time, the reaction mixture was quenched with saturated aqueous NH_4Cl. Aqueous workup followed by flash chromatography (10% ethyl ether/hexanes) afforded 0.59 g (4.85 mmol) of 2-methyl-6-hepten-3-one in a 31% yield. **9b** was prepared from this ketone according to the general procedure for the preparation of **4a** in a 44% yield (two steps): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (d, J = 7.08 Hz, 2.1H), 0.88 (d, J = 6.91 Hz, 0.9H), 0.98 (d, J = 6.87 Hz, 0.9H), 1.04 (d, J = 6.89 Hz, 2.1H), 1.49−1.64 (m, 2H), 1.76−1.81 (m, 1H), 1.86−2.05 (m, 2H), 2.19 (s, 2.1H), 2.22 (s, 0.9H), 3.41 (s, 0.3H), 3.50 (s, 0.7H), 4.90−5.04 (m, 2H), 5.69−5.82 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.14, 17.77, 18.68, 18.76, 26.75, 27.75, 28.37, 29.45, 30.95, 31.16, 62.57, 63.83, 69.13, 69.22, 115.16, 125.30, 128.23, 129.04, 137.48, 137.72, 204.78, 205.03; IR (neat) 2923.9, 2852.4, 1725.7, 1462.8, 1377.7, 1274.2 cm^{-1}; HRMS calcd for $C_{11}H_{18}O_2$ (M + H)$^+$ 183.1385, found 183.1381; LRMS (EI) *m*/*z* 183 (6), 139 (90), 127 (36), 99 (58), 81 (38), 69 (37), 55 (52), 43 (100).

3,4-Epoxy-4-ethyl-5-methyl-7-octen-2-one (9c). To a stirred solution of 22 mmol of LDA at −78 °C was added dropwise a solution of 3-pentanone (1.73 g, 20 mmol) in 20 mL of THF. After the addition of the substrate was complete, the reaction mixture was stirred for an additional 20 min period at −78 °C. Then, allyl bromide (2.42 g, 20 mmol) in 20 mL of THF was added slowly dropwise. The reaction mixture was warmed to room temperature with continued stirring for 3 h. After this period, the reaction mixture was quenched with saturated aqueous NH_4Cl. Aqueous workup followed by flash chromatography (10% ethyl ether/hexanes) afforded 0.74 g (5.86 mmol) of 4-methyl-7-hepten-3-one in a 30% yield. **9c** was prepared from this ketone according to the general procedure for the preparation of **4a** in an 23% (two steps): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.76−0.83 (m, 4.92H), 1.01 (d, J = 6.76 Hz, 1.08H), 1.45−1.58 (m, 1H), 1.64−2.03 (m, 3.36H), 2.19 (s, 1.08H), 2.20 (s, 1.92H), 2.31−2.39 (m, 0.64H), 3.42 (s, 0.64H), 3.47 (s, 0.36H), 4.92−5.03 (m, 2H), 5.47−5.58 (m, 0.36H), 5.68−5.79 (m, 0.64H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.66, 7.88, 15.63, 16.05, 20.72, 20.95, 28.37, 28.63, 35.70, 36.29, 37.12, 38.04, 62.26, 63.08, 69.50, 69.67, 116.26, 116.59, 136.13, 136.51, 204.84, 204.95; IR (neat) 2924.7, 1717.7, 1457.9, 1356.2, 1186.2 cm^{-1}; HRMS calcd for $C_{11}H_{18}O_2$ (M + H)$^+$ 183.1385, found 183.1374; LRMS (EI) *m*/*z* 153 (55), 139 (50), 113 (100), 99 (87), 81 (67), 69 (95), 57 (92).

3,4-Epoxy-4-methyl-6-hepten-2-one (13a) was prepared from 4-penten-2-ol according to the procedure for the preparation of **9a** to afford **13a** in 21% overall yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20 (s, 1.29H), 1.36 (s, 1.71H), 2.16 (s, 1.29H), 2.19 (s, 1.71H), 2.15−2.40 (m, 2H), 3.37 (s, 0.43H), 3.38 (s, 0.57H), 5.00−5.12 (m, 2H), 5.60−5.75 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.50, 22.02, 28.02, 28.39, 37.10, 42.27, 62.77, 63.18, 63.86, 65.17, 118.68, 119.10, 132.10, 132.39, 203.82, 204.41; IR (neat) 2917.3, 2848.8, 1720.3, 1260.2, 1018.8 cm^{-1}; HRMS calcd for $C_8H_{12}O_2$ (M + H)$^+$ 141.0916, found 141.0892; LRMS (EI) *m*/*z* 99 (21), 83 (5), 67 (6), 53 (7), 43 (100).

