Stereochemical Investigations of Samarium(II) Iodide-Promoted 5-Exo and 6-Exo Ketyl–Olefin Radical Cyclization Reactions

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Samarium(II) iodide (SmI_2)-promoted ketyl cyclizations of several substituted, unsaturated ketones, providing various cyclopentyl and cyclohexyl systems, have been investigated. The resulting experiments provide stereochemical insight into these reactions and in addition outline the synthetic potential of these 5-exo and 6-exo radical cyclization processes.

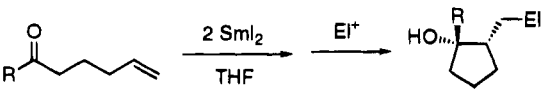
Introduction

Despite their relatively recent inception,[1] radical cyclization procedures have matured quickly,[2] and the regiochemical as well as stereochemical preferences of many neutral radical cyclization reactions have been delineated.[3] Although many of these studies have involved neutral alkenyl radical and related chain cyclization reactions, few have addressed the inherently more stereoselective ketyl–olefin systems.[4] The purpose of this report is to provide stereochemical insight into this process and to outline the synthetic potential of the samarium(II) iodide-promoted intramolecular ketyl–olefin coupling reaction as well.

Early reports from our laboratory detailed a novel method for promoting highly stereoselective radical cyclization reactions of several unsaturated β-keto esters and β-keto amides (eq 1, $El^+ = H^+$).[5] While ketyl radical anion cyclization procedures had been known for some time,[6] the unique characteristics associated with the SmI_2-promoted cyclization process permitted exceptional stereochemical control via chelation of the Lewis basic functional groups to the oxophilic samarium(III) ion.[5]

(1)

More recently we reported the ability of samarium(II) iodide–HMPA mixtures to promote the cyclization of unactivated olefinic ketones resulting in the formation of various five-, six-, and eight-membered rings in good to excellent yield (eq 2).[7] In the case of a single cyclopentyl system, the organosamarium species formed was found to be stable and could subsequently be trapped by a variety of electrophiles. The yields and/or stereoselectivities obtained following cyclization of these substrates were revealed to exceed those obtained by similar reactions induced photochemically, electrochemically, or by other chemical means.[4] While evidence was provided that 5-exo- and 6-exo-trig radical cyclizations of achiral unsubstituted systems proceeded with excellent diastereoselectivities, the potential of controlling relative stereochemistry at three stereocenters from chiral substrates was also apparent.



(2)

El = H^+, CO_2, aldehydes, ketones, PhSSPh, etc.

The studies described herein further detail the SmI_2-promoted 5-exo- and 6-exo reductive cyclization reaction of substituted olefinic ketones. Experiments have been conducted to determine the range of ketones applicable to this cyclization reaction, and potential difficulties that may arise in attempted sequential reactions have also been determined. In addition, the source of the modest stereoselectivity observed in these cyclization processes has been detailed.

Results and Discussion

Initial experiments were performed to determine the effect of substitution about the ketyl radical on the ensuing radical cyclization rates and to examine the diastereoselectivities inherent in these reactions (Scheme 1). As indicated by the entries in Table 1, there is an inverse relationship between the 5-exo-trig radical cyclization rates and the size of the ketone substituent.

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(1) (a) Lamb, R. C.; Ayers, P. W.; Toney, M. K. *J. Am. Chem. Soc.* **1963**, *85*, 3483. (b) Julia, M. *Pure Appl. Chem.* **1967**, *15*, 167. (c) Julia, M. *Acc. Chem. Res.* **1971**, *4*, 386 and references cited therein.

(2) (a) RajanBabu, T. V. *Acc. Chem. Res.* **1991**, *24*, 139. (b) Jasperse, C.; Curran, D. P.; Fevig, T. L. *Chem. Rev.* **1991**, *91*, 1237. (c) Thebtaranonth, C.; Thebtaranonth, Y. *Tetrahedron* **1990**, *46*, 1385. (d) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds;* Pergamon Press: New York, 1986. (e) Curran, D. P. *Synthesis* **1988**, 417. (f) Ramaiah, M. *Tetrahedron* **1987**, *43*, 3541. (g) Hart, D. J. *Science* **1984**, *223*, 883.

(3) (a) Beckwith, A. L. J. *Tetrahedron* **1981**, *37*, 3073. (b) Beckwith, A. L. J.; Schiesser, C. H. *Tetrahedron* **1985**, *41*, 3925. (c) Spellmeyer, D. C.; Houk, K. N. *J. Org. Chem.* **1987**, *52*, 959. (c) Hanessian, S.; Dhanoa, D. S.; Beaulieu, P. L. *Can. J. Chem.* **1986**, *65*, 1859.

(4) (a) Inokuchi, T.; Kawafuchi, H.; Torii, S. *J. Org. Chem.* **1991**, *56*, 4983. (b) Shono, T.; Nishiguchi, I.; Ohmizu, H.; Mitani, M. *J. Am. Chem. Soc.* **1978**, *100*, 545. (c) Sowinski, A. F.; Whitesides, G. M. *J. Org. Chem.* **1979**, *44*, 2369. (d) Little, R. D.; Fox, D. P.; Hijfte, L. V.; Dannecker, R.; Sowell, G.; Wolin, R. L.; Moëns, L.; Baizer, M. M. *J. Org. Chem.* **1988**, *53*, 2287. (e) Pyne, S.; Corey, E. J. *Tetrahedron Lett.* **1983**, *24*, 2821. (f) Pattenden, G.; Robertson, G. M. *Tetrahedron Lett.* **1983**, *24*, 4617. (g) Shono, T.; Nishiguchi, I.; Ohmizu, H.; Mitani, M. *J. Am. Chem. Soc.* **1978**, *100*, 545. (h) Belotti, D.; Cossy, J.; Pete, J. P.; Portella, C. *J. Org. Chem.* **1986**, *51*, 4196. (i) Fukuzawa, S.; Nakanishi, A.; Fujinami, T.; Sakai, S. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1669. (j) Enholm, E. J.; Trivellas, A. *J. Am. Chem. Soc.* **1989**, *111*, 6463. (k) Shim, S. C.; Hwang, J.-T.; Kang, H.-Y.; Chang, M. H. *Tetrahedron Lett.* **1990**, *31*, 4765. (l) Bannai, K.; Tanaka, T.; Okamura, N.; Hazato, A.; Sugiura, S.; Manabe, K.; Tomimori, K.; Kato, Y.; Kurozumi, S.; Noyori, R. *Tetrahedron* **1990**, *46*, 6689.

(5) (a) Molander, G. A.; Kenny, C. *Tetrahedron Lett.* **1987**, *28*, 4367. (b) Molander, G. A.; Kenny, C. *J. Am. Chem. Soc.* **1989**, *111*, 8236.

(6) (a) Stork, G.; Malhotra, S.; Thompson, H.; Uchibayashi, M. *J. Am. Chem. Soc.* **1965**, *87*, 1148. (b) Eakin, M.; Martin, J.; Parker, W. *J. Chem. Soc., Chem. Commun.* **1965**, 206.

(7) (a) Molander, G. A.; Kenny, C. *J. Org. Chem.* **1991**, *56*, 1439. (b) Molander, G. A.; McKie, J. A. *J. Org. Chem.* **1991**, *57*, 3132. (c) Molander, G. A.; McKie, J. A., *J. Org. Chem.* **1994**, *59*, 3186.

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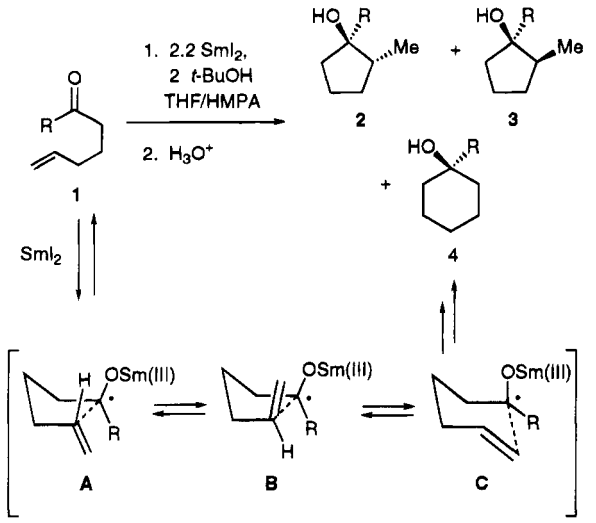
Table 1. Samarium(II) Iodide-Promoted Cyclization of Olefinic Ketones 1 to Yield Substituted Cyclopentanols 2 and 3 (Scheme 1)

entry	substrate	R	% isoltd yield 2 + 3 (diast ratio, 2:3)	% yield 4	reaction time
1	**1a**	Me	86 (>150:1)	–	15 min
2	**1b**	*i*-Pr	85 (23:1)	3	30 min
3	**1c**	*t*-Bu	78 (3:1)	4	8 h
4	**1d**	Ph	48 (<1:150)	–	2 h

Scheme 1



Although the diastereoselectivity decreased with increasing steric size of the pendant alkyl group, the overall yields remained surprisingly high. It is remarkable that even in the case of entry 3 a cis relationship between the methyl and *tert*-butyl groups is retained in the major product.[8] Radical cyclization of the analogous *tert*-butyl-substituted alkyl radical (2,2-dimethyloct-7-en-3-yl radical) resulted in a 1.6:1 (trans:cis) mixture of diastereomeric 1-*tert*-butyl-2-methylcyclopentanes in 57% yield.[9] Additionally, in the 2,2-dimethyloct-7-en-3-yl radical cyclization, reduced uncyclized material (7,7-dimethyloct-1-ene) was formed in 43% yield as a result of the decreased cyclization rate relative to substrates with less steric hindrance vicinal to the radical center. In analogy to 5-hexenyl radical cyclizations, the ketyl–olefin cyclization may be predicted to proceed through a chairlike transition state. Therefore, in the transition state leading to cyclized product, the ketone substituent (R) is nearly eclipsed with the developing methylene radical center (**A** in Scheme 1). The trans relationship of the π-system and the ketyl oxygen has precedent and is likely electronic in nature, although steric elements may also play a significant role.[2d,3a] As the steric requirements of the alkyl substituent (R) increase, steric repulsion between R and the olefin are relieved in the transition state leading to the minor diastereomeric product (**B** in Scheme 1). However, this conformation occurs at the expense of eclipsing the ketyl oxygen functionality with the π-system. It is also noteworthy that in the case of the *tert*-butyl- and isopropyl-substituted cases a small amount of six-membered ring product **4** was detected. In this case, steric repulsion of the olefin and alkyl group as well as unfavorable interactions between the ketyl oxygen and π-system are alleviated at the expense of poor orbital overlap in the 6-endo-trig transition state (**C** in Scheme 1).

Unexpectedly (in light of relative reduction potentials), the slowest reacting substrate was phenyl ketone **1d**. Although the reaction required approximately 12 h for completion, only a trace of reduced, uncyclized material was present in the reaction mixture. In addition, only a single diastereomeric cyclized product was detected by NMR and GC analyses. This product was isolated in 48% yield and it was proven to be the cis isomer **3d**.[8] It is of note that attempted electrochemical cyclization of **1d** has been reported to afford 1-phenyl-5-hexen-1-ol as the only isolable product.[4g] Furthermore, a detailed study of the cyclization of 1-phenyl-5-hexenyl radical verified that that reaction was reversible and the resulting product yields were determined to be temperature and concentration dependent.[1c,10] A mixture of *trans*-1-phenyl-2-methylcylopentane, phenylcyclohexane, and 1-phenyl-5-hexene was formed under all conditions studied. It is uncertain whether the formation of the cis isomer **3d** over the trans isomer **2d** is a kinetic phenomenon or if it is due to thermodynamic equilibration of the cyclopentylmethyl radical. Analysis of the reaction mixture of substrate **1d** with SmI_2 following a premature quench indicated the presence of starting material and a single diastereomeric cyclic product **3d**, with no evidence of six-membered ring product **4d**, indicating that the observed product may actually be kinetic in origin.

