# Sequential Nucleophilic Acyl Substitution/Alkenyl Transfer Reactions Mediated by Samarium(II) Iodide

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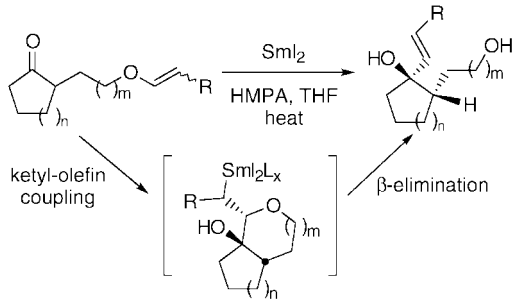
Samarium(II) iodide ($SmI_2$) has been employed in a one-pot, three-step, nucleophilic acyl substitution/ketyl−olefin coupling/$\beta$-elimination reaction sequence. This novel protocol combines two recently developed $SmI_2$-mediated processes to permit the net delivery of an alkenyl moiety to a ketone carbonyl generated as an intermediate along the sequential reaction pathway. A remarkable measure of stereocontrol over three to five contiguous stereocenters is established in the process as a result of the excellent facial selectivity conveyed in the ketyl−olefin coupling reaction. Unique to the $SmI_2$-mediated process, the relative asymmetric induction engendered in these addition reactions is complementary to more traditional nucleophilic addition reactions in that the alkenyl group is delivered to the carbonyl center by an attached tether. Moreover, the protocol avoids the basic reaction conditions characteristic of alkenylmagnesium halides and alkenyllithium reagents.

## Introduction

Previous research from these laboratories has focused on the development of sequential carbon−carbon bond-forming reactions mediated by $SmI_2$.[1] Investigations in this area have demonstrated high degrees of stereo- and chemoselectivity in a variety of one-pot processes. As demonstrated in these reported examples, $SmI_2$ is a truly distinguished reagent in that it has the ability to sustain a multitude of reactions that may be either radical or anionic in a single reaction vessel. Additionally, the sequential processes can be carried out in virtually any order (e.g., radical/anionic, anionic/anionic, or anionic/radical, etc.). Because few, if any, currently available reagents have the ability to perform both radical and carbanionic processes in this manner in a single reaction vessel, we have chosen to develop reaction processes that may be singly mediated by $SmI_2$.

We recently reported the development of a novel sequential ketyl−olefin coupling/$\beta$-elimination reaction (a radical/anionic process) that was mediated by $SmI_2$ (Scheme 1).[2] The overall course of events in this previously developed procedure resulted in the net addition of an alkenyl species to a ketone carbonyl. Indeed, there were certain perceived advantages to pursuing this line of research. Notably, the introduction of the alkenyl species in this reaction was directed by a tether to the reaction center, providing a stereochemical outcome complementary to alkenylmetallic carbonyl addition reactions. Furthermore, this novel protocol did not suffer the consequences of a strongly basic reaction mixture (e.g., substrate enolization) that often plague more traditional magnesium- and lithium-based organometallic addition reactions.

**Scheme 1**




In view of these recent discoveries, we sought to explore the feasibility of linking the sequential ketyl−olefin coupling/$\beta$-elimination reaction with the recently developed nucleophilic acyl substitution (NAS) reaction that is also mediated by $SmI_2$.[3] Scheme 2 outlines a representative example of the proposed three-step reaction sequence that was anticipated to proceed via an anionic/radical/anionic process. The sequential process was expected to proceed first through initial generation of a pendant organosamarium species that would be poised to effect an intramolecular nucleophilic acyl substitution on the ester, liberating a cycloalkanone. The ketone should subsequently suffer a radical ketyl−olefin coupling reaction, generating an exocyclic organosamarium species that would undergo a rapid $\beta$-elimination (or competitive protonation).

There were certain attractive advantages to employing this sequential three-step, one-pot procedure. The $SmI_2$-mediated procedure was anticipated to allow excellent stereocontrol over several contiguous stereocenters. Indeed, the sense and magnitude of asymmetric induction established in these alkenyl group transfer reactions occurs as a result of the high diastereoselectivity im-

(1) (a) Molander, G. A.; Harris, C. R. *Tetrahedron* **1998**, *54*, 3321. (b) Molander, G. A.; Harris, C. R. *Chem. Rev.* **1996**, *96*, 307 and references therein. (c) Molander, G. A.; Harris, C. R. *J. Org. Chem.* **1997**, *62*, 2944. (d) Molander, G. A.; del Pozo Losada, C. *J. Org. Chem.* **1997**, *62*, 2935. (e) Molander, G. A.; Alonso-Alija, C. *Tetrahedron* **1997**, *53*, 8067. (f) Molander, G. A.; Harris, C. R. *J. Am. Chem. Soc.* **1996**, *118*, 4059. (g) Molander, G. A.; Harris, C. R. *J. Am. Chem. Soc.* **1995**, *117*, 3705. (h) Molander, G. A.; McKie, J. A. *J. Org. Chem.* **1992**, *57*, 3132. (i) Molander, G. A.; Kenny, C. *J. Org. Chem.* **1991**, *56*, 1439. (j) Molander, G. A.; Harring, L. S. *J. Org. Chem.* **1990**, *55*, 6171.

(2) Molander, G. A.; Harris, C. R. *J. Org. Chem.* **1998**, *63*, 812.

(3) (a) Molander, G. A.; McKie, J. A. *J. Org. Chem.* **1993**, *58*, 7216. (b) Molander, G. A.; Shakya, S. R. *J. Org. Chem.* **1994**, *59*, 3445.

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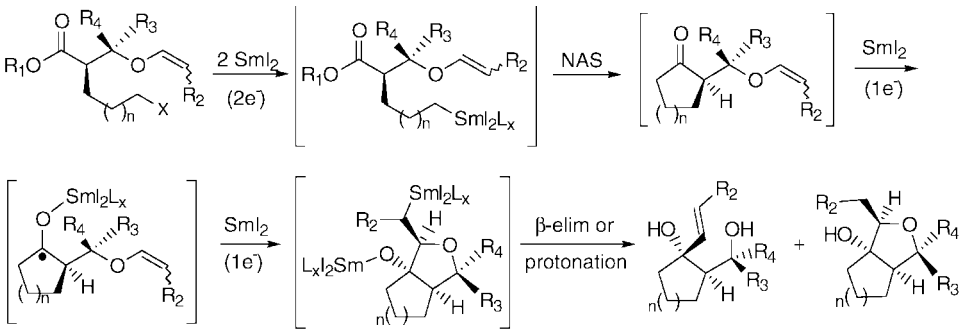
**Scheme 2**




parted by $SmI_2$ during the intermediate ketyl−olefin coupling reaction that sets the stereochemistry observed in the final products. As discussed previously, the introduction of the alkenyl species is directed by a tether to the reacting center, providing a stereochemistry that is complementary to the more traditional alkenylmetallic carbonyl addition reactions. Moreover, it was anticipated that the substrates required for these three-step, one-pot sequential series could be readily obtained, diastereomerically enriched, from $\beta$-hydroxy esters via a directed aldol-type condensation between an ester and an aldehyde.

