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SEQUENTIAL EPOXIDE FRAGMENTATION/RADICAL CYCLIZATIONS MEDIATED BY SAMARIUM(II) IODIDE

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ABSTRACT

A sequential reductive coupling process promoted by samarium(II) iodide is described. Cascade epoxide ring opening and two sequential radical cyclizations lead to a variety of bicyclo[m.n.0] systems as mixtures of diastereomers.

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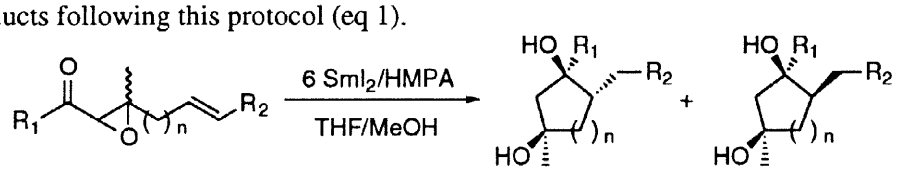
INTRODUCTION

The formation of several carbon-carbon bonds in a one pot process, increasing the molecular complexity of desired products from relatively simple precursors in a single operation, provides obvious efficiencies in organic synthesis.[1] The exceptional properties that samarium(II) iodide (SmI_2) exhibits in promoting such sequential reactions have been reviewed.[2] Its ability to carry out both one- and two electron reactions in any order and the high chemoselectivity demonstrated enhance the versatility of this reagent in these tandem processes. Herein we report a sequential transformation promoted by SmI_2 that results in the formation of bicyclo[m.n.0] systems with creation of two carbon-carbon bonds in the overall process.

Previous research has demonstrated that SmI_2 efficiently promotes domino epoxide ring opening/ketyl-olefin coupling reactions that provide access to a variety of stereodefined *cis*-1,3-cyclopentanediols and *cis*-1,3-cyclohexanediols.[1e] Thus, α,β-epoxy ketones bearing remote olefins were converted to the corresponding cyclized products following this protocol (eq 1).



(1)

R_1=Me, Et, *i*-Pr, *t*-Bu; R_2=H, Ph, COOEt; n=1, 2

In all cases, complete selectivity for *cis*-1,3-diols was achieved, owing to the formation of a samarium(III) chelate between the ketyl-oxygen and the β-hydroxy group in the cyclization step. The diastereoselectivity at the R_2CH_2-bearing stereocenter was substrate dependent. In the formation of *cis*-1,3-cyclopentanediols the diastereoselectivity was excellent. In the case of *cis*-1,3-cyclohexanediols, the reaction suffered from a lack of diastereoselectivity.

This tandem process proceeded via a series of electron transfer reactions. Electron transfer from SmI_2 to the carbonyl generated a ketyl that induced epoxide ring opening. The carbonyl of the resultant

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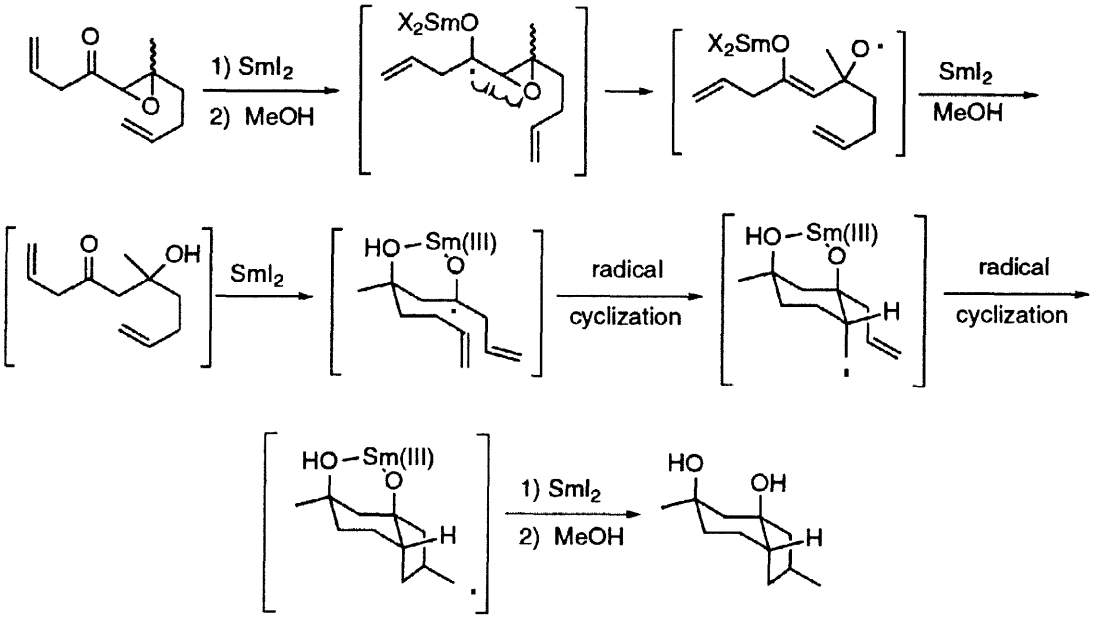
β-hydroxy ketone then suffered reduction by a second electron transfer, and this ketyl cyclized onto the available alkene. The methylene radical formed was reduced and protonated to afford the observed products.

We envisioned the possibility of trapping this methylene radical with alkenes or alkynes strategically located in the initial α,β-epoxy ketones before its subsequent reduction (Scheme 1).

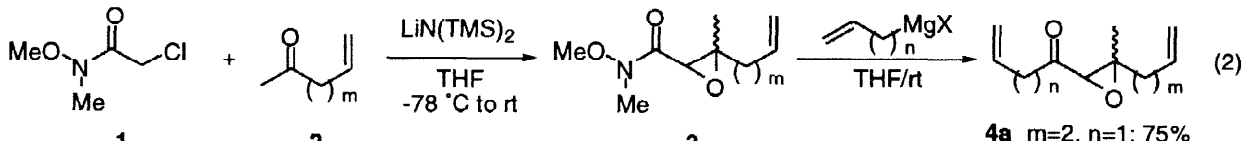
Scheme 1.



Herein we describe the results of studies directed toward this goal. A combination of three sequential SmI_2-promoted reactions is demonstrated: an epoxide ring opening followed by two radical cyclizations. This protocol provides entry into bicyclo[m.n.0] systems in a "one pot" process derived from the cleavage of a carbon-oxygen bond and the creation of two carbon-carbon bonds.

RESULTS AND DISCUSSION

In order to study the scope of the reaction, a variety of α,β-epoxy ketones bearing remote olefins and another properly functionalized lateral chain were prepared. The initial studies on the development of the sequential processes were concentrated primarily in the use of olefins as the radical acceptors to effect the second cyclization. Access to substrates **4a-d** was obtained through Darzen's condensation of Weinreb amide **1** with ketones **2** to afford the epoxy amides **3**. Subsequently, treatment with the corresponding organomagnesium compound provided substrates **4a-d** (eq 2).

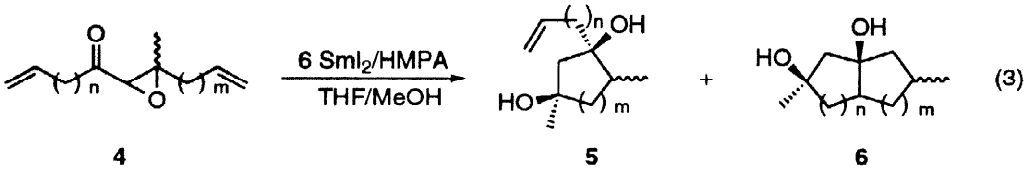


1 **2** **3**

4a m=2, n=1; 75%
4b m=1, n=1; 18%
4c m=1, n=2; 19%
4d m=2, n=2; 44%

(2)

These substrates were subjected to the tandem process mediated by SmI_2 under the conditions described in our earlier work,[1e] affording the desired bicyclic systems after workup and flash chromatography (eq 3, Table 1).



4 5 6 (3)

For substrates **4a** and **4b** the sequential process proceeded to provide exclusively the bicyclic products **6a** and **6b**, respectively, as mixtures of diastereomers. The selectivity in the formation of the *cis*- or *trans*-fused bicyclics was dependent on the ketyl olefin cyclization step. This selectivity was better in the formation of five-membered rings, and that explains the enhanced diastereoselection found in the product **6b** as compared to that of **6a**. The second cyclization proceeded without a template to control the stereochemistry, and the bicyclics were always obtained as a mixture of diastereomers at the methyl-bearing stereocenter. Exclusive formation of *cis*-diols was observed as a result of a samarium(III) chelate in the cyclization step. The undesired reduction/protonation reaction of the methylene radical became very important for substrates **4c** and **4d**. Thus, compounds **5c** and **5d** were obtained as the major products of the reaction. In these cases, the second cyclization step provides a six-membered ring, and the slower rate of the reaction compared to the formation of five-membered rings allows reduction of the radical prior to cyclization.[3] Although the cyclization process took place, the bicyclic systems **6c** and **6d** were generated in low yields as mixtures of diastereomers.