In addition to studying the 5-exo cyclization process with appropriate achiral substrates, we also had an interest in examining the 6-exo process with homologous unsaturated ketones. In the event, it was determined that although methyl ketone **5a** cyclized in excellent yield and diastereoselectivity, increasing the ketone substituent size to ethyl (**5b**) then isopropyl (**5c**) resulted in a gradual decrease in the yield of the 6-exo cyclization product (Scheme 2, Table 2). Interestingly, the diastereoselectivity remained nearly identical for both of these latter substrates despite the significant increase in the size of the ketone substituent. Although ethyl ketone **5b** cyclized in moderate yield with only 15% reduced uncyclized material (**9b**) present in the reaction mixture, isopropyl ketone **5c** cyclized in only 37% yield. The second major product isolated from the reaction mixture in this latter case was 7-endo product **8c**. In addition, reduced products **9c** and **10c** were each isolated in 15% yield. Evidently, **10c** arises from intramolecular allylic hydrogen atom abstraction (**G** in Scheme 2).

In a previous report it was suggested that uncyclized, reduced product **9** resulted from hydrogen atom abstraction from THF.[7b] However, a more recent investigation on the SmI_2-promoted reductive cyclization of olefinic ketones has indicated that THF is not a significant source of hydrogen atoms under protic conditions.[7c] As indicated by the products isolated following cyclization of substrates **5c** and **5d** in Table 2, the reduced uncyclized material may arise from intramolecular allylic hydrogen atom abstraction. In accord with our previous findings,[7c] the reduced material may also be formed by a net two-electron reduction of the ketone functionality followed by protonation by *t*-BuOH present in the reaction mixture. This mechanism of ketone reduction is supported by entry 4 in Table 2. Addition of 20 equiv of *t*-BuOH

(8) Proof of stereochemistry was established by a comparison of the products generated in this study with known diastereomers prepared by addition of the appropriate Grignard reagents to 2-alkylcyclopentanones. Ashby, E. C.; Laemmle, J. T. *Chem. Rev.* **1975**, *75*, 521.

(9) Beckwith, A. L. J.; Cliff, M. D.; Schiesser, C. H. *Tetrahedron* **1992**, *48*, 4641.

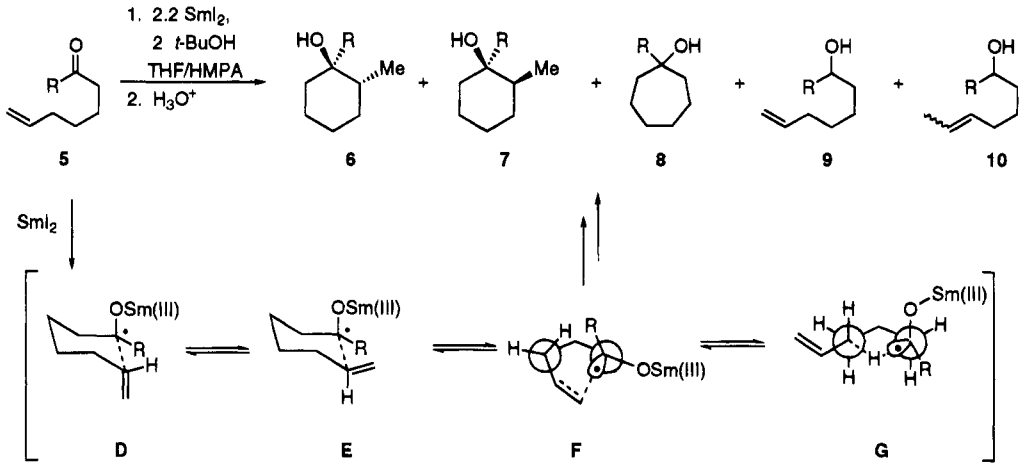
(10) Walling, C.; Cioffari, A. *J. Am. Chem. Soc.* **1972**, *94*, 6064.

Table 2. Reductive Cyclization of Olefinic Ketones 5 To Provide Substituted Cyclohexanols 6 and 7 (Scheme 2)

entry	substrate	R	% isoltd yield **6** + **7** (diast ratio, **6**:**7**)	% yield **8**	% yield **9**	% yield **10**	reaction time (h)
1	**5a**	Me	91 (36:1)	–	–	–	<0.25
2	**5b**	Et	73 (5:1)	–	15	–	2
3	**5c**	*i*-Pr	37 (5:1)	25	15	15	8
4	**5c**[a]	*i*-Pr	20 (5:1)	16	50	10	4
5	**5d**	*t*-Bu	7 (5:1)	7	50	30	32
6	**5e**	Ph	–	–	64	–	30

[a] Twenty equivalents of *t*-BuOH were added.

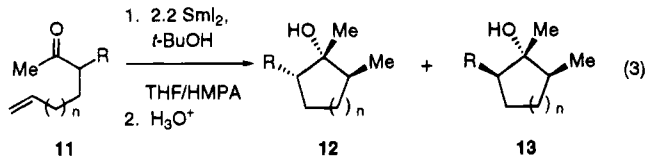
Scheme 2



resulted in a more rapid consumption of starting material and a significant increase in reduced byproduct **9c**.

With both the *tert*-butyl-substituted and phenyl-substituted unsaturated ketones **5d** and **5e**, respectively, the major products were the reduced, uncyclized alcohols **9d** and **9e**. Reactions with **5d** and **5e** both required 32 h for complete consumption of starting material.

Although excellent diastereoselectivities were observed at two stereocenters in the case of the methyl ketones as well as several cyclic ketones previously studied,[7b] we anticipated the potential of simultaneously controlling the relative stereochemistry over three stereocenters using chiral, unsaturated ketone substrates (eq 3). The



(3)

diastereoselectivity was predicted to be controlled through cyclization via a chairlike transition state with the substituents at the existing stereocenter preferentially occupying pseudoequatorial positions. Despite the fact that similar neutral radical cyclization reactions result in the formation of all possible diastereomers,[11] we were optimistic that the inherent preference for the trans relationship between the ketyl oxygen and developing methylene radical would set the relative stereochemistry at these two positions and additionally permit asymmetric induction at a third center. Along these lines we first prepared the substrates in Table 3 to investigate asymmetric induction in the radical cyclization process. Entries 1 and 2 indicate that while substitution at the position adjacent to the carbonyl of substituted 6-hepten-2-ones results in minimal preference for additional relative asymmetric induction at this stereogenic center, the relative stereochemistry of the two stereocenters created by carbon–carbon bond formation remain intact. Thus, despite the possibility of forming four diastereomers in the case of substrate **11b**, only two diastereomers are produced. Additionally, the major diastereomeric product **12b** is the diastereomer predicted assuming a chairlike transition state with the isopropyl group in a pseudoequatorial position. In slight contrast to the 5-exo-trig ketyl radical cyclizations, modest stereoselectivity over three stereocenters was observed upon cyclization of substrates **11c** and **11d**. Surprisingly, increasing the alkyl substituent from methyl to isopropyl resulted in a drop in stereoselectivity, and a third diastereomer was also formed.

Table 3. Investigation of Relative Asymmetric Induction in the Cyclization of Substrates 11

entry	substrate	R	*n*	% isoltd yield **12** + **13**	diast ratio **12**:**13**
1	**11a**	Me	1	83	1:1
2	**11b**	*i*-Pr	1	89	3:1
3	**11c**	Me	2	89	6:1
4	**11d**	*i*-Pr	2	93	9:2:1

Stereochemical assignments for products generated in this series were based mostly upon NMR spectral data. While the stereochemical assignments of the separated isomers of **12a** and **13a** as well as **12c** and **13c** were established by symmetry arguments, the relative stereochemistry of the diastereomeric pairs **12b**, **13b** and **12d**, **13d** was not quite as straightforward. However, a chemical shift tendency was evident in the ^{13}C spectra of these compounds. As a result of steric compression effects (the γ-gauche effect)[12] the C-1 methyl group (C1-

(11) Feldman, K. S.; Romanelli, A. L.; Ruckle, R. E., Jr.; Jean, G. *J. Org. Chem.* **1992**, *57*, 100.

(12) (a) Wehrli, F. W.; Wirthlin, T. *Interpretation of Carbon-13 NMR Spectra*; Heyden: London, 1976. (b) Whitesell, J. A.; Minton, M. A. *J. Am. Chem. Soc.* **1987**, *109*, 225 and references cited therein.

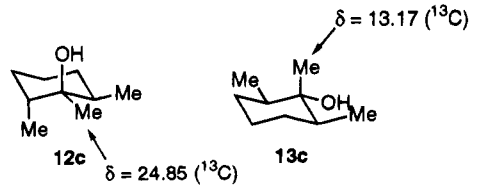


Figure 1. Chemical shift correlation of diastereomers **12c** and **13c**.

Table 4. ^{13}C NMR Chemical Shift Correlation of Products 12 and 13

product	C-1 Me (ppm)	C1 (ppm)	product	C-1 Me (ppm)	C1 (ppm)
12a	22.65	81.57	**12c**	24.85	74.06
13a	14.93	80.64	**13c**	13.17	75.32
12b	25.50	81.43	**12d**	26.90	75.50
13b	14.89	80.93	**13d**	14.83	76.22

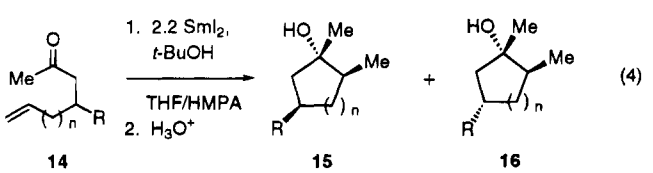
Table 5. Investigation of Relative Asymmetric Induction in the Cyclization of Substrates 14

entry	substrate	R	*n*	% isoltd yield **15** + **16**	diast. ratio **15**:**16**
1	**14a**	Me	1	73	7:1[a]
2	**14b**	Ph	1	82	5:1
3	**14c**	*i*-Pr	1	85	3:1
4	**14d**	Me	2	86	4:1
5	**14e**	Ph	2	89	3:1
6	**14f**	*i*-Pr	2	93	2:1
7	**14g**	OH	2	95	1:4
8	**14h**	OTBS	2	93	1:1

[a] The intermediate-cyclized organosamarium was trapped with $(PhSe)_2$ to provide the reported compound.

Me in Table 4) was shifted significantly upfield (as determined by $^{13}C-^{1}H$ HETCOR experiments) in diastereomer **13**. For example, in considering the two diastereomeric products **12c** and **13c**, the lowest energy conformation of the minor diastereomer (**13c**, Figure 1) consists of the C-1 methyl group in an axial orientation subject to 4 gauche butane interactions. The equatorial C-1 methyl group corresponding to the lowest energy chair conformation of the major diastereomer (**12c**, Figure 1) was subject to two gauche butane interactions [the chair flip isomer is 0.70 kcal higher in energy (MM2*) and is subject to three gauche butane interactions]. The ^{13}C chemical shift of the C-1 methyl group in the minor diastereomer was 13.17 ppm while the same resonance for the major diastereomer occurred at 24.85 ppm. A similar upfield shift of the C-1 methyl group was apparent for the analogous cyclopentyl systems.

