Sequenced Reactions with Samarium(II) Iodide. Tandem Intramolecular Nucleophilic Acyl Substitution/Intramolecular Barbier Cyclizations

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Abstract: Samarium(II) iodide has been employed to promote a tandem intramolecular nucleophilic acyl substitution/intramolecular Barbier cyclization sequence, generating bicyclic and tricyclic ring systems in excellent yield and high diastereoselectivity. Additionally, a highly versatile ring expansion–cyclization sequence allows entry into several different naturally occurring tricyclic ring systems containing seven- and eight-membered rings.

Introduction

The ability to sequence carbon–carbon bond-forming reactions provides obvious efficiencies in selective organic synthesis.[1] Sequential methods are attractive because elaborate products may be accessed in a single, one-pot process from relatively simple precursors. Important contributions to this area have been realized utilizing a combination of cationic,[2] anionic,[3] radical,[4] pericyclic,[5] carbenoid,[6] and transition metal catalyzed[7] processes.

With the storehouse of information concerning the relative reactivities of various functional groups with samarium(II) iodide (SmI_2),[8] the sequencing of organic reactions with this reductive coupling agent has also become possible, and several examples have been reported that demonstrate high degrees of stereoselectivity and chemoselectivity in such multistep, one-pot processes.[9] The high chemoselectivity of SmI_2 as a reducing agent thus provides several advantages over other approaches. For instance, a wide variety of organic functional groups are tolerated under standard reaction conditions. Furthermore, the chemoselectivity that SmI_2 displays is largely solvent dependent. Consequently, the reductant may be finely tuned using solvent effects to react in a directed manner.

Previous research from this laboratory has demonstrated that SmI_2 in conjunction with catalytic Fe(III) species or strong ligand donors promotes the nucleophilic acyl substitution of halosubstituted carboxylic acid derivatives.[10] Likewise, the ability to perform SmI_2-promoted Barbier-type cyclization reactions between ketones and a variety of alkyl halides has

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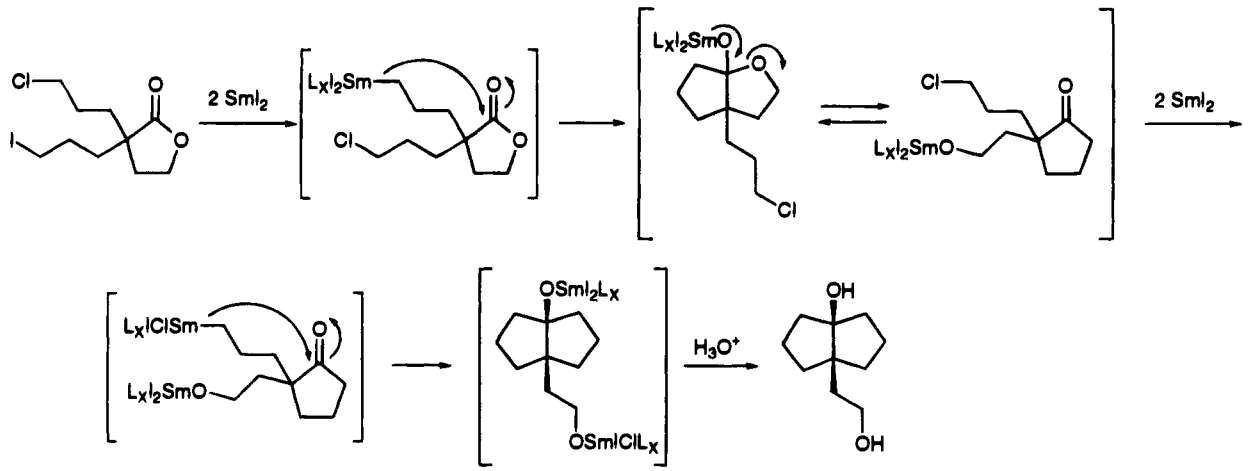
Scheme 1



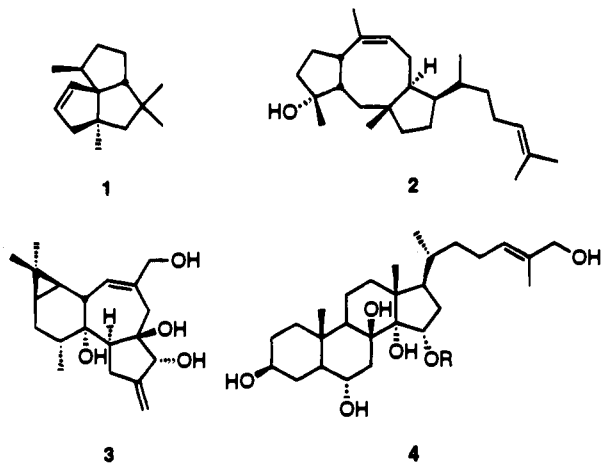


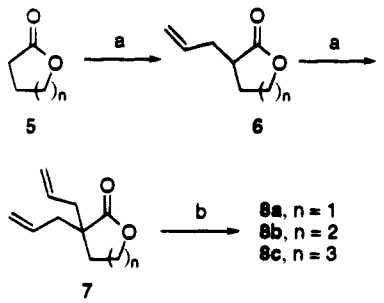
Figure 1. Ring systems accessible through SmI_2 induced sequential reactions.

been demonstrated.[11] In the present contribution the strong reducing ability and high chemoselectivity of SmI_2 is exploited in a sequential intramolecular nucleophilic acylation/Barbier-type cyclization process that facilitates access to a variety of synthetically useful bicyclic and tricyclic ring systems. This sequential process provides a unique entry into bicyclo[*m.n.*0] and tricyclic [*m.n.*0.0] ring systems commonly found in nature (Figure 1). Included is an approach to the angular triquinane skeleton of sesquiterpenes such as silphinene (**1**). Furthermore, a highly versatile ring expansion/anionic cyclization protocol provides entry into the ophiobolane (ophiobolin F, **2**) ring system of sesterterpenes, access to the 6:7:5 ring system of phorbol (**3**), and an approach to the sesquiterpene ring system of steroids such as cholestane (**4**).

Results and Discussion

The initial studies on the development of the sequential process concentrated primarily on ester and lactone functionalities containing differentially substituted halides. A representative example is shown in Scheme 1. Thus, the cyclization is believed to proceed through the initial formation of an organosamarium species.[10,11a,12] Presumably, attack on the lactone results in formation of a tetrahedral intermediate that collapses to liberate the ketone, which subsequently suffers attack by a newly generated organosamarium, generating the desired fused ring system.

Scheme 2[a]



[a] (a) LDA, THF, −78 °C; then allyl bromide, HMPA. (b) 2 equiv dicyclohexylborane; then NaOAc, ICl, MeOH.

Paramount in this tandem cyclization process, which clearly sets SmI_2 chemistry apart from virtually every other related method, is the ability to sequence the formation of the organosamarium species so that formation of carbon−carbon bonds may be effectively directed. Alkyl halides are reduced to organosamariums in the expected order (I > Br > Cl), which parallels the reduction potential of these species.[13] Hence, the first organosamarium species is formed from the alkyl iodide, with subsequent formation of an organosamarium species from the alkyl chloride. In the presence of SmI_2 and 5 equiv of hexamethylphosphoramide (HMPA), it was found that the sequential cyclization reaction was complete in approximately 45 min to 1 h using a diiodo-substituted substrate. The same reductive coupling using one alkyl chloride group and one alkyl iodide group took approximately 6 h for completion. Preliminary competion studies utilizing one alkyl bromide and one alkyl iodide group under identical reaction conditions resulted in products generated from competitive reduction of both alkyl halides. Hence, all sequenced reactions were performed using diiodides (where the sequence of reactions was inconsequential) or alkyl iodide/alkyl chloride combinations for substrates where the order of side-chain reactions was significant.

With these results in hand, a series of substrates was prepared to demonstrate this sequential process. Access to substrates **8a−c** and **18** (Table 1) was obtained through dialkylation of the appropriate ester or lactone with allyl bromide[14] followed by a one-pot hydroboration/iodination[15] sequence to afford the desired diiodide substrates as depicted in Scheme 2.

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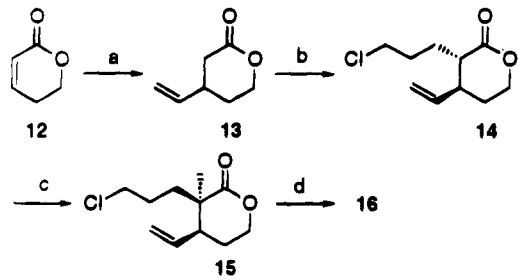
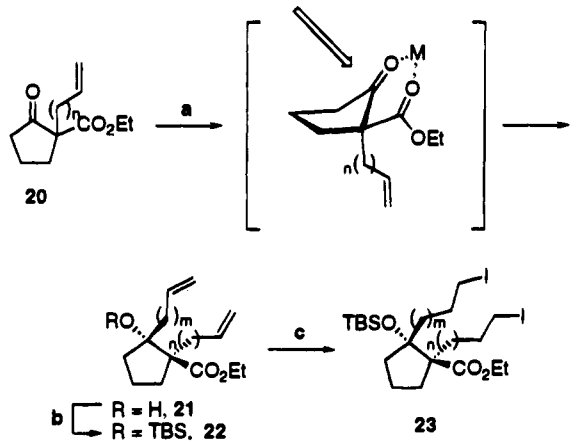
Scheme 3[a]



[a] (a) vinylmagnesium bromide, CuCl, THF, −78 °C. (b) LDA, THF, −78 °C; then 1-chloro-3-iodopropane, HMPA, −40 °C. (c) LDA, THF, −78 °C; then MeI, HMPA, −40 °C. (d) Dicyclohexylborane, THF; then NaOAc, ICl, MeOH.