4,5-Epoxy-5-methyl-7-octen-3-one (13b) was prepared from 4-penten-2-ol according to the procedure for the preparation of **9a** to afford **13b** in 23% overall yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.98 (t, J = 7.27 Hz, 3H), 1.13 (s, 1.38H), 1.32 (s, 1.62H), 2.08−2.55 (m, 4H), 3.36 (s, 1H), 4.95−5.08 (m, 2H), 5.57−5.72 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.11, 16.35, 21.93, 34.10, 34.43, 36.95, 42.25, 62.67, 63.06, 63.39, 64.65, 118.48, 118.98, 132.16, 132.53, 206.23, 206.67; IR (neat) 3097.7, 2978.8, 2938.3, 1720.7, 1380.5 cm^{-1}; HRMS calcd for $C_9H_{14}O_2$ (M + H)$^+$ 155.1072, found 155.1090; LRMS (EI) *m*/*z* 113 (57), 97 (36), 83 (11), 69 (13), 57 (100), 43 (71).

4,5-Epoxy-2,5-dimethyl-7-octen-3-one (13c) was prepared from 4-penten-2-ol according to the procedure for the preparation of **9a** to afford **13c** in 22% overall yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.02−1.08 (m, 6H), 1.13 (s, 1.80H), 1.37 (s, 1.20H), 2.11−2.42 (m, 2H), 2.70−2.80 (m, 1H), 3.45 (s, 0.4H), 3.46 (s, 0.6H), 5.00−5.12 (m, 2H), 5.61−5.80 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.31, 16.82, 17.17, 17.69, 21.88, 22.62, 31.56, 36.78, 38.86, 42.37, 62.73, 63.04, 63.40, 63.96, 118.62, 119.06, 132.20, 132.60, 208.97; IR (neat) 2972.5, 2933.8, 1716.3, 1467.3, 1384.0, 1001.3 cm^{-1}; HRMS calcd for $C_{10}H_{16}O_2$ 168.1150, found 168.1142; LRMS (EI) *m*/*z* 127 (18), 97 (28), 85 (17), 71 (32), 43 (100).

4,5-Epoxy-2,2,5-trimethyl-7-octen-3-one (13d) was prepared from 4-penten-2-ol according to the procedure for the preparation of **9a** to afford **13d** in 17% overall yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.07 (s, 1.65H), 1.08 (s, 4.95H), 1.10 (s, 4.05H), 1.33 (s, 1.35H), 2.10−2.12 (m, 1H), 2.28−2.42 (m, 1H), 3.64 (s, 0.55H), 3.68 (s, 0.45H), 4.93−5.09 (m, 2H), 5.48−5.62 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.92, 21.67, 26.02, 26.04, 36.20, 42.32, 43.42, 43.47, 60.95, 62.13, 63.15, 63.52, 118.67, 119.11, 132.19, 132.75, 208.93, 209.04; IR (neat) 2966.3, 2916.4, 1712.0, 1478.2, 1398.6, 1065.0 cm^{-1}; HRMS calcd for $C_{11}H_{18}O_2$ (M + H)$^+$ 183.1385, found 183.1407; LRMS (EI) *m*/*z* 141 (27), 99 (28), 83 (10), 69 (9), 57 (100).

1,2-Epoxy-2-methyl-4-pentenyl phenyl ketone (13e) was prepared from 4-penten-2-ol according to the procedure for the preparation of **9a** to afford **13e** in 29% overall yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.18 (s, 1.35H), 1.50 (s, 1.65H), 2.11−2.29 (m, 1.10H), 2.40−2.58 (m, 0.90H), 4.04 (s, 0.55H), 4.05 (s, 0.45H), 4.89−4.94 (m, 1.10H), 5.16−5.22 (m, 0.90H), 5.53-5.61 (m, 0.55H), 5.79−5.84 (m, 0.45H), 7.41−7.46 (m, 2H), 7.53−7.57 (m, 1H), 7.90−7.93 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.56, 21.64, 37.21, 42.16, 62.68, 63.20, 63.47, 64.13, 118.89, 119.33, 128.18, 128.20, 128.83, 128.85, 132.26, 132.36, 133.85, 135.75, 193.94, 194.15; IR (neat) 2979.9, 1693.6, 1641.6, 1597.6, 1449.6, 1383.2 cm^{-1}; HRMS calcd for $C_{13}H_{14}O_2$ (M + H)$^+$ 203.1072, found 203.1077; LRMS (EI) *m*/*z* 185 (16), 161 (68), 105 (100), 77 (65), 43 (65).