1,3-Asymmetric induction was next examined by synthesizing substrates substituted at the 4-position of 6-hepten-2-one and 7-octen-2-one and subjecting them to reductive cyclization with SmI_2. Only moderate diastereoselectivity was achieved in these cases as indicated in Table 5 (eq 4). Interestingly, in analogy with the results



(4)

discussed above, there appears to be an inverse relationship between diastereoselectivity and substituent size. These results indicate that while the major diastereomer in the case of the alkyl-substituted examples can in

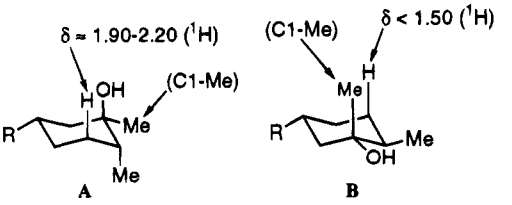


Figure 2. Chemical shift correlations of compounds **15d–f** and **16d–f**.

Table 6. ^{13}C NMR Chemical Shift Correlation of Products 15 and 16

product	C-1 Me (ppm)	C1 (ppm)	product	C-1 Me (ppm)	C1 (ppm)
15d	29.15	72.98	**16e**	20.11	73.31
16d	20.13	73.12	**15f**	29.39	72.99
15e	29.41	72.99	**16f**	20.19	73.48

general be rationalized by invoking a chairlike transition state with the substituent in an equatorial position, the minor diastereomer is likely to arise from a boatlike or some alternative transition structure. A boatlike transition structure with the substituent in an equatorial position has been suggested as a minimum energy pathway leading to the minor diastereomer in some substituted 5-hexenyl radical reactions.[3c]

Stereochemical assignments in this series were again made by NMR analysis. The ^{1}H NMR spectra provided useful information in certain instances. In the case of the cyclohexanol products, the axial C-3 proton signal was shifted noticeably downfield ($\delta \approx 1.90-2.20$, **A** in Figure 2) appearing as a triplet of triplets (the geminal coupling constant and the 180° vicinal coupling constant are similar) when the hydroxyl group at C-1 was in an axial position (and the C-2 methyl was also axial). However, when the hydroxyl group was in an equatorial position the same C-3 proton was obscured ($\delta < 1.50$, **B** in Figure 2) by the additional resonances. Interestingly, the axial proton at C-5 was not similarly shifted downfield. Furthermore, the same compressional effects as alluded to previously were observed in the ^{13}C NMR of cyclohexanol compounds **15d–f** and **16d–f** (Table 6). In addition to these chemical shift tendencies, the relative stereochemistry of **15e** and **16e** was supported by NOE and coupling constant data. The chemical shift of the benzylic proton signal for the major diastereomer was observed at 2.94 ppm and was split into a triplet of triplets, supporting the assignment as an axial proton deshielded by the axial C-1 hydroxyl group. The axial C-3 proton signal was evident at 2.12 ppm as a triplet of triplets as discussed above and exhibited an NOE with the axial benzylic proton signal at $\delta = 2.94$. The benzylic proton signal for the minor diastereomer also appeared as a triplet of triplets, but its chemical shift (2.67) was considerably upfield because it was not subject to the deshielding effects of the C-1 hydroxyl group. An NOE between the C-1 methyl group and the benzylic proton for the minor diastereomer further supported the stereochemistry shown. This NOE was absent in the major diastereomer (Figure 3).

Cyclization of hydroxy ketone **14g** resulted in an inverted 4:1 mixture of diastereomers when compared to the alkyl-substituted examples (Table 5, entry 7). The stereochemistry in this case was established by single crystal X-ray analysis of the major diastereomeric diol **16g**. Chelation with the samarium(III) ion or intramolecular hydrogen bonding may account for the observed

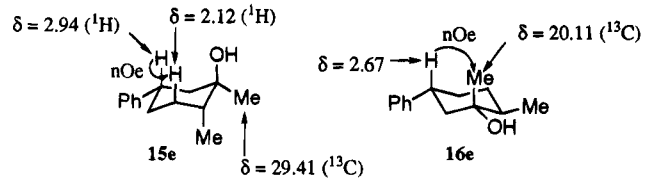


Figure 3. Chemical shift and NOE correlation of compounds **15e** and **16e**.

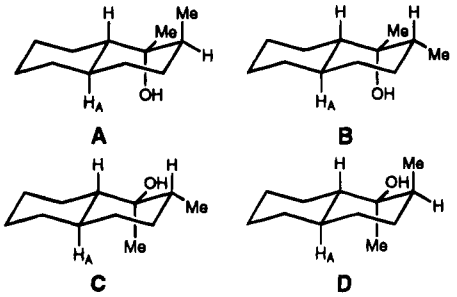
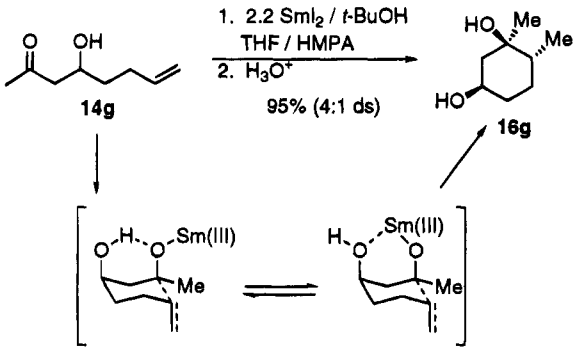


Figure 4. Possible diastereomers generated in SmI_2-induced cyclization of **17**.

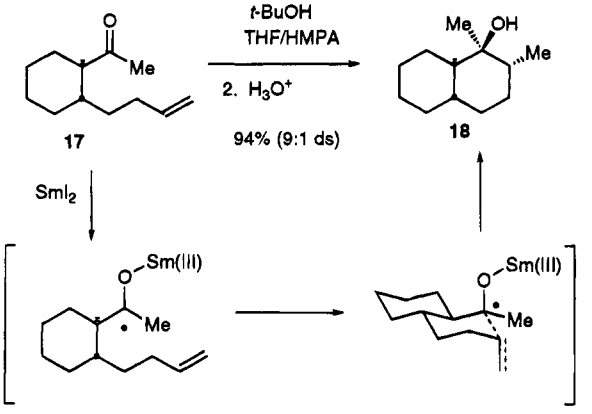
Scheme 3



diastereomeric ratio (Scheme 3). Unfortunately, attempted cyclization without HMPA in the reaction mixture (in an attempt to facilitate samarium chelation) resulted in ketone reduction without cyclization. In a similar vein, silyl ether **14h** was subjected to reductive cyclization in order to determine if the diastereoselection could be reversed through a nonchelating intermediate. Unfortunately, a 1:1 mixture of diastereomers was obtained. It is unclear whether the observed diastereomeric ratio was a result of the silyl ether exerting no steric bias in the transition state leading to product or whether some degree of chelation of the silyl ether by samarium is offsetting any steric influence.

Substrate **17** also cyclized in excellent yield and diastereoselectivity (Scheme 4). The stereochemistry of the major diastereomer was verified by a combination of ^1H NMR and ^{13}C NMR spectroscopy. The ring fusion must be trans because of the stereochemistry of the initial substrate **17**. Four stereoisomers are still possible (**A**–**D**, Figure 4). Isomers **C** and **D** can be ruled out on the basis of two-dimensional COSY spectra and by comparing chemical shifts observed in d_5-pyridine to those observed in $CDCl_3$.[13] Proton H_A appears as an apparent triplet of triplets (J = 14 Hz and 4.6 Hz) centered at 1.94 ppm in $CDCl_3$. The downfield position of H_A is indicative of the 1,3-diaxial relationship between this proton and the electronegative hydroxyl group, and this is further substantiated by a downfield chemical shift of 0.55 ppm in d_5-pyridine relative to that measured in $CDCl_3$. (The

Scheme 4

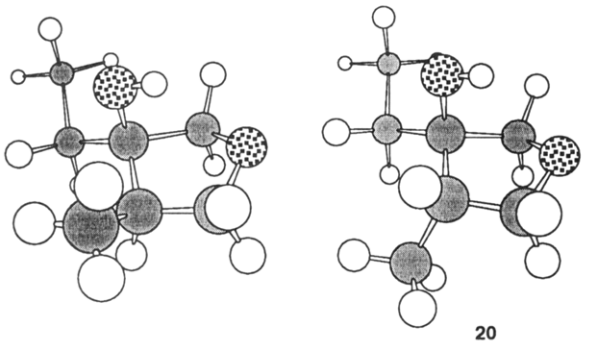


solvent-induced chemical shift differences for protons oriented with a 1,3-diaxial relationship to hydroxyl groups is typically 0.2–0.4 ppm[13]). Having established the orientation of the hydroxyl group in the rigid *trans*-decalin system, the last remaining stereocenter to assign is that possessing the methyl group adjacent to the hydroxyl group. This methyl doublet experiences a downfield shift of only 0.05 ppm upon a change of solvent from $CDCl_3$ to d_5-pyridine, in line with that expected for a methyl group trans diaxially disposed to a hydroxyl group. Thus, because the extent of vicinal deshielding experienced in pyridine solvent is a function of the dihedral angle of the O–C–C–CH_3 unit [with the largest deshielding observed for dihedral angles approaching 0° and negligible shift differences ($\Delta\delta \approx 0.03$ ppm) for dihedral angles of 180°], the methyl group and the hydroxy group must be aligned in a trans diaxial orientation. This is further substantiated by the ^{13}C chemical shift of this methyl group (δ 15.7 ppm, assigned by DEPT). The relative upfield position of this methyl group is characteristic of an axially disposed methyl group.[12] Thus product **18** can be assigned as diastereomer **A**, with the cyclization process again rationalized by invoking a chairlike transition structure (Scheme 4). Interestingly, the minor isomer appears to be diastereomer **D**, as assigned by NMR. Thus the ^{13}C chemical shifts of the methyl groups (δ 15.3, 14.8) are consistent with the isomer in which both methyl groups are axial.

A potential limitation of the ketyl radical cyclization reaction arises when electronegative heteroatoms that can act as leaving groups are placed α to the ketone in the initial substrate. In these instances, reductive elimination of the α-substituent (with concomitant formation of the corresponding enolate) may become competitive with radical cyclization.[14] Although five-membered ring formation is fast enough to permit the desired 5-exo cyclization (eq 5), attempted annulation to provide the analogous six-membered ring failed (eq 6). In this latter case, alkoxide elimination with enolate formation presumably preceeds the slower 6-exo radical cyclization.

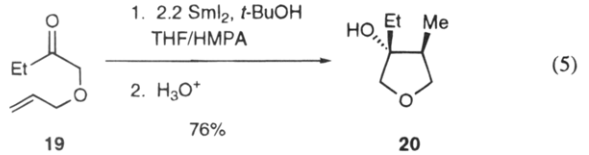
The stereochemistry of **20** was inferred from ^1H NMR coupling constants. Observation of the coupling constants in the proton NMR spectrum of **20** led us to postulate that the furanyl ring system was fairly rigid. Subsequent MM2* minimization of both possible diastereomers supported this hypothesis. The apparent global

(13) Demarco, P. V.; Farkas, E.; Doddrell, D.; Mylari, B. L.; Wenkert, E. *J. Am. Chem. Soc.* **1968**, *90*, 5480.
(14) Molander, G. A.; Hahn, G. *J. Org. Chem.* **1986**, *51*, 1135.