Scheme 4[a]

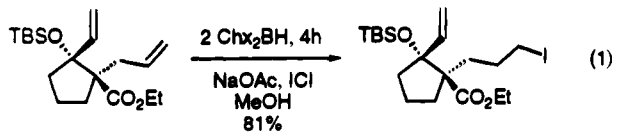


[a] (a) Allyl bromide, Zn, DMF. (b) TBSOTf, 2,6-lutidine, CH_2Cl_2. (c) Dicyclohexylborane, THF; then NaOAc, ICl, MeOH.

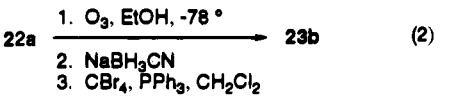
Substrates **8d**, **8e**, and **10** (Table 1) were obtained by simple dialkylation of γ-butyrolactone or ϵ-caprolactone with the appropriate dihalide followed by a Finkelstein reaction. Substrate **16** (Scheme 3) was obtained by Michael addition of vinyl cuprate to 5,6-dihydro-(2*H*)-pyran-2-one (**12**)[3h,16] followed by dialkylation and subsequent hydroboration/iodination to afford the desired dihalide (**16**). Methylation of **14** provided a 3:1 mixture of diastereomeric products separable by flash chromatography resulting from alkylation anti to the β-vinyl group.[17]

Substrates **23a** and **23c** (Table 1) were obtained by alkylation of ethyl 2-oxocyclopentanecarboxylate with either allyl bromide or 4-bromo-1-butene followed by stereoselective addition of an allylzinc reagent,[18] protection of the resultant tertiary alcohol,[19] and subsequent hydroboration/iodination (Scheme 4). Stereoselectivities in the allylzinc addition ranged from 10 to 12:1. The observed stereoselectivity is apparently the result of chelation controlled nucleophilic addition of the allylzinc reagent, with addition occurring from the less hindered face of the chelated carbonyl.[20]

The general one-pot hydroboration/iodination protocol was not feasible for the preparation of **23b** because hydroboration of the olefin adjacent to the quaternary center did not proceed under the various conditions attempted. Instead, treatment of the appropriate diene[21] resulted in exclusive hydroboration/iodination at only the allylic olefin (eq 1).



Consequently, an alternative route to this substrate was required. Thus, ozonolysis of the one-carbon homologated substrate **22a** ($n = 1, m = 2$) followed by reduction with $NaBH_3CN$[22] and subsequent halogenation resulted in the desired bromide **23b** as depicted in eq 2.



Initial sequencing studies focused on diiodide substrates, for which the results are depicted in Table 1. Optimum reaction conditions for these substrates involved slow, dropwise addition of the substrate (0.03−0.04 M in THF) to a 0.10−0.15 M solution of SmI_2 in THF containing 5 equiv of HMPA at 0 °C. Reactions were found to be complete after approximately 1−1.5 h in most cases. Reactions of allylic halides, which possess a more positive reduction potential than aliphatic halides,[13] were found to be complete after approximately 45 min to 1 h even in the absence of HMPA. Rapid addition of the substrate resulted in the formation of side products and in general a 30−40% reduction in the yield of the desired product. Presumably, the diminished yield and resultant complex reaction mixture was the result of intermolecular reactions of the organosamarium and unreacted lactone or ketone functionality. Catalytic Fe(DBM)$_3$ was also found to promote the reactions of diiodides but with a noticeable diminution in yield (approximately a 15−20% reduction in the yield of the desired bicyclic product). Consequently, all reactions were performed using 5 equiv of HMPA which was required for formation of an organosamarium from the alkyl chloride.

Reactions of γ-lactone (**8a**) and ϵ-lactone (**8c**) (entries 1 and 3, Table 1) proceeded uneventfully to provide the desired bicyclic products as single diastereomers in high yield. As demonstrated previously,[11] α,α-dialkyl substitution of 2-(ω-iodoalkyl)cycloalkanones provides exclusive formation of the cis-fused bicyclic product in intramolecular Barbier-type cyclizations. Surprisingly, δ-lactone **8b** (entry 2, Table 1) proceeded equally well with formation of a single product although similar systems have been shown to undergo an intramolecular Meerwein−Ponndorf−Verley (MPV) redox reaction in the presence of SmI_2 (eq 3).[23] Apparently, under the current reaction conditions intramolecular hydride transfer is much slower than cyclization. Presumably, HMPA precludes chelation between the two reacting centers required for the MPV reaction, allowing the second cyclization to occur.

Although attempts at synthesizing 6-membered rings *via* intermediate organolithiums have proven difficult in Barbier-type reactions and intramolecular nucleophilic acyl substitution reactions,[24] organosamariums undergo such reactions with high diastereoselectivity and little loss in yield (entry 4). Addition-

(16) Nakagawa, M.; Tonozuka, M.; Obi, M.; Kiuchi, M.; Hino, T.; Ban, Y. *Synthesis* **1974**, 510.

(17) (a) Caine, D. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 3, Chapter 1.1. (b) Evans, D. A. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press, Inc.: Orlando, 1984; Vol. 3, pp 1−110.

(18) Shono, T.; Ishifune, M.; Kashimura, S. *Chem. Lett.* **1990**, 449.

(19) Corey, E. J.; Cho, H.; Rücker, C.; Hua, D. H. *Tetrahedron Lett.* **1981**, *22*, 3455.

(20) (a) Still, W. C.; McDonald, J. H., III. *Tetrahedron Lett.* **1980**, *21*, 1031. (b) Still, W. C.; Schneider, J. A. *Tetrahedron Lett.* **1980**, *21*, 1035.

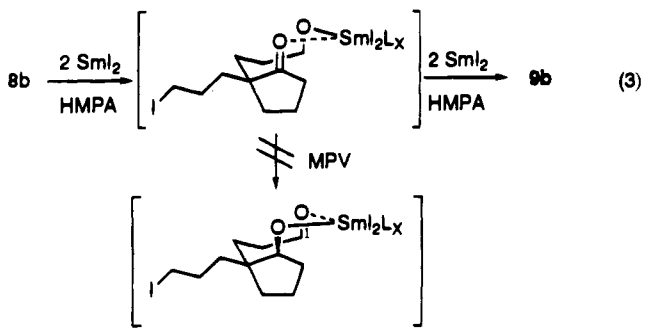
(21) Prepared by addition of vinylmagnesium bromide to ethyl 2-oxo-1-(2-propenyl)cyclopentanecarboxylate according to the general procedure outlined in: Kinney, W. A.; Coghlan, M. J.; Paquette, L. A. *J. Am. Chem. Soc.* **1985**, *107*, 7352.

(22) (a) Evans, D. A.; Bender, S. L.; Morris, J. *J. Am. Chem. Soc.* **1988**, *110*, 2506. (b) Danishefsky, S.; Berman, E. M.; Ciufolini, M.; Etheredge, S. J.; Segmuller, B. E. *J. Am. Chem. Soc.* **1985**, *107*, 3891.

(23) Molander, G. A.; McKie, J. A. *J. Am. Chem. Soc.* **1993**, *115*, 5821.

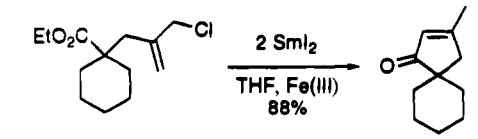
Table 1. Sequential Cyclization of Dihalides To Yield Bicyclo[*m*.3.0] Ring Systems and Angular Tricyclic Systems

entry	substrate	product	% isolated yield
1	**8a** (n, m, R) = (1, 1, H)	**9a**	83
2	**8b** (2, 1, H)	**9b**	97
3	**8c** (3, 1, H)	**9c**	91
4	**8d** (3, 2, H)	**9d**	78
5	**8e** (1, 1, Me)	**9e**	79
6	**10**	**11**	96
7	**16**	**17**	74
8	**18**	**19**	64
9	**23a** (X, n, m) = (I, 2, 2)	**24a**	88
10	**23b** (Br, 1, 1)	**24b**	84
11	**23c** (I, 1, 2)	**24c**	86

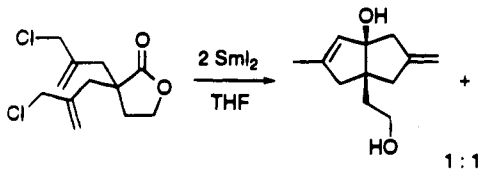


(3)

ally, utilizing a secondary alkyl halide precursor (entry 5) provides **8e** as a 1:1 mixture of the expected diastereomeric products, attesting to the broad applicability of this reaction sequence. As indicated in entry 6, allylic halides react in the absence of HMPA to form the desired bicyclic product. Somewhat surprisingly, no isomerization of the olefin occurs in this instance. In a related nucleophilic acyl substitution reaction run under similar reaction conditions, the major product isolated was the isomer in which the double bond was conjugated with the ketone (eq 4).[10a] Apparently, olefin isomerization occurs much more slowly than cyclization in the present case. By contrast, the allylic chloride substrates provide products resulting from olefin isomerization prior to cyclization in addition to **11** (eq 5).



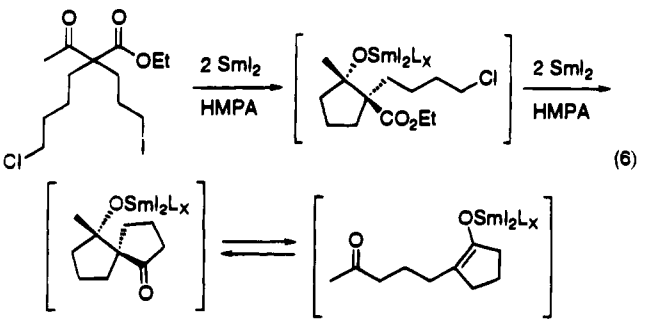
(4)



(5)

Entry 7 provides an indication of the excellent relative face selectivity achieved by the organosamarium in the Barbier-type cyclization following the initial nucleophilic acyl substitution. Cyclization of **16** (a 20:1 mixture of diastereomers) provided a 20:1 mixture of **17** and its diastereomer in high yield.