Ethyl 6,7-Epoxy-6-methyl-8-oxo-2-nonenoate (18b). Ozone was bubbled through a solution of 5-hexen-2-one (1.96 g, 20 mmol) and $NaHCO_3$ (3.36 g, 40 mmol) in 40 mL of 50% $MeOH/CH_2Cl_2$ at −78 °C until a blue color persisted. Then, Me_2S was added (12.42 g, 200 mmol), and the reaction mixture was stirred and warmed to room temperature. The resultant crude reaction mixture was diluted with brine (50 mL), extracted with ether, dried over $MgSO_4$, and concentrated in vacuo. This crude was used in the next step without further purification. To a suspension of NaH (0.53 g, 22 mmol) in 20 mL of THF at 0 °C was added slowly dropwise a solution of triethyl phosphonoacetate (4.48 g, 20 mmol) in 20 mL of THF and the mixture stirred for 20−30 min at 0 °C after the addition was finished. Then, a solution of the keto aldehyde (obtained in the ozonolysis) in 30 mL of THF was added dropwise. When the addition of the substrate was complete, the reaction mixture was stirred for an additional 2 h at 0 °C. The reaction mixture was then quenched with saturated aqueous NH_4Cl. Aqueous workup followed by flash chromatography (50% ethyl ether/hexanes) afforded 2.04 g (12 mmol) of ethyl 6-oxo-2-heptenoate in a 60% yield as a 97:3 mixture of the trans and cis diastereomers, respectively. **18a** was prepared from this keto ester according to the general procedure for the preparation of **4a**, in 35% yield after flash chromatography with 33% ethyl ether/hexanes: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.21−1.25 (m, 3H), 1.22 (s, 1.5H), 1.39 (s, 1.5H), 1.59−1.83 (m, 2H), 2.17 (s, 1.5H), 2.20 (s, 1.5H), 2.22−2.34 (m, 2H), 3.36 (s, 0.5H), 3.37 (s, 0.5H), 4.09−4.16 (m, 2H), 5.75−5.83 (m, 1H), 6.76−6.93 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.24, 16.19, 21.20, 27.59, 28.00, 28.07, 28.43, 30.64, 36.41, 60.31, 62.65, 63.20, 64.57, 65.64, 122.29, 146.86, 146.97, 166.25, 203.88, 203.93; IR (neat) 2981.8, 1719.5, 1694.6, 1270.9, 1186.7, 1043.1 cm^{-1}; HRMS calcd for $C_{12}H_{18}O_4$ $(M + H)^+$ 227.1283, found 227.1263; LRMS (EI) *m/z* 127 (10), 114 (19), 99 (24), 81 (18), 71 (17), 55 (19), 43 (100).

3,4-Epoxy-4-methyl-8-phenyl-7-octen-2-one (18a) was prepared following the procedure described above for the preparation of **18a** by ozonolysis of 5-hexen-2-one, and subsequent Horner-Emmons reaction with the keto aldehyde using diethyl phosphonoacetate to afford after flash choromatography (20% ethyl ether/hexanes) 0.70 g of the Wittig adduct (3.3 mmol) in a 20% yield. Following the procedure described for the synthesis of **4a**, **18b** was obtained in a 62% yield (two steps): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28 (s, 1.71H), 1.44 (s, 1.29H), 1.66−1.89 (m, 2H), 2.20−2.38 (m, 2H), 2.15 (s, 1.71H), 2.18 (s, 1.29H), 3.38 (s, 0.43H), 3.42 (s, 0.57H), 6.06−6.21 (m, 1H), 6.35−6.39 (m, 1H), 7.18−7.20 (m, 1H), 7.24−7.34 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.14, 22.04, 27.98, 28.37, 28.57, 28.89, 31.84, 37.76, 63.04, 63.61, 64.74, 65.64, 125.89, 127.10, 127.13, 128.45, 128.49, 128.71, 128.77, 130.73, 130.79, 137.17, 204.17; IR (neat) 2952.2, 1718.3, 1654.5, 1436.7, 1275.7, 1199.7 cm^{-1}; HRMS calcd for $C_{15}H_{18}O_2$ $(M + H)^+$ 213.1127, found 213.1137; LRMS (EI) *m/z* 137 (10), 109 (12), 99 (43), 81 (14), 68 (16), 53 (10), 43 (100).

Ethyl 5,6-Epoxy-5,8-dimethyl-8-oxo-2-octenoate (18c) was prepared according to the procedure for the preparation of ethyl 2-oxo-6-heptenoate described in the synthesis of **18a** by ozonolysis of **13c** and further Horner−Emmons reaction with triethyl phosphonoacetate at −78 °C in a 38% yield (two steps). **18c** was obtained as the trans diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.05−1.11 (m, 6H), 1.20 (s, 3H), 1.34 (t, J = 7.13 Hz, 3H), 2.45−2.60 (m, 2H), 2.72−2.83 (m, 1H), 3.47 (s, 1H), 4.13−4.19 (q, J = 7.13 Hz, 2H), 5.88−5.93 (m, 1H), 6.76−6.89 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.23, 16.64, 16.80, 17.78, 31.59, 38.88, 40.50, 60.52, 62.62, 125.33, 141.56, 165.84, 208.59; IR (neat) 2972.8, 2935.0, 1719.9, 1657.5, 1270.3, 1199.8 cm^{-1}; HRMS calcd for $C_{14}H_{20}O_4$ 240.1362, found 240.1360; LRMS (EI) *m/z* 169 (13), 127 (48), 95 (40), 85 (47), 71 (54), 55 (34), 43 (100).