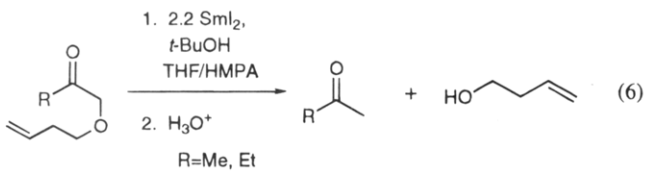


δ Ha1 = 4.21 ppm J (Ha1Hm1) = 8.2 Hz
δ Hm1 = 3.47 ppm J (Ha1Hx1) = 6.5 Hz
δ Hx1 = 2.10 ppm J (Hm1Hx1) = 3.2 Hz

Figure 5. MM2* Minimized geometries of product **20** and its diastereomer.



(5)

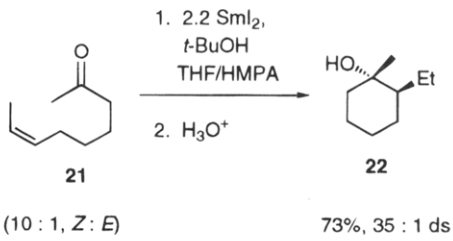


(6)

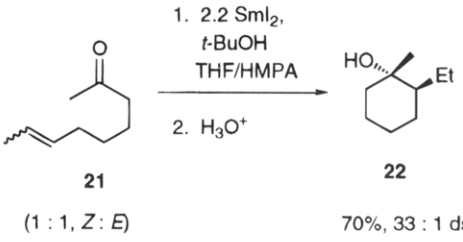
minimum energy structure consisted of a conformation in which the hydroxyl functionality formed an intramolecular hydrogen bond with the furanyl oxygen (Figure 5). The semirigid structure likely aided in the well-defined coupling constants observed in the ^{1}H NMR spectrum. The chemical shift and coupling constant data listed in Figure 5 were consistent with those of the observed product **20**. The most highly deshielded proton signal appeared as a doublet of doublets and could therefore be assigned to protons Ha or Hm. The most probable choice is Ha because it is likely deshielded by the hydroxyl functionality. Furthermore, the geminal coupling constant as well as the relatively large vicinal coupling constant for Ha (6.5 Hz vs 3.2 Hz) are most accurately explained by structure **20**.

Substrates **21** and **23** (eqs 7–9) were prepared to determine the effects of olefin geometry on the resulting cyclized product yield and stereochemistry. Subjecting substrate **21** as a 10:1 mixture of cis:trans isomers to the cyclization conditions resulted in isolation of cyclized product **22** in 73% yield as a 35:1 mixture of isomers (eq 7). Cyclization of a 1:1 mixture of cis:trans isomers (eq 8) resulted in a 33:1 mixture of diastereomers in 70% yield. Thus, the double bond isomer appears to have minimal effect on the resulting six-membered ring yield and stereochemistry. Similarily, substrate **23** also cyclized to form a single diastereomeric product (**24**) in high yield (eq 9).

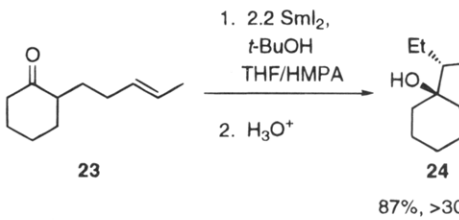
As supported by previous studies,[7b] an advantage of SmI_2-promoted reductive cyclization reactions over other reductive methods is the potential of effecting sequential radical cyclization/nucleophilic addition and substitution reactions. Our earlier studies indicated that this process was possible in cases that were initiated by a 5-exo-trig radical cyclization reaction.[7b] As verified by the results



(7)



(8)



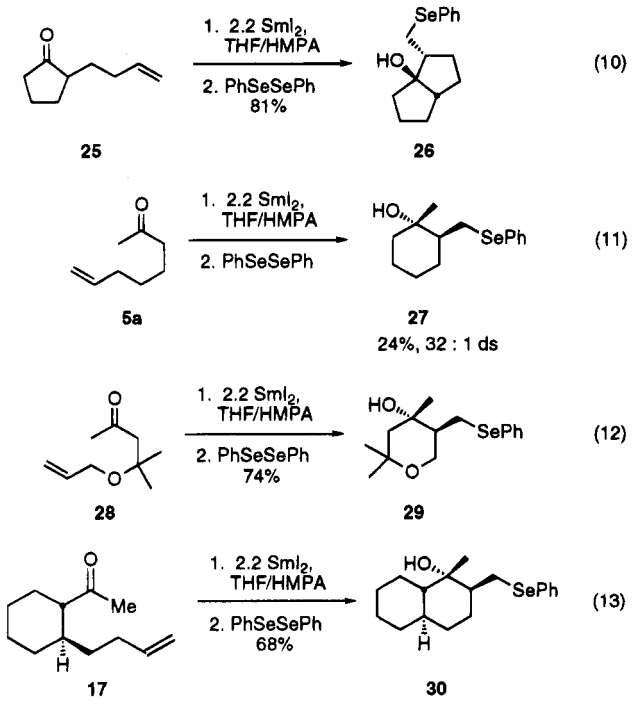
(9)

in eq 10, this tandem sequence appears to be general for cyclopentanoid systems. However, the slower cyclization rates associated with six-membered ring formation results in significantly lower yields of the desired products in certain instances. Consequently, attempted sequential radical cyclization/nucleophilic substitution as indicated in eq 11 resulted in a low yield of isolated product, presumably because of competitive intermolecular addition of the intermediate organosamarium species with unreacted ketone starting material. Although addition of the electrophile following cyclization resulted in a diminished yield of cyclized and trapped product, simultaneous addition of the substrate and electrophile might be expected to permit higher yields of the desired product at the expense of limiting the potential electrophiles compatible with this process.[7a,15] Additionally, substrates with cyclization rates greater than the acyclic unsubstituted case in eq 11 were expected to be amenable to this tandem sequence. As indicated by the results displayed in eqs 12 and 13, this hypothesis appears to hold in the case of the two substrates studied.

Conclusions

The samarium(II) iodide-promoted cyclization of several unsaturated ketones proceeds in excellent yield in the case of relatively unhindered ketones. Although five-membered ring formation proceeds even in the case of *tert*-butyl ketones, six-membered ring formation is severely impeded in the case of isopropyl and *tert*-butyl ketones. Additionally, the excellent diastereoselectivity for most ketyl cyclizations, attributed to the inherent preference for the largest possible dihedral angle between the ketyl oxygen and developing methylene radical center, is offset by increasing the size of the ketone substituent. Modest stereoselectivity is also observed over three stereocenters in most cases, and the relative stereochemistry of the major diastereomer can be pre-

(15) Molander, G. A.; Harring, L. S. *J. Org. Chem.* **1990**, *55*, 6171.



dicted invoking a chairlike transition state. Sequential radical cyclization/nucleophilic substitution appears to be general for reactions that are initiated by a 5-exo radical cyclization process, while examples that are initiated by a 6-exo radical cyclization reaction are only successful in instances when the radical cyclization process is relatively rapid.

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 weighed and stored under and inert atmosphere. CH_2I_2 was purchased from Aldrich and was distilled prior to use. Standard benchtop techniques were employed for handling air-sensitive reagents, and all reactions were carried out under Ar.

2-Methyl-7-octen-3-one (1b). To a solution of LDA (10 mmol) in 15 mL of THF at 0 °C was added 3-methyl-2-butanone *N,N*-dimethylhydrazone (1.14 g, 9 mmol) in 10 mL of THF. The resulting suspension was allowed to stir for 2 h at 0 °C, at which time 4-bromo-1-butene (1.45 g, 10 mmol) was added. After warming to room temperature the reaction mixture was stirred for an additional 2 h. Aqueous workup afforded the crude alkylated hydrazone. The hydrazone was dissolved in 40 mL of acetone, and 5 g of wet Amberlyst ion-exchange resin was added. After the reaction mixture was stirred for 3 h at room temperature, 80 mL of Et_2O was added, and the ion-exchange resin was removed by filtration. The organic layer was dried, concentrated, and purified by flash chromatography to provide the title compound (1.03 g, 82%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.79–5.63 (m, 1H), 5.02–4.85 (m, 2H), 2.60–2.48 (m, 1H), 2.40 (t, J = 7.3 Hz, 2H), 1.99 (q, J = 7.2 Hz, 2H), 1.67–1.57 (m, 2H), 1.03 (d, J = 6.8 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 214.74, 138.08, 115.07, 40.75, 39.30, 33.05, 22.61, 18.14.

2,2-Dimethyl-7-octen-3-one (1c). Following the hydrazone alkylation procedure described for **1b**, the title compound was prepared in 87% yield from 3,3-dimethyl-2-butanone *N,N*-dimethylhydrazone and 4-bromo-1-butene. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.79–5.62 (m, 1H), 4.95–4.83 (m, 2H), 2.42 (t, J = 7.3 Hz, 2H), 2.01–1.94 (m, 2H), 1.64–1.54 (m, 2H), 1.06 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 215.68, 138.15, 114.94, 43.96, 35.37, 33.00, 26.27, 22.75.

1-Phenyl-5-hexenone (1d). Following the hydrazone alkylation procedure described for **1b**, the title compound was prepared in 92% yield from acetophenone *N,N*-dimethylhydrazone and 4-bromo-1-butene. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.98–7.91 (m, 2H), 7.57–7.41 (m, 3H), 5.86–5.73 (m, 1H), 5.08–4.49 (m, 2H), 2.95 (t, J = 7.3 Hz, 2H), 2.17–2.10 (m, 2H), 1.88–1.78 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 200.22, 138.02, 137.00, 132.89, 128.52, 127.97, 115.24, 37.59, 33.08, 23.15.

8-Nonen-3-one (5b). Following the hydrazone alkylation procedure described for **1b**, the title compound was prepared in 68% yield from 2-butanone *N,N*-dimethylhydrazone and 5-bromo-1-pentene. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.80–5.65 (m, 1H), 4.97–4.82 (m, 2H), 2.42–2.32 (m, 4H), 2.24–1.96 (m, 2H), 1.60–1.48 (m, 2H), 1.38–1.27 (m, 2H), 0.99 (t, J = 7.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 211.71, 138.45, 114.54, 42.08, 35.74, 33.41, 28.35, 23.23.

2-Methyl-8-nonen-3-one (5c). Following the hydrazone alkylation procedure described for **1b**, the title compound was prepared in 82% yield from 3-methyl-2-butanone *N,N*-dimethylhydrazone and 5-bromo-1-pentene. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.83–5.71 (m, 1H), 5.04–4.85 (m, 2H), 2.61–2.50 (m, 1H), 2.41 (t, J = 7.5 Hz, 2H), 2.06–1.98 (m, 2H), 1.60–1.28 (m, 4H), 1.05 (d, J = 6.9 Hz, 6H).