Cyclization of **18** (entry 8, Table 1) afforded the corresponding bicyclic hydroxy ester in modest yield. The reduced yield is likely the result of subsequent ring opening of the initially formed aldolate to the cyclooctanone carboxylate enolate.[25] The reaction of **18** with SmI_2 was initiated and quenched at −20 °C. Prolonged stirring or warmer reaction temperatures resulted in considerable decomposition of the bicyclic hydroxyester **19**. Other dicarbonyl substrates proved even less manageable. For example, while initial cyclization of the dihalide depicted in eq 6 provided the resulting hydroxyester with good diastereoselectivity and in high yield, reduction of the chloride (requiring ambient reaction temperatures) and subsequent cyclization provided a highly strained spirocyclic ring system which suffered a retro-aldol reaction, providing a complex mixture of both cyclic and acyclic products. Consequently, further efforts with related dicarbonyl substrates were not pursued.



(6)

Entries 9, 10, and 11 (Table 1) demonstrate the broad applicability of this protocol for the formation of angularly fused tricyclic ring systems. Furthermore, these examples attest to the ability of SmI_2 to promote reactions at sterically hindered carbonyl centers.

(24) (a) Cooke, M. P., Jr.; Houpis, I. N. *Tetrahedron Lett.* **1985**, *26*, 4987. (b) Souchet, M.; Clark, R. D. *Synlett* **1990**, 151.

(25) (a) Molander, G. A.; Etter, J. B.; Zinke, P. W. *J. Am. Chem. Soc.* **1987**, *109*, 453. (b) Molander, G. A.; Kenny, C. *J. Am. Chem. Soc.* **1989**, *111*, 8236. (c) Heathcock, C. H. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 2, Chapter 1.6.5.

Table 2. Sequential Cyclization of Dihalides To Yield Bicyclo[*n*.3.0] and Tricyclo[*m.n*.0.0]Systems

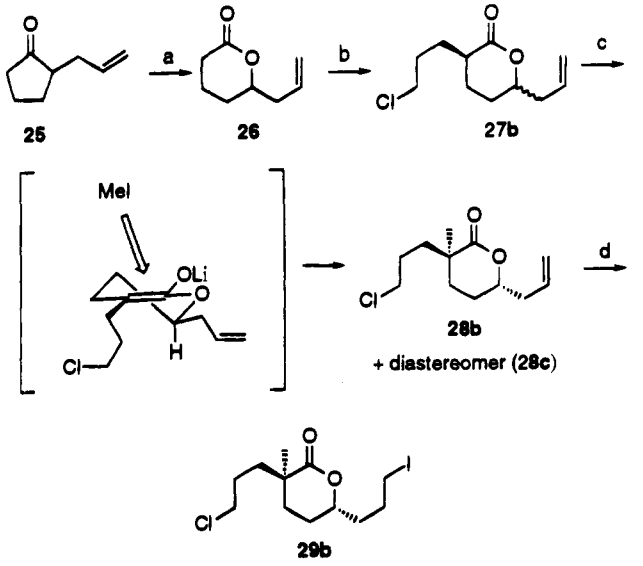
entry	substrate	product	% isolated yield
1	**29a** (n = 1)	$R^1 = R^4 = H$, $R^3 = OH$, $R^2 = CH_2CH_2CH_2I$	**30a** 58
2	**29b** (n = 2)	$R^1 = CH_2CH_2CH_2I$, $R^2 = R^4 = H$, $R^3 = OH$	**30b** 68
3	**29c** (n = 2)	$R^1 = R^3 = H$, $R^4 = OH$, $R^2 = CH_2CH_2CH_2I$	**30c** 65
4	**34a** R' = $CH_2CH_2CH_2Cl$, R = H		**35a** 67
5	**34b** R' = H, R = $CH_2CH_2CH_2Cl$		**35b** 72
6	**34c**	(R, n, m, o) = (H, 1, 1, 1)	**35c** 91
7	**34d**	(H, 2, 1, 1)	**35d** 83
8	**38**	(Me, 2, 0, 2)	**39** 80

As discussed earlier, SmI_2 is unique in that reduction of the halide species occurs at rates allowing carbon−carbon bonds to be formed sequentially and in a directed manner. This characteristic was exploited in a sequential ring expansion/cyclization process to afford both bicyclic and tricyclic products in excellent yield and high diastereoselectivity (Table 2).

Two strategies were used to gain access to substrates required for these studies. Access to substrates **29b** and **29c**, as depicted in Scheme 5, was gained through Baeyer−Villiger oxidation of 2-(2-propenyl)cyclopentanone (**25**), alkylation with 1-chloro-3-iodopropane followed by alkylation with methyl iodide, and finally the general hydroboration/iodination sequence described above. A 2.5:1 ratio of diastereomers, separable by flash chromatography, was obtained in the alkylation of **27b** with methyl iodide. The major diastereomer from this alkylation proved to be **29b**. Substrate **29a** was prepared similarly from dihydro-5-(2-propenyl)furan-2(3*H*)-one.[18]

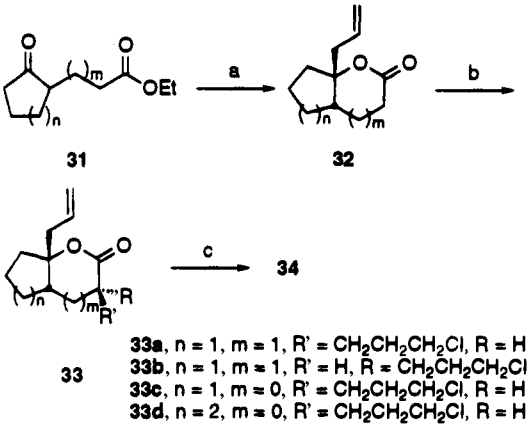
All other substrates in Table 2 were obtained through addition of an allylzinc reagent to the appropriate keto ester or formyl ester (entry 1) followed by *in situ* cyclization to generate the fused bicyclic or monocyclic lactone in one step (Scheme 6). Stereoselectivity in the addition of allylzinc to these substrates parallels those observed previously for addition to keto esters, ranging from 5 to 10:1, to generate the cis-fused lactone

Scheme 5[a]



[a] (a) mCPBA, CH_2Cl_2. (b) LDA, THF, −78 °C; then 1-chloro-3-iodopropane, HMPA. (c) LDA, THF, −78 °C; then methyl iodide, HMPA. (d) Dicyclohexylborane, THF; then NaOAc, ICl, MeOH.

Scheme 6[a]



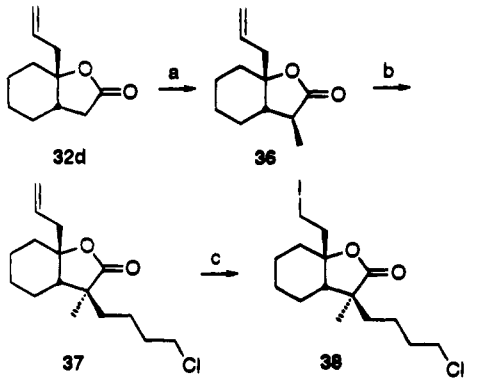
[a] (a) Allyl bromide, Zn, DMF. (b) LDA, THF, −78 °C; then 1-chloro-3-iodopropane, HMPA. (c) Dicyclohexylborane; then NaOAc, ICl, MeOH.

exclusively after *in situ* lactonization. In general, no trans-fused lactone resulting from lactonization of the minor diastereomer was generated under these reaction conditions but rather the intermediates persisted as the hydroxy ester. Subsequent alkylation of the lactone followed by the hydroboration/iodination sequence developed previously provided access to the requisite substrates. Alkylation of the bicyclic lactones proceeded with fair to excellent diastereoselectivity. Alkylation of **32a** provided a 2.5:1 mixture of diastereomers. The major diasteromer of this alkylation (**33a**) resulted from alkylation on the less sterically hindered top face of the bicyclic lactone. Likewise, alkylation of **32c** provided a single diastereomeric product resulting from alkylation of the less sterically hindered top face of the bicyclic lactone.[17]

Substrate 3δ (Scheme 7) required similar conditions to those of **23b** in that hydroboration of a vinyl group on the quaternary carbon was not possible. Instead, ozonolysis of the one-carbon homologated alkene followed by reduction and subsequent halogenation provided the desired substrate **38**.

With the requisite substrates in hand, the sequential cyclization reactions were examined. In the event, cyclization of **29a** afforded **30a** as a 5:1 mixture of diastereomeric products in good yield. Likewise, **29b** afforded **30b** as an 10:1 mixture of

Scheme 7[a]



[a] (a) LDA, THF, −78 °C; then methyl iodide, HMPA, −40 °C. (b) LDA, THF, −78 °C; then 1-chloro-4-iodobutane, HMPA, −40 °C. (c) O_3, EtOH, −78 °C; then $NaCNBH_3$; then TMSI, CH_3CN.

diastereomeric products, and cyclization of **29c** afforded **30c** as an 8:1 mixture of diastereomeric products. The stereochemistry of the bicyclic products was established in part by comparing ^1H NMR chemical shifts observed in pyridine-d_5 to those observed in $CDCl_3$.[26] Thus, the bridgehead methyl group experiences 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−CH_3 unit, with the largest deshielding observed for dihedral angles approaching 0°. The corresponding chemical shift difference in the trans-fused ring isomers is essentially 0. The ^1H NMR of **30b** in pyridine-d_5 shows a 0.26 ppm change in chemical shift downfield relative to the spectrum obtained in $CDCl_3$ (TMS internal standard), indicating a cis-fused ring junction. The corresponding ^1H NMR of the minor diastereomer obtained from cyclization of **29b** shows a 0.004 ppm change in chemical shift downfield, indicating that the ring fusion is trans (i.e., the bridgehead methyl group experiences no deshielding effect). Similar findings were observed in the ^1H NMR spectrum of **30c** in pyridine-d_5. The fused bicyclic product **30c** shows a 0.23 ppm change in the chemical shift of the bridgehead methyl resonance in pyridine-d_5 relative to that observed in $CDCl_3$. Likewise, ^1H NMR of the major diastereomer obtained from cyclization of **29a** displays a 0.27 ppm change in chemical shift downfield, again suggesting a cis-fused ring junction.