5,8-Dimethyl-1,6-nonadien-7-ol (21). To a suspension of *t*-BuOK (2.61 g, 22 mmol) in 20 mL of THF at 0 °C was added dropwise a solution of diethyl (cyanomethyl)phosphonate (3.54 g, 20 mmol) in 20 mL of THF. After the addition was complete, the reaction mixture was stirred for 20−30 min at 0 °C. Then, a solution of 5-hexen-2-one (1.96 g, 20 mmol) in 20 mL of THF was added slowly dropwise, and after the addition was complete, stirring was continued for 3 h. The reaction mixture was quenched with saturated aqueous NH_4Cl. Aqueous workup and concentration in vacuo afforded a crude mixture that was used without further purification. This crude mixture was disolved in 30 mL of THF and treated at 0 °C with DIBAH (22 mL of a 1.0 M solution in hexanes, 22 mmol). The reaction mixture was stirred for 1 h at 0 °C and quenched with water. Aqueous workup followed by flash chromatography (20% ethyl ether/hexanes) afforded 1.88 g (11.2 mmol) of the α,β-unsaturated aldehyde in 56% yield as a mixture 2:1 of the trans:cis diastereomers. The treatment of a solution of this mixture in 20 mL of THF at 0 °C with isopropylmagnesium bromide (6.72 mL of a 2.0 M solution in THF, 13.44 mmol), continued stirring for 1 h at 0 °C, quenching with saturated aqueous NH_4Cl, and aqueous workup afforded the allylic alcohol **21** as a mixture 2:1 of the trans:cis diastereomers. After several flash chromatographies (10% ethyl ether/hexanes), the trans isomer was separated in a 99% purity and used in the Sharpless epoxidation: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83 (d, J = 6.88 Hz, 3H), 0.92 (d, J = 6.62 Hz, 3H), 1.65 (s, 3H), 1.60−1.71 (m, 1H), 2.09 (m, 3H), 2.11−2.20 (m, 2H), 4.01−4.06 (m, 1H), 4.90−5.01 (m, 2H), 5.17−5.20 (m, 1H), 5.71−5.82 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.74, 18.09, 18.39, 32.08, 34.46, 39.04, 73.62, 114.66, 126.54, 138.30, 138.56; IR (neat) 3374.1, 2956.7, 2927.0, 1465.7, 1381.9, 1008.2 cm^{-1}.

Preparation of the SmI_2 Solution. Samarium metal (0.827 g, 5.5 mmol) was added under a flow of argon to an oven-dried, round-bottomed flask containing a magnetic stirring bar and a septum inlet. To the samarium was added 20 mL of THF followed by CH_2I_2 (1.473 g, 5.0 mmol). The mixture was stirred at room temperature for 2 h. The resulting deep blue solution was used directly to effect the following sequential reactions.

General Procedure for the SmI_2-Promoted Sequential Reactions of α,β-Epoxy Ketones. To the SmI_2 (5.0 mmol) in THF was added HMPA (4.93 g, 27.5 mmol), and Ar was bubbled through the solution for 10 min. A solution of the α,β-epoxy ketone (0.83 mmol), and MeOH (1 mL) in 30 mL of THF was added over 1 h. After the starting material was consumed, aqueous workup followed by flash chromatography and/or Kugelrohr distillation afforded the title compounds. For the cases in Table 4, no HMPA was added to the samarium solution.

1,3,4-Trimethyl-1,3-cyclohexanediol (5a, 6a) was prepared from **4a** according to the general procedure described above to afford after flash chromatography (75% ethyl ether/hexanes) 0.115 g (0.73 mmol) of a 12:1 mixture of diastereomers **5a**:**6a** in 88% yield. **5a** (major): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (d, J = 7.23 Hz, 3H), 1.11 (s, 3H), 1.15 (s, 3H), 1.21−1.28 (m, 1H), 1.39−1.54 (m, 4H), 1.69−1.73 (m, 1H), 2.15−2.24 (m, 1H), 3.40−3.70 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.88, 24.33, 28.74, 31.10, 32.60, 38.67, 43.41, 71.15, 74.34; IR (neat) 3328.5, 2965.7, 2929.9, 1457.9, 1175.0 cm^{-1}; HRMS calcd for $C_9H_{18}O_2$ 158.1307, found 158.1301; LRMS (EI) *m/z* 140 (10), 125 (15), 101 (47,), 83 (18,), 43 (100). Anal. Calcd for $C_9H_{18}O_2$: C, 68.31; H, 11.46. Found: C, 68.09; H, 11.55. **6a** (minor): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (d, J = 6.59 Hz, 3H), 1.11 (s, 3H), 1.16 (s, 3H), 1.18−1.40 (m, 4H), 1.55−1.70 (m, 2H), 1.72−1.76 (m, 1H), 2.80−3.30 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.82, 26.40, 28.40, 31.08, 39.07, 39.98, 49.49, 71.56, 72.64; IR (neat) 3346.4, 2931.8, 1457.6, 1367.8, 1119.3, 1033.3 cm^{-1}; HRMS calcd for $C_9H_{18}O_2$ 158.1307, found 158.1295; LRMS (EI) *m/z* 141 (10), 123 (14), 101 (33), 82 (17), 43 (100). Anal. Calcd for $C_9H_{18}O_2$: C, 68.31; H, 11.46. Found: C, 69.74; H, 11.65.