2,2-Dimethyl-8-nonen-3-one (5d). Following the hydrazone alkylation procedure described for **1b**, the title compound was prepared in 91% yield from 3,3-dimethyl-2-butanone *N,N*-dimethylhydrazone and 5-bromo-1-pentene. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.81–5.68 (m, 1H), 4.98–4.85 (m, 2H), 2.43 (t, J = 7.2 Hz, 2H), 2.04–1.96 (m, 2H), 1.58–1.27 (m, 4H), 1.08 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 215.92, 138.60, 114.47, 43.98, 36.11, 33.56, 28.45, 26.28, 23.31.

1-Phenyl-6-heptenone (5e). Following the hydrazone alkylation procedure described for **1b**, the title compound was prepared in 74% yield from acetophenone *N,N*-dimethylhydrazone and 5-bromo-1-pentene. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.94–7.90 (m, 2H), 7.55–7.39 (m, 3H), 5.83–5.71 (m, 1H), 5.03–4.89 (m, 2H), 2.95 (t, J = 7.3 Hz, 2H), 2.79–2.03 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 200.32, 138.50, 136.97, 132.87, 128.51, 127.99, 114.60, 38.28, 33.49, 28.45, 23.66.

3-Methyl-6-hepten-2-one (11a). To a solution of LDA (11 mmol, 1 M in THF) at 0 °C was added propanal *N,N*-dimethylhydrazone (1.0 g, 10 mmol) in 10 mL of THF. After 2 h at 0 °C 4-bromo-1-butene (1.76 g, 13 mmol) was added and the reaction mixture was warmed to room temperature. Following an additional 4 h, aqueous workup and hydrazone cleavage (Amberlyst, acetone) afforded crude 2-methyl-5-hexenal. This crude product was dissolved in 20 mL of THF and cooled to 0 °C. MeLi (15 mmol, 7.5 mL of a 2M solution in Et_2O) was added slowly and the resulting solution was warmed to room temperature. After an additional 1 h at room temperature an aqueous workup was performed. The resulting crude alcohol was dissolved in 30 mL of acetone and was oxidized to the corresponding ketone with PDC (4.51 g, 12 mmol). Aqueous workup followed by flash chromatography afforded the title compound (0.57 g, 45%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.79–5.62 (m, 1H), 4.98–4.84 (m, 2H), 2.61–2.55 (m, 1H), 2.23–1.34 (m, 4H), 2.07 (s, 3H), 1.02 (d, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 212.48, 137.89, 114.97, 46.16, 31.65, 31.18, 28.02, 16.00.

3-(2-Propyl)-6-hepten-2-one (11b). Following the general procedure described for **11a**, the title compound was prepared in 42% yield from 3-methylbutanal *N,N*-dimethylhydrazone and 4-bromo-1-butene. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.78–5.64 (m, 1H), 4.97–4.83 (m, 2H), 2.28–2.21 (m, 1H), 2.09 (s, 3H), 2.01–1.43 (m, 5H), 0.87 (d, J = 6.6 Hz, 3H), 0.85 (d, J = 6.6 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 212.89, 138.18, 114.97, 59.03, 31.88, 30.30, 29.91, 27.42, 20.99, 19.58.

3-(2-Propyl)-7-octen-2-one (11d). Following the general procedure described for **11a**, the title compound was prepared in 59% yield from 3-methylbutanal *N,N*-dimethylhydrazone and 5-bromo-1-pentene. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.79–5.63 (m, 1H), 4.98–4.84 (m, 2H), 2.41–2.24 (m, 1H), 2.06 (s, 3H), 2.03–1.31 (m, 7H), 0.84 (d, J = 6.6 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 213.05, 138.32, 114.67, 59.94, 33.73, 29.92, 29.87, 27.98, 26.91, 21.02, 19.71.

4-Methyl-6-hepten-2-one (14a). $TiCl_4$-promoted addition of allyltrimethylsilane to 3-penten-2-one provided the title compound in 63% yield. ^1H NMR (300 MHz, $CDCl_3$): δ 5.77–5.62 (m, 1H), 5.01–4.93 (m, 2H), 2.40 (dd, J = 15.9, 5.1 Hz, 1H), 2.16 (dd, J = 15.9, 7.6 Hz, 1H), 2.18–1.91 (m, 3H), 2.08 (s, 3H), 0.86 (d, J = 6.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 208.88, 136.60, 116.46, 50.17, 41.04, 30.40, 28.80, 19.63.

4-Phenyl-6-hepten-2-one (14b). $TiCl_4$-promoted addition of allyltrimethylsilane to 4-phenyl-3-buten-2-one provided the title compound in 71% yield. ^1H NMR (300 MHz, $CDCl_3$): δ 7.39–7.21 (m, 5H), 5.77–5.62 (m, 1H), 5.08–4.96 (m, 2H), 3.36–3.27 (m, 1H), 2.83 (dd, J = 16.5, 6.6 Hz, 1H), 2.76 (dd, J = 16.5, 7.7 Hz, 1H), 2.44–2.41 (m, 2H), 2.38 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 207.72, 144.00, 136.12, 128.42, 127.39, 126.39, 116.72, 49.36, 40.76, 40.55, 30.56.

4-(2-Propyl)-6-hepten-2-one (14c). $TiCl_4$-promoted addition of allyltrimethylsilane to 6-methyl-3-hepten-2-one provided the title compound in 76% yield. ^1H NMR (300 MHz, $CDCl_3$): δ 5.79–5.65 (m, 1H), 4.96–4.84 (m, 2H), 2.34 (dd, J = 16.4, 5.8 Hz, 1H), 2.18 (dd, J = 16.4, 7.3 Hz, 1H), 2.08 (s, 3H), 1.99–1.61 (m, 4H), 1.41–1.13 (m, 2H), 0.79 (d, J = 7.1 Hz, 3H), 0.76 (d, J = 7.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 209.28, 138.69, 114.39, 45.17, 38.71, 31.45, 30.42, 30.19, 29.38, 19.28, 18.25.

4-Phenyl-7-octen-2-one (14e). To a suspension of CuCN (1.35 g, 15 mmol) in 20 mL of THF was added TMEDA (1.75 g, 15 mmol). The mixture was allowed to stir for 10 min at room temperature and then it was cooled to −78 °C. 3-Butenylmagnesium bromide (20 mmol, 20 mL of a 1 M solution in THF) was added dropwise over 10 min, and the resulting suspension was stirred for an additional 20 min. TMSCl (1.63 g, 15 mmol) was added followed by a precooled solution of 4-phenyl-3-buten-2-one (2.19 g, 15 mmol) in 15 mL of THF. Upon complete reaction (ca. 30 min), the reaction mixture was quenched with aqueous NH_4Cl·NH_4OH (10:1). Extractive workup (Et_2O) afforded the TMS enol ether that was hydrolyzed with 1 M HCl. Flash chromatography yielded the title compound (2.24 g, 74%). ^1H NMR (300 MHz, $CDCl_3$): δ 7.36–7.20 (m, 5H), 5.84–5.72 (m, 1H), 5.03–4.94 (m, 2H), 3.25–3.14 (m, 1H), 2.81 (dd, J = 16.1, 7.1 Hz, 1H), 2.74 (dd, J = 16.1, 7.1 Hz, 1H), 2.06 (s, 3H), 1.98–1.90 (m, 2H), 1.82–1.64 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 207.77, 144.02, 138.17, 128.47, 127.49, 126.40, 114.72, 50.72, 40.53, 35.36, 31.35, 30.51.

4-(2-Propyl)-7-octen-2-one (14f). CuCN-promoted conjugate addition of 3-butenylmagnesium bromide to 6-methyl-3-hepten-2-one as described for **14e**, provided the title compound in 76% yield. ^1H NMR (300 MHz, $CDCl_3$): δ 5.79–5.65 (m, 1H), 4.96–4.84 (m, 2H), 2.34 (dd, J = 16.4, 5.8 Hz, 1H), 2.18 (dd, J = 16.4, 7.3 Hz, 1H), 2.08 (s, 3H), 1.99–1.61 (m, 4H), 1.41–1.13 (m, 2H), 0.79 (d, J = 7.1 Hz, 3H), 0.76 (d, J = 7.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 209.28, 138.69, 114.39, 45.17, 38.71, 31.45, 30.42, 30.19, 29.38, 19.28, 18.25.

4-Hydroxy-7-octen-2-one (14g). To a solution of acetone *N,N*-dimethylhydrazone (1.0 g, 10 mmol) in 15 mL of THF at −78 °C was added *n*-BuLi (11 mmol, 6.9 mL of a 1.6 M solution in hexanes) and the reaction mixture was warmed to 0 °C. After stirring for 2 h at 0 °C the reaction was cooled to −78 °C. 4-Pentenal (1.18 g, 12 mmol) in 15 mL of THF was added, and the solution was stirred for an additional 2 h. The reaction was warmed to room temperature and quenched with aqueous $NaHCO_3$. Hydrazone cleavage (Amberlyst, acetone) followed by flash chromoatography afforded the title compound (1.02 g, 72%). ^1H NMR (300 MHz, $CDCl_3$): δ 5.86–5.70 (m, 1H), 5.07–4.91 (m, 2H), 4.08–3.97 (m, 1H), 3.01 (br s, 1H), 2.62-2.49 (m, 2H), 2.21–2.05 (m, 2H), 2.14 (s, 3H), 1.61–1.42 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 209.92, 138.12, 114.93, 66.86, 49.84, 35.33, 30.68, 29.62.

4-(*tert*-Butyldimethylsiloxy)-7-octen-2-one (14h). To a solution of 4-hydroxy-7-octen-2-one (**14g**, 0.426 g, 3 mmol) in 10 mL of DMF were added imidazole (0.272 g, 4 mmol) and TBDMSCl (0.60 g, 4 mmol), and the resulting mixture was stirred at room temperature overnight. Aqueous workup afforded the title compound (0.668 g, 87%). ^1H NMR (300 MHz, $CDCl_3$): δ 5.84–5.70 (m, 1H), 5.02–4.91 (m, 2H), 4.19–4.11 (m, 1H), 2.60 (dd, J = 15.0, 6.6 Hz, 1H), 2.46 (dd, J = 15.0, 5.4 Hz, 1H), 2.14 (s, 3H), 2.10–2.01 (m, 2H), 1.58–1.49 (m, 2H), 0.84 (s, 9H), 0.04 (s, 3H), 0.00 (s, 3H).

***trans*-[2-(3-Butenyl)cyclohexyl] Methyl Ketone (17).** CuCN-promoted conjugate addition of 3-butenylmagnesium bromide to 1-acetylcyclohexene, as described for **14e**, afforded the title compound as a 1:1 mixture of diastereomers. Isomerization with *t*-BuOH/*t*-BuOH in THF afforded a 9:1 mixture of diastereomers. Flash chromatography afforded a 50:1 mixture of trans:cis isomers (2.30 g, 64%). ^1H NMR (300 MHz, $CDCl_3$): δ 5.78–5.64 (m, 1H), 4.97–4.85 (m, 2H), 2.20–0.82 (m, 14H), 2.08 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 213.20, 138.68, 114.40, 57.72, 37.73, 33.89, 30.59, 30.46, 29.63, 28.99, 25.63, 25.58.