Additional evidence for the stereochemical assignments made for cyclization products **30b** and **30c** lies in observations of the OH stretching vibrations seen in the IR spectrum performed at high dilution. At high dilution (approximately 0.02 M in CCl_4), **30b** shows only the "free" hydroxyl (3621.4 cm^{-1}) whereas **30c** displays both a "free" hydroxyl (3613.5 cm^{-1}) and a strong intramolecular hydrogen-bonded OH stretch (3420.2 cm^{-1}). These results are expected if the two hydroxyl groups are on the same face of the molecule as in **30c**. Molecular models indicated that there should be considerable ability for intramolecular hydrogen bonding in **30c** but not in **30b**.

Cyclization of the diastereomeric bicyclic lactones **34a** and **34b** afforded **35a** and **35b**, respectively, each as a single diastereomeric product. Cyclization products **35a** and **35b** possess a C-2 axis of symmetry and a mirror plane, respectively, as indicated by ^{13}C NMR. Hence, contrary to the α,α-disubstituted systems, Barbier-type cyclizations in this series generate the trans-fused ring junction on the existing eight-membered ring. The stereochemical assignments for **35a** and **35b** were further verified by observing the OH stretching

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

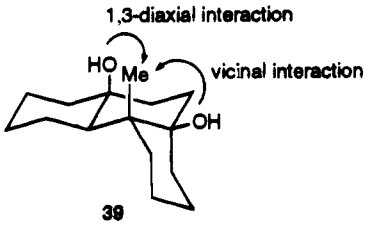


Figure 2. Interactions of the hydroxyl groups with the bridgehead methyl group influencing solvent-induced chemical shift differences.

vibrations of each molecule at high dilution in a nonpolar solvent (0.03 M in CCl_4). The IR spectrum of tricyclic product **35a** shows only a very sharp "free" hydroxyl band (3615.7 cm^{-1}) at high dilution whereas **35b** shows both "free" hydroxyl (3607.6 cm^{-1}) and a shallow, broad band (3471.3 cm^{-1}) attributed to intramolecular hydrogen bonding at high dilution.

Cyclization of **34c** with SmI_2 affords **35c** as a single diastereomeric product in excellent yield. ^{13}C NMR indicates that **35c** does not possess a C-2 axis of symmetry as would be expected if the second ring junction formed were trans. Hence the Barbier-type cyclization proceeds to generate the cis-fused ring junction on the existing seven-membered ring. Cyclization of **34d** and **38** proceeds equally well to generate the desired tricyclic products in excellent yield and very high diastereoselectivity. Cyclization of **34d** affords a single product, **35d**, while **38** cyclizes to generate **39** as a 40:1 mixture of diastereomeric products. Although α,α-disubstituted ketones have previously been observed to form exclusively the cis-fused ring product,[11] the cis stereochemistry of the ring junction in **39** from Barbier-type cyclization was further verified by comparing the chemical shift differences of the bridgehead methyl group in pyridine-d_5 relative to those in $CDCl_3$. The solvent-induced chemical shift difference of the methyl singlet was 0.56 ppm (downfield in pyridine-d_5 relative to the spectrum obtained in $CDCl_3$). Although this chemical shift is substantially larger than those generally observed for methyl groups vicinally situated to hydroxyl groups (which generally experience a 0.00 to 0.27 ppm chemical shift difference depending on the dihedral angle between the hydroxyl and methyl groups), the methyl group in **39** also suffers a 1,3-diaxial interaction with a second hydroxyl group (Figure 2). The solvent-induced chemical shift difference of a methyl group experiencing 1,3-diaxial interaction with a hydroxyl substituent is generally 0.20−0.40 ppm.[26] In the present system, the additive effect of vicinal hydroxyl substitution and the 1,3-diaxial interaction between the observed methyl group and the second hydroxyl group combine to provide a stronger deshielding effect than either interaction alone. Hence, the solvent-induced chemical shift is significantly larger than that expected from a single interaction.

It deserves note at this point that each of the intermediate alkoxy ketone species resulting from nucleophilic acyl substitution in entries 1−7 (Table 2) should exist nearly exclusively as the intramolecular hemiacetal.[10a] The fact that the intramolecular Barbier-type reaction ensues attests to the long-lived nature of the intermediate organosamarium species. The only other products observed in these cyclizations (primarily with substrates **34a** and **34b**, accounting for approximately 10−15% of the reaction mixture) result from simple reduction of the chloride to the corresponding alkane prior to sequential cyclization. However, slow addition of substrate at high dilution over 5−6 h allows nearly exclusive formation of the desired tricyclic system.

Conclusions

The SmI_2-promoted intramolecular nucleophilic acyl substitution/Barbier cyclization sequence has been utilized to convert

a variety of suitable substrates to bicyclic and tricyclic alcohols efficiently with excellent diastereoselectivity. Substrates for the reaction are readily prepared by classic alkylation and carbonyl addition chemistry in a relatively few steps. The overall transformation represents a highly effective means by which simple starting materials can be converted to relatively complex products in a one-pot process.

Experimental Section

Reagents. Tetrahydrofuran (THF) was distilled immediately prior to use from benzophenone ketyl under Ar. Samarium metal was purchased from Cerac Inc., Milwaukee, WI, and was weighed and stored under an inert atmosphere. CH_2I_2 was purchased from Aldrich Chemicals and was distilled prior to use and stored under argon over copper turnings. HMPA was purchased from either Aldrich or Sigma Chemicals and was distilled from either Na(0) or CaH_2 at 0.04 mm Hg and stored over 4 Å molecular sieves under Ar. Standard benchtop techniques were employed for handling air-sensitive reagents,[27] and all reactions were carried out under argon.

Dihydro-3-(2-propenyl)furan-2(3*H*)-one (6a). General Procedure for Alkylation of Esters and Lactones.[14] To a stirred solution of 22.0 mmol of LDA at −78 °C was added dropwise over 1.0−1.5 h a 1.0 M solution of γ-butyrolactone (1.72 g, 20.0 mmol) in THF. After the addition of the substrate was complete, the reaction mixture was stirred an additional 20−30 min at −78 °C. After this period of stirring, allyl bromide (2.90 g, 24.0 mmol) in 4.2 mL of HMPA was added slowly dropwise. After addition of the halide was complete, the reaction mixture was warmed to −30 °C with continued stirring for 2−3 h. After this period, TLC/GC analysis revealed the complete consumption of the starting material. The reaction mixture was quenched with saturated aqueous NH_4Cl. Aqueous workup followed by flash chromatography (7% EtOAc/hexanes) afforded 4.58 g (17.8 mmol) of **6a** in 89% yield after Kugelrohr distillation (ot 90−100 °C at 0.05 mm Hg): ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.73 (m, 1H), 5.07 (m, 2H), 4.29 (m, 1H), 4.15 (m, 1H), 2.58 (m, 2H), 2.26 (m, 2H), 1.94 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 179.25, 134.74, 118.04, 66.88, 39.08, 34.58, 28.04.

Tetrahydro-3-(2-propenyl)-2(2*H*)-pyranone (6b) was prepared from δ-valerolactone according to the general procedure for the preparation of **6a** by alkylation with allyl bromide to afford **6b** in 73% yield after flash chromatography with 15% EtOAc/hexanes followed by Kugelrohr distillation (ot 70−80 °C at 0.05 mm Hg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.77 (m, 1H), 5.07 (m, 2H), 4.26 (m, 2H), 2.55 (m, 2H), 2.27 (m, 1H), 2.03 (m, 1H), 1.86 (m, 2H), 1.52 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.82, 135.10, 117.45, 68.50, 39.33, 35.47, 24.12, 21.95.

3-(2-Propenyl)oxepan-2-one (6c) was prepared from ϵ-caprolactone according to the general procedure for the preparation of **6a** by alkylation with allyl bromide. Purification of the crude product by flash chromatography (8% EtOAc/hexanes) provided 1.98 g (13.0 mmol, 65%) of **6c**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.57 (m, 1H), 5.04 (m, 2H), 4.21 (m, 2H), 2.55 (m, 2H), 1.11 (m, 1H), 1.98−1.32 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.18, 135.90, 117.15, 68.39, 42.35, 36.48, 28.96, 28.76, 28.20.

Dihydro-3,3-bis(2-propenyl)furan-2(3*H*)-one (7a) was prepared from **6a** according to the general procedure for the preparation of **6a** by a second alkylation with allyl bromide. Purification of the crude product by flash chromatography (8% EtOAc/hexanes) followed by Kugelrohr distillation (ot 100−110 °C at 0.05 mm Hg) afforded 3.16 g (19.0 mmol, 95%) of **7a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.69 (m, 2H), 5.02 (m, 4H), 4.14 (t, 2H, J = 7.50 Hz), 2.28 (m, 4H), 2.10 (t, 2H, J = 7.50 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.45, 132.49, 119.54, 65.23, 45.91, 40.67, 30.25.