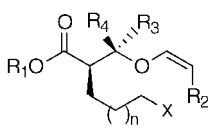
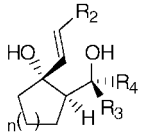
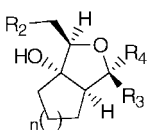
## Results and Discussion

To test the proposed sequence, a series of enol ether substrates with appropriately substituted pendant haloalkyl chains and ester functionalities was synthesized. Substrates comprising a variety of substitution patterns were examined to determine the scope and limitations of this sequential three-step, one-pot procedure. The results of this study are depicted in Tables 1 and 2. Optimized reaction conditions for the nucleophilic acyl substitution/alkenyl transfer protocol were determined to involve the dropwise addition of the enol ether substrate (0.05−0.06 M in THF) to a vigorously stirred solution of $SmI_2$ (0.12 M in THF) with 4 equiv of HMPA [or 10% (V/V) of tetramethylguanidine (TMG)] at ambient temperature. In general, the sequential reactions were found to be complete after the substrate addition was effected but were allowed to proceed for an additional 2 h to ensure consumption of the starting substrate before an aqueous workup. Tetramethylguanidine was found to work well as the cosolvent with this sequential protocol when alkyl iodides were employed as substrates. However, HMPA cosolvent, providing a more strongly reducing environment, was required for alkyl chloride substrates.[4] Additives such as nickel(II) iodide or $Fe(acac)_3$, which have previously been shown to enhance the reducing ability of $SmI_2$,[5] were found to be inadequate in executing these transformations.

Substrates **1**, **3**, and **5** (entries 1−3, Table 1) were converted in good yield and with a high degree of stereocontrol to the corresponding diastereomeric cyclopentanols **2a** and **4a**. Substrate **1**, a 1.3:1 mixture of diastereomeric esters inseparable by flash column chromatography, was converted to a 1.3:1 mixture of diastereomeric diols in 73% combined yield. Likewise the chloride **3** and iodide **5** (each a 1.5:1 mixture of diastereomeric halides), when subjected to the standard $SmI_2$/HMPA reaction conditions, were converted to a 1.5:1 mixture of diastereomeric diols in 71% and 77% yields, respectively. Tetramethylguanidine was found to be an adequate cosolvent with iodide **5** as a substrate, providing a similar yield.

Next, substrates with larger alkyl groups in the $R_3$ and/or $R_4$ position were investigated. In the event, subjection of substrates **6**, **8**, **10**−**12**, and **14** (entries 4−9, Table 1, each >95% diastereomerically pure) to the standard reaction conditions afforded the desired cyclic diols in moderate yield. Interestingly, substrates with the larger *i*-Pr alkyl group in the $R_3/R_4$ position afforded a larger amount of the protonated intermediate resulting from

**Table 1. Sequential NAS/Ketyl−Olefin Coupling/ $\beta$-Elimination Reactions Mediated by $SmI_2$**

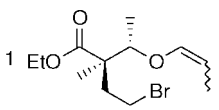
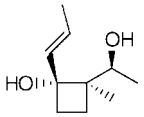
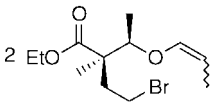
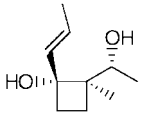
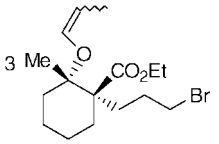
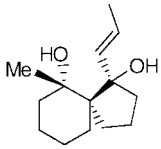
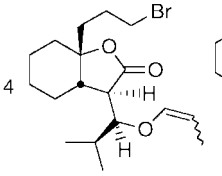
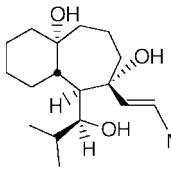
| entry | | substrate[a] | products (% isolated yield) | |
|---|---|---|---|---|
| | |  |  |  |
| 1 | **1** | $R_1$ = Me, $R_2$ = H, $R_3$ = Me/H $R_4$ = H/Me, n =1, X = Cl | **2a** (73%) | **2b** (0%)[b] |
| 2 | **3** | $R_1$ = Me, $R_2$ = H, $R_3$ =Et/H $R_4$ = H/Et, n =1, X = Cl | **4a** (71%) | **4b** (<5%)[c] |
| 3 | **5** | $R_1$ = Me, $R_2$ = H, $R_3$ =Et/H $R_4$ = H/Et, n =1, X = I | **4a** (77%) | **4b** (<5%)[c] |
| 4 | **6** | $R_1$ = *t*-Bu, $R_2$ =H, $R_3$ = *i*-Pr $R_4$ = H, n = 1, X = I | **7a** (70%) | **7b** (23%) |
| 5 | **8** | $R_1$ = *t*-Bu, $R_2$ = H, $R_3$ = H $R_4$ = *i*-Pr, n =1, X = I | **9a** (69%) | **9b** (25%)[d] |
| 6 | **10** | $R_1$ = Me, $R_2$ = H, $R_3$ = *i*-Pr $R_4$ = H, n = 1, X = Cl | **7a** (60-64%) | **7b** (21-25%) |
| 7 | **11** | $R_1$ = Me, $R_2$ = H, $R_3$ = H $R_4$ = *i*-Pr, n = 1, X = Cl | **9a** (60-70%) | **9b** (14-23%)[d] |
| 8 | **12** | $R_1$ = Et, $R_2$ = Me, $R_3$ = *i*-Pr $R_4$ = H, n = 2, X = Br | **13a** (60-64%) | **13b** (21-25%) |
| 9 | **14** | $R_1$ = Et, $R_2$ =Me, $R_3$ = H $R_4$ = *i*-Pr, n = 2, X =Br | **15a** (60%) | **15b** (40%) |

[a] Terminally substituted olefin substrates were a 2−3:1 mixture of *Z* and *E* olefin isomers, respectively. [b] A 1.3:1 mixture of diastereomeric substrates afforded a 1.3:1 mixture of diastereomeric diols. [c] A 1.5:1 mixture of diastereomeric substrates afforded a 1.5:1 mixture of diastereomeric diols. [d] Trapped, bicyclic product was isolated as a 3:1 mixture of the expected isomer (shown) plus the diastereomer epimeric at C-2.

(4) (a) Inanaga, J.; Ishikawa, M.; Yamaguchi, M. *Chem. Lett.* **1987**, 1485. (b) Ruder, S. M. *Tetrahedron Lett.* **1992**, *33*, 2621. (c) Hasegawa, E.; Curran, D. P. *J. Org. Chem.* **1993**, *58*, 5008. (d) Namy, J.-L.; Colomb, M.; Kagan, H. B. *Tetrahedron Lett.* **1994**, *35*, 1723. (e) Cabri, W.; Candiani, I.; Colombo, M.; Franzoi, L.; Bedeschi, A. *Tetrahedron Lett.* **1995**, *36*, 949. (f) Girard, P.; Namy, J. L.; Kagan, H. B. *J. Am. Chem. Soc.* **1980**, *102*, 2693.

(5) (a) Machrouhi, F.; Hamann, B.; Namy, J.-L.; Kagan, H. B. *Synlett* **1996**, 633. (b) Molander, G. A.; McKie, J. A. *J. Org. Chem.* **1991**, *57*, 3132.