5-Oxa-7-octen-3-one (19). To a solution of 1-hydroxybutan-2-one (0.44 g, 5 mmol) in 4 mL of allyl bromide was added 3 g of $CaSO_4$. This suspension was cooled to 0 °C and Ag_2O (1.98 g, 8 mmol) was added in several portions over 30 min. The reaction mixture was warmed to room temperature and allowed to stir an additional 10 h. Et_2O was added and the reaction mixture was filtered through Celite. Solvent removal followed by flash chromatography afforded the title compound (0.60 g, 94%). ^1H NMR (300 MHz, $CDCl_3$): δ 5.94–5.81 (m, 1H), 5.20–5.17 (m, 2H), 4.01 (s, 2H), 3.98 (d, J = 4.5 Hz, 2H), 2.45 (q, J = 7.3 Hz, 2H), 1.04 (t, J = 7.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 209.88, 134.80, 116.82, 75.84, 71.01, 33.02, 7.12.

5-Oxa-8-nonen-3-one. The title compound was prepared from 1-hydroxybutan-2-one and 1-iodo-3-butene in 62% yield as described for **19**. ^1H NMR (300 MHz, $CDCl_3$): δ 5.88–5.72 (m, 1H), 5.12–4.99 (m, 2H), 4.03 (s, 2H), 3.52 (t, J = 6.8 Hz, 2H), 2.46 (q, J = 7.3 Hz, 2H), 2.39–2.32 (m, 2H), 1.04 (t, J = 7.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 209.88, 134.80, 116.72, 75.84, 71.01, 33.02, 31.07, 7.12.

6,6-(Ethylenedioxy)heptanal. 7-Octen-2-one was protected as the acetal with ethylene glycol and treated with ozone to afford the title compound. ^1H NMR (300 MHz, $CDCl_3$): δ 9.74 (s, 1H), 3.92–3.74 (m, 4H), 2.42 (t, J = 7.1 Hz, 2H), 1.61–1.51 (m, 4H), 1.37–1.25 (m, 2H), 1.28 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 202.56, 109.71, 64.47, 43.68, 38.73, 23.58, 23.43, 22.04.

(*Z*)-7-Nonen-2-one (21). To (ethyl)triphenylphosphonium iodide (2.60 g, 7 mmol) in 15 mL of THF at room temperature was added *t*-BuOK (0.78 g, 7 mmol) and the suspension was stirred for 2 h. 6,6-(Ethylendioxy)heptanal (0.86 g, 5 mmol) in 15 mL of THF was added, and the reaction mixture was stirred overnight. Aqueous workup, acetal cleavage (1 M HCl and THF), and flash chromatography afforded the title compound as a 10:1 mixture of cis:trans isomers. ^1H NMR (300 MHz, $CDCl_3$): δ 5.48–5.27 (m, 2H), 2.39 (t, J = 7.3 Hz, 2H), 2.10 (s, 3H), 2.06–1.97 (m, 2H), 1.57 (d, J = 6.2 Hz, 3H), 1.62–1.51 (m, 2H), 1.38–1.27 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 209.19, 130.11, 124.12, 43.59, 29.77, 28.46, 26.48, 23.38, 23.24, 12.66.

(*E*)-Ethyl 5-[2,2-(Ethylenedioxy)cyclohexyl]-2-pentenoate. A solution of 2-(3-butenyl)cyclohexanone (2.25 g, 14.8 mmol), ethylene glycol (1.86 g, 30 mmol), TsOH (0.02 g), and 50 mL of benzene was heated at reflux with azeotropic removal of water for 2 h. The ethylene ketal was isolated after aqueous workup. Ozonolysis of this material followed by reduction of the ozonide with triphenylphosphine afforded the crude aldehyde. Triethyl phosphonoacetate (2.92 g, 13 mmol) in 20 mL of THF was added slowly to a suspension of NaH (12 mmol, 0.48 g of a 60% dispersion in mineral oil) in 30 mL of THF at 0 °C. The resulting solution was warmed to room temperature and stirred for 2 h. The aldehyde (1.98 g, 10 mmol) in 20 mL was added the above solution, and the resulting solution was stirred and additional 12 h. Aqueous workup afforded the title compound (2.51 g, 63%). ^1H NMR (300 MHz, $CDCl_3$): δ 6.92 (dt, J = 15.6, 6.8 Hz, 1H), 5.77 (dt, J = 15.6, 1.5 Hz, 1H), 4.13 (q, J = 7.0 Hz, 2H), 3.93–3.86 (m, 4H), 2.38–2.05 (m, 2H), 1.75–1.18 (m, 11H), 1.24 (t, J = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.79, 149.64, 121.08, 110.63, 64.71, 64.59, 60.03, 43.98, 34.58, 30.07, 28.88, 26.51, 24.43, 23.67, 14.17.

2-[(*E*)-5-Hydroxy-3-pentenyl]cyclohexanone. To a solution of ethyl 5-[2,2-(ethylenedioxy)cyclohexyl]-2-pentenoate (1.47 g, 5.48 mmol) in 60 mL of Et_2O at −40 °C was added

DIBAH (1.72 g, 12.1 mmol) in 30 mL of Et_2O. The resulting solution was warmed to −5 °C and stirred overnight. The reaction was quenched with 1 mL of H_2O, and 8 g of Na_2SO_4 was added. The crude product in 20 mL of THF at 0 °C was treated with 10 mL of 1 M HCl to effect acetal cleavage. Usual workup afforded the title compound. ^1H NMR (300 MHz, $CDCl_3$): δ 5.60−5.57 (m, 2H), 4.02−4.00 (m, 2H), 2.30−1.17 (m, 14H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 213.44, 132.41, 129.37, 63.45, 49.76, 41.92, 33.77, 29.53, 28.65, 27.89, 24.74.

2-[(*E*)-3-Pentenyl]cyclohexanone (23). To a solution of (*E*)-5-[2,2-(ethylenedioxy)cyclohexyl]-2-pentenol (0.44 g, 1.96 mmol) in 10 mL of THF at 0 °C was added pyridine·SO_3 complex (0.48 g, 3 mmol). The resulting suspension was stirred for 4 h at 0 °C prior to the addition of LAH (0.45 g, 12 mmol) in 15 mL of THF. This solution was warmed to room temperature and stirred for 6 h. The reaction was quenched with $Na_2SO_4·10H_2O$ and extracted with Et_2O. The crude product in THF at 0 °C was treated with 1 M HCl to cleave the acetal. Aqueous workup and flash chromatography afforded the title compound (0.178 g, 55%). ^1H NMR (300 MHz, $CDCl_3$): δ 5.42−5.28 (m, 2H), 2.39−1.11 (m, 13H), 1.58 (d, J = 4.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 213.36, 130.88, 125.12, 49.75, 41.92, 33.70, 29.86, 29.04, 27.92, 24.75, 17.78.

4,4-Dimethyl-5-oxa-7-octen-2-one (28). The title compound was prepared from 4-hydroxy-4-methyl-2-pentanone and allyl bromide, as described for **19**, in 48% yield. ^1H NMR (300 MHz, $CDCl_3$): δ 5.87−5.79 (m, 1H), 5.25−5.18 (m, 2H), 4.05 (s, 2H), 3.91 (d, J = 5.1 Hz, 2H), 2.18 (s, 3H), 1.26 (s, 6H).

Preparation of SmI_2 Solution. Samarium metal (0.301 g, 2.00 mmol) was added under a flow of Ar to an oven-dried round-bottomed flask containing a magnetic stirring bar and a septum inlet. To the samarium was added 12 mL of THF followed by CH_2I_2 (0.492 g, 1.84 mmol). The mixture was stirred at room temperature for 2 h. The resulting deep blue solution was used directly to effect the following reductive cyclization reactions.

General Procedure for Cyclization of Olefinic Ketones. To the SmI_2 (1.84 mmol) in THF was added HMPA (2.63 g, 17.4 mmol), and Ar was bubbled through the solution for 10 min. A solution of the olefinic ketone (0.83 mmol) and *t*-BuOH (1.64 mmol) in 30 mL of THF was added over 1.5 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 6, no *t*-BuOH was added with the substrate and after the substrate was consumed, $(PhSe)_2$ (1.66 mmol) in 5 mL of THF was added to the reaction. Following an additional 30 min the reaction was quenched and worked up as usual.

2-Methyl-1-(2-propyl)cyclopentanol (2b) (**1b**, 0.106 g, 0.76 mmol): yield 0.092 g (85%) as a 23:1 mixture of diastereomers. ^1H NMR (300 MHz, $CDCl_3$): δ 2.17−2.04 (m, 1H), 1.88−1.52 (m, 6H), 1.32−1.23 (m, 1H), 1.02 (br s, 1H), 0.88 (d, J = 6.8 Hz, 3H), 0.87 (d, J = 6.6 Hz, 3H), 0.76 (d, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 88.94, 42.84, 35.31, 32.08, 31.70, 20.52, 17.42, 17.28, 16.84. IR (CCl_4): 3610, 3425, 2945 cm^{-1}. HRMS Calcd for $C_9H_{18}O$: 142.1358. found 142.1362. LRMS (EI) *m/e*: 142 (15), 99 (100), 81 (41).

1-*tert*-Butyl-2-methylcyclopentanol (2c). (**1c**, 0.116 g, 0.75 mmol), yield 0.091 g (78%) as a 3:1 mixture of diastereomers. ^1H NMR (300 MHz, $CDCl_3$): (major) δ 2.22−1.16 (m, 7H), 1.16 (br s, 1H), 0.98 (s, 9H), 0.93 (d, J = 7.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): (major) δ 88.81, 44.12, 36.70, 33.11, 26.85, 25.79, 20.46, 19.98; (minor) δ 85.45, 38.02, 37.70, 35.19, 30.56, 24.92, 22.60, 15.73. IR (CCl_4): 3620, 2980 cm^{-1}. HRMS Calcd for $C_{10}H_{20}O$: 138.1409 (M − H_2O). Found 138.1409. LRMS (EI) *m/e*: 138 (20), 123 (100), 95 (20), 81 (65).

2-Methyl-1-phenylcyclopentanol (3d) (**1d**, 0.162 g, 0.93 mmol): yield 0.079 g (48%) as a single diastereomer. ^1H NMR (300 MHz, $CDCl_3$): δ 7.46−7.43 (m, 2H), 7.36−7.30 (m, 2H), 7.24−7.19 (m, 1H), 2.26−1.53 (m, 7H), 1.52 (br s, 1H), 0.83 (d, J = 6.8 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 146.06, 128.08, 126.44, 125.02, 83.80, 45.25, 43.19, 31.76, 21.62, 11.91. IR (CCl_4): 3605, 3492, 3055, 2956, 2871 cm^{-1}. HRMS (EI) Calcd for $C_{12}H_{16}O$: 176.1201. Found 176.1216. LRMS (EI) *m/e*: 176 (38), 133 (100), 120 (35), 105 (61).

2-Methyl-1-ethylcyclohexanol (6b, 7b) (**5b**, 0.127 g, 0.91 mmol): yield 0.094 g (73%) as a 5:1 mixture of diastereomers. ^1H NMR (300 MHz, $CDCl_3$): δ 1.67−0.98 (m, 12H), 0.83 (t, J = 7.4 Hz, 3H), 0.82 (d, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): (major) δ 73.35, 40.85, 35.49, 31.03, 30.01, 23.29, 22.63, 15.11, 6.68. IR (CCl_4): 3612, 3415, 2935 cm^{-1}. LRMS (EI) *m/e*: (major) 142 (2), 113 (88), 95 (52), 85 (100), 72 (42), 57 (53); (minor) 142 (1), 113 (81), 95 (40), 85 (100), 72 (41), 57 (44).