3-Ethyl-1,4-dimethyl-1,3-cyclohexanediol (5b, 6b) was prepared from **4a** according to the general procedure described above to afford after flash chromatography (75% ethyl ether/hexanes) 0.122 g (0.71 mmol) of a 10:1 mixture of diastereomers **5b**:**6b** in 86% yield. **5b** (major): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83 (d, J = 7.27 Hz, 3H), 0.85 (t, J = 7.45 Hz, 3H), 1.13 (s, 3H), 1.20−1.26 (m, 1H), 1.30−1.41 (m, 3H), 1.43−1.52 (m, 3H), 1.75−1.79 (m, 1H), 2.11−2.19 (m, 1H), 3.20−4.30 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 5.99, 15.37, 24.26, 31.09, 32.87, 33.15, 35.55, 42.48, 71.01, 75.83; IR (neat) 3332.7, 2926.7, 1456.8, 1173.8 cm^{-1}; HRMS calcd for $C_{10}H_{20}O_2$ 172.1463,

found 172.1468; LRMS (EI) *m/z* 154 (10), 143 (8), 125 (45), 115 (55), 57 (100), 43 (47). Anal. Calcd for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70. Found: C, 69.53; H, 11.77. **6b** (minor): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.82 (t, J = 7.54 Hz, 3H), 0.86 (d, J = 6.48 Hz, 3H), 0.89−1.30 (m, 1H), 1.17 (s, 3H), 1.28−1.47 (m, 5H), 1.50−1.72 (m, 3H), 2.80−3.20 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.16, 14.40, 26.28, 31.25, 33.10, 37.06, 39.00, 45.19, 71.48, 74.96; IR (neat) 3370.8, 2927.9, 1696.0, 1458.4, 1172.2 cm^{-1}; HRMS calcd for $C_{10}H_{20}O_2$ 172.1463, found 172.1458; LRMS (EI) *m/z* 154 (18), 137 (24), 125 (81), 115 (73), 96 (48), 81 (48), 57 (100). Anal. Calcd for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70. Found: C, 70.87; H, 11.01.

3-Isopropyl-1,4-dimethyl-1,3-cyclohexanediol (5c, 6c) was prepared from **4a** according to the general procedure described above to afford after flash chromatography (75% ethyl ether/hexanes) 0.112 g (0.60 mmol) of a 10:1 mixture of diastereomers **5c**:**6c** in 72% yield. **5c** (major): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.81−0.88 (m, 9H), 1.14 (s, 3H), 1.19−1.24 (m, 2H), 1.40−1.46 (m, 2H), 1.48−1.55 (m, 1H), 1.68−1.72 (m, 1H), 1.82−1.86 (m, 1H), 2.11−2.20 (m, 1H), 3.08 (br s, 1H), 4.04 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.02, 15.11, 16.07, 24.57, 31.23, 32.71, 33.34, 34.87, 40.14, 65.79, 70.83, 76.99; IR (neat) 3260.4, 2960.6, 2919.4, 1474.7, 1449.1 cm^{-1}; HRMS calcd for $C_{11}H_{22}O_2$ 186.1620, found 186.1617; LRMS (EI) *m/z* 168 (10), 143 (28), 125 (100), 97 (30), 71 (72), 43 (53). Anal. Calcd for $C_{11}H_{22}O_2$: C, 70.92; H, 11.90. Found: C, 71.16; H, 12.12. **6c** (minor): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.79 (d, J = 7.57 Hz, 3H), 0.84 (d, J = 6.49 Hz, 3H), 0.92 (d, J = 7.57 Hz, 3H), 1.02−1.13 (m, 1H), 1.18 (s, 3H), 1.21−1.45 (m, 2H), 1.48−1.84 (m, 5H), 2.74 (br s, 1H), 3.03 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.03, 16.44, 17.40, 26.52, 31.47, 34.45, 36.08, 38.98, 39.09, 71.37, 76.87; IR (neat) 3335.5, 2960.3, 2929.6, 2873.8, 1461.7, 1373.7 cm^{-1}; HRMS calcd for $C_{11}H_{22}O_2$ (M − CH_3) 171.1385, found 171.1397, (M − H_2O) 168.1515, found 168.1514; LRMS (EI) *m/z* 168 (12), 143 (52), 125 (90), 97 (63), 85 (54), 71 (91), 43 (100). Anal. Calcd for $C_{11}H_{22}O_2$: C, 70.92; H, 11.90. Found: C, 71.19; H, 12.00.