**Table 2. Sequential NAS/Ketyl−Olefin Coupling/ β-Elimination Reactions Mediated by $SmI_2$**

| entry | substrate[a] | product (% isolated yield) |
|---|---|---|
| 1 |  **16a** |  **17a** (74%)[b] |
| 2 |  **16b** |  **17b** (69%)[c] |
| 3 |  **18** |  **19** (76%)[d] |
| 4 |  **20** |  **21** (80%)[c] |

[a] Internal olefin substrates were a 2−3:1 mixture of *Z* and *E* olefin isomers, respectively. [b] The product was isolated as a 5:1 mixture of *E* and *Z* olefin isomers. [c] The product was isolated as a 4:1 mixture of *E* and *Z* olefin isomers. [d] The product was isolated as a 10:1 mixture of *E* and *Z* olefin isomers.

incomplete β-elimination of the bicyclic intermediate. Although we have previously observed the presence of trapped intermediate without the deliberate addition of a proton source,[1c,f,g] it is interesting in this context to observe the dependence of the alkyl group on the ratio of the desired β-elimination product to protonated intermediate.

Substrate **6**, derived from the syn β-hydroxy *tert*-butyl ester, (entry 4, Table 1) afforded the desired cyclic diol **7a** as a single diastereomer in 70% yield in addition to 23% of the trapped bicyclic intermediate **7b**. Interestingly, the organosamarium species that is generated in the initial step of this sequential process is readily able to attack even the very bulky *tert*-butyl ester group. The stereochemistry of the desired cyclic diol **7a** was assigned largely on the basis of correlation to the all-carbon ketyl−olefin coupling products that have been previously investigated.[6] The stereochemistry of the bicyclic intermediate was also assigned with correlation to the all-carbon analogues. However, the stereochemistry could be further authenticated by two-dimensional (2D) NMR (COSY) and NOE experiments. Thus, the 2D NMR spectrum of **7b** exhibited coupling between $H_a$ and $H_c$ (Figure 1) consistent with these protons both existing on the same face of the molecule. Additionally, an NOE experiment was performed on the bicyclic compound **7b** during which protons $H_a$, $H_b$, and $H_c$ were irradiated. The results of this study are depicted in Figure 1. Thus, irradiation of $H_a$ revealed a 9% NOE in the resonance

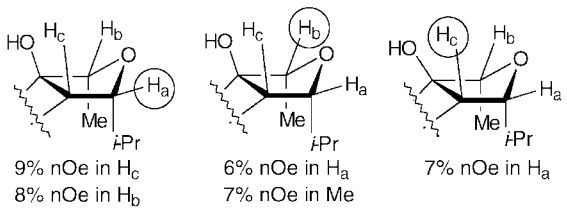



**Figure 1.** Results of NOE studies for diol **7b**.

for $H_c$ and an 8% NOE in the signal for $H_b$. Likewise, irradiation of $H_c$ afforded a 7% NOE in the signal for $H_a$ while irradiation of $H_b$ afforded a 6% NOE enhancement in the signal of $H_a$. Finally, the stereochemistry of the bicyclic product **7b** was established further by comparing $^1$H NMR chemical shifts observed in pyridine-$d_5$ to those observed in $CDCl_3$.[7] Thus, the ring fusion methine $H_c$ should experience a large deshielding effect in cis-fused bridged bicyclic alcohols owing to coordination of pyridine at the vicinally situated hydroxyl functionality. The extent of vicinal deshielding is a function of the dihedral angle of the O−C−C−H unit, with the largest deshielding observed for dihedral angles approaching 0°. The corresponding chemical shift difference in the trans ring fused isomers (dihedral angle approaching 180°) is essentially 0. In alcohol **7b**, the ring fusion methine $H_c$ experiences a 0.33 ppm chemical shift downfield in pyridine-$d_5$ relative to the spectrum obtained in $CDCl_3$. This is consistent with a cis-fused ring junction.[7] A significant chemical shift difference is observed in $H_a$ and $H_b$ (0.18 and 0.46 ppm, respectively), indicative of a small dihedral angle between the 1,3-disubstituted $H_a$ and vicinally substituted $H_b$. These results are also consistent with previous related studies.[7,8]

Substrate **8** (entry 5, Table 1) derived from the anti β-hydroxy ester, afforded the desired cyclic diol **9a** as a single diastereomer in 69% yield along with a 25% yield of the trapped bicyclic intermediate **9b** as a 3:1 mixture of diastereomers epimeric at C-2. The latter were inseparable by flash column chromatography. The stereochemistry of the cyclic diol **9a** was assigned, as above, on the basis of analogy with the all-carbon cyclization analogues that have been previously reported.[8,9] The stereochemistry of the bicyclic intermediate was determined in a similar manner and further validated by a 2D $^1$H NMR experiment. Thus, the 2D NMR spectrum of diastereomeric **9b** exhibited no coupling between $H_a$ and $H_c$ (Figure 1), consistent with $H_a$ and $H_c$ being oriented on opposite faces of the molecule with an approximately 90° dihedral angle. Finally, the stereochemistry of the bicyclic diastereomeric products **9b** was confirmed by comparing $^1$H NMR chemical shifts observed in pyridine-$d_5$ to those observed in $CDCl_3$. Thus, the major diastereomer of the 3:1 mixture was assigned to be the predicted stereoisomer **9b** (shown in Table 1) with the C-2 methyl group and hydroxyl oriented trans to one another. Further NMR studies demonstrated that in the major diastereomer $H_b$ experiences a 0.44 ppm chemical shift downfield in pyridine-$d_5$ relative to the spectrum obtained in $CDCl_3$, consistent with a small dihedral angle (or cis orientation) between $H_b$ and the

(6) Molander, G. A.; McKie, J. A. *J. Org. Chem.* **1995**, *61*, 872.

(7) Demarco, P. V.; Farkas, E.; Doddrell, D. Mylari, B. L.; Wenkert, E. *J. Am. Chem. Soc.* **1968**, *90*, 5480.

(8) Molander, G. A.; Kenny, C. *J. Am. Chem. Soc.* **1989**, *111*, 8236.

(9) (a) Molander, G. A.; McKie, J. A. *J. Org. Chem.* **1992**, *57*, 3132. (b) Molander, G. A.; Kenny, C. *J. Org. Chem.* **1991**, *56*, 1439.

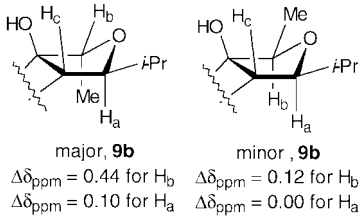



**Figure 2.** Results of NMR studies for diols **9b**.

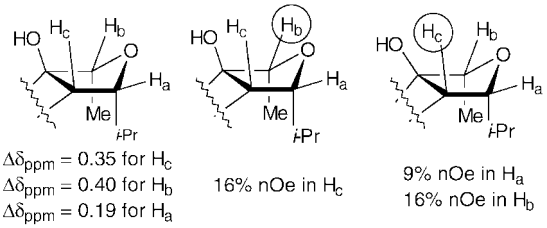



**Figure 3.** Results of NOE studies for diol **13b**.

hydroxyl group (Figure 2). In the minor diastereomer, $H_b$ experiences a much smaller, nearly insignificant, 0.12 ppm chemical shift downfield in pyridine-$d_5$ relative to the spectrum obtained in $CDCl_3$. This is consistent with a large dihedral angle (or trans orientation) between $H_b$ and the hydroxyl group (Figure 2). Furthermore, the ring fusion methine, $H_c$, experiences a 0.33 ppm chemical shift downfield in pyridine-$d_5$ relative to the spectrum obtained in $CDCl_3$ (for both diastereomers of **9b**), consistent with a cis-fused ring junction between $H_c$ and the hydroxyl group (Figure 2).