2-Methyl-1-(2-propyl)cyclohexanol (6c, 7c) (**4c**, 0.149 g, 0.97 mmol): yield 0.056 g (37%) as a 5:1 mixture of diastereomers. ^1H NMR (300 MHz, $CDCl_3$): δ 1.92−1.22 (m, 10H), 1.02 (br s, 1H), 0.89 (d, J = 7.1 Hz, 3H), 0.83 (d, J = 6.8 Hz, 3H), 0.82 (d, J = 6.8 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): (major) δ 74.60, 35.20, 33.47, 30.05, 28.85, 21.74, 19.56, 15.96, 15.27, 15.24; (minor) δ 74.94, 36.26, 34.29, 30.72, 28.95, 25.86, 21.38, 17.30, 16.20, 14.39. IR (CCl_4): 3625, 3454, 2980 cm^{-1}. LRMS (EI) *m/e*: (major) 156 (4), 113 (100), 95 (73), 86 (16), 71 (19), 69 (22); (minor) 156 (1), 113 (100), 95 (57), 86 (10), 71 (16), 69 (17).

1,2,5-Trimethylcyclopentanol (12a) (**11a**, 0.106 g, 0.84 mmol): yield 0.089g (83%) as a 1:1 mixture of diastereomers. ^1H NMR (400 MHz, $CDCl_3$): (**13a**, low R_f diastereomer) δ 1.84−1.76 (m, 4H), 1.19 (br s, 1H), 1.13−1.06 (m, 2H), 0.89 (d, J = 6.1 Hz, 6H), 0.84 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 80.64, 44.88, 28.45, 14.93, 13.83. IR (CCl_4): 3450, 1920 cm^{-1}. LRMS (EI) *m/e*: 128 (11), 113 (4), 85 (100), 72 (47), 71 (40), 43 (72). Anal. Calcd for $C_8H_{16}O$: C, 74.94; H, 12.58. Found: C, 74.87; H, 12.26.

***(1R*,2R*,5R*)*-1,2,5-Trimethylcyclopentanol (12a).** ^1H NMR (400 MHz, $CDCl_3$): δ 1.98−1.83 (m, 1H), 1.81−1.67 (m, 1H), 1.56 (br s, 1H), 1.34−1.08 (m, 4H), 1.10 (s, 3H), 0.92 (d, J = 6.7 Hz, 3H), 0.87 (d, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 81.57, 44.72, 41.66, 30.51(2C), 22.65, 17.77, 13.23. LRMS (EI) *m/e*: 128 (17), 113 (12), 85 (100), 43 (67).

1,5-Dimethyl-2-(2-propyl)cyclopentanol (12b) (**11b**, 0.154 g, 1.00 mmol): yield 0.139 g (89%) as a 3:1 mixture of diastereomers. ^1H NMR (300 MHz, $CDCl_3$): δ 1.87−1.20 (m, 8H), 1.16 (s, 2.25H), 1.03 (d, J = 6.4 Hz, 0.75H), 0.98 (d, J = 6.6 Hz, 2.25H), 0.92 (s, 0.75H), 0.89 (d, J = 6.8 Hz, 4.5H), 0.87 (d, J = 6.4 Hz, 0.75H), 0.84 (d, J = 6.6 Hz, 0.75H). ^{13}C NMR (75 MHz, $CDCl_3$): (major) δ 81.43, 54.28, 47.64, 30.80, 28.21, 27.17, 25.50, 23.31, 21.42, 16.43; (minor) δ 80.90, 56.60, 46.16, 30.04, 27.60, 26.25, 22.51, 21.52, 14.89, 13.23. IR (CCl_4): 3612, 3495, 2936 cm^{-1}. LRMS (EI) *m/e*: (major) 156 (11), 141 (8), 138 (2), 85 (100), 72 (81), 71 (63); (minor) 156 (10), 141 (12), 138 (2), 85 (100), 72 (73), 71 (68). Anal. Calcd for $C_{10}H_{20}O$: C, 76.86; H, 12.90. Found: C, 76.72; H, 12.78.

1,6-Dimethyl-2-(2-propyl)cyclohexanol (12d) (**11d**, 0.168 g, 1.00 mmol): yield 0.159 g (93%) as a 9:2:1 mixture of diastereomers (separable). ^1H NMR (400 MHz, C_6D_6): (major) δ 2.01 (dhept, J = 6.9, 2.5 Hz, 1H), 1.87(tt, J = 12.9, 4.5 Hz, 1H), 1.47−1.32 (m, 5H), 1.24−1.13 (m, 2H), 1.03 (s, 3H), 1.02 (d, J = 6.9 Hz, 3H), 0.91 (d, J = 6.9 Hz, 3H), 0.80 (d, J = 7.3 Hz, 3H), 0.68 (br s, 1H); (minor) δ 2.18 (dhept, J = 8.7, 1.8 Hz, 1H), 1.58−1.01 (m, 8H), 0.97 (d, J = 7.0 Hz, 3H), 0.88 (d, J = 6.7 Hz, 3H), 0.85 (s, 3H), 0.80 (d, J = 6.9 Hz, 3H), 0.61 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): (major) δ 75.50, 44.87, 42.16, 28.69, 26.90, 26.10, 23.66, 20.97, 20.60, 18.32, 15.82; (minor) δ 76.22, 55.00, 45.04, 32.66, 26.26, 25.18, 24.89, 24.80, 19.25, 15.17, 14.83. IR (CCl_4): 3612, 2942, 2871 cm^{-1}. HRMS Calcd for $C_{11}H_{22}O$: 170.1671. Found 170.1675. LRMS (EI) *m/e*: 170 (38), 155 (30), 113 (45), 99 (32), 85 (100), 43 (90). Anal. Calcd for $C_{11}H_{22}O$: C, 77.58; H, 13.02. Found: C, 77.50; H, 13.02.

1,4-Dimethyl-2-[(phenylseleno)methyl]cyclopentanol (15a) (**14a**, 0.102 g, 0.81 mmol): yield 0.168 g (73%) as a 7:1 mixture of diastereomers. ^1H NMR (300 MHz, $CDCl_3$): (major) δ 7.57−7.43 (m, 2H), 7.32−7.21 (m, 3H), 3.05 (dd, J = 11.6, 6.5 Hz, 1H), 2.78 (dd, J = 11.6, 8.3 Hz, 1H), 2.18−1.32 (m, 7H), 1.24 (s, 3H), 0.96 (d, J = 6.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 132.55, 130.40, 129.12, 126.89, 80.66, 51.27, 50.29, 41.24, 29.65, 29.17, 25.15, 21.06. IR (CCl_4): 3612, 3506, 3062, 2942, 2864 cm^{-1}. HRMS Calcd for $C_{14}H_{20}OSe$: 284.0679. Found 284.0683. LRMS (EI) *m/e*: 284 (30), 158 (12), 127 (45), 109 (73), 69 (49), 43 (100).

1,2-Dimethyl-4-phenylcyclopentanol (15b) (**14b**, 0.162 g, 0.86 mmol): yield 0.134 g (82%) as a 5:1 mixture of diastereomers. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39–7.14 (m, 5H), 3.44–3.32 (m, 0.83H), 3.26–3.15 (m, 0.17H), 2.45–1.32 (m, 5H), 1.56 (br s, 1H), 1.29 (s, 2.H), 1.26 (s, 0.5H), 1.02 (d, J = 7.1 Hz, 2.5H), 0.99 (d, J = 6.8 Hz, 0.5H). ^{13}C NMR (75 MHz, $CDCl_3$): (major) δ 145.41, 128.32, 127.01, 125.87, 80.91, 49.15, 45.69, 42.28, 41.01, 25.02, 16.60; (minor) δ 147.49, 128.39, 127.13, 125.75, 81.01, 49.62, 45.09, 40.68, 40.51, 22.56, 14.67. IR (CCl_4): 3603, 3368, 3053, 3026, 2954 cm^{-1}. LRMS (EI) *m/e*: (major) 190 (2), 172 (58), 157 (76), 147 (100), 117 (78), 105 (47), 91 (74); (minor) 190 (6), 172 (28), 157 (32), 147 (100), 117 (66), 105 (44), 91 (57). Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.53. Found: C, 82.25; H, 9.92.

1,2-Dimethyl-4-(2-propyl)cyclopentanol (15c) (**14c**, 0.120 g, 0.78 mmol): yield 0.103 g (85%) as a 3:1 mixture of diastereomers. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.07–1.20 (m, 8H), 1.12 (s, 2.25H), 1.09 (s, 0.75H), 0.86 (d, J = 7.1 Hz, 3H), 0.82 (d, J = 6.6 Hz, 3H), 0.81 (d, J = 6.6 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): (major) δ 80.84, 45.92, 45.42, 43.51, 38.80, 34.06, 24.73, 21.45, 21.10, 16.37; (minor) δ 80.49, 45.84, 44.05, 41.74, 35.90, 34.20, 22.14, 20.87, 20.76, 14.41. IR (CCl_4): 3603, 3404, 2954, 2873 cm^{-1}. LRMS (EI) *m/e*: 156 (1), 113 (100), 71 (93). Anal. Calcd for $C_{10}H_{20}O$: C, 76.86; H, 12.90. Found: C, 76.58; H, 13.05.

1,2-Dimethyl-5-phenylcyclohexanol (15e) (**14e**, 0.184 g, 0.91 mmol): yield 0.165 g (89%) as a 3:1 mixture of diastereomers. ^{1}H NMR (400 MHz, $CDCl_3$): (major) δ 7.34–7.19 (m, 5H), 2.94 (tt, J = 11.8, 4.7 Hz, 1H), 2.12 (tt, J = 13.2, 4.7 Hz, 1H), 1.76–1.57 (m, 5H), 1.48 (qq, J = 13.2, 2.9 Hz, 1H), 1.37 (br s, 1H), 1.19 (s, 3H), 1.03 (d, J = 7.3 Hz, 3H); (minor) δ 7.35–7.17 (m, 5H), 2.67 (tt, J = 12.6, 3.4 Hz, 1H), 1.91 (ddd, J = 12.4, 3.1, 2.2 Hz, 1H), 1.87–1.82 (m, 1H), 1.72 (dq, J = 13.5, 3.8 Hz, 1H), 1.64–1.15 (m, 5H), 1.18 (s, 3H), 0.95 (d, J = 6.7 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): (major) δ 147.06, 128.29, 126.89, 125.88, 72.99, 41.20, 39.17, 38.39, 29.41, 28.64, 26.97, 16.01; (minor) δ 146.17, 128.34, 126.70, 126.03, 73.31, 49.54, 42.13, 42.01, 34.18, 32.32, 20.11, 14.94. IR (CCl_4): 3395, 3035, 2927 cm^{-1}. LRMS (EI) *m/e*: (major) 180 (64), 147 (100), 144 (52), 129 (60), 104 (90), 91 (56); (minor) 180 (52), 147 (100), 144 (65), 129 (40), 104 (87), 91 (62). Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.10; H, 9.91.