Table 1. Sequential Cyclizations of Substrates 4a-d to Yield 5 and 6.

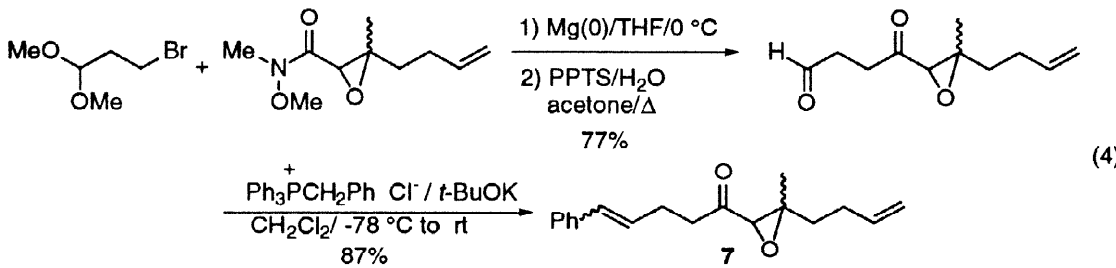
substrate	m	n	T (°C)	*cis/trans* ratio (**6**)[a]	% yield **5**	% yield **6**
4a	2	1	0	5.25/1	-	72
4a	2	1	-20	4/1	-	70
4b	1	1	0	18/1	-	61
4b	1	1	-20	37/1	-	60
4c	1	2	0	3/1	43	22
4c	1	2	rt	3/1	40	27
4d	2	2	0	2/1	67	14
4d	2	2	rt	2/1	56	26

[a] The ratios of diastereomers at the ring junctures were determined by fused silica capillary GC analysis of the reaction mixtures. All bicyclics were obtained as a mixture of diastereomers in the methyl-bearing stereocenter.

The stereochemistry of the bicyclic products was established by single crystal X-ray analysis of the major diastereomeric diol of compound **6a**. A *cis* relative relationship between the methyl-bearing stereocenter and both hydroxyl functionalities, and a *cis* fusion at the ring juncture was found to be the stereochemistry of the major products. The structural assignment of **5c** and **5d** was performed by spectroscopic techniques. High dilution IR spectra of these compounds revealed two hydroxyl resonances (hydrogen bonded and non-hydrogen bonded). Pyridine-d_5/$CDCl_3$ difference ^1H NMR showed a 0.040 ppm

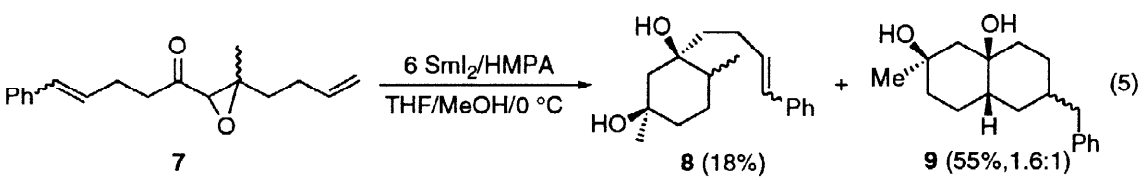
downfield shift of the methyl group in pyridine-d_5 relative to the spectrum in $CDCl_3$ for the major diastereomer of **5c**, and a 0.036 ppm shift for the major isomer of **5d**.[4] Both experiments indicate a *cis*-1,3-diol stereochemistry, and a trans relative relationship between the methyl-bearing stereocenter and the hydroxyl functionalities, respectively.

With the data of Table 1 in hand, it was apparent that when the second cyclization step leads to a six-membered ring the efficiency of the sequential process dramatically dropped off because the reduction-protonation reaction became competitive. The use of activated olefins was anticipated to increase the rate of addition of the intermediate free radicals to the alkenes, increasing the yield of cyclized product.[5] Compound **7**, bearing an activated olefin, was synthesized in an effort to avoid the reductive side reaction by increasing the rate of the second cyclization step. This substrate was obtained by reaction of the corresponding Grignard reagent of 3-bromopropionaldehyde dimethylacetal with Weinreb amide **3** (m=2). Deprotection of the acetal and a subsequent Wittig reaction provided **7** in good yield (eq 4).



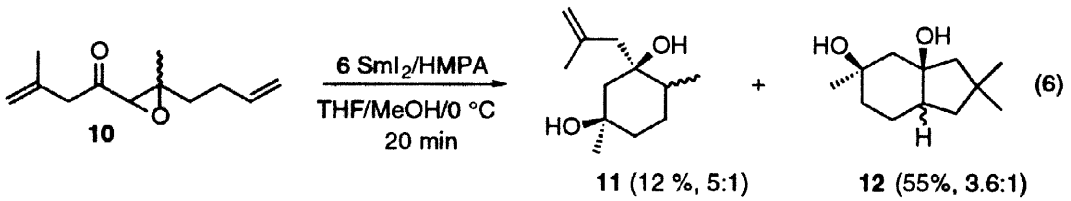
(4)

Subjecting substrate **7** to the standard reaction conditions provided the desired bicyclic **9** as the major product, plus the monocyclic product **8** resulting from the reduction-protonation of the terminal methylene radical after the ketyl-olefin cyclization step (eq 5).



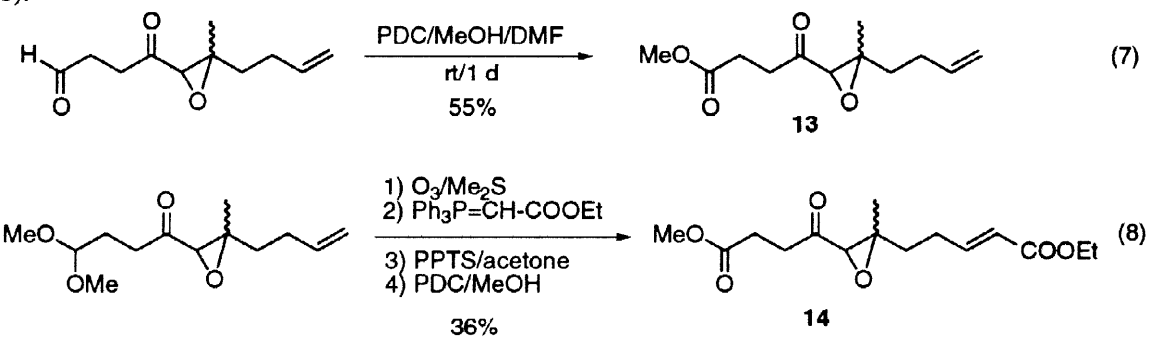
(5)

In order to investigate the effect of substitution patterns about the alkenes on the cyclization, substrate **10** was prepared. This substrate also had the advantage that the number of potential diastereomers produced from it would be reduced, thereby facilitating analysis of the crude reaction mixtures. Darzen's condensation of Weinreb amide **3** (m=2) with methallylmagnesium bromide afforded the substrate. Exposure to SmI_2 led to a mixture of the diastereomeric bicyclic isomers **12** bearing a gem-dimethyl group, plus a small amount of the undesired products **11** (eq 6). The stereochemistry of **12** was assigned by comparison of its ^1H NMR to compounds **6a**. Again, the major diastereomer was determined to be the *cis*-fused bicyclic. High dilution IR spectra (0.2 M in CCl_4) of the major bicyclic showed two hydroxyl absorbances (hydrogen bonded and non-hydrogen bonded), confirming the *cis*-diol configuration.

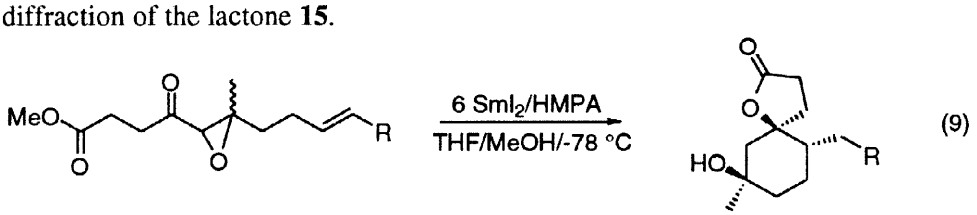


11 (12 %, 5:1) **12** (55%, 3.6:1)

The next phase of our study was to investigate the tandem process using other functionalities as acceptors, this time hoping to trap the anions generated upon reduction of the initially generated cyclized radicals. Substrates **13** and **14**, functionalized with ester electrophiles, were assembled as depicted below (eqs 7 and 8).