Substrates **10** and **11** (entries 6−7, Table 1) derived from the syn and anti $\beta$-hydroxy methyl esters, respectively, afforded the desired cyclic diols **7a** and **9a** (each a single diastereomer, previously identified) in 60−64% and 60−70% yields, respectively. In addition, 21−25% and 14−23% yields of the trapped bicyclic products **7b** (a single diastereomer) and **9b** (a 3:1 mixture of diastereomers, previously identified) were also obtained.

Substrates **12** and **14** (entry 8 and 9, Table 1) derived from the syn and anti $\beta$-hydroxy ethyl esters, respectively, afforded the desired cyclic diols **13a** and **15a**, respectively, in 60−64% yields as single diastereomers. These products too were contaminated with 21−25% and 40% yields of the trapped bicyclic intermediates, **13b** and **15b**, respectively, each as a single diastereomer. As discussed above, the stereochemistry of these cyclic diols was assigned on the basis of the previous precedent established for these types of cyclization events. The stereochemistry of the bicyclic intermediates was corroborated on the basis of 2D, NOE, and pyridine-$d_5$ $^1H$ NMR experiments.

Thus, **12**, derived from the syn $\beta$-hydroxy ester derivative, afforded the cyclic diol **13a** as well as the trapped bicyclic intermediate **13b** as single diastereomers. The 2D $^1H$ NMR of **13b** (but not **15b**) demonstrated coupling between $H_a$ and $H_c$ (Figure 3) consistent with a cis-oriented relationship. Additionally, an NOE experiment was performed on the bicyclic compound **13b** during which protons $H_a$, $H_b$, and $H_c$ were irradiated. The results of this experiment are depicted in Figure 3. Irradiation of $H_c$ afforded a 9% NOE in $H_a$ and a 16% NOE in $H_b$, the latter of which was reciprocal. These results indicate that $H_c$ and $H_b$ exist in a cis orientation. Pyridine-$d_5$ $^1H$ NMR experiments also confirmed the

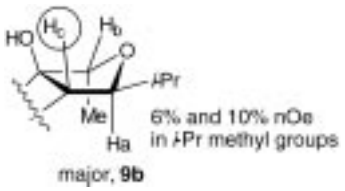



**Figure 4.** Results of NOE studies for diol **15b**.

expected stereochemistry (Figure 3). Thus, in bicyclic compound **13b** the ring fusion methine $H_c$ experiences a 0.35 ppm chemical shift downfield in pyridine-$d_5$ relative to the spectrum obtained in $CDCl_3$. This is again consistent with a previously observed cis-fused ring junction. A significant chemical shift difference was observed in $H_a$ and $H_b$ of 0.19 and 0.40 ppm, respectively, indicative of a small dihedral angle between the 1,3-disubstituted $H_a$ and vicinally substituted $H_b$, and also consistent with the stereochemistry demonstrated in previous studies.

Finally, **14**, derived from the anti $\beta$-hydroxy ester derivative, afforded the cyclic diol **15a** as well as the trapped bicyclic intermediate **15b** as a single diastereomer. The 2D $^1H$ NMR of **15b** demonstrated no coupling between $H_a$ and $H_c$ (Figure 4), consistent with a dihedral angle approaching 90°. An NOE experiment performed on **15b** demonstrated NOE enhancement of the *i*-Pr methyl groups upon irradiation of $H_c$, consistent with the cis orientation of the *i*-Pr group and $H_c$ (Figure 4).

The remainder of the substrates examined are displayed in Table 2. Studies employing these substrates explored the diversity of ring sizes and ring fusions that could be accessed in the cascade of reactions leading to products. Entries 1 and 2 demonstrate the ability to create stereodefined cyclobutanols. Thus, treatment of **16a** and **16b** with $SmI_2$ afforded the desired $\beta$-elimination products **17a/b** in good yield, each as single diastereomeric products at the newly generated stereocenters, and a 5:1 and 4:1 mixture, respectively, of the diastereomeric olefin isomers. The stereochemistry of the diastereomers was not proven rigorously in these examples but is based on previously reported studies on these types of cyclization reactions.[8,9]

Appropriate substitution also permits the facile construction of spirocyclic systems. For example, the spirocyclic diol **19** was generated in 76% yield as a 10:1 mixture of *E* and *Z* olefin isomers from the cyclic ester **18.** The stereochemistry of the intermediate product that was generated in this cyclization sequence for the all-carbon analogue has been previously solved by single-crystal X-ray analysis.[1c]

Finally, the complex trans-fused bicyclic triol **21** was generated from the readily prepared bicyclic lactone **20** in 80% yield as a single diastereomer at the newly generated stereocenters and a 4:1 mixture of diastereomeric olefins (trans, major). The stereochemistry of the desired cyclized product is based on previously reported studies[1g] and by single-crystal X-ray analysis of a crucial intermediate in the substrate synthesis.

## Conclusion

The nucleophilic acyl substitution/alkenyl transfer process described herein is a three-step, one-pot protocol developed to provide a novel method for the introduction of an alkenyl moiety to a carbonyl species in good yield

while maintaining a high degree of stereocontrol over three to five stereocenters. The method is complementary to the more familiar methods of adding alkenyl functionality to a carbonyl carbon and is uniquely suited to the strengths of $SmI_2$ as a reductive coupling agent. Four-, five-, six-, and (by ring expansion) seven-membered rings can be constructed in a stereodefined manner. The excellent stereocontrol exhibited in these transformations is created by directing nucleophilic attack to the carbonyl carbon through the tethered alkenyl group, the latter of which which may be placed in the substrate readily through simple condensation chemistry of an ester with an aldehyde. It has been demonstrated that a variety of structural motifs can be accessed. Finally, the sequential $SmI_2$ protocol developed herein is quite mild, avoiding the strongly basic conditions characteristic of other alkenyl group delivery reactions.

## Experimental Section

**Reagents.** Tetrahydrofuran (THF) was distilled immediately prior to use from benzophenone ketyl under Ar. Samarium metal and iodine were purchased from Aldrich Chemicals and used without further purification. Standard benchtop techniques were employed for handling air-sensitive reagents,[10] and all reactions were carried out under argon.

**(1*R**,2*S**)-1-Ethenyl-2-(1′(*S**)-hydroxyethyl)cyclopentanol, 2a-major** was prepared from a 1.3:1 mixture of methyl (2*R**,3*R*/S**)-2-(3-chloropropyl)-4-oxa-5-hexenoate according to the general $SmI_2$ reaction conditions described above to afford the cyclization/elimination products in 73% combined yield after flash column chromatography with 20% EtOAc/hexanes (from lower $R_f$, major, anti aldol): $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 6.15 (dd, $J$ = 10.8, 17.4 Hz, 1H), 5.33 (dd, $J$ = 1.39, 17.4 Hz, 1H), 5.15 (dd, $J$ = 1.39, 10.8 Hz, 1H), 3.90 (m, 1H), 1.94−1.76 (m, 4H), 1.72−1.65 (m, 3H), 1.43 (bs, 2H), 1.15 (d, $J$ = 6.45 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 141.82, 112.32, 82.69, 67.19, 57.35, 41.18, 23.96, 22.39, 21.35; IR (neat) 3394.4, 3086.5, 1639.9 cm$^{-1}$; HRMS calcd for $C_9H_{14}O$ (M − $H_2O$)$^+$ 138.1045, found 138.1017; LRMS (EI$^+$) *m/z* 138 (6), 123 (12), 109 (22), 95 (16), 83 (34), 68 (100), 55 (51), 43 (33), 27 (23). Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 68.74; H, 10.45.