1,2-Dimethyl-5-(2-propyl)cyclohexanol (15f) (**14f**, 0.168 g, 1.00 mmol): yield 0.162 g (95%) as a 2:1 mixture of diastereomers. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.92–0.98 (m, 10H), 1.10 (s, 2H), 1.01 (s, 1H), 0.86 (d, J = 7.3 Hz, 2H), 0.85 (d, J = 6.8 Hz, 1H), 0.82–0.77 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): (major) δ 72.99, 38.85, 38.77, 37.08, 32.57, 29.39, 28.52, 22.40, 19.72, 19.51, 15.95; (minor) δ 73.48, 45.95, 42.57, 41.91, 32.51, 32.15, 29.36, 20.19, 19.70, 19.61, 14.95. IR (CCl_4): 3603, 3476, 2918 cm^{-1}. LRMS (EI) *m/e*: (major) 170 (1), 127 (100), 71 (95); (minor) 170 (1), 127 (100), 71 (68). Anal. Calcd for $C_{11}H_{22}O$: C, 77.58; H, 13.02. Found: C, 77.52; H, 13.36.

1,2-Dimethyl-1,5-cyclohexanediol (15g) (**14g**, 0.114 g, 0.80 mmol): yield 0.109 g (95%) as a 4:1 mixture of diastereomers. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.96–3.88 (m, 0.20H), 3.77–3.69 (m, 0.80H), 2.98 (br s, 2H), 1.89–1.07 (m, 7H), 1.14 (s, 0.60H), 1.03 (s, 2.40H), 0.89 (d, J = 7.5 Hz, 0.60H), 0.86 (d, 2.40H). ^{13}C NMR (75 MHz, $CDCl_3$): (major) δ 73.40, 68.20, 45.62, 40.59, 31.77, 26.72, 23.72, 15.00; (minor) δ 74.16, 67.50, 43.63, 39.07, 29.80, 27.91, 26.85, 15.67. IR (CCl_4): 3210, 2921 cm^{-1}. HRMS Calcd for $C_8H_{16}O_2$: 144.1150. Found 144.1142. LRMS (EI) *m/e*: (major) 144 (3), 126 (40), 111 (60), 97 (42), 87 (82), 72 (65), 58 (61), 43 (100); (minor) 144 (1), 126 (35), 111 (48), 97 (28), 87 (70), 72 (55), 58 (40), 43 (100). Anal. Calcd for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found: C, 66.41; H, 11.29.

5-(*tert*-Butyldimethylsiloxy)-1,2-dimethylcyclohexanol (15h) (**14h**, 0.305 g, 1.19 mmol): yield 0.286 g (93%) as a ca. 1:1 mixture of diastereomers. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.98–3.87 (m, 1H), 2.02–1.33 (m, 8H), 1.15 (s, 1.5H), 1.03 (s, 1.5H), 0.85 (s, 4.5H), 0.84 (s, 4.5H), 0.03 (s, 1.5H), 0.02 (s, 1.5H), 0.00 (s, 1.5H), −0.01 (s, 1.5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 73.80, 72.75, 69.33, 68.32, 45.54, 40.45, 40.09, 31.46, 26.99, 26.40, 25.78, 25.69, 25.23, 25.20, 25.16, 25.12, 18.01, 17.89, 15.52, 15.46, −4.89, −4.92, −5.03, −5.13. IR (CCl_4): 3612, 3495, 2936, 2864 cm^{-1}. HRMS Calcd for $C_{14}H_{30}O_2Si$: 258.2015. Found 258.2025. LRMS (EI) *m/e*: 258 (2), 201 (32), 109 (100), 75 (86). Anal. Calcd for $C_{14}H_{30}O_2Si$: C, 65.06; H, 11.70. Found: C, 64.81; H, 11.97.

(1*R,2*S**,3*R**,6*S**)-2,3-Dimethylbicyclo[4.4.0]decan-2-ol (18)** (**17**, 0.155 g, 0.86 mmol): yield 0.147 g (94%) as a 9:1: 0.3 mixture of diastereomers. ^{1}H NMR (400 MHz, $CDCl_3$): (major) δ 1.94 (tt, J = 13.2, 4.4 Hz, 1H), 1.77–1.54 (m, 5H), 1.35 (br s, 1H), 1.33–0.95 (m, 7H), 1.07 (s, 3H), 0.91 (d, J = 7.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): (major) δ 73.84, 45.01, 40.96, 37.34, 34.42, 28.02, 27.93, 26.81, 26.46, 26.19, 24.99, 15.56. IR (CCl_4): 3619, 2921, 2850 cm^{-1}. HRMS Calcd for $C_{12}H_{22}O$: 182.1671. Found 182.1678. LRMS (EI) *m/e*: 182 (20), 167 (18), 149 (15), 135 (10), 125 (100), 85 (18), 67 (20), 43 (55). Anal. Calcd for: C, 79.06; H, 12.16. Found: C, 79.31; H, 11.95.

(3*R,4*S**)-3-Ethyl-4-methyltetrahydrofuran-3-ol (20)** (**19**, 0.122 g, 0.95 mmol): yield 0.094 g (76%) as a single diastereomer by GC and NMR analyses. ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.21 (dd, J = 8.2, 6.5 Hz, 1H), 3.65 (d, J = 9.4 Hz, 1H), 3.62 (d, J = 9.4 Hz, 1H), 3.47 (dd, J = 8.2, 3.2 Hz, 1H), 2.25 (br s, 1H), 2.10 (dp, J = 6.5, 3.2 Hz, 1H), 1.61-1.51 (m, 2H), 0.97 (t, J = 7.4 Hz, 3H), 0.92 (d, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 82.99, 76.68, 75.13, 43.70, 25.59, 15.54, 8.11. IR (CCl_4): 3428, 2949, 2878 cm^{-1}. HRMS Calcd for $C_7H_{14}O_2$: 130.0994. Found 130.0988. LRMS (EI) *m/e*: 130 (10), 85 (35), 71 (42), 57 (100). Anal. Calcd for $C_7H_{14}O_2$: C, 64.58; H, 10.84. Found: C, 64.92; H, 11.19.

2-Ethyl-1-methylcyclohexanol (22) (**21**, 0.127 g, 0.91 mmol, a 10:1, cis:trans, mixture of diastereomers): yield 0.094 g (73%) as a 35:1 mixture of diastereomers. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.86–0.88 (m, 12H), 1.08 (s, 3H), 0.92 (t, J = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 73.10, 49.83, 41.96, 28.04, 25.41, 23.97, 21.76, 20.90, 12.39. IR (CCl_4): 3462, 2009 cm^{-1}. HRMS (EI) Calcd for $C_9H_{18}O$: 142.1358. Found 142.1353. LRMS (EI) *m/e*: 142 (23), 99 (25), 71 (100), 58 (30), 43 (57).

9-Ethylbicyclo[4.3.0]nonan-1-ol (24) (**23**, 0.138 g, 0.83 mmol): yield 0.121 g (87%) as a single diastereomer. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.95–1.81 (m, 2H), 1.68–0.97 (m, 15H), 0.86 (t, J = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 78.37, 52.92, 45.04, 27.94, 26.09, 23.98, 23.32, 21.72, 21.13, 20.24, 12.92. IR (CCl_4): 3612, 3485, 2928, 2857 cm^{-1}. HRMS Calcd for $C_{11}H_{20}O$: 168.1514. Found 168.1505. LRMS (EI) *m/e* 168 (31), 111 (100), 98 (99), 83 (31), 55 (40).

(1*R,2*R**,5*R**)-2-[(Phenylseleno)methyl]bicyclo[3.3.0]-octan-1-ol (26)** (**25**, 0.113 g, 0.82 mmol): yield 0.196 g (81%) as a single diastereomer. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.58–7.43 (m, 2H), 7.31–7.22 (m, 3H), 3.01–2.94 (m, 2H), 2.28–2.05 (m, 4H), 1.87–1.00 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 132.50, 130.28, 129.12, 126.91, 92.51, 51.70, 50.32, 36.63, 34.83, 31.50, 29.34, 28.14, 25.66. IR (CCl_4): 3615, 3421, 3020, 2940 cm^{-1}. HRMS Calcd for $C_{15}H_{20}OSe$: 296.0679. Found 296.0687. LRMS (EI) *m/e*: 296 (50), 158 (28), 139 (100), 121 (65), 69 (52), 55 (76).

(1*R,2*R**)-1-Methyl-2-[(phenylseleno)methyl]cyclohexan-1-ol (27)** (**5a**, 0.111 g, 0.88 mmol): yield 0.059 g (24%) as a 32:1 mixture of diastereomers. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.56–7.48 (m, 2H), 7.31–7.20 (m, 3H), 3.41 (dd, J = 11.8, 3.8 Hz, 1H), 2.55 (dd, J = 11.8, 10.1 Hz, 1H), 2.08–2.00 (m, 1H), 1.75–1.02 (m, 8H), 1.47 (br s, 1H), 1.14 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 132.04, 131.21, 129.04, 126.54, 73.44, 48.76, 42.43, 29.73, 29.13, 25.52, 24.08, 20.47. IR (CCl_4): 3605, 3471, 3062, 2928, 2857 cm^{-1}. HRMS Calcd for $C_{14}H_{20}OSe$: 284.0679. Found 284.0681. LRMS (EI) *m/e*: 284 (21), 158 (12), 127 (18), 109 (31), 43 (100).

(4*R,5*R**)-2,2,4-Trimethyl-5-[(phenylseleno)methyl]tetrahydropyran-4-ol (29)** (**28**, 0.091 g, 0.58 mmol): yield 0.135 g (74%): mp 64–65 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.47–7.44 (m, 2H), 7.21–7.18 (m, 3H), 4.00 (dd, J = 12.0, 3.0 Hz, 1H), 3.55 (dd, J = 12.0, 5.8 Hz, 1H), 3.06 (dd, J = 12.2, 3.4 Hz, 1H), 2.72 (t, J = 12.2 Hz, 1H), 1.67–1.56 (m, 1H), 1.54 (d, J = 13.8 Hz, 1H), 1.42 (d, J = 13.8 Hz, 1H), 1.35 (br s, 1H), 1.26 (s, 3H), 1.18 (s, 3H), 1.14 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 132.45, 130.38, 129.08, 126.86, 72.16, 71.16, 61.39, 47.99, 46.54, 28.43, 27.94, 26.78, 25.38. IR (CCl_4): 3605, 3420,

3075, 2945 cm^{-1}. HRMS Calcd for $C_{15}H_{22}O_2Se$: 314.0785. Found 314.0796. LRMS (EI) *m/e*: 314 (100), 198 (49), 99 (85), 43 (65).

***(1R*,2R*,3S*,6R*)*-2-Methyl-3-[(phenylseleno)methyl]-bicyclo[4.4.0]decan-2-ol (30)** (**17**, 0.140 g, 0.78 mmol): yield 0.179 g (68%) as a single diastereomer by GC and NMR analyses. ^1H NMR (300 MHz, $CDCl_3$): δ 7.53–7.49 (m, 2H), 7.29–7.23 (m, 3H), 3.04 (dd, J = 11.5, 2.5 Hz, 1H), 2.93 (t, J = 11.5 Hz, 1H), 1.94–1.60 (m, 7H), 1.42–0.93 (m, 9H), 1.16 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 132.79, 130.57, 129.03, 126.86, 73.79, 46.89, 46.16, 37.18, 34.29, 28.09, 27.72, 26.70, 26.61, 26.09, 24.93, 23.75. IR (CCl_4): 3612, 3492, 3069, 2921, 2850 cm^{-1}. HRMS Calcd for $C_{12}H_{26}OSe$: 338.1149. Found 338.1159. LRMS (EI) *m/e*: 338 (21), 181 (35), 163 (21), 137 (15), 95 (18), 81 (22), 43 (100).

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Supplementary Material Available: ^1H and ^{13}C NMR spectra of compounds for which no elemental analysis was obtained (91 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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