Performing the SmI_2 reaction under standard conditions resulted in the formation of the spirolactones **15** and **16**, with good yields and diastereoselectivities. Replacement of the unactivated olefin in **13** with the activating ester group (**14**) permitted the reaction to be performed in the absence of HMPA and at lower temperatures (-78 °C), generating the final products with increased stereoselectivity (eq 9). It was evident from these studies that attack of the ketyl oxygen-centered organosamarium on the methyl ester was faster than the reaction of the organosamarium intermediate, affording the spirolactones instead of the desired bicyclo[m.n.0] systems. The stereochemistry of these compounds was unambiguously established by single crystal X-ray diffraction of the lactone **15**.



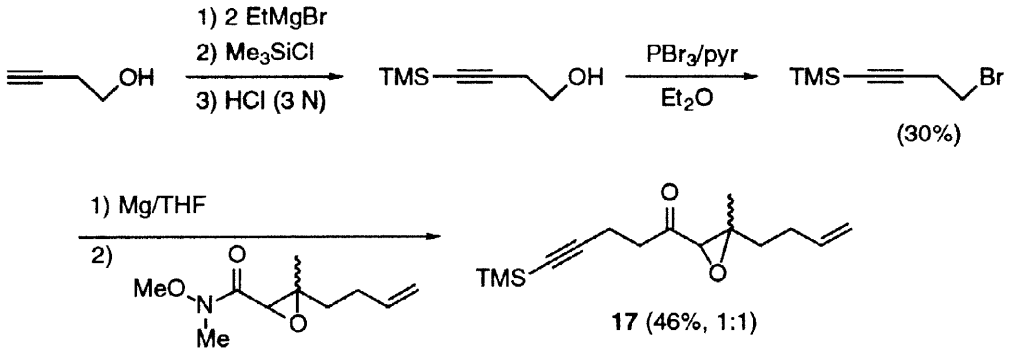
13 (R=H)
14 (R=COOEt)

15 (R=H, 77%, 10:1)
16 (R=COOEt, 77%, 18:1)

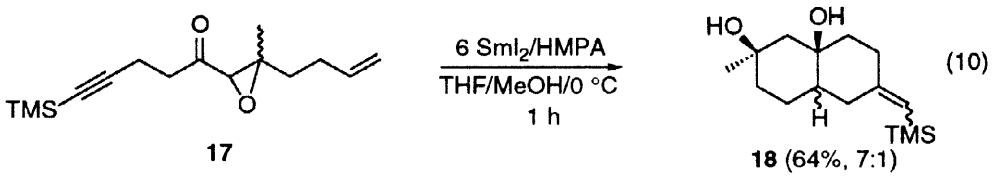
All attempts to effect tandem processes using other functional groups as either radical or electrophilic acceptors were unsuccessful. α,β-Epoxy ketones containing aldehydes, ketones, nitriles, α,β-unsaturated esters and α,β-unsaturated amides in the pendant chain were prepared and subjected to the standard reaction conditions, providing in all cases either the monocyclic systems or the acyclic diols resulting from opening of the epoxide and reduction of the ketone.

Extension of the successful sequential protocol to alkynes was examined next. Thus, substrate **17** was prepared as depicted in Scheme 2.

Scheme 2.

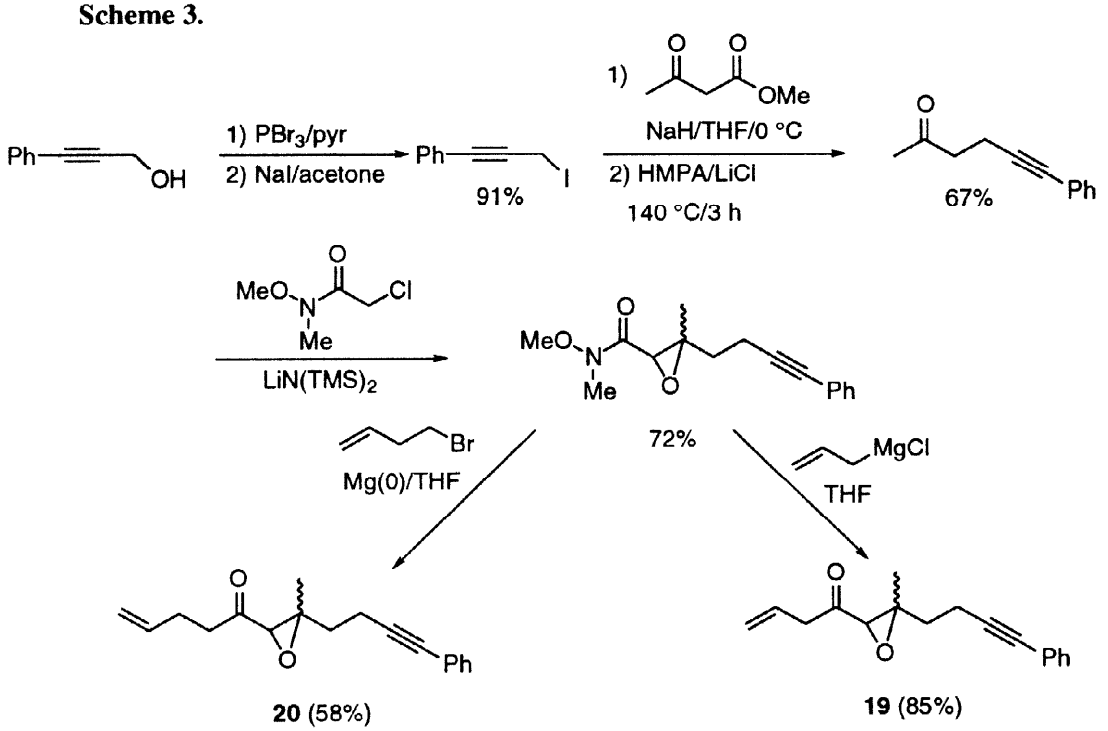


Reaction of **17** with SmI_2 provided the desired bicyclic product **18** as a 7:1 mixture of the *cis* and *trans* ring-fused isomers (eq 10). Again the major product was the *cis*-fused bicyclic system.



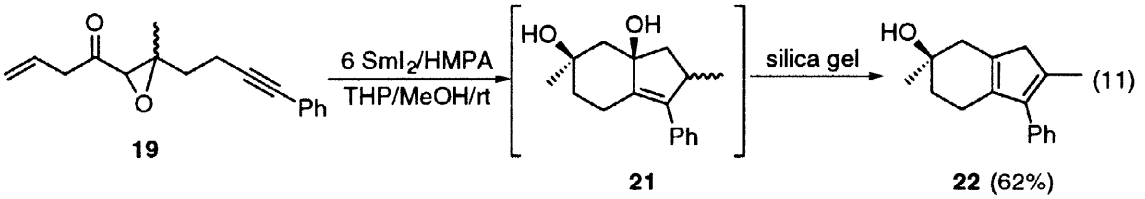
Finally, efforts were directed at extending this protocol to incorporate the use of alkynes in the ketyl olefin cyclization step. The synthesis of the substrates **19** and **20** was accomplished as depicted in Scheme 3.

Scheme 3.

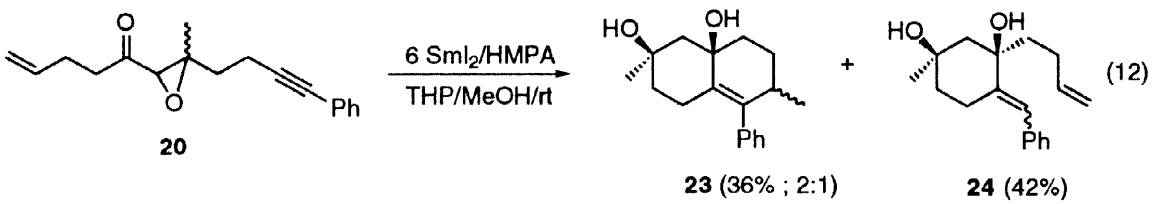


Substrates **19** and **20** were subjected to reductive cyclization under slightly modified reaction conditions. In these tandem processes, a vinylidene radical is formed upon the first cyclization step. It is known that vinylidene radicals can easily abstract a hydrogen from THF. To avoid this process, which would

interrupt a second radical cyclization, THP was utilized as the solvent for the reactions.[6] Utilizing this protocol, higher yields of bicyclic products could be attained. The formation of substantial amounts of **21** from **19** can be attributed to the facility of creating a five-membered ring in the second step of the two-step process (eq 11). The initial product of this reaction, tertiary allylic alcohol **21**, proved to be somewhat unstable. During the purification process a dehydration/isomerization took place, resulting in the formation of **22.**



With the cyclization of **20,** a slower rate of formation of the second six-membered ring through the radical cyclization process results in the formation of the monocyclic system **24** as the major product (eq 12).[3]



CONCLUSIONS

The synthetic utility of samarium(II) iodide in a novel sequential transformation has been described. The epoxide ring opening/double cyclization process results in the construction of bicyclic systems in which stereochemical control about the diol stereocenters is virtually complete. Unfortunately, stereoselectivity about the remaining stereocenters created is highly substrate dependent. Additionally, although five-membered rings can be synthesized efficiently utilizing a variety of alkene and alkyne radical acceptors, six-membered ring synthesis requires activated alkenes and alkynes in the final step of the sequential process. Even with these limitations, the increase in molecular complexity permits the process to be a synthetically viable one for the construction of a variety of useful bicyclo[m.n.0] systems.