Tetrahydro-3,3-bis(2-propenyl)pyran-2(2*H*)-one (7b) was prepared according to the general procedure for the preparation of **6a** by alkylation of **6b** with allyl bromide. Purification of the crude product by flash chromatography (12% EtOAc/hexanes) afforded **7b** in 90% yield after Kugelrohr distillation (ot 100−110 °C at 0.05 mm Hg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.74 (m, 2H), 5.10 (m, 4H), 4.26 (m, 2H), 2.54 (dd, J = 6.59, 13.67 Hz, 2H), 2.19 (dd, J = 8.06, 13.67 Hz, 2H), 1.81 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.97, 133.23 (2), 119.19 (2), 70.22, 45.88, 43.80 (2), 28.58, 21.04.

3,3-Bis(2-propenyl)oxepan-2-one (7c) was prepared according to the general procedure for the preparation of **6a** by alkylation of **6c** with allyl bromide. Purification of the crude product by flash chromatography (8% EtOAc/hexanes) afforded 2.21 g (12.1 mmol, 67%) of **7c**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.75 (m, 2H), 5.04 (m, 4H), 4.27 (m, 2H), 2.36 (d, 4H, J = 6.59 Hz), 1.75 (m, 4H), 1.62 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.58, 133.41, 118.71, 68.10, 50.32, 41.16, 32.01, 28.42, 22.53.

Dihydro-3,3-bis(3-iodopropyl)furan-2(2*H*)-one (8a). General Procedure for One-Pot Hydroboration−Iodination Reactions.[15] BH_3·SMe_2 complex (0.49 mL of a 10.0 M solution, 4.9 mmol) was added to cyclohexene (0.95 g, 11.5 mmol) in 10 mL of THF at 0 °C. The resultant solution was stirred for 3 h at 0 °C during which time a white precipitate formed. After this period of stirring, **7a** (0.66 g, 4.0 mmol) in 3 mL of THF was added dropwise to the 0 °C cooled solution. After addition of the substrate was complete, the reaction mixture was allowed to warm slowly to room temperature (rt) during which time the white precipitate disappeared and the reaction mixture became clear and colorless. The reaction mixture was allowed to stir for an additional 3 h after coming to rt. After this period of time, NaOAc (0.94 g, 11.5 mmol, 1 M in methanol) and ICl (0.78 g, 4.8 mmol, 1 M in methanol) were added successively. The resultant reaction mixture was stirred for 30 min at rt, quenched with saturated aqueous $NaHSO_4$, and then subjected to aqueous workup. The crude workup mixture was concentrated *in vacuo* and then dissolved in THF and cooled to 0 °C, whereupon a solution of 1.34 mL of 3 N NaOAc and 0.84 mL of 30% H_2O_2 was added. The reaction mixture was allowed to warm slowly to rt and was stirred for an additional 1−2 h. Aqueous workup followed by flash chromatography with EtOAc/hexanes afforded 1.37 g (3.24 mmol, 81%) of **8a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.26 (t, J = 7.05 Hz, 2H), 3.16 (t, J = 6.10 Hz, 4H), 2.14 (t, J = 7.20 Hz, 2H), 1.60−2.10 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.20, 65.03, 44.77, 36.28, 32.44, 27.96, 5.97.

Tetrahydro-3,3-bis(3-iodopropyl)-2(2*H*)-pyranone (8b) was prepared from **7b** according to the general procedure for preparation of **8a** to afford **8b** in 50% yield after flash chromatography with 11−12% EtOAc/hexanes: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.30 (t, J = 5.40 Hz, 2H), 3.12 (m, 4H), 1.81 (m, 10H), 1.62 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.84, 70.12, 44.91, 39.92 (2), 29.97, 28.33 (2), 21.06, 6.22 (2).

3,3-Bis(3-iodopropyl)oxepan-2-one (8c) was prepared from **7c** according to the general procedure for the preparation of **8a**. Purification of the crude product by flash chromatography afforded 1.80 g (4.01 mmol, 80%) of **8c**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.34 (m, 2H), 3.17 (m, 4H), 1.92−1.62 (m, 14H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.49, 68.57, 49.54, 37.88, 32.84, 28.62, 27.93, 22.71, 7.02.

3-(4-Chlorobutyl)oxepan-2-one was prepared according to the general procedure for the preparation of **6a** by alkylation of ϵ-caprolactone with 1-chloro-4-iodobutane to afford the desired alkylated product (0.69 g, 3.4 mmol) in 20% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.23 (m, 2H), 3.52 (t, J = 6.60 Hz, 2H), 2.51 (m, 1H), 2.02−1.33 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.36, 68.27, 44.83, 42.79, 32.53, 31.94, 30.03, 28.71, 28.26, 24.67.

3-(4-Iodobutyl)-3-(3-iodopropyl)oxepan-2-one (8d) was prepared according to the general procedure for the alkylation of **6a** by alkylation of 3-(4-chlorobutyl)oxepan-2-one with 1-chloro-3-iodopropane. The crude reaction mixture was filtered through a short plug of silica to remove the HMPA then subjected to a Finkelstein reaction with NaI to generate the diiodide **8d** (0.72 g) in 45% yield (2 steps): ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.28 (m, 2H), 3.16 (t, J = 6.70 Hz, 4H), 1.78 (m, 10H), 1.62 (m, 4H), 1.38 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.78, 68.42, 49.91, 37.72, 35.78, 33.69, 32.84, 28.64, 28.09, 24.89, 22.73, 6.95, 6.26.

Dihydro-3-chloropropylfuran-2(3*H*)-one was prepared according to the general procedure for the preparation of **6a** by alkylation of γ-butyrolactone with 1-chloro-3-iodopropane. The crude product was purified by flash chromatography to afford the desired alkylated product as a clear yellow liquid in 71% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.34 (m, 1H), 4.18 (m, 1H), 3.55 (t, J = 6.30 Hz, 2H), 2.53 (m, 1H),

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

2.40 (m, 1H), 2.03−1.79 (m, 4H), 1.63 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.92, 66.40, 44.40, 38.55, 30.10, 28.66, 27.70.

Dihydro-3-(3-iodobutyl)-3-(3-iodopropyl)furan-2(3*H*)-one (8e) was prepared according to the general procedure for the preparation of **6a** by alkylation of dihydro-3-chloropropylfuran-2(3*H*)-one with (±)-1,3-diiodobutane. The crude reaction mixture, isolated as a 1:1 mixture of diastereomers, was filtered through a short plug of silica to remove residual HMPA, then subjected to a Finkelstein reaction with NaI to afford **8e** in 65% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.26 (t, J = 7.20 Hz, 2H), 4.17 (m, 1H), 3.16 (m, 2H), 2.14 (m, 2H), 1.91 (dd, J = 3.42, 6.84 Hz, 3H), 1.87−1.56 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.06(2), 65.10, 65.06, 44.86, 44.68, 37.12(2), 36.90, 36.77, 35.88, 35.67, 35.28(2), 32.85, 32.18, 29.27, 28.89, 28.81, 28.03, 5.96, 5.94.

***cis*-5-(2-Hydroxyethyl)bicyclo[3.3.0]octan-1-ol (9a). General Procedure for SmI_2 Promoted Sequential Reactions of Diiodides.** To Sm (0.478 g, 3.18 mmol) in 25 mL of THF at rt was added CH_2I_2 (0.766 g, 2.86 mmol). The resultant blue-green reaction mixture was stirred vigorously for 2.5 h. Then, HMPA (3 mL) was added and the resultant deep purple solution was stirred for 15 min at rt, then cooled to 0 °C. Diiodide **8a** (0.265 g, 0.628 mmol) was then added slowly dropwise over 2−2.5 h as a 0.03−0.04 M solution in THF. After the substrate addition was complete, the reaction mixture was allowed to warm to rt and stirred for 2.0 h. After this period, the reaction mixture was subjected to TLC/GC analysis and found to be complete. A single product was formed. The reaction mixture was quenched with saturated aqueous $NaHCO_3$, then subjected to aqueous workup. The crude product was purified by flash chromatography (40% EtOAc/hexanes) and recrystallized from EtOAc/hexanes to afford **9a** as a white solid in 83% isolated yield: mp 98−99 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.74 (t, J = 6.0 Hz, 2H), 3.05 (s, 2H), 1.54−1.80 (m, 10H), 1.40−1.51 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 89.70, 59.59, 53.03, 42.11, 39.37, 38.60, 22.90; IR ($CHCl_3$) 3605.1, 3402.9, 2990.3, 2947.1 cm^{-1}; LRMS (EI) *m/z* 128 (100), 109 (49), 97 (94), 41 (45); HRMS (EI$^+$) calcd for $C_{10}H_{18}O_2$ 170.1307, found 170.1307. Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66. Found: C, 70.24; H, 11.09.

***cis*-5-(3-Hydroxypropyl)bicyclo[3.3.0]octan-1-ol (9b)** was prepared from **8b** according to the general procedure for the preparation of **9a** to afford **9b** in 97% yield after flash chromatography with 35% EtOAc/hexanes: mp 62.5−63.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.65 (t, J = 6.54 Hz, 2H), 1.82 (m, 2H), 1.66 (m, 2H), 1.58 (m, 6H), 1.46 (m, 6H), 1.31 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 90.27, 63.76, 52.93, 42.08 (2), 38.31 (2), 32.41, 29.18, 22.72 (2); IR ($CHCl_3$) 3606.2 cm^{-1}; LRMS (EI$^+$) *m/z* 184 (50), 167 (85), 156 (100), 142 (100), 124 (90), 92 (100). Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.70; H, 10.94. Found: C, 71.56; H, 10.88.

***cis*-5-(4-Hydroxybutyl)bicyclo[3.3.0]octan-1-ol (9c)** was prepared from **8c** as described above for **9a**. Purification by flash chromatography (EtOAc/hexanes) and recrystallization from EtOAc/hexanes afforded **9c** in 91% isolated yield: mp 90.5−91.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.65 (t, J = 6.35 Hz, 2H), 1.78 (m, 2H), 1.60 (m, 8H), 1.44 (bs, 2H), 1.40 (m, 6H), 1.26 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 90.28, 62.81, 53.13, 42.04, 38.20, 36.03, 33.60, 22.69, 21.98; IR ($CHCl_3$) 3605.5, 3464.0, 2993.3, 1013.7 cm^{-1}; LRMS (EI) *m/z* 156 (47), 126 (94), 108 (56), 97 (100), 41 (57); HRMS (EI$^+$) calcd for $C_{12}H_{22}O_2$ 198.1620, found 198.1617.