**(1*R**,2*S**)-1-Ethenyl-2-(1′(*R**)-hydroxyethyl)cyclopentanol, 2a-minor** (from higher $R_f$, minor, syn aldol): $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 6.06 (dd, $J$ = 10.8, 17.2 Hz, 1H), 5.38 (dd, $J$ = 1.49, 17.2 Hz, 1H), 5.18 (dd, $J$ = 1.49, 10.8 Hz, 1H), 3.70 (m, 1H), 2.37 (bs, 2H), 1.92−1.74 (m, 5H), 1.66−1.58 (m, 1H), 1.23 (m, 1H), 1.14 (d, $J$ = 6.15 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 140.04, 112.63, 82.93, 70.20, 56.68, 39.42, 25.82, 22.95, 19.84; IR (neat) 3374.3, 3080.2 cm$^{-1}$; HRMS calcd for $C_9H_{14}O$ (M − $H_2O$)$^+$ 138.1045, found 138.1043; LRMS (EI$^+$) *m/z* 138 (5), 123 (13), 109 (18), 95 (22), 83 (31), 68 (100), 55 (53), 43 (26), 27 (22). Anal. Calcd for $C_9H_{16}O_2$: C, 69.20; H, 10.32. Found: C, 68.85; H, 10.53.

**(1*R**,2*R**)-1-Ethenyl-2-[1(*R*/S**)-hydroxypropyl]cyclopentan-1-ol, 4a. General Procedure for the $SmI_2$-Mediated NAS/Alkenyl Transfer Reactions. 4a** was prepared from either methyl (2*R**,3*R*/S**)-2-(3-chloropropyl)-3-ethyl-4-oxa-5-hexenoate or methyl (2*R**,3*R*/S**)-2-(3-iodopropyl)-3-ethyl-4-oxa-5-hexenoate according to the following general procedure. Samarium metal (0.54 g, 3.61 mmol) and iodine (0.82 g, 3.25 mmol) were stirred together vigorously for 2 h at ambient temperature. During this time period the color of the reaction mixture progressed from a dark orange to lime green to a brilliant blue color. Then 3 mL of HMPA (with chloride or iodide substrate) or 4 mL of tetramethylguanidine (TMG, with iodide substrate) was added to the blue colored solution, and the reaction mixture became deep violet in color (with HMPA cosolvent) or a deep teal color (with TMG cosolvent). Methyl 3-ethyl-2-(2-iodopropyl)-4-oxa-5-hexenoate (a 1.5:1 mixture of diastereomers) (0.21 g, 0.65 mmol) in 15 mL of dry THF was added dropwise over 2.5 h to a vigorously stirred solution of $SmI_2$ (1.50 mmol, 0.11 M in THF) and 3 mL of HMPA. After the addition of the substrate was complete, the reaction mixture was stirred for 1 h. TLC at this time showed the complete consumption of the starting material and formation of a major new product. The reaction was then quenched with saturated aqueous $NaHCO_3$, filtered through a plug of Florisil to remove the precipitated salts, and concentrated *in vacuo* to remove the THF solvent, and then the resultant aqueous layer was subjected to an aqueous workup. Flash column chromatography with 25% EtOAc/hexanes afforded a 1.5:1 mixture of diastereomeric products in 77% (from the iodide) or 71% (from the chloride) combined yield after flash chromatography with 25% EtOAc/hexanes (major diastereomer, lower $R_f$): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 6.18 (dd, $J$ = 10.8, 17.4 Hz, 1H), 5.33 (dd, $J$ = 1.48, 17.4 Hz, 1H), 5.14 (dd, $J$ = 1.48, 10.8 Hz, 1H), 3.62 (m, 1H), 1.92 (m, 1H), 1.88−1.65 (m, 6H), 1.45−1.40 (m, 4H), 0.90 (t, $J$ = 7.40 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 142.21, 112.27, 82.92, 72.24, 55.51, 41.06, 28.91, 23.43, 21.64, 10.45; IR (neat) 3392.1, 1639.9 cm$^{-1}$; HRMS calcd for $C_{10}H_{18}O_2$ 170.1307, found 170.1304; LRMS (EI$^+$) *m/z* 170 (5), 152 (8), 137 (9), 123 (26), 111 (28), 95 (46), 82 (100), 67 (52), 55 (73), 41 (28), 27 (18); (minor diastereomer, higher $R_f$) $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 6.06 (dd, $J$ = 10.8, 17.2 Hz, 1H), 5.38 (dd, $J$ = 1.62, 17.2 Hz, 1H), 5.17 (dd, $J$ = 1.62, 10.8 Hz, 1H), 3.48 (m, 1H), 3.12 (s, 1H), 2.21 (d, $J$ = 3.32 Hz, 1H), 1.95 (m, 1H), 1.88−1.72 (m, 4H), 1.64−1.43 (m, 2H), 1.36−1.18 (m, 2H), 0.92 (t, $J$ = 7.41 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 140.14, 112.53, 82.91, 75.14, 54.37, 39.23, 28.97, 25.53, 19.85, 9.06; IR (neat) 3392.1, 1635.2 cm$^{-1}$; HRMS calcd for $C_{10}H_{18}O_2$ 170.1307, found 170.1300; LRMS (EI$^+$) *m/z* 170 (5), 152 (100), 141 (49), 137 (58), 123 (22), 111 (18), 95 (45), 82 (88), 67 (70), 55 (99), 41 (48), 27 (51).

**(1*R**,2*S**)-1-(1′(*E*)-propenyl)-2-(1′(*R**)-hydroxy-2-methylpropyl)cyclopentan-1-ol (7a)** was prepared from *tert*-butyl (2*R**,3*S**)-2-(3-iodopropyl)-3-(2-propyl)-4-oxa-5-hexenoate according to the general $SmI_2$ reaction conditions described above to afford the desired cyclization/elimination product in 70% yield along with 23% of the protonated intermediate (from minor diastereomer, higher $R_f$, syn aldol): mp 79.5−80.5 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 6.19 (dd, $J$ = 17.4, 10.8 Hz, 1H), 5.33 (dd, $J$ = 1.39, 17.4 Hz, 1H), 5.14 (dd, $J$ = 1.50, 10.8 Hz, 1H), 3.35 (m, 1H), 2.09 (m, 1H), 1.87−1.79 (m, 4H), 1.72−1.40 (m, 4H), 1.39 (m, 1H), 0.92 (d, $J$ = 6.65 Hz, 3H), 0.85 (d, $J$ = 6.75 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 142.25, 112.29, 83.18, 75.91, 53.01, 40.97, 32.12, 23.47, 21.73, 19.59, 18.45; IR ($CHCl_3$) 3596.1, 3034.8, 1634.0, 1514.2 cm$^{-1}$; HRMS calcd for $C_{11}H_{18}O$ (M − $H_2O$)$^+$ 166.1358, found 166.1369; LRMS (EI$^+$) *m/z* 166 (80), 151 (100), 123 (47), 96 (98), 81 (78), 55 (83), 41 (80).