ACKNOWLEDGMENT. We thank the National Institutes of Health (GM 35249) for their generous support of this work. Additional support from the Ministerio de Educacion y Ciencia of Spain for a Postdoctoral Fellowship to C. d. P. L. is gratefully acknowledged. Finally, we thank Dr. Bruce Noll for performing the X-ray crystallographic structure determinations.

EXPERIMENTAL SECTION

Reagents. Tetrahydrofuran (THF) was distilled immediately prior to use from benzophenone ketyl under Ar. Samarium metal was purchased from Cerac Inc., Milwaukee, WI, and was weighed and stored under an inert atmosphere. HMPA was purchased from either Aldrich or Sigma Chemicals and was distilled

from either Na(0) or CaH_2 at 0.04 mm Hg and stored over 4Å molecular sieves under Ar. Standard benchtop techniques were employed for the handling of air sensitive reagents, and all reactions were carried out under argon.

5,6-Epoxy-6-methyl-1,9-decadien-4-one (4a) was prepared according to the following general procedure. To a stirred solution of the Weinreb's amide **3**[1c] (m=2, 0.60 g, 3 mmol) in 20 mL of dry THF at rt was added dropwise allylmagnesium chloride (1.8 mL of a 2.0 M solution in THF, 3.6 mmol), and the reaction mixture was stirred for an additional 30 min period. Then, TLC revealed the complete comsumption of the starting material, and the reaction mixture was quenched with saturated aqueous NH_4Cl. Aqueous workup followed by flash chromatography (20% ethyl ether/hexanes) afforded 0.44 g (2.44 mmol) of **4a** in 82% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22 (s, 1.53H), 1.39 (s, 1.47H), 1.51-1.93 (m, 2H), 2.02-2.24 (m, 2H), 3.25-3.29 (m, 2H), 3.40 (s, 0.51H), 3.43 (s, 0.49H), 4.90-5.22 (m, 4H), 5.64-5.96 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.3, 22.0, 29.2, 29.6, 31.5, 37.3, 45.7, 45.9, 63.4, 63.9, 64.3, 65.26, 115.4, 115.5, 119.6, 119.7, 129.1, 129.1, 137.2, 137.2, 203.7, 203.8; IR (neat) 3078.8, 2970.0, 2931.7, 1721.8, 1641.0, 1404.5 cm^{-1}; HRMS calcd for $C_{11}H_{17}O_2$ (M+H)$^+$: 181.1229, found 181.1201; LRMS (EI) *m/z* 125 (22), 111 (19), 97 (18), 81 (19), 69 (94), 55 (42), 41 (100).

5,6-Epoxy-6-methyl-1,8-nonadien-4-one (4b) was prepared from **3** (m=1) according to the general procedure for the preparation of **4a** to afford **4b** in 55% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.21 (s, 1.29H), 1.39 (s, 1.71H), 2.12-2.43 (m, 2H), 3.24-3.28 (m, 2H), 3.44 (s, 0.57H), 3.46 (s, 0.43H), 5.01-5.21 (m, 4H), 5.52-5.93 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.4, 21.8, 36.9, 42.1, 45.6, 45.9, 62.9, 63.23, 63.3, 64.5, 118.6, 119.0, 119.5, 119.6, 128.9, 129.0, 131.9, 132.3, 203.2, 203.5; IR (neat) 3080.5, 2981.5, 2931.5, 1721.9, 1641.3, 1445.5, 1405.3 cm^{-1}; HRMS calcd for $C_{10}H_{15}O_2$ (M+H)$^+$: 167.1072, found 167.1041; LRMS (EI) *m/z* 125 (20), 97 (22), 83 (18), 69 (100), 53 (12), 41 (98).

6,7-Epoxy-7-methyl-1,9-decadien-5-one (4c) was prepared according to the following general procedure. A solution of 4-bromo-1-butene (0.54 g, 4 mmol) in 20 mL of dry THF was added slowly to a slurry of magnetically stirred Mg powder (0.49 g, 20 mmol) in 15 mL of dry THF at 0 °C. After the addition was complete, the reaction mixture was stirred for two more hours at 0 °C. A solution of the Weinreb's amide **3** (m=1, 0.60 g, 3 mmol) in 15 mL of dry THF was treated with the Grignard reagent (added via cannula to the solution of **3**). The resultant solution was stirred at rt for 30 min and quenched after that period with saturated aqueous NH_4Cl. Aqueous workup followed by flash chromatography (20% ethyl ether/hexanes) afforded 0.30 g (1.68 mmol) of **4c** in 56% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20 (s, 1.68H), 1.38 (s, 1.32H), 2.14-2.42 (m, 4H), 2.53-2.62 (m, 2H), 3.39 (s, 0.60H), 3.40 (s, 0.40H), 4.92-5.13 (m, 4H), 5.60-5.81 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.5, 22.0, 27.1, 37.1, 39.9, 40.3, 42.3, 62.9, 63.3, 63.5, 68.9, 115.7, 118.7, 119.1, 132.1, 132.5, 136.6, 205.1, 205.6; IR (neat) 3079.3, 2979.6, 2927.9, 1721.0, 1641.6, 1408.0 cm^{-1}; HRMS calcd for $C_{11}H_{17}O_2$ (M+H)$^+$: 181.1228, found 181.1224; LRMS (EI) *m/z* 139 (51), 97 (28), 83 (26), 55 (100), 41 (53).

6,7-Epoxy-7-methyl-1,10-undecadien-5-one (4d) was prepared from **3** (m=2) and 4-bromo-1-butene according to the general procedure for the preparation of **4c** to afford **4d** in 48% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20 (s, 1.47H), 1.38 (s, 1.43H), 1.47-1.80 (m, 2H), 2.00-2.22 (m, 2H), 2.25-2.35 (m, 2H), 2.50-2.65 (m, 2H), 3.34 (s, 0.49H), 3.37 (s, 0.51H), 4.91-5.07 (m, 4H), 5.62-5.82 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.2, 22.0, 27.1, 27.1, 29.2, 29.6, 31.5, 37.3, 39.9, 40.2, 63.2, 63.7, 64.4, 65.4, 115.3, 115.4, 115.5, 115.5, 136.5, 137.1, 137.2, 205.4; IR (neat) 3078.2, 2977.6, 2926.9, 1721.3, 1641.5, 1407.1 cm^{-1}; HRMS calcd for $C_{12}H_{19}O_2$ (M+H)$^+$: 195.1385, found 195.1348; LRMS (EI) *m/z* 139 (21), 111 (18), 97 (23), 83 (70), 71 (41), 55 (100).

6,7-Epoxy-7-methyl-1-phenyl-1,10-undecadien-5-one (7) was prepared according to the following general procedure. Reaction of 3-bromopropionaldehyde dimethylacetal (0.73 g, 4 mmol) with the Weinreb's amide **3** (m=2, 0.60 g, 3 mmol) and Mg powder (0.49 g, 20 mmol) according to the procedure described for the synthesis of **4c** afforded the corresponding α,β-epoxy ketone with the pendant acetal. A solution of this crude acetal, pyridinium *p*-toluensulfonate (PPTS, 0.38 g, 1.5 mmol)[7] and water (1 mL) in 40 mL of acetone was