***cis*-6-(4-Hydroxybutyl)bicyclo[4.3.0]nonan-1-ol (9d)** was prepared from **8d** as described above for **9a** to afford the desired product as a white solid in 78% yield. The crude product was purified by flash chromatography (30% EtOAc/hexanes) followed by recrystallization from EtOAc/hexanes: mp 128.0−128.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.65 (t, J = 6.40 Hz, 2H), 2.11 (m, 1H), 1.79−1.01 (m, 21H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 82.61, 63.01, 47.36, 35.89, 33.86, 33.22, 30.71, 30.59, 23.73, 21.32, 21.01, 18.56; IR ($CHCl_3$) 3605.5, 3454.0, 2991.4, 2944.3, 1069.9 cm^{-1}; LRMS (EI) *m/z* 170 (92), 140 (98), 121 (100), 97 (96), 79 (73), 67 (79), 55 (88), 41 (97). Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.54; H, 11.40. Found: C, 73.65; H, 11.72.

(1*R,2*R**,5*R**)-5-(2-Hydroxyethyl)-2-methylbicyclo[3.3.0]octan-1-ol (9e)** was prepared from **8e** (a 1:1 mixture of diastereomers) according to the general procedure for the preparation of **9a**. Purification of the crude product by flash chromatography followed by Kugelrohr distillation afforded **9e** as a white solid in 79% yield (1:1 mixture of diastereomers epimeric at C-2, separable by flash chromatography): mp 85.5−87.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) low R_f diastereomer, δ 3.73 (t, J = 6.30 Hz, 2H), 2.70 (s, 2H), 1.87−1.02 (m, 13H), 0.96 (d, J = 6.59 Hz, 3H), high R_f diastereomer, δ 3.69 (t, J = 6.10 Hz, 2H), 3.34 (s, 2H), 1.76−1.50 (m, 8H), 1.49−1.38 (m, 3H), 1.29 (m, 2H), 0.95 (d, J = 6.59 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), low R_f diastereomer, δ 91.13, 59.70, 53.17, 44.65, 41.06, 39.41, 36.51, 36.38, 30.00, 23.76, 13.54, high R_f diastereomer, δ 89.67, 59.47, 53.95, 44.68, 39.73, 39.37, 39.09, 38.20, 31.80, 22.10, 13.36; IR ($CHCl_3$) 3633.5, 3598.0, 3315.6, 1130.4, 1088.6 cm^{-1}; LRMS (EI) *m/z* 184 (15), 141 (100), 128 (99), 97 (98), 41 (52). Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.70; H, 10.94. Found: C, 71.84; H, 11.00.

Dihydro-3-(2-(chloromethyl)-2-propenyl)furan-2(3*H*)-one was prepared according to the general procedure for the preparation of **6a** by alkylation of γ-butyrolactone with 3-chloro-2-(chloromethyl)-1-propene to afford the desired alkylated product in 56% yield after flash chromatography with 15% EtOAc/hexanes: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.24 (s, 1H), 5.02 (s, 1H), 4.35 (dt, J = 2.93, 9.03 Hz, 1H), 4.20 (m, 1H), 4.05 (s, 2H), 2.78 (m, 2H), 2.42 (m, 1H), 2.32 (m, 1H), 2.07 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.61, 142.04, 116.80, 66.42, 47.82, 37.71, 34.19, 28.66.

Dihydro-3,3-bis(2-(chloromethyl)-2-propenyl)furan-2(3*H*)-one was prepared from dihydro-3-(2-(chloromethyl)-2-propenyl)furan-2(2*H*)-one according to the general procedure for the preparation of **6a** to afford the desired alkylated product in 61% yield after flash chromatography (17% EtOAc/hexanes): ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.36 (s, 2H), 5.10 (s, 2H), 4.21 (t, J = 7.32 Hz, 2H), 4.02 (m, 4H), 2.62 (d, J = 13.6 Hz, 2H), 2.42 (d, J = 14.4 Hz, 2H), 2.31 (t, J = 7.57 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.63, 140.51, 120.22, 65.42, 48.53, 45.95, 39.85, 30.81.

Dihydro-3-bis(2-(iodomethyl)-2-propenyl)furan-2(3*H*)-one (10). Sodium iodide (1.50 g, 10.0 mmol) and dihydro-3,3-bis(2-(chloromethyl)-2-propenyl)furan-2(3*H*)-one (0.263 g, 1.0 mmol) in 10 mL acetone were heated at reflux for 24 h. After this period of stirring, the reaction mixture was cooled to rt and concentrated *in vacuo*, and the resultant aqueous layer was extracted with ether. The combined organic layers were washed with saturated $NaHSO_3$ and brine, dried over $MgSO_4$, and concentrated *in vacuo*. Flash chromatography with 15% EtOAc/hexanes afforded **10** in 99% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.45 (s, 2H), 5.02 (s, 2H), 4.21 (t, J = 7.32 Hz, 2H), 3.92 (m, 4H), 2.70 (d, J = 14.64 Hz, 2H), 2.42 (d, J = 14.40 Hz, 2H), 2.30 (t, J = 7.32 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.49, 142.06, 119.44, 65.40, 45.90, 40.73, 30.97, 10.86.

***cis*-3,7-Bis(methylene)-5-(2-hydroxyethyl)bicyclo[3.3.0]octan-1-ol (11)** was prepared from **10** according to the general procedure of **9a**, except no HMPA was required, to afford **11** in 96% yield after flash chromatography with 23% EtOAc/hexanes: mp 104.5−105 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.84 (s, 4H), 3.77 (t, J = 6.10 Hz, 2H), 2.57 (s, 4H), 2.43 (d, J = 16.36 Hz, 2H), 2.23 (d, J = 16.60 Hz, 2H), 1.76 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.20 (2), 107.62(2), 87.72, 59.75, 53.59, 46.34 (2), 43.85 (2), 37.29; IR ($CHCl_3$) 3606.1, 3431.9, 2910.2, 1657.6 cm^{-1}; LRMS (EI) *m/z* 194 (55), 176 (55), 163 (80), 145 (100), 139 (70), 121 (98). Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.18; H, 9.38.

Tetrahydro-4-ethenylpyran-2(2*H*)-one (13).[3h] To a stirred solution of vinyl magnesium bromide (22.5 mmol) in 50 mL of THF at −78 °C was added 2.23 g (22.5 mmol) of CuCl, and the resultant orange-red heterogeneous mixture was stirred vigorously for 1.5 h. After this period, 5,6-dihydropyran-2(2*H*)-one (**12**)[16] (1.47 g, 15.0 mmol) was added slowly dropwise over 30 min as a 0.5 M solution in THF. The reaction mixture was monitored by TLC/GC and determined to be complete after 1.5 h at −78 °C. The reaction was quenched by transferring the reaction mixture via cannula to a vigorously stirred solution of ice/NH_4Cl. The resultant mixture was stirred until a bright blue color was apparent, then an aqueous workup followed by Kugelrohr distillation of the crude reaction mixture provided **13** as a clear colorless liquid (1.10 g, 8.70 mmol) in 58% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.73 (m, 1H), 5.04 (m, 2H), 4.38 (m, 1H), 4.25 (m, 1H), 2.64 (m, 2H), 2.31 (m, 1H), 1.95 (m, 1H), 1.66 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.59, 139.43, 115.06, 68.19, 35.33, 34.96, 28.38.

(3*R,4*R**)-Tetrahydro-3-(3-chloropropyl)-4-ethenylpyran-2(2*H*)-one (14)** was prepared according to the general procedure used for **6a** by alkylation of **13** with 1-chloro-3-iodopropane. The crude product was purified by flash chromatography (10−12% EtOAc/hexanes) to afford **14** as a clear colorless liquid in 50% yield: ^{1}H NMR (300 MHz,

$CDCl_3$) δ 5.67 (m, 1H), 5.11 (m, 2H), 4.29 (m, 2H), 3.50 (m, 2H), 2.37 (m, 2H), 2.04−1.68 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.07, 139.25, 116.42, 66.98, 44.81, 44.19, 40.56, 29.80, 29.14, 26.56.

(3*R,4*S**)-Tetrahydro-3-(3-chloropropyl)-4-ethenyl-3-methylpyran-2(2*H*)-one (15)** was prepared according to the general procedure of **6a** by alkylation of **14** with methyl iodide. The crude product was purified by flash chromatography (12% EtOAc/hexanes) to afford a 2.5:1 mixture of diastereomers in 75% yield (major diastereomer, **15**): ^1H NMR (300 MHz, $CDCl_3$) δ 5.61 (m, 1H), 5.15 (m, 2H), 4.40 (m, 1H), 4.27 (m, 1H), 3.49 (m, 2H), 2.54 (m, 1H), 2.10−1.50 (m, 6H), 1.22 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.88, 175.33, 135.86, 135.73, 117.84, 117.68, 68.59, 68.06, 46.51, 45.90, 45.22, 44.97, 44.60, 42.07, 34.86, 31.87, 31.83, 27.93, 27.37, 25.18, 23.20, 22.02.

(3*R,4*S**)-Tetrahydro-3-(3-chloropropyl)-4-(2-iodoethyl)-3-methylpyran-2(2*H*)-one (16)** was prepared from **15** according to the general procedure for the preparation of **8a**. The crude product was purified by flash chromatography to afford a 20:1 mixture of diastereomers (major isomer **16**) in 45% yield: ^1H NMR (300 MHz, $CDCl_3$) δ 4.42 (m, 1H), 4.25 (m, 1H), 3.57 (m, 1H), 3.49 (m, 1H), 3.39 (m, 1H), 3.07 (m, 1H), 2.06−1.31 (m, 9H), 1.18 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.69, 68.63, 46.38, 44.94, 37.84, 34.16, 32.36, 28.01, 23.46, 21.94, 4.03.