**(1*R**,2*R*/S**,4*R**,5*S**)-2-Methyl-3-oxa-4-(2-propyl)bicyclo-[3.3.0]octan-1-ol (7b)**: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 3.58 (q, $J$ = 6.43 Hz, 1H), 3.40 (dd, $J$ = 6.16, 10.2 Hz, 1H), 2.23 (m, 1H), 1.82 (m, 1H), 1.75−1.61 (m, 4H), 1.54 (m, 2H), 1.43 (m, 1H), 1.21 (d, $J$ = 6.42 Hz, 3H), 1.01 (d, $J$ = 6.42 Hz, 3H), 0.82 (d, $J$ = 6.69 Hz, 3H); $^1$H NMR (500 MHz, pyr-$d_5$) $\delta$ 4.04 (q, $J$ = 6.45 Hz, 1H), 3.58 (dd, $J$ = 6.15 Hz, 1H), 2.56 (m, 1H), 1.89−1.78 (m, 6H), 1.69 (m, 1H), 1.50 (m, 1H), 1.36 (d, $J$ = 6.35 Hz, 3H), 1.14 (d, $J$ = 6.35 Hz, 3H), 0.80 (d, $J$ = 6.65 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 91.81, 86.03, 82.35, 55.48, 36.41, 28.55, 27.36, 26.16, 20.50, 19.02, 14.16; IR (neat) 3372.4, 1691.8 cm$^{-1}$; HRMS calcd for $C_{11}H_{19}O$ (M − H)$^+$ 183.1385, found 183.1396; LRMS (*EI*$^+$) *m/z* 183 (38), 167 (15), 155 (23), 141 (41), 97 (100). Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.70; H, 10.94. Found: C, 71.69; H, 11.03.

**(1*R**,2*S**)-1-(1′(*E*)-Propenyl)-2-(1′(*S**)-hydroxy-2-methylpropyl)cyclopentan-1-ol (9a)** was prepared from *tert*-butyl-(2*R**,3*R**)-2-(3-iodopropyl)-3-(2-propyl)-4-oxa-5-hexenoate according to the general $SmI_2$ reaction conditions described above to afford the desired cyclization/elimination product in 69% yield along with 25% (a 3:1 mixture of

(10) Brown, H. C. *Organic Syntheses via Boranes*; Wiley: New York, 1975.

diastereomers) of the protonated intermediate (from anti aldol): $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 6.06 (dd, $J$ = 10.8, 17.2 Hz, 1H), 5.36 (dd, $J$ = 1.69, 17.3 Hz, 1H), 5.16 (dd, $J$ = 1.59, 10.8 Hz, 1H), 3.45 (dd, $J$ = 2.08, 10.4 Hz, 1H), 2.03 (m, 1H), 1.86−1.70 (m, 6H), 1.65−1.58 (m, 2H), 1.23 (m, 1H), 0.93 (d, $J$ = 7.05 Hz, 3H), 0.83 (d, $J$ = 6.85 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 140.18, 112.51, 82.88, 77.82, 52.05, 39.13, 31.06, 25.14, 19.87, 19.84, 13.98; IR (neat) 3336.2, 1465.0 cm$^{-1}$; HRMS calcd for $C_{11}H_{18}O$ $(M - H_2O)^+$ 166.1358, found 166.1371; LRMS ($EI^+$) $m/z$ 166 (100), 151.61, 96 (98), 81 (79), 55 (81), 41 (58). Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.70; H, 10.94. Found: C, 71.75; H, 11.19.

**(1*R**,2*R*/S**,4*S**,5*S**)-2-Methyl-3-oxa-4-(2-propyl)bicyclo-[3.3.0]octan-1-ol (9b).** The trapped intermediate was isolated as a 3:1 mixture of diastereomeric products epimeric at C-2 which were not separable by flash column chromatography: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 3.89 (q, $J$ = 6.42 Hz, 0.75H), 3.45 (q, $J$ = 6.42 Hz, 0.25H), 3.15 (dd, $J$ = 8.57, 5.09 Hz, 0.75H), 3.01 (dd, $J$ = 7.50, 7.50 Hz, 0.25H), 2.17 (m, 1H), 2.06 (m, 1H), 1.92−1.75 (m, 3H), 1.67 (m, 1H), 1.59−1.40 (m, 3H), 1.23 (d, $J$ = 6.16 Hz, 0.75H), 1.18 (d, $J$ = 6.42 Hz, 2.25H), 0.96 (d, $J$ = 6.69 Hz, 0.75H), 0.93 (d, $J$ = 6.42 Hz, 2.25H), 0.88 (d, $J$ = 6.69 Hz, 0.75H), 0.85 (d, $J$ = 6.69 Hz, 2.25H); $^1$H NMR (500 MHz, $d_5$-pyr) $\delta$ 4.33 (q, $J$ = 6.35 Hz, 0.75H), 3.57 (q, $J$ = 6.25 Hz, 0.25H), 3.25 (dd, $J$ = 5.66, 8.44 Hz, 0.75H), 3.03 (dd, $J$ = 7.74, 7.74 Hz, 0.25H), 2.51 (m, 0.75H), 2.36 (m, 0.25H), 2.19−2.12 (m, 1H), 2.09−1.98 (m, 1H), 1.96−1.90 (m, 1H), 1.89−1.76 (m, 3H), 1.67 (m, 1H), 1.52 (d, $J$ = 5.98 Hz, 0.75H), 1.46 (m, 1H), 1.37 (d, $J$ = 6.25 Hz, 2.25H), 1.09 (d, $J$ = 6.65 Hz, 0.75H), 1.03 (d, $J$ = 6.55 Hz, 2.25H), 0.89 (d, $J$ = 6.75 Hz, 0.75H), 0.86 (d, $J$ = 6.65 Hz, 2.25H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 92.27, 90.57, 79.23, 55.95, 34.62, 32.63, 32.07, 26.06, 19.06, 18.35, 14.84; IR (neat) 3410.0 cm$^{-1}$; HRMS calcd for $C_{11}H_{19}O_2$ $(M - H)^+$ 183.1385, found 183.1382; LRMS ($EI^+$) $m/z$ 183 (100), 167 (40), 141 (81), 123 (22), 97 (98), 81 (32), 43 (62).

**(1*R**,2*S**)-1-(1′(*E*)-Propenyl)-2-(1′(*R**)-hydroxy-2-methylpropyl)cyclohexan-1-ol (13a)** was prepared from (2*R**,3*S**,5*E*/*Z*) ethyl 2-(4′-bromo)-3-(2′-propyl)-4-oxa-5-heptenoate according to the general $SmI_2$ reaction conditions described above to afford the desired cyclization/$\beta$-elimination product in 55% yield and the trapped intermediate (34%) after flash column chromatography with 12% EtOAc/hexanes on 10% (w/w) $AgNO_3$-doped silica gel (from major aldol product, syn aldol): mp 116−117 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 5.86 (m, 2H), 4.05 (bs, 1H), 3.44 (dd, $J$ = 1.98, 9.92 Hz, 1H), 2.82 (bs, 1H), 1.79−1.68 (m, 6H), 1.62−1.47 (m, 4H), 1.36 (tq, $J$ = 3.47, 13.2, 13.3 Hz, 1H), 1.24 (tq, $J$ = 3.67, 12.9, 26.1 Hz, 1H), 0.95 (m, 1H), 0.92 (d, $J$ = 6.95 Hz, 3H), 0.80 (d, $J$ = 6.75 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 132.19, 124.60, 78.34, 75.50, 48.70, 41.79, 28.90, 25.80, 25.57, 23.19, 20.00, 18.16, 13.46; IR ($CHCl_3$) 3622.4, 3455.2, 3038.1, 1464.8, 1450.1 cm$^{-1}$; HRMS calcd for $C_{13}H_{24}O_2$ 212.1776, found 212.1799; LRMS ($EI^+$) $m/z$ 212 (2), 194 (21), 169 (23), 151 (53), 137 (22), 111 (63), 97 (94), 84 (73), 69 (100), 55 (57), 41 (94). Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.54; H, 11.60. Found: C, 73.52; H, 11.60.