heated at reflux for 3 h. The mixture was then cooled to rt and the acetone was removed under reduced pressure. Aqueous workup followed by flash chomatography (33% ethyl ether/hexanes) afforded 0.45 g (2.31 mmol) of the corresponding aldehyde in 77% yield (both steps). To a suspension of t-BuOK (0.33 g, 2.77 mmol) in 15 mL of dry CH_2Cl_2 at 0 °C was added slowly benzyl triphenylphosphonium chloride (1.08 g, 2.77 mmol) and the mixture stirred for 20-30 min at 0 °C after the addition was finished. The reaction mixture was then cooled to -78 °C and a solution of the aldehyde (obtained before) in 20 mL of dry THF was added dropwise, and when the addition was complete, the reaction was warmed to rt with continued stirring overnight. The reaction mixture was then quenched with saturated aqueous NH_4Cl after TLC analysis revealed the complete consumption of the starting material. Aqueous workup followed by flash chromatography (50% ethyl ether/hexanes) afforded 0.54 g (2.01 mmol) of **7** in 87% yield: ^1H NMR (400 MHz, $CDCl_3$) δ 1.20 (s, 0.87H), 1.22 (s, 0.87H), 1.49 (s, 0.63H), 1.51 (s, 0.63H), 1.50-1.82 (m, 2H), 1.95-2.22 (m, 2H), 2.48-2.71 (m, 4H), 3.35 (s, 0.29H), 3.38 (s, 0.29H), 3.39 (s, 0.21H), 3.42 (s, 0.21H), 4.90-5.05 (m, 2H), 5.52-5.83 (m, 1.50H), 6.10-6.20 (m, 0.50H), 6.38-6.47 (m, 1H), 7.15-7.35 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.3, 16.3, 22.1, 22.3, 22.4, 26.6, 29.3, 29.6, 31.6, 37.4, 37.4, 40.5, 40.8, 41.0, 41.2, 63.3, 63.8, 64.4, 64.5, 65.4, 65.5, 115.5, 126.0, 126.9, 127.2, 128.3, 128.5, 128.7, 130.2, 130.3, 131.1, 137.1, 137.2, 137.3, 205.4; IR (neat) 2929.5, 1715.9, 1640.5, 1493.8, 1447.3, 1406.3 cm^{-1}; HRMS calcd for $C_{18}H_{22}O_2$: 270.1620, found 270.1609; LRMS (EI) *m/z* 205 (15), 180 (23), 157 (13), 130 (78), 91 (51).

5,6-Epoxy-2,6-dimethyl-1,9-decadien-4-one (10) was prepared from **3** (m=2) according to the general procedure for the preparation of **4c** by reaction with methallyl chloride (0.36 g, 4 mmol) to afford **10** in 40% yield after flash chromatography with 20% ethyl ether/hexanes: ^1H NMR (400 MHz, $CDCl_3$) δ 1.22 (s, 1.62H), 1.39 (s, 1.38H), 1.54-1.82 (m, 2H), 1.74 (s, 1.62H), 1.75 (s, 1.38H), 2.04-2.30 (m, 2H), 3.12-3.30 (m, 2H), 3.43 (s, 0.46H), 3.47 (s, 0.54H), 4.80-5.17 (m, 4H), 5.66-5.87 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.0, 21.9, 22.6, 22.8, 29.2, 29.6, 31.3, 37.3, 50.2, 50.2, 63.6, 64.0, 65.0, 115.4, 115.4, 115.6, 115.7, 137.2, 137.2, 137.8, 137.8, 203.4, 203.5; IR (neat) 3078.1, 2975.0, 2930.5, 1719.5, 1642.1, 1404.4 cm^{-1}; HRMS calcd for $C_{12}H_{18}O_2$: 194.1307, found 194.1312; LRMS (EI) *m/z* 139 (27), 111 (30), 97 (32), 83 (88), 71 (33), 55 (100).

Methyl 5,6-Epoxy-6-methyl-4-oxo-9-decenoate (13) was prepared according to the following general procedure.[8] To a solution of the aldehyde (0.39 g, 2 mmol) described in the synthesis of **7** in methanol (0.48 mL, 12 mmol) and dry dimethylformamide (10 mL) at rt under an argon atmosphere, was added pyridinium dichromate (PDC, 4.50 g, 12 mmol) and the reaction mixture was stirred for 20 h. After this period, the solution was poured into hexanes (150 mL)/water (50 mL) and filtered over Celite. The aqueous layer was extracted with hexanes (3 x 50 mL) and the combined hexane extracts were dried over magnesium sulfate. Removal of the solvent and flash chromatography with 50% ethyl ether/hexanes gave **13** in 55% yield: ^1H NMR (400 MHz, $CDCl_3$) δ 1.21 (s, 2.01H), 1.38 (s, 0.99H), 1.51-1.62 (m, 1.34H), 1.72-1.80 (m, 0.66H), 2.01-2.20 (m, 2H), 2.52-2.61 (m, 2H), 2.65-2.88 (m, 2H), 3.38 (s, 0.33H), 3.40 (s, 0.67H), 3.60 (s, 3H), 4.88-5.02 (m, 2H), 5.61-5.81 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.1, 22.0, 27.1, 27.2, 29.3, 29.6, 31.4, 35.5, 35.9, 37.4, 51.9, 63.4, 63.9, 64.4, 65.4, 115.3, 115.5, 137.3, 137.3, 172.8, 204.3; IR (neat) 3077.5, 2951.5, 1740.0, 1731.9, 1640, 1211.4 cm^{-1}; HRMS calcd for $C_{11}H_{15}O_4$: (M-CH_3) 211.0970, found 211.1023, (M-H_2O) 208.1099, found 208.1107; LRMS (EI) *m/z* 171 (16), 115 (72), 81 (17), 55 (90), 41 (100).

Methyl 5,6-Epoxy-10-ethoxycarbonyl-6-methyl-4-oxo-9-decenoate (14) was prepared according to the following general procedure. Ozone was bubbled through a solution of the acetal (0.49 g, 2 mmol) described in the synthesis of **7** and $NaHCO_3$ (0.34 g, 4 mmol) in 8 mL of 50% MeOH/CH_2Cl_2 at -78 °C until a blue color persisted. Then, Me_2S was added (1.24 g, 20 mmol) and the reaction mixture was stirred and warmed to rt. The resultant crude reaction mixture was diluted with brine (10 mL), extracted with ether, dried over $MgSO_4$, and concentrated in vacuo. This crude was used in the next step without further purification. To a solution of this aldehyde (obtained in the ozonolysis) in 20 mL of CH_2Cl_2 at -78 °C was added slowly (carbethoxymethylene)triphenylphosphorane (0.77 g, 2.2 mmol) and the reaction was warmed to rt with

continued stirring overnight. Aqueous workup followed by flash chromatography (50% ethyl acetate/hexanes) afforded 0.52 g (1.66 mmol) of the corresponding acetal. This acetal was converted in the corresponding aldehyde by the reaction with PPTS following the procedure described in the synthesis of **7**. Next, this aldehyde was converted to the methyl ester **14** by oxidation with PDC as described in the synthesis of **13** to provide after aqueous workup and flash chromatography (33% ethyl acetate/hexanes) 0.22 g (0.73 mmol) of **14** in 44% yield (both steps): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.19-1.27 (m, 3H), 1.21 (s, 1.65H), 1.39 (s, 1.35H), 1.55-1.90 (m, 3H), 2.36-2.44 (m, 2H), 2.48-2.82 (m, 3H), 3.22 (s, 0.55H), 3.39 (s, 0.45H), 3.61 (s, 3H), 4.10-4.17 (m, 2H), 5.78-5.83 (m, 1H), 6.82-6.92 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 16.1, 27.1, 27.6, 35.5, 36.4, 51.9, 53.3, 60.3, 63.0, 64.2, 122.3, 147.0, 166.3, 172.8, 204.1; IR (neat) 2953.8, 1715.8, 1652.0, 1368.1, 1269.0, 1200.3 cm^{-1}; HRMS calcd for $C_{15}H_{23}O_6$ $(M+H)^+$: 283.1182, found 283.1179; LRMS (EI) *m/z* 221 (12), 171 (21), 137 (10), 115 (100), 71 (33).

6,7-Epoxy-7-methyl-11-trimethylsilyl-1-undecen-10-yn-5-one (17) was prepared from **3** (m=2) and 4-bromo-1-(trimethylsilyl)-1-butyne[9] according to the general procedure for the preparation of **4c** to afford **17** in 46% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.08 (s, 4.32H), 0.09 (s, 4.68H), 1.21 (s, 1.44H), 1.40 (s, 1.56H), 1.50-1.68 (m, 2H), 1.74-1.82 (m, 0.52H), 2.01-2.21 (m, 2H), 2.45-2.51 (m, 2H), 2.61-2.81 (m, 1.48H), 3.48 (s, 1.52H), 3.50 (s, 0.48H), 4.90-5.05 (m, 2H), 5.62-5.82 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 0.0, 13.9, 13.9, 16.3, 22.0, 29.3, 29.7, 31.5, 37.4, 39.8, 40.3, 63.4, 63.9, 64.4, 64.5, 65.3, 65.5, 85.3, 105.1, 115.5, 115.6, 137.2, 104.1, 104.1; IR (neat) 2960.2, 2176, 1722.3, 1407.5, 1249.9 cm^{-1}; HRMS calcd for $C_{15}H_{25}SiO_2$ $(M+H)^+$: 265.1624, found 265.1613; LRMS (EI) *m/z* 209 (12), 179 (5), 151 (35), 111 (31), 97 (36), 73 (100).