3-*tert*-Butyl-1,4-dimethyl-1,3-cyclohexanediol (5d, 6d) was prepared from **4a** according to the general procedure described above to afford after flash chromatography (75% ethyl ether/hexanes) 0.017 g (0.083 mmol) of a 7:1 mixture of diastereomers **5d**:**6d** in 10% yield. **5d** (major): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.95 (s, 9H), 1.04 (d, J = 7.17 Hz, 3H), 1.19 (s, 3H), 1.20−1.24 (m, 1H), 1.41−1.68 (m, 4H), 1.91−1.97 (m, 1H), 2.23−2.34 (m, 1H), 2.62 (br s, 1H), 3.99 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.18, 25.97, 27.31, 31.49, 33.06, 36.30, 36.36, 38.37, 71.21, 79.78; IR (neat) 3473.3, 2967.9, 2930.5, 1397.7, 1377.4, 1159.8 cm^{-1}; HRMS calcd for $C_{12}H_{24}O_2$ (M − H_2O) 182.1671, found 182.1652, (M − CH_3) 185.1542, found 185.1534; LRMS (EI) *m/z* 182 (4), 143 (27), 125 (94), 83 (29), 57 (86), 41 (100). Anal. Calcd for $C_{12}H_{24}O_2$: C, 71.95; H, 12.07. Found: C, 71.92; H, 12.44.

3,4-Dimethyl-1,3-cyclohexanediol (10a, 11a) was prepared from **9a** according to the general procedure described above to afford after flash chromatography with ethyl ether 0.088 g (0.61 mmol) of a 3:1 mixture of diastereomers **10a**:**11a** in 74% yield.[3c]

1-Isopropyl-3,4-dimethyl-1,3-cyclohexanediol (10b, 11b) was prepared from **9b** according to the general procedure described above to afford after flash chromatography (75% ethyl ether/hexanes) 0.060 g (0.33 mmol) of a 3:1 mixture of diastereomers **10b**:**11b** in 40% yield. **10b** (major): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (d, J = 7.18 Hz, 3H), 0.89 (d, J = 6.83 Hz, 6H), 1.12 (s, 3H), 1.23−1.31 (m, 2H), 1.37−1.40 (m, 1H), 1.46−1.55 (m, 3H), 1.71−1.75 (m, 1H), 2.18−2.25 (m, 1H), 2.80−3.50 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.92, 16.62, 16.73, 24.12, 27.53, 28.92, 38.54, 38.63, 38.95, 74.12, 75.31; IR (neat) 3324.0, 2960.4, 2877.7, 1455.9, 1380.8, 1168.9 cm^{-1}; HRMS calcd for $C_{11}H_{22}O_2$ (M − H_2O) 168.1514, found 168.1507, (M − CH_3) 171.1385, found 171.1407; LRMS (EI) *m/z* 168 (7), 143 (45), 125 (48), 83 (58), 69 (61), 55 (42), 43 (100). Anal. Calcd for $C_{11}H_{22}O_2$: C, 70.92; H, 11.70. Found: C, 71.30; H, 12.30.

1,3,4-Trimethyl-1,3-cyclopentanediol (14a, 15a) was prepared from **13a** according to the general procedure described above to afford after flash chromatography with ethyl ether 0.073 g (0.51 mmol) of a >100:1 mixture of diastereomers **14a**:**15a** in 61% yield. **14a** (major): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (d, J = 6.88 Hz, 3H), 1.19 (s, 3H), 1.30 (s, 3H), 1.17−1.24 (m, 1H), 1.33−1.40 (m, 1H), 1.70−1.81 (m, 2H), 2.19−2.23 (m, 1H), 2.60−2.90 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.24, 23.68, 28.35, 44.97, 50.25, 53.38, 78.68, 82.59; IR (neat) 3363.1, 2963.9, 2929.5, 1457.8, 1376.8, 1245.3 cm^{-1}; HRMS calcd for $C_8H_{16}O_2$ (M − H_2O) 126.1045, found 126.1053; LRMS (EI) *m/z* 126 (8), 111 (35), 101 (13), 83 (42), 71 (57), 55 (50), 43 (100). Anal. Calcd for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found: C, 63.79; H, 11.64.

3-Ethyl-1,4-dimethyl-1,3-cyclopentanediol (14b, 15b) was prepared from **13b** according to the general procedure described above to afford after flash chromatography with ethyl ether 0.085 g (0.54 mmol) of a 100:1 mixture of diastereomers **14b**:**15b** in 65% yield. **14b** (major): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83 (d, J = 7.13 Hz, 3H), 0.91 (t, J = 7.43 Hz, 3H), 1.29 (s, 3H), 1.34−1.40 (m, 1H), 1.42−1.58 (m, 2H), 1.61−1.65 (m, 1H), 1.72−1.76 (m, 1H), 2.14−2.20 (m, 1H), 2.22−2.30 (m, 1H), 2.40−2.90 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.13, 18.40, 28.60, 28.95, 44.22, 50.19, 50.41, 78.57, 85.35; IR (neat) 3372.4, 2963.2, 2929.9, 1458.5, 375.8, 1149.1 cm^{-1}; HRMS calcd for $C_9H_{18}O_2$ (M − H_2O) 140.1201, found 140.1187; LRMS (EI) *m/z* 140 (10), 125 (18), 111 (41), 97 (25), 83 (40), 71 (35), 57 (100). Anal. Calcd for $C_9H_{18}O_2$: C, 68.31; H, 11.46. Found: C, 67.52; H, 11.90.