**(1*R**,2*R**,4*S**,5*S**)-2-Ethyl-3-oxa-9-(2′-propyl)bicyclo-[4.3.0]nonan-1-ol (13b)** (intermediate, from major aldol product, syn aldol): mp 51−52 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 3.50 (dd, $J$ = 15.3, 5.36 Hz, 1H), 3.36 (dd, $J$ = 8.83, 4.27 Hz, 1H), 1.95 (m, 1H), 1.90 (m, 1H), 1.73−1.56 (m, 4H), 1.51−1.38 (m, 6H), 1.33−1.22 (m, 1H), 0.97 (t, $J$ = 7.54 Hz, 3H), 0.93 (d, $J$ = 6.75 Hz, 3H), 0.91 (d, $J$ = 6.84 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 86.57, 82.09, 76.66, 47.34, 33.14, 28.93, 22.72, 21.30, 21.04, 20.96, 19.21, 17.89, 11.08; IR ($CHCl_3$) 3599.7, 3448.0 cm$^{-1}$; HRMS calcd for $C_{13}H_{22}O$ $(M - H_2O)^+$ 194.1671, found 194.1678; LRMS ($EI^+$) $m/z$ 194 (5), 169 (100), 151 (38), 123 (42), 111 (98), 95 (58), 81 (58), 67 (38), 57 (68), 41 (74).

**(1*R**,2*S**)-1-(1′(*E*)-Propenyl)-2-(1′(*S**)-hydroxy-2-methylpropyl)cyclohexan-1-ol (15a)** was prepared from ethyl (2*R**,3*R**,5*E*/*Z*)-2-(4′-bromo)-3-(2′-propyl)-4-oxa-5-heptenoate according to the general $SmI_2$ reaction conditions described above to afford the desired cyclization/$\beta$-elimination product in 60% yield and the trapped intermediate (40%) after flash column chromatography with 12% EtOAc/hexanes on 10% (w/w) $AgNO_3$-doped silica gel (from high $R_f$, minor, anti aldol−ether diastereomer): mp 53.0−54.5 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 6.09 (m, $J$ = 15.6 (not resolved) Hz, 1H), 5.87 (dq, $J$ = 15.6, 6.45 Hz, 1H), 3.62 (d, $J$ = 8.83 Hz, 1H), 1.80 (m, 1H), 1.74 (dd, $J$ = 1.59, 6.45 Hz, 2H), 1.74−1.58 (m, 5H), 1.53 (bs, 2H), 1.50−1.36 (m, 3H), 1.30−1.23 (m, 2H), 0.97 (d, $J$ = 6.55 Hz, 3H), 0.83 (d, $J$ = 6.75 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 133.95, 124.13, 74.32, 73.53, 50.35, 43.00, 31.03, 25.89, 23.64, 22.10, 19.82, 19.39, 18.14; IR ($CHCl_3$) 3597.6, 3034.1, 1518.0, 1472.1, 1450.2 cm$^{-1}$; HRMS calcd for $C_{13}H_{22}O$ $(M - H_2O)^+$ 194.1671, found 194.1679; LRMS ($EI^+$) $m/z$ 212 (2), 194 (78), 179 (100), 167 (77), 153 (42), 111 (98), 97 (81), 69 (91), 56 (52), 41 (86).

**(1*R**,2*R**,4*R**,5*S**)-2-Ethyl-3-oxa-9-(2′-propyl)bicyclo-[4.3.0]nonan-1-ol (15b)** (trapped intermediate product, from minor aldol ether product, anti aldol): $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 3.61 (dd, $J$ = 10.2, 4.28 Hz, 1H), 3.54 (dd, $J$ = 10.4, 2.94 Hz, 1H), 2.03 (m, 1H), 1.75−1.46 (m, 9H), 1.37 (m, 1H), 1.23−1.13 (m, 2H), 1.01 (d, $J$ = 6.42 Hz, 3H), 1.00 (t, $J$ = 7.23 Hz, 3H), 0.81 (d, $J$ = 6.42 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 91.16, 84.78, 81.01, 49.83, 33.90, 28.07, 26.41, 23.34, 22.60, 21.87, 20.51, 19.00, 12.32; IR ($CHCl_3$) 3598.1, 1468.0, 1451.9 cm$^{-1}$; HRMS calcd for $C_{13}H_{23}O_2$ $(M - H)^+$ 211.1698, found 211.1718; LRMS ($EI^+$) $m/z$ 212 (2), 169 (77), 154 (33), 111 (100), 98 (73), 81 (60), 67 (54), 55 (74), 41 (97). Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.54; H, 11.39. Found: C, 73.66; H, 11.57.

**(1*R**,2*S**)-2-[(1′*R**)-Hydroxyethyl]-2-methyl-1-[1′(*E*/*Z*)-propenyl]cyclobutan-1-ol (17a)** was prepared from ethyl (2*R**,3*R**,5*Z*/*E*)-2-(2-bromoethyl)-2,3-dimethyl-4-oxa-5-heptenoate according to the general $SmI_2$ cyclization/elimination procedure described above to afford the desired cyclobutanol as a 5:1 mixture of *E*/*Z* olefin isomers, respectively, in 74% combined yield (from lower $R_f$ substrate): Trans, lower $R_f$ product: mp 73−74 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 5.87 (m, 1H), 5.83 (dq, $J$ = 15.5, 5.89 Hz, 1H), 3.84 (q, $J$ = 6.43 Hz, 1H), 2.04 (dd, $J$ = 6.43, 8.83 Hz, 2H), 1.77 (d, $J$ = 5.09 Hz, 3H), 1.63 (bs, 2H), 1.39−1.32 (m, 2H), 1.15 (s, 3H), 0.96 (d, $J$ = 6.42 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 133.51, 124.03, 76.54, 71.36, 51.63, 31.64, 23.64, 17.94, 16.65, 12.62; IR (neat) 3592.2, 1378.7 cm$^{-1}$; HRMS calcd for $C_{10}H_{16}O$ $(M - H_2O)^+$ 152.1201, found 152.1213; LRMS ($EI^+$) $m/z$ 152 (3), 137 (79), 124 (100), 109 (22), 84 (51), 69 (98) Cis, higher $R_f$ product: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 5.75−5.67 (m, 2H), 3.75 (q, $J$ = 6.35 Hz, 1H), 2.13−2.07 (m, 1H), 2.05−2.01 (m, 1H), 1.74 (d, $J$ = 5.36 Hz, 3H), 1.60−1.49 (m, 2H), 1.23 (bs, 2H), 1.14 (s, 3H), 0.99 (d, $J$ = 6.35 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 132.89, 127.68, 77.74, 71.48, 52.37, 34.22, 24.25, 16.84, 14.80, 12.77; HRMS calcd for $C_{10}H_{16}O$ $(M - H_2O)^+$ 152.1201, found 152.1201; LRMS ($EI^+$) $m/z$ 152 (13), 137 (100), 124 (98), 109 (18), 84 (20), 69 (98).