5,6-Epoxy-6-methyl-10-phenyl-1-decen-9-yn-4-one (19) was prepared according to the following general procedure. Sodium iodide (30 g, 200 mmol) was added to a stirred solution of 1-bromo-3-phenyl-2-butyne[8b] (3.9 g, 20 mmol) in 100 mL of acetone. The resultant solution was heated at reflux for 12 h. After this period, the reaction mixture was cooled to rt and the solvent was removed *in vacuo*. The resultant reaction mixture was diluted in ether, washed with saturated aqueous sodium thiosulfate and brine, and then dried over $MgSO_4$. The crude reaction mixture was utilized in the next step without further purification. Methyl acetoacetate (11.61 g, 100 mmol) in 40 mL of dry THF was added dropwise via cannula to a stirred slurry of NaH (4.4 g of a 60% dispersion in mineral oil, 110 mmol) at 0 °C. After the addition of the substrate was complete and H_2 evolution had ceased, the reaction mixture was warmed to rt and stirred for 2 h. After this period of time, the reaction mixture was cooled to 0 °C, and a solution of 1-iodo-3-phenyl-2-butyne (the crude mixture obtained before) in 40 mL of THF was added dropwise, and the reaction mixture was then warmed to rt and stirred for 3 h. The reaction was then quenched at rt by the careful addition of saturated aqueous NH_4Cl and subjected to an aqueous workup. Flash chromatography with 25% ethyl ether/hexanes afforded the corresponding alkylated methyl acetoacetate. A solution of this acetoacetate, LiCl (12.72 g, 300 mmol) and H_2O (5.4 g, 300 mmol) in 15 mL of HMPA was heated at 140 °C for 6 h with vigorous stirring. TLC analysis of the reaction mixture after this period of time showed complete consumption of starting material. The reaction mixture was cooled to rt and quenched with water. An aqueous workup followed by flash chromatography with 50% ethyl ether/hexanes provided 2.10 g (12.2 mmol) of 6-phenyl-5-hexan-2-one in a 61% yield (four steps). Darzen's condensation of this ketone with **1** and subsequent treatment with allylmagnesium chloride (2.0 M in THF) afforded **19** in 85% yield after aqueous workup and flash chromatography with 20% ether/hexanes: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28 (s, 1.26H), 1.49 (s, 1.74H), 1.24-1.40 (m, 2H), 2.45-2.56 (m, 2H), 3.20-3.40 (m, 3H), 3.46 (s, 0.58H), 3.64 (s, 0.42H), 5.02-5.21 (m, 2H), 5.78-5.91 (m, 1H), 7.20-7.29 (m, 3H), 7.29-7.40 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.5, 15.8, 16.1, 21.9, 31.0, 36.9, 45.7, 46.0, 62.8, 63.5, 64.1, 65.1, 81.4, 81.7, 88.5, 119.6, 119.7, 123.4, 123.5, 127.8, 127.9, 128.2, 128.3, 129.0, 129.1, 131.5, 145.2, 203.3, 203.4; IR (neat) 3079.3, 2971.4, 2929.9, 2236.1, 1721.3, 1490.2 cm^{-1}; HRMS calcd for $C_{17}H_{17}O_2$ $(M-H)^+$: 253.1229, found 253.1203; LRMS (EI) *m/z* 115 (15), 99 (10), 85 (11), 69 (42), 55 (32), 43 (100).

6,7-Epoxy-7-methyl-11-phenyl-1-undecen-10-yn-5-one (20) was prepared from the same Weinreb amide obtained in the Darzen's condensation described in the preparation of **19** by treatment with 3-butenylmagnesium bromide according to the general procedure for the preparation of **4c**, to afford **20** in 58% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28 (s, 1.08H), 1.49 (s, 1.92H), 1.76-1.84 (m, 2H), 2.25-2.39 (m, 2H), 2.49-2.63 (m, 4H), 3.42 (s, 0.64H), 3.62 (s, 0.36H), 4.89-5.00 (m, 2H), 5.52-5.65 (m, 1H), 7.22-7.30 (m, 3H), 7.30-7.42 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.5, 15.8, 16.0, 22.0, 27.1, 27.2, 31.0, 36.9, 40.1, 40.5, 62.7, 63.4, 64.3, 65.4, 81.3, 88.4, 115.5, 115.6, 123.5, 127.9, 128.1, 128.3, 128.3, 131.5, 136.5, 205.0, 205.2; IR (neat) 2729.9, 1720.3, 1641.0, 1490.1, 1407.1, 1070.7 cm^{-1}; HRMS calcd for $C_{18}H_{19}O_2$ $(M-H)^+$: 267.1385, found 267.1385; LRMS (EI) *m/z* 220 (5), 205 (37), 185 (10), 155 (11), 115 (40), 43 (100).

Preparation of the SmI_2 Solution. Samarium metal (0.541 g, 3.6 mmol) was added under a flow of argon to an oven-dried, round-bottomed flask containing a magnetic stirring bar and a septum inlet. To the samarium was added I_2 (0.761 g, 3.0 mmol), followed by 20 mL of dry THF. The mixture was stirred at rt for 2 h. The resulting deep blue solution was used directly to effect the following sequential reactions.

General Procedure for the SmI_2 Promoted Sequential Reactions of α,β-Epoxy Ketones. To the SmI_2 (3.0 mmol) in THF was added HMPA (3.23 g, 18 mmol), and Ar was bubbled through the solution for 10 min. A solution of the α,β-epoxy ketone (0.5 mmol) and MeOH (1 mL) in 30 mL of THF was added over 1 h. After the starting material was consumed, aqueous workup followed by flash chromatography and/or Kugelrohr distillation afforded the title compounds. For the case of substrate **14**, no HMPA was added to the SmI_2 solution.

***cis*-3,8-Dimethylbicyclo[4.3.0]nonan-1,8-diol (6a)** was prepared from **4a** according to the general procedure described above to afford after flash chromatography (50% ethyl acetate/hexanes) 0.066 g (0.36 mmol) of a 5.25:1 mixture of diastereomers **6a** in 72% yield. **6a** (major): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.96 (d, J = 6.91 Hz, 0.33H), 1.02 (d, J = 6.85 Hz, 2.67H), 1.20 (s, 2.67H), 1.22-1.30 (m, 2H), 1.37-1.48 (m, 4.33H), 1.57-1.62 (m, 1H), 1.66-1.75 (m, 1H), 1.82-1.87 (m, 1H), 1.90-2.09 (m, 3H), 2.65 (br s, 1H), 3.23 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.0, 19.3, 22.5, 23.4, 27.6, 28.6, 31.0, 32.4, 33.0, 34.2, 37.0, 38.6, 42.0, 43.0, 45.3, 45.5, 48.0, 49.1, 70.7, 70.8, 79.5, 80.0; IR (neat) 3345.8, 2932.1, 2865.7, 1455.8, 1207.6, 1166.3 cm^{-1}; LRMS (EI) *m/z* 166 (60), 151 (12), 123 (20), 108 (52), 98 (66), 43 (100). Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.70; H, 10.94. Found: C, 71.36; H, 10.80. **6a** (minor): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85-0.93 (m, 1.99H), 0.98 (d, J = 6.97 Hz, 2.01H), 1.16 (s, 0.99H), 1.20 (s, 2.01H), 1.20-1.61 (m, 6H), 1.65-1.78 (m, 2H), 1.81-1.96 (m, 2H), 2.10-2.31 (m, 1H), 3.00-3.25 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.6, 14.8, 15.5, 21.4, 23.1, 24.3, 29.0, 31.2, 31.3, 33.2, 35.8, 36.2, 39.8, 42.7, 43.1, 45.8, 46.6, 48.3, 71.0, 72.0, 76.0, 81.4; IR (neat) 3308.6, 2931.1, 2865.3, 1453.4, 1372.4, 1174.6 cm^{-1}; HRMS calcd for $C_{11}H_{20}O_2$: 184.1463, found 184.1460; LRMS (EI) *m/z* 166 (42), 151 (11), 123 (21), 108 (85), 98 (37), 43 (100). Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.70; H, 10.94. Found: C, 70.94; H, 11.20.

***cis*-3,7-Dimethylbicyclo[3.3.0]octan-1,7-diol (6b)** was prepared from **4b** according to the general procedure described above to afford after flash chromatography (50% ethyl acetate/hexanes) 0.051 g (0.30 mmol) of a 37:1 mixture of diastereomers **6b** in 60% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 (d, J = 6.47 Hz, 1.80H), 0.97 (d, J = 6.11 Hz, 1.20H), 1.12-1.28 (m, 2H), 1.29 (s, 1.20H), 1.30 (s, 1.80H), 1.32-1.40 (m, 0.6H), 1.44-1.55 (m, 0.4H), 1.57-1.64 (m, 1H), 1.78-1.98 (m, 3H), 2.01-2.13 (m, 1.06H), 2.21-2.36 (m, 0.4H), 2.43-2.55 (m, 1H), 2.60-2.90 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.0, 19.4, 26.2, 26.8, 32.9, 37.4, 40.1, 44.1, 48.0, 48.1, 49.3, 51.4, 54.0, 54.2, 54.9, 81.4, 84.4, 91.4, 92.4; IR (neat) 3382.6, 2951.7, 2929.0, 1465.5, 1402.7, 1374.9 cm^{-1}; HRMS calcd for $C_9H_{15}O_2$ $(M-CH_3)$: 155.1072, found 155.1054; LRMS (EI) *m/z* 152 (18), 137 (11), 109 (41), 94 (52), 67 (31), 43 (100).