(1*R,4*S**,5*S**)-4-(2-Hydroxyethyl)-5-methylbicyclo[3.3.0]octan-1-ol (17)** was prepared from a 20:1 mixture of **16** and its diastereomer according to the general procedure for **9a**. Purification of the crude product by flash chromatography (30% EtOAc/hexanes) followed by Kugelrohr distillation afforded **17** as a clear colorless oil (20:1 mixture of diastereomers) in 74% yield: ^1H NMR (300 MHz, $CDCl_3$) δ 3.64 (m, 2H), 1.90−1.24 (m, 15H), 1.10 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 89.80, 62.40, 52.82, 45.60, 41.68, 40.34, 34.53, 33.80, 28.45, 22.17, 21.64; IR ($CHCl_3$) 3383.5, 2956.0, 1454.3, 1377.0, 1315.3, 1188.7, 1015.8 cm^{-1}; HRMS (EI^+) calcd for $C_{11}H_{20}O_2$ 184.1463, found 184.1473; LRMS (EI) *m/z* 184 (12), 142 (100), 97 (99). Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.70; H, 10.94. Found: C, 71.25; H, 11.23.

Diethyl 2,2-Bis(2-propenyl)malonate. Diethyl malonate (4.80 g, 30.0 mmol) was added slowly dropwise (neat) to a stirred slurry of NaH (1.22 g of a 65% dispersion in mineral oil) in 50 mL of DMF at 0 °C. After the substrate addition was complete and H_2 evolution had ceased, the reaction mixture was allowed to warm to rt and stirred for 1−2 h. After this period, the reaction mixture was cooled to 0 °C and allyl bromide (6.05 g, 50.0 mmol) was added slowly dropwise. The reaction mixture was allowed to come to rt and stirred overnight. After this time, the resultant yellow mixture was added slowly dropwise to a stirred slurry of NaH (1.22 g of a 65% dispersion in mineral oil) in 50 mL of DMF at 0 °C over a period of 1−2 h. After the addition was complete and H_2 evolution had ceased. the reaction mixture was warmed to rt and stirred for 2 h. Then the reaction mixture was cooled to 0 °C and allyl bromide (6.05 g, 50.0 mmol) was added slowly dropwise. After the addition was complete, the resultant mixture was warmed to rt and stirred overnight. TLC/GC analysis after this period showed complete consumption of starting material and formation of a single product. The reaction mixture was quenched with saturated aqueous $NaHCO_3$. Aqueous workup followed by distillation of the crude product afforded the dialkylated product in 76% yield: bp 66−67 °C at 0.05 mm Hg; ^1H NMR (300 MHz, $CDCl_3$) δ 5.61 (m, 2H), 5.07 (m, 4H), 4.15 (q, J = 7.33 Hz, 4H), 2.60 (d, J = 7.32 Hz, 4H), 1.21 (t, J = 7.08 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.72 (2), 132.28 (2), 119.13 (2), 61.20 (2), 57.30, 36.67 (2), 14.09 (2); IR (neat) 1732.6, 1641.8 cm^{-1}.

Diethyl 2,2-bis(3-iodopropyl)malonate (18) was prepared from **17** according to the general procedure for the preparation of **8a** to afford **18** in 51% yield: ^1H NMR (300 MHz, $CDCl_3$) δ 4.17 (q, J = 7.08 Hz, 4H), 3.14 (t, J = 6.59 Hz, 4H), 1.95 (m, 4H), 1.72 (m, 4H), 1.24 (t, J = 7.08 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.00 (2), 61.44 (2), 56.37, 33.63 (2), 28.24 (2), 14.11 (2), 5.76 (2); IR (neat) 1728.1 cm^{-1}.

Ethyl *cis*-5-Hydroxybicyclo[3.3.0]octanecarboxylate (19). Diiodomethane (0.83 g, 3.11 mmol) was added to a vigorously stirred solution of Sm (0.52 g, 3.45 mmol) in 30 mL of dry THF. The resultant blue-green reaction mixture was stirred for 2.5 h at rt, and then HMPA (2.5 mL) was added and the resultant deep purple solution was stirred for 15 min at rt. Then, the reaction mixture was cooled to −20 °C ($CaCl_2/H_2O$/Dry Ice bath)[28] and substrate **18** (0.301 g, 0.690 mmol) was added slowly dropwise over 2 h as a 0.03 M solution in THF. After the substrate addition was complete, the reaction was quenched at −20 °C with saturated aqueous $NaHCO_3$. Aqueous workup followed by flash chromatography (10% EtOAc/hexanes) afforded **19** in 64% yield (ot 70−80 °C at 0.05 mm Hg): ^1H NMR (300 MHz, $CDCl_3$) δ 4.15 (q, J = 7.08 Hz, 2H), 2.81 (s, 1H), 2.32 (m, 2H), 1.73 (m, 6H), 1.53 (m, 4H), 1.25 (t, J = 7.08 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.76, 92.45, 61.62, 60.72, 41.50 (2), 37.35 (2), 23.80 (2), 14.21; IR (neat) 3507.8, 1704.4 cm^{-1}; HRMS calcd for $C_{11}H_{18}O_3$ 198.1256, found 198.1262; LRMS (EI^+) *m/z* 198 (10), 180 (30), 152 (98), 124 (75), 108 (80), 97 (100).

(1*R,2*S**)-Ethyl 1-(3-Butenyl)-2-hydroxy-2-(2-propenyl)cyclopentanecarboxylate (21a). General Procedure for the Reaction of Allylzinc with β-Keto Esters.**[18] To a stirred solution of ethyl 1-(3-butenyl)-2-oxocyclopentanecarboxylate (**20a**)[29] (2.52 g, 10.0 mmol) and allyl bromide (1.81 g, 15.0 mmol) in 10 mL of DMF at rt was added unactivated zinc metal (0.98 g, 15.0 mmol) in one portion. After approximately 5−10 min, the reaction mixture turned from clear and colorless to cloudy gray and became very hot. The reaction mixture was stirred for an additional 1−2 h during which time the exotherm subsided. TLC/GC analysis at this time revealed complete consumption of starting material and the production of a 10:1 mixture of diastereomeric products. The reaction mixture was quenched with saturated aqueous NH_4Cl and filtered through a plug of Celite to remove the metal salts. Aqueous extraction followed by flash chromatography with 5% EtOAc/hexanes afforded **21a** (single diastereomer) in 56% yield: ^1H NMR (400 MHz, $CDCl_3$) δ 5.91 (m, 1H), 5.79 (m, 1H), 5.10 (m, 2H), 4.96 (m, 2H), 4.15 (m, 2H), 2.05 (m, 2H), 2.17 (m, 3H), 1.83 (m, 2H), 1.70 (m, 4H), 1.51 (m, 2H), 1.27 (t, J = 7.11 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.50, 138.52, 133.89, 118.70, 114.47, 82.66, 60.38, 60.27, 41.88, 35.00, 31.60, 30.22, 29.79, 18.72, 14.23.

(1*R,2*R**)-Ethyl 2-Hydroxy-1,2-bis(2-propenyl)cyclopentanecarboxylate (21b)** was prepared from 1-(3-propenyl)-2-oxocyclopentanecarboxylate (**20b**) according to the general procedure for the preparation of **21a** to afford a 12:1 mixture of diastereomeric products (major isomer **21b**) after flash chromatography with 3% EtOAc/hexanes and Kugelrohr distillation (ot 110−115 °C at 0.05 mm Hg), 64% yield (major diastereomer): ^1H NMR (300 MHz, $CDCl_3$) δ 5.83 (m, 1H), 5.62 (m, 1H), 5.05 (m, 4H), 4.13 (m, 2H), 2.75 (dd, J = 6.84, 13.92 Hz, 1H), 2.07 (m, 4H), 1.91 (s, 1H), 1.75 (m, 5H), 1.25 (t, J = 7.08 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.22, 134.63, 133.81, 118.76, 117.92, 82.50, 60.43, 59.99, 41.96, 37.03, 34.69, 29.83, 18.35, 14.20.

(1*R,2*S**)-Ethyl 1-(3-Butenyl)-2-((*tert*-butyldimethylsilyl)oxy)-2-(3-propenyl)cyclopentanecarboxylate (22a).**[19] 2,6-Lutidine (2.66 g, 25.0 mmol) and (*tert*-butyldimethyl)silyl triflate (5.28 g, 20.0 mmol) were added successively to a solution of **21a** (3.66 g, 10.0 mmol) in dichloromethane (10 mL) at 0 °C. The reaction mixture was stirred for 1 h at 0 °C and then 2 h at rt. TLC after this period of time showed complete consumption of the starting material. The reaction mixture was quenched with 0.1 N HCl and then subjected to aqueous workup. Flash chromatography with 1% EtOAc/hexanes afforded **22a** in 90% yield: ^1H NMR (400 MHz, $CDCl_3$) δ 5.83 (m, 2H), 4.97 (m, 4H), 4.09 (m, 2H), 2.23 (d, J = 7.14 Hz, 2H), 2.15 (m, 2H), 1.88 (m, 4H), 1.66 (m, 2H), 1.48 (m, 2H), 1.25 (t, J = 7.11 Hz, 3H), 0.88 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.47, 138.99, 134.59, 117.34, 114.01, 86.08, 61.52, 60.10, 42.91, 36.19, 32.15, 30.41, 29.68, 25.99 (3), 19.32, 18.70, 14.19, −1.98, −2.01.