**(1*R**,2*S**)-2-[1′(*S**)-Hydroxyethyl]-2-methyl-1-[(1′*E*/*Z*)-propenyl]cyclobutan-1-ol (17b)** was prepared from ethyl (2*R**,3*S**,5*Z*/*E*)-2-(2-bromoethyl)-2,3-dimethyl-4-oxa-5-heptenoate according to the general $SmI_2$ cyclization/elimination procedure described above to afford the desired cyclobutanol as a 4:1 mixture of *E*/*Z* olefin isomers, respectively, in 69% combined yield (from higher $R_f$ substrate): Cis, higher $R_f$ product: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 5.67 (dd, $J$ = 11.8, 1.09 Hz, 1H), 5.59 (dq, $J$ = 11.8, 6.85 Hz, 1H), 3.83 (q, $J$ = 6.35 Hz, 1H), 2.18−2.13 (m, 1H), 2.05 (m, 1H), 1.83 (d, $J$ = 7.05 Hz, 3H), 1.68 (m, 2H), 1.54 (m, 2H), 1.13 (s, 3H), 1.04 (d, $J$ = 6.35 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 132.39, 127.61, 71.69, 52.35, 35.21, 24.45, 17.77, 14.94, 14.45; HRMS calcd for $C_{10}H_{16}O$ $(M - H_2O)^+$ 152.1201, found 152.1209; LRMS ($EI^+$) $m/z$ 152 (31), 142 (41), 137 (100), 109 (64), 84 (62), 69 (98), 41 (61). Trans, lower $R_f$ product: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 5.76−5.66 (m, 2H), 3.75 (q, $J$ = 6.35 Hz, 1H), 2.09 (m, 1H), 2.03 (m, 1H), 1.74 (d, $J$ = 5.16 Hz, 3H), 1.59−1.49 (m, 4H), 1.13 (s, 3H), 0.98 (d, $J$ = 6.35 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 132.79, 123.75, 75.89, 71.73, 51.58, 32.45, 24.96, 17.89, 17.79, 13.15; IR (neat) 3414.2, 1449.9 cm$^{-1}$; HRMS calcd for $C_{10}H_{16}O$ $(M - H_2O)^+$ 152.1201, found 152.1197; LRMS ($EI^+$) $m/z$ 152 (19), 137 (100), 124 (92), 109 (33), 84 (49), 69 (98).

**(2*R**,7*S**)-2-Methyl-7-[1(*E*)-propenyl]spiro[5.3.0]heptane-2,7-diol (19)** was prepared from ethyl (1*R**,2*S**)-1-(3-bro-

mopropyl)-2-methyl-2-[1(*E*/*Z*)-propenyloxy]cyclopentanecarboxylate according to the $SmI_2$ reaction conditions described above to afford the desired alkenyl transfer product as a 10:1 mixture of *E* and *Z* olefin isomers in 76% combined yield after flash column chromatography with 15% EtOAc/hexanes. Trans olefin: mp 85.0−86.5 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 5.99 (m, 1H), 5.76 (dq, $J$ = 6.43, 15.5 Hz, 1H), 2.09 (m, 2H), 1.88 (m, 1H), 1.74 (dd, $J$ = 6.43, 1.61 Hz, 3H), 1.71−1.56 (m, 6H), 1.46−1.39 (m, 4H), 1.33 (s, 3H), 1.28 (m, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 137.06, 121.56, 83.51, 74.33, 55.44, 39.66, 38.90, 27.62, 25.17, 23.65, 23.17, 21.20, 17.85, 16.78; IR ($CHCl_3$) 3608.0, 3561.3, 3038.4, 3026.1, 1663.1 cm$^{-1}$. Cis olefin: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 5.81 (m, $J$ = 12.3 Hz, unresolved, 1H), 5.44 (m, 1H), 2.32 (s, 1H), 2.13 (m, 2H), 1.94 (d, $J$ = 7.34 Hz, 2H), 1.86−1.76 (m, 2H), 1.69−1.53 (m, 6H), 1.49−1.29 (m, 4H), 1.39 (s, 3H), 1.23 (m, 2H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 134.68, 122.65, 86.61, 74.04, 56.22, 41.08, 38.98, 27.42, 25.44, 23.79, 23.30, 21.30, 17.07, 14.63; HRMS calcd for $C_{14}H_{22}O$ (M − $H_2O$)$^+$ 206.1671, found 206.1687; LRMS (EI$^+$) *m*/*z* 206 (33), 148 (52), 122 (73), 97 (34), 79 (68), 55 (53), 43 (100). Anal. Calcd for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78. Found: C, 75.02; H, 10.86.

**(1*R**,5*S**,6*S**,7*R**)-6-(2-Methylpropan-1-ol)-5-(1(*E*/*Z*)-propenyl)bicyclo[5.4.0]undecane-1,5-diol (21)** was prepared from (1*R**,4*S**,5*S**)-1-(3′-bromo)-4-[2-oxa-1′(*S**)-(2-propyl)-3(*E*/*Z*)-pentenyl]-2-oxabicyclo[4.3.0]nonan-3-one according to the general $SmI_2$ reaction conditions described above to afford the desired cyclization−elimination product as a 1:4 mixture of cis and trans olefin isomers, respectively, in 80% combined yield after flash column chromatography with 15% EtOAc/hexanes: mp 61−63 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 5.84 (m, 0.75H), 5.76 (dq, $J$ = 15.5 Hz, 1H), 5.63 (m, 0.25H), 3.76 (m, 0.25H), 3.43 (m, 0.75H), 2.03−1.80 (m, 6H), 1.69 (m, 3H), 1.63−1.41 (m, 9H), 1.37−1.15 (m, 5H), 1.01 (d, $J$ = 6.96 Hz, 0.6H), 0.92 (d, $J$ = 6.96 Hz, 2.4H), 0.87 (d, $J$ = 6.69 Hz, 2.4H), 0.82 (d, $J$ = 6.69 Hz, 0.6H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 138.01, 125.06, 123.25, 81.10, 80.92, 75.95, 72.90, 65.82, 59.34, 44.06, 42.90, 35.62, 32.00, 30.96, 28.98, 27.74, 27.05, 21.47, 21.07, 20.48, 19.32, 18.68, 18.23, 18.06, 17.83, 17.33, 15.57, 13.90; IR ($CHCl_3$) 3587.6, 3381.8, 3034.4, 1450.6 cm$^{-1}$; HRMS calcd for $C_{18}H_{30}O_2$ (M − $H_2O$)$^+$ 278.2246, found 278.2243; LRMS (EI$^+$) *m*/*z* 278 (22), 235 (28), 217 (100), 205 (71), 189 (21), 133 (32), 122 (24), 107 (33), 97 (56), 79 (40), 69 (98), 55 (52), 41 (91). Anal. Calcd for $C_{18}H_{32}O_3$: C, 72.93; H, 10.88. Found: C, 73.15; H, 11.08.

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**Supporting Information Available:** Complete experimental details for the preparation of all of the substrates described herein, $^1$H and $^{13}$C NMR spectral data for all of the compounds prepared, and X-ray data for one of the intermediates en route to substrate **20** (128 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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