1,4-Dimethyl-3-(3-butenyl)-1,3-cyclopentanediol (5c) was prepared from **4c** according to the general procedure described above to afford after flash chromatography (33% ethyl acetate/hexanes) 0.037 g (0.20 mmol) of a 6:1 mixture of diastereomers **5c** in 40% yield. **5c** (major): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86 (d,

J = 7.14 Hz, 3H), 1.12-1.21 (m, 1H), 1.30 (s, 3H), 1.35-1.41 (m, 1H), 1.44-1.62 (m, 2H), 1.65-1.81 (m, 2H), 2.08-2.32 (m, 3H), 2.65-2.85 (br s, 2H), 4.92-5.06 (m, 2H), 5.80-5.91 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.6, 28.7, 28.8, 35.8, 44.8, 50.2, 50.8, 78.7, 85.1, 114.6, 139.2; IR (neat) 3374.2, 2963.3, 2872.9, 1640.5, 1448.2, 1375.9 cm^{-1}; HRMS calcd for $C_{11}H_{18}O$ (M-H_2O)$^+$: 166.1358, found 166.1357; LRMS (EI) *m/z* 166 (23), 149 (71), 129 (48), 111 (65), 83 (100), 69 (60). Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.70; H, 10.94. Found: C, 70.47; H, 11.01.

***cis*-4,8-Dimethylbicyclo[4.3.0]nonan-1,8-diol (6c)** was prepared from **4c** according to the general procedure described above to afford after flash chromatography (50% ethyl acetate/hexanes) 0.025 g (0.135 mmol) of a 3:1 mixture of diastereomers **6c** in 27% yield. **6c** (major): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (d, J = 6.91 Hz, 2.58H), 0.94 (d, J = 7.31 Hz, 0.42H), 1.19-1.32 (m, 3.42H), 1.33 (s, 2.58H), 1.37-1.57 (m, 7H), 1.92-2.00 (m, 2H), 2.16-2.31 (m, 1.72H), 2.50-2.53 (m, 0.28H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.0, 26.5, 29.5, 30.2, 32.8, 35.3, 43.4, 46.8, 53.3, 77.8, 80.1; IR (neat) 3381.9, 2923.2, 2852.9, 1455.8, 1377.2, 1018.5 cm^{-1}; LRMS (EI) *m/z* 166 (34), 151 (45), 123 (62), 108 (59), 95 (25), 43 (100). Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.70; H, 10.94. Found: C, 71.84; H, 10.87.

1,4-Dimethyl-3-(3-butenyl)-1,3-cyclohexanediol (5d) was prepared from **4d** according to the general procedure described above to afford after flash chromatography (33% ethyl acetate/hexanes) 0.055 g (0.28 mmol) of a 3:1 mixture of diastereomers **5d** in 56% yield. **5d** (major): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86 (d, J = 7.23 Hz, 3H), 1.15 (s, 3H), 1.20-1.30 (m, 2H), 1.40-1.56 (m, 5H), 1.60-1.82 (m, 1H), 2.00-2.23 (m, 3H), 3.30-3.50 (br s, 2H), 4.90-5.04 (m, 2H), 5.76-5.87 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.5, 24.2, 26.4, 31.2, 33.1, 36.2, 39.6, 42.5, 71.1, 75.7, 114.5, 139.2; IR (neat) 3330.3, 2964.2, 2941.6, 1450.8, 1421.7, 1216.7 cm^{-1}; LRMS (EI) *m/z* 180 (22), 141 (28), 125 (60), 109 (12), 83 (77), 55 (100). Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18. Found: C, 72.32; H, 11.15.

***cis*-4,9-Dimethylbicyclo[4.4.0]decan-1,9-diol (6d)** was prepared from **4d** according to the general procedure described above to afford after flash chromatography (50% ethyl acetate/hexanes) 0.026 g (0.13 mmol) of a 3:1 mixture of diastereomers **6d** in 26% yield. **6d** (major): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85 (d, J = 6.88 Hz, 1.98H), 0.88-1.02 (m, 2.02H), 1.18 (s, 1.98H), 1.12-1.22 (m, 3.02H), 1.20-1.50 (m, 7H), 1.50-1.65 (m, 2H), 1.71-1.81 (m, 1H), 2.12-2.27 (m, 1H), 2.90-3.20 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.8, 22.1, 22.8, 23.0, 27.1, 29.1, 31.3, 32.5, 33.2, 33.2, 34.1, 35.1, 35.8, 37.5, 40.9, 41.2, 42.0, 71.5, 71.6, 73.6, 74.1; IR (neat) 3322.7, 2921.8, 1455.3, 1374.5, 1214.9, 1160.7 cm^{-1}; HRMS calcd for $C_{12}H_{22}O_2$: 198.1620, found 198.1642; LRMS (EI) *m/z* 130 (38), 165 (10), 141 (5), 112 (42), 71 (26), 43 (100). Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18. Found: C, 72.67; H, 11.33.

***cis*-4-Benzyl-9-methylbicyclo[4.4.0]decan-1,8-diol (9)** was prepared from **7** according to the general procedure described above to afford after flash chromatography (50% ethyl acetate/hexanes) 0.075 g (0.275 mmol) of a 1.6:1 mixture of diastereomers **9** in 55% yield. **9** (major): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92-1.13 (m, 2H), 1.20 (s, 1.83), 1.21 (s, 1.17H), 1.30-1.51 (m, 6H), 1.51-1.72 (m, 3H), 1.74-1.86 (m, 2H), 2.12-2.35 (m, 1H), 2.48 (d, J = 8.07 Hz, 1.22H), 2.71 (d, J = 6.96 Hz, 0.78H), 2.80-3.30 (br s, 2H), 7.09-7.20 (m, 3H), 7.21-7.40 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.7, 22.9, 26.5, 30.2, 31.2, 31.6, 33.0, 33.1, 34.8, 35.0, 35.1, 36.1, 37.5, 39.4, 40.4, 41.0, 41.1, 41.7, 43.4, 71.5, 73.6, 73.8, 125.7, 128.1, 128.2, 128.9, 128.9, 140.8, 141.5; IR (neat) 3312.3, 2921.4, 1452.1, 1167.4, 1020.2 cm^{-1}; LRMS (EI) *m/z* 274 (4), 256 (47), 238 (11), 188 (21), 165 (39), 147 (43), 91 (100). Anal. Calcd for $C_{18}H_{26}O_2$: C, 8.79; H, 9.55. Found: C, 78.88; H, 9.51.

***cis*-3,3,8-Trimethylbicyclo[4.3.0]nonan-1,8-diol (12)** was prepared from **10** according to the general procedure described above to afford after flash chromatography (50% ethyl acetate/hexanes) 0.054 g (0.275 mmol) of a 3.6:1 mixture of diastereomers **12** in 55% yield. **12** (major): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.98 (s, 3H), 1.04 (s, 3H), 1.19 (s, 3H), 1.31-1.62 (m, 9H), 1.93-2.05 (m, 1H), 2.12-2.22 (m, 1H), 2.75-2.90 (br s, 1H), 3.35-3.50 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.0, 31.2, 32.1, 32.9, 33.2, 33.8, 42.9, 43.5, 44.6,

55.4, 70.9, 80.0; IR (neat) 3342.2, 2927.4, 2862.9, 1451.7, 1420.9, 1159.9 cm^{-1}; HRMS calcd for $C_{12}H_{20}O$ $(M-H_2O)^+$: 180.1514, found 180.1504; LRMS (EI) *m/z* 180 (44), 165 (31), 137 (20), 125 (21), 112 (42), 43 (100). Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18. Found: C, 73.09; H, 11.15.

7-Hydroxy-7,10-dimethyl-1-oxaspiro[5.4]decan-2-one (15) was prepared from **13** according to the general procedure described above to afford after flash chromatography (40% ethyl acetate/hexanes) 0.076 g (0.385 mmol) of a 10:1 mixture of diastereomers **15** in 77% yield. **15** (major): ^1H NMR (400 MHz, $CDCl_3$) δ 0.93 (d, J = 7.29 Hz, 3H), 1.17 (s, 3H), 1.33-1.41 (m, 1H), 1.52-1.57 (m, 2H), 1.64-1.69 (m, 1H), 1.75-1.79 (m, 1H), 1.81-1.92 (m, 2H), 2.02-2.11 (m, 2H), 2.45-2.61 (m, 2H), 3.15-3.25 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 24.6, 28.4, 30.0, 32.0, 32.8, 36.6, 43.0, 69.7, 90.2, 175.5; IR (neat) 3443.9, 2933.7, 1769.9, 1732.0, 1455.7, 1106.4 cm^{-1}; LRMS (EI) *m/z* 180 (20), 165 (5), 141 (48), 125 (14), 99 (45), 43 (100). Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.63; H, 9.18.