3-Isopropyl-1,4-dimethyl-1,3-cyclopentanediol (14c, 15c) was prepared from **13c** according to the general procedure described above to afford after flash chromatography with ethyl ether 0.094 g (0.55 mmol) of a 50:1 mixture of diastereomers **14c**:**15c** in 66% yield. **14c** (major): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.82 (d, J = 7.33 Hz, 3H), 0.87 (d, J = 6.85 Hz, 3H), 0.89 (d, J = 6.92 Hz, 3H), 1.31 (s, 3H), 1.47−1.52 (m, 1H), 1.63−1.67 (m, 1H), 1.68−1.72 (m, 1H), 1.77−1.81 (m, 1H), 2.09−2.15 (m, 1H), 2.35−2.41 (m, 1H), 2.80 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.28, 17.73, 19.34, 29.60, 31.49, 43.53, 49.36, 50.41, 78.70, 88.15; IR (neat) 3382.2, 2966.6, 2934.2, 1377.5, 1244.1, 1151.2 cm^{-1}; HRMS calcd for $C_{10}H_{20}O_2$ 172.1463, found 172.1467; LRMS (EI) *m/z* 154 (28), 129 (46), 111 (55), 83.43, 69 (60), 55 (50), 43 (100). Anal. Calcd for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70. Found: C, 69.72; H, 12.01.

3-*tert*-Butyl-1,4-dimethyl-1,3-cyclopentanediol (14d, 15d) was prepared from **13d** according to the general procedure described above to afford after flash chromatography with ethyl ether 0.125 g (0.67 mmol) of a 2:1 mixture of diastereomers **14d**:**15d** in 81% yield. **14d** (major): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 (s, 9H), 1.06 (d, J = 7.01 Hz, 3H), 1.27 (s, 3H), 1.52−1.58 (m, 1H), 1.69−1.73 (m, 1H), 1.81−1.85 (m, 1H), 1.94−2.00 (m, 1H), 2.27−2.35 (m, 1H), 2.50−3.00 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.69, 26.00, 27.80, 37.12, 37.42, 49.60, 50.23, 78.71, 87.63; IR (neat) 3380.9, 2958.8, 2874.5, 1395.8, 1375.5, 1128.1 cm^{-1}; HRMS calcd for $C_{11}H_{22}O_2$ (M − CH_3) 171.1385, found 171.1396, (M − H_2O) 168.1514, found 168.1510; LRMS (EI) *m/z* 143 (10), 129 (37), 111 (77), 95 (11), 83 (32), 69 (60), 57 (100). Anal. Calcd for $C_{11}H_{22}O_2$: C, 70.92; H, 11.90. Found: C, 71.24; H, 11.96. **15d** (minor): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.99 (s, 9H), 1.00 (d, J = 7.01 Hz, 3H), 1.83 (s, 3H), 1.45−1.49 (m, 1H), 1.68−1.71 (m, 1H), 1.93−1.96 (m, 1H), 2.18−2.25 (m, 1H), 2.38−2.44 (m, 1H), 2.60−2.90 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.80, 26.59, 29.99, 36.62, 45.22, 45.44, 51.78, 77.60, 90.07; IR (neat) 3310.5, 2962.7, 2952.4, 1483.3, 1373.9, 1263.0 cm^{-1}; HRMS calcd for $C_{11}H_{22}O_2$ (M − CH_3) 171.1385, found 171.1376, (M − H_2O) 168.1514, found 168.1501; LRMS (EI) *m/z* 129 (16), 111 (28), 95 (8), 83 (22), 69 (37), 57 (94), 43 (100). Anal. Calcd for $C_{11}H_{22}O_2$: C, 70.92; H, 11.90. Found: C, 70.58; H, 12.01.