10-Ethoxycarbonylmethyl-7-hydroxy-7-methyl-1-oxaspiro[5.4]decan-2-one (16) was prepared from **14** according to the general procedure described above to afford after flash chromatography (40% ethyl acetate/hexanes) 0.104 g (0.385 mmol) of a 17:1 mixture of diastereomers **16** in 77% yield. **16** (major): ^1H NMR (400 MHz, $CDCl_3$) δ 1.17 (s, 3H), 1.22 (t, J = 7.15 Hz, 3H), 1.38-1.62 (m, 4H), 1.78-1.88 (m, 2H), 2.00-2.11 (m, 2H), 2.21-2.37 (m, 3H), 2.54-2.58 (m, 2H), 3.10-3.20 (br s, 1H), 4.11 (q, J = 7.15 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 22.2, 28.1, 30.0, 31.9, 33.0, 33.5, 38.6, 43.9, 61.0, 69.4, 88.6, 171.9, 174.9; IR (neat) 3478.3, 2933.3, 1769.9, 1731.9, 1127.7, 1026.2 cm^{-1}; HRMS calcd for $C_{14}H_{22}O_5$: 270.1467, found 270.1445; LRMS (EI) *m/z* 224 (5), 206 (6), 182 (15), 141 (59), 91 (45), 43 (100). Anal. Calcd for $C_{14}H_{22}O_5$: C, 62.20; H, 8.20. Found: C, 62.69; H, 8.36.

***cis*-9-Methyl-4-[(trimethylsilyl)methylene]bicyclo[4.4.0]decan-1,9-diol (18)** was prepared from **17** according to the general procedure described above to afford after flash chromatography (20% ethyl acetate/hexanes) 0.086 g (0.32 mmol) of a 7:1 mixture of diastereomers **18** in 64% yield. **18** (major): ^1H NMR (400 MHz, $CDCl_3$) δ 0.11 (s, 4.05H), 0.12 (s, 4.95H), 0.80-0.97 (m, 3H), 1.08-1.38 (m, 5H), 1.38-1.70 (m, 4H), 1.70-1.90 (m, 2.95H), 1.90-2.11 (m, 1.45H), 2.11-2.48 (m, 2H), 4.70-4.76 (m, 0.45H), 4.85-4.95 (m, 0.55H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -0.1, -0.1, 13.1, 15.3, 15.4, 24.2, 24.3, 30.9, 31.2, 33.0, 33.1, 36.0, 36.2, 36.5, 38.8, 39.6, 39.7, 42.0, 42.3, 70.8, 71.0, 75.6, 75.8, 103.2, 103.6, 106.5, 107.5; IR (neat) 3344.2, 2961.6, 1662.3, 1419.9, 1249.8, 1160.7 cm^{-1}; LRMS (EI) *m/z* 221 (12), 193 (11), 143 (21), 125 (45), 73 (100). Anal. Calcd for $C_{15}H_{28}SiO_2$: C, 67.11; H, 10.51. Found: C, 67.26; H, 10.31.

3,8-Dimethyl-4-phenylbicyclo[4.3.0]-1,4-nonadien-8-ol (22) was prepared from **19** according to the general procedure described above to afford after flash chromatography (33% ethyl acetate/hexanes) 0.074 g (0.31 mmol) of **22** in 62% yield: ^1H NMR (400 MHz, $CDCl_3$) δ 1.31 (s, 3H), 1.55-1.86 (m, 3H), 1.98 (s, 3H), 2.10-2.25 (m, 1H), 2.25-2.50 (m, 2H), 2.62-2.65 (m, 1H), 2.88-2.90 (m, 1H), 7.12-7.49 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.4, 21.7, 28.6, 35.9, 40.4, 42.2, 67.8, 126.4, 128.0, 129.0, 134.0, 136.4, 137.1, 137.6, 140.5; IR (neat) 3373.9, 2935.8, 1653.0, 1599.0, 1491.9, 1442.1 cm^{-1}; HRMS calcd for $C_{17}H_{20}O$: 240.1514, found 240.1509; LRMS (EI) *m/z* 222 (12), 207 (11), 167 (5), 129 (14), 99 (20), 43 (100).

***cis*-1,9-Dimethyl-4-phenylbicyclo[4.4.0]-4-decen-1,9-diol (23)** was prepared from **20** according to the general procedure described above to afford after flash chromatography (33% ethyl acetate/hexanes) 0.049 g (0.18 mmol) of **23** in 36% yield. (major): ^1H NMR (400 MHz, $CDCl_3$) δ 0.78 (d, J = 6.99 Hz, 2.25H), 0.81 (d, J = 7.16 Hz, 0.75H), 1.16 (s, 2.25H), 1.21 (s, 0.75H), 1.18-1.39 (m, 2H), 1.39-2.11 (m, 6H), 2.11-2.79 (m, 3H), 6.98-7.30 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.8, 22.8, 29.0, 30.6, 35.4, 36.8, 40.0, 49.7, 70.9, 72.2, 126.2, 128.0, 128.2, 128.5, 134.3, 141.7; IR (neat) 3354.0, 2927.9, 1639.8, 1447.8, 1373.8, 1157.3 cm^{-1}; HRMS calcd for $C_{18}H_{22}O$ $(M-H_2O)^+$: 254.1671, found 254.1676; LRMS (EI) *m/z* 254 (41), 236 (12), 211 (37), 170 (33), 155 (40), 84 (100).

REFERENCES

(1) (a) Molander, G. A.; Kenny, C. *J. Org. Chem.* **1991**, *56*, 1439. (b) Molander, G. A.; McKie, J. A. *J. Org. Chem.* **1992**, *57*, 3132. (c) Molander, G. A.; Harris, C. R. *J. Am. Chem. Soc.* **1995**, *117*, 3705. (d) Molander, G. A.; Harris, C. R. *J. Am. Chem. Soc.* **1996**, *118*, 4059. (e) Molander, G. A.; del Pozo Losada, C. *J. Org. Chem.* **1997**, *62*, 2935. (f) Molander, G. A.; Alonso-Alija, C. *Tetrahedron* **1997**, *53*, 8067. (g) Molander, G. A.; Harris, C. R. *J. Org. Chem.* **1997**, *62*, 2944. For reviews on sequential processes see: (h) Ho, T.-L. *Tandem Organic Reactions*; Wiley-Interscience: New York, 1992. (i) Tietze, L. F.; Beifuss, U. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 131. (j) Wender, P. A.; Miller, B. L. In *Organic Synthesis, Theory and Applications*; Hudlicky, T., Ed.; JAI Press: Greenwich, CT, 1993; Vol. 2, p 27.

(2) Molander, G. A.; Harris, C. R. *Chem. Rev.* **1996**, *96*, 307.

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

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

(5) (a) Enholm, E. J.; Trivellas, A. *Tetrahedron Lett.* **1989**, *30*, 1063 (b) Fukuzawa, S.-I.; Iida, M.; Fujinami, T.; Sakai, S. *J. Chem. Soc., Chem. Commun.* **1987**, 920. (c) Kito, M.; Sakai, T.; Yamada, K.; Matsuda, F.; Shirahama, H. *Synlett* **1992**, 158. (d) Curran, D. P.; Fevig, T. L.; Jasperse, C. P.; Totleben, M. J. *Synlett* **1992**, 943. (e) Baldwin, J. E., Turner, S. C. M.; Moloney, M. G. *Tetrahedron* **1994**, *50*, 9425.

(6) Namy, J. L.; Colomb, M.; Kagan, H. B. *Tetrahedron Lett.* **1994**, *35*, 1723.

(7) (a) Sterzycki, R. *Synthesis* **1979**, 724. (b) Hagiwara, H.; Uda, H. *J. Chem. Soc., Chem. Commun.* **1987**, 1351.

(8) O'Connor, B.; Just, G. *Tetrahedron Lett.* **1987**, *28*, 3235.

(9) 4-Bromo-1-(trimethylsilyl)-1-butyne was prepared from 3-butyn-1-ol according to the following general procedures: (a) Overman, L. E.; Brown, M. J.; McCann, S. F. in *Organic Synthesis;* White, J. D., Ed.; New York 1989; Collect. Vol. 68, p 182. (b) Miller, B. *Synth. Commun.* **1972**, *2*, 267.