4-Benzyl-2,3-dimethyl-1,3-cyclohexanediol (19a, 20a) was prepared from **18a** according to the general procedure described above to afford after flash chromatography (66% ethyl ether/hexanes) 0.136 g (0.63 mmol) of a 2.55:1 mixture of diastereomers **19a**:**20a** in 82% yield. **19a** (major): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22 (s, 3H), 1.27 (s, 3H), 1.16−1.24 (m, 1H), 1.41−1.45 (m, 1H), 1.50−1.55 (m, 2H), 1.63−1.67 (m, 1H), 1.86−1.98 (m, 2H), 2.28−2.35 (m, 1H), 2.72−2.77 (m, 1H), 3.50 (br s, 1H), 3.70 (br s, 1H), 7.12−7.19 (m, 3H), 7.24−7.29 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.69, 28.89, 31.21, 32.67,

34.68, 44.28, 45.99, 71.28, 74.08, 125.95, 128.42, 128.90, 141.00; IR (neat) 3330.6, 2964.5, 2935.4, 1453.6, 1374.0, 1191.3 cm^{-1}; HRMS calcd for $C_{15}H_{22}O_2$ (M − H_2O) 1216.1514, found 216.1522; LRMS (EI) *m*/*z* 216 (31), 198 (20), 158 (42), 118 (68), 101 (50), 91 (70), 43 (100). Anal. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 74.99; H, 9.63. **20a** (minor): ^1H NMR (400 MHz, $CDCl_3$) δ 1.17 (s, 3H), 1.23 (s, 3H), 1.18−1.35 (m, 3H), 1.41−1.47 (m, 2H), 1.53−1.59 (m, 1H), 1.77−1.81 (m, 1H), 2.33−2.40 (m, 1H), 2.70 (br s, 1H), 3.03−3.07 (m, 1H), 3.50 (br s, 1H), 7.14−7.18 (m, 3H), 7.24−7.28 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.55, 28.56, 31.17, 35.68, 38.73, 47.39, 49.87, 71.57, 72.65, 125.64, 128.19, 129.24, 141.65; IR (neat) 3337.0, 2928.0, 1452.6, 1185.8 cm^{-1}; HRMS calcd for $C_{15}H_{22}O_2$ (M − H_2O) 216.1514, found 216.1528; LRMS (EI) *m*/*z* 216 (39), 198 (16), 158 (40), 118 (62), 91 (80), 43 (100). Anal. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 75.76; H, 9.63.

Ethyl (1*R,3*R**,4*S**)-1,3-dimethyl-4-(carboxylatomethyl)-1,3-cyclohexanediol (19b, 20b)** was prepared from **18b** according to the general procedure described above to afford after flash chromatography (66% ethyl ether/hexanes) 0.163 g (0.71 mmol) of a 50:1 mixture of diastereomers **19b**:**20b** in 85% yield. **19b** (major): ^1H NMR (400 MHz, $CDCl_3$) δ 1.14 (s, 3H), 1.18 (s, 3H), 1.24 (t, J = 7.18 Hz, 3H), 1.32−1.55 (m, 1H), 1.58−1.63 (m, 5H), 2.15−2.23 (m, 2H), 2.25−2.35 (m, 1H), 3.10−3.60 (br s, 2H), 4.12 (q, J = 7.10 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.22, 21.39, 28.24, 30.95, 32.86, 35.08, 40.76, 44.06, 60.59, 70.99, 73.42, 173.08; IR (neat) 3357.7, 2968.8, 2932.7, 1732.3, 1290.8, 1184.1 cm^{-1}; HRMS calcd for $C_{12}H_{22}O_4$ (M − H_2O) 212.1412, found 212.1414; LRMS (EI) *m*/*z* 167 (10), 151 (6), 115 (14), 101 (42), 43 (100). Anal. Calcd for $C_{12}H_{22}O_4$: C, 62.58; H, 9.63. Found: C, 61.85; H, 10.03.

Ethyl (1*R,3*S**,4*S**)-1-methyl-3-isopropyl-4-(carboxylatomethyl)-1,3-cyclohexanediol (19c, 20c)** was prepared from **18c** according to the general procedure described above to afford after flash chromatography (66% ethyl ether/hexanes) 0.163 g (0.67 mmol) of a 50:1 mixture of diastereomers **19c**:**20c** in 81% yield. **19c** (major): ^1H NMR (400 MHz, $CDCl_3$) δ 0.90−0.93 (m, 6H), 1.23 (t, J = 7.31 Hz, 3H), 1.33 (s, 3H), 1.57−1.64 (m, 3H), 1.83−1.94 (m, 2H), 2.32−2.38 (m, 1H), 2.41−2.46 (m, 1H), 2.51−2.57 (m, 2H), 3.09 (br s, 1H), 4.08−4.13 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.23, 16.34, 17.82, 29.42, 31.84, 37.76, 45.87, 47.56, 49.86, 60.59, 78.53, 87.04, 172.70; IR (neat) 3422.4, 2967.2, 1734.1, 1372.5, 1257.2, 1160.7 cm^{-1}; HRMS calcd for $C_{13}H_{24}O_4$ (M − H_2O) 226.1569, found 226.1552, (M − CH_3) 229.1440, found 229.1431; LRMS (EI) *m*/*z* 226 (17), 209 (38), 183 (41), 137 (52), 109 (50), 71 (56), 43 (100). Anal. Calcd for $C_{13}H_{24}O_4$: C, 63.91; H, 9.90. Found: C, 63.20; H, 10.36.

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Supporting Information Available: Copies of ^1H NMR and ^{13}C NMR spectra of synthesized compounds (70 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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