(1*R,2*R**)-Ethyl 1,2-Bis(2-propenyl)-2-((*tert*-butyldimethylsilyl)oxy)cyclopentanecarboxylate (22b)** was prepared from **21b** according to the general procedure for the preparation of **22a** to afford **22b** in 88% yield after flash chromatography with 1−2% EtOAc/hexanes: ^1H NMR (300 MHz, $CDCl_3$): δ 5.86 (m, 1H), 5.61 (m, 1H), 5.01 (m, 4H), 4.08 (q, J = 7.08 Hz, 2H), 5.71 (dd, J = 6.35, 13.48 Hz, 1H), 2.24 (m, 2H), 2.10 (m, 2H), 1.90 (m, 1H), 1.77 (m, 1H), 1.65 (m, 3H), 1.24 (t, J = 7.08 Hz, 3H), 0.90 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.11, 135.43, 134.48, 117.52, 117.48, 85.84, 61.20, 61.16, 43.08, 37.71, 36.22, 30.06, 25.95 (3), 19.04, 18.64, 14.14, −2.06 (2).

(1*R,2*S**)-Ethyl 2-((*tert*-butyldimethylsilyl)oxy)-1-(4-iodobutyl)-2-(3-iodopropyl)cyclopentanecarboxylate (23a)** was prepared from **22a** according to the general procedure for the preparation of **8a** to afford **23a** in 63% yield after flash chromatography with 1% EtOAc/

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hexanes: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.13 (m, 2H), 3.13 (m, 4H), 2.18 (m, 1H), 2.04 (m, 1H), 1.94 (m, 1H), 1.74 (m, 7H), 1.51 (m, 4H), 1.28 (t, J = 7.12 Hz, 3H), 1.19 (m, 2H), 0.88 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.66, 86.51, 62.59, 60.50, 40.03, 37.60, 34.18, 31.97, 31.89, 28.17, 26.62, 26.07 (3), 19.96, 18.84, 14.37, 7.58, 6.79, −2.01, −2.19.

(1*R,2*S**)-Ethyl 2-((*tert*-Butyldimethylsilyl)oxy)-2-(2-hydroxyethyl)-1-(3-hydroxypropyl)cyclopentanecarboxylate.**[22] Ozone was bubbled through a solution of **22a** (0.73 g, 2.0 mmol) in 5 mL of ethanol at −78 °C until a blue color persisted. Then, the reaction mixture was purged with argon at −78 °C for 5 min, and subsequently $NaCNBH_3$ (0.63g, 10.0 mmol) was added carefully to the stirred −78 °C solution and the pH was monitored and kept between 3 and 4. (**CAUTION!! HCN evolved!!**) After addition of the reducing agent was complete, the reaction mixture was warmed to rt and stirred for several hours with the pH maintained between 3 and 4. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ and concentrated *in vacuo* (water bath 30−33 °C). The resultant crude reaction mixture was diluted with a small amount of brine, extracted with EtOAc, dried over $MgSO_4$, and concentrated *in vacuo*. The crude reaction mixture was flash chromatographed with 40% EtOAc/hexanes to afford the diol which was directly subjected to bromination: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.12 (m, 2H), 3.89 (m, 1H), 3.71 (m, 1H), 3.58 (m, 2H), 2.17 (m, 1H), 1.78 (m, 11H), 1.48 (m, 1H), 1.35 (m, 1H), 1.25 (t, J = 7.13 Hz, 3H), 0.88 (s, 9H), 0.12 (s, 3H), 0.11 (s, 3H).

(1*R,2*S**)-Ethyl 2-(2-Bromoethyl)-1-(3-bromopropyl)-2-((*tert*-butyldimethylsilyl)oxy)cyclopentanecarboxylate (23b).** PPh_3 (1.40 g, 5.25 mmol) and CBr_4 (1.70 g, 5.0 mmol) were added to a stirred solution of the crude diol (1*R**,2*S**)-ethyl 2-((*tert*-butyldimethylsilyl)oxy)-2-(2-hydroxyethyl)-1-(3-hydroxypropyl)cyclopentanecarboxylate and the resultant cloudy-white reaction mixture was stirred overnight. After this period of stirring, the reaction mixture was filtered through a plug of Celite and then subjected to flash chromatography (2% EtOAc/hexanes) to afford **23b** in 42% yield from the starting diene, **22a**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.14 (q, J = 7.13 Hz, 2H), 3.71 (m, 1H), 3.35 (m, 2H), 3.46 (m, 1H), 2.19 (m, 2H), 2.01 (m, 2H), 1.70 (m, 8H), 1.28 (t, J = 7.14 Hz, 3H), 0.90 (s, 9H), 0.15 (s, 3H), 0.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.22, 87.31, 62.56, 60.83, 43.42, 38.42, 34.27, 32.51, 32.37, 29.38, 28.28, 25.99 (3), 20.19, 18.82, 14.18, −2.43, −2.52.

(1*R,2*R**)-Ethyl 1,2-bis(3-iodopropyl)-2-((*tert*-butyldimethylsilyl)oxy)cyclopentanecarboxylate (23c)** was prepared from **22c** according to the general procedure for the preparation of **8a** to afford **23c** in 52% yield after flash chromatography with 1−2% EtOAc/hexanes: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.12 (m, 2H), 3.13 (m, 4H), 2.04 (m, 4H), 1.84 (m, 4H), 1.52 (m, 6H), 1.23 (t, J = 7.32 Hz, 3H), 0.90 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.43, 86.56, 62.15, 60.53, 40.00, 37.57, 34.34, 32.04, 29.94, 28.07, 26.11 (3), 20.00, 18.80, 14.29, 7.47, 7.40, −2.02, −2.17.

(1*R,5*R**,10*R**)-1-((*tert*-Butyldimethylsilyl)oxy)tricyclo[8.3.0.0^{5},^{10}]-tridecan-1-ol (24a)** was prepared from **23a** according to the general procedure for the preparation of **9a** to afford **24a** in 88% yield after flash chromatography with 1−3% EtOAc/hexanes: mp 62−62.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.27 (bs, 1H), 1.92 (m, 1H), 1.72 (m, 5H), 1.52 (m, 8H), 1.32 (m, 4H), 1.24 (m, 2H), 0.84 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 86.59, 74.30, 53.78, 39.84, 37.96, 32.98, 32.30, 31.46, 25.98 (3), 24.03, 23.65, 21.85, 18.90, 18.75, 18.41, −1.83, −2.26; IR ($CHCl_3$) 3473.6 cm^{-1}; HRMS calcd for $[C_{19}H_{37}O_2Si]^+ - H^+$ 323.2406, found 323.2416; LRMS (EI^+) *m/z* 323 (30), 307 (100), 291 (60), 267 (30), 249 (80), 175 (100), 75 (95).

(1*R,4*R**,8*S**)-4-((*tert*-Butyldimethylsilyl)oxy)tricyclo[6.3.0.0^{4,8}]-nonan-1-ol (24b)** was prepared from **23b** according to the general procedure of **9a** to afford **24b** as a single diastereomer in 84% yield: mp 100−101 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.17 (m, 1H), 1.90 (m, 1H), 1.82 (m, 2H), 1.71 (m, 3H), 1.56 (m, 5H), 1.37 (m, 3H), 1.25 (m, 2H), 0.86 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 91.76, 89.47, 64.14, 42.58, 41.74, 38.46, 38.16, 35.94, 34.84, 25.82 (3), 24.52, 23.86, 18.15, −2.51, −2.59; IR ($CHCl_3$) 3603.8 cm^{-1}; LRMS (EI^+) m/z 296 (5), 279 (10), 239 (100), 147 (58), 119 (60), 91 (47), 75 (98); HRMS (EI^+) calcd for $C_{17}H_{32}O_2Si$ 296.2172, found 296.2163. Anal. Calcd for $C_{17}H_{32}O_2Si$: C, 68.86; H, 10.88. Found: C, 68.91; H, 10.83.

(1*R,4*R**,9*S**)-4-((*tert*-Butyldimethylsilyl)oxy)tricyclo[7.3.0.0^{4,9}]-undecan-1-ol (24c)** was prepared from **23c** according to the general procedure for the preparation of **9a** to afford **24c** in 86% yield after flash chromatography with 4% EtOAc/hexanes: mp 92.5−93.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.07 (m, 2H), 1.76 (m, 9H), 1.50 (m, 7H), 1.20 (s, 1H), 0.87 (s, 9H), 0.08 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 84.38, 82.41, 58.51, 38.07, 37.61, 34.96, 34.20, 33.49, 32.08, 25.93 (3), 20.11 19.57, 18.68, 18.28, −2.23, −2.29; IR ($CHCl_3$) 3602.7 cm^{-1}; LRMS (EI) *m/z* 310 (10), 253 (80), 235 (100), 161 (100), 75 (65). Anal. Calcd for $C_{18}H_{34}O_2Si$: C, 69.62; H, 11.03. Found: C, 69.82; H, 11.15.

Tetrahydro-6-(2-propenyl)pyran-2(2*H*)-one (26b). To a mechanically stirred solution of 2-(2-propenyl)cyclopentanone (**25**)[30] (6.54 g, 52.8 mmol) in 100 mL of methylene chloride at 0 °C was added $NaHCO_3$ (12.2 g, 145.1 mmol) followed by the slow addition of 20.0 g (58.0 mmol) of mCPBA as a 50% mixture of mCPBA/benzoic acid. The reaction mixture was stirred at 0 °C for 4 h and then warmed to rt for 1 h. GC analysis at this time revealed the complete consumption of starting material. After the reaction was complete, the careful addition of 100 mL of saturated aqueous $NaHCO_3$ and 100 mL of saturated aqueous $NaHSO_3$ was followed by an aqueous workup. The crude product was purified by flash chromatography to afford **26b** as a clear colorless oil in 60% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.78 (m, 1H), 5.11 (m, 2H), 4.30 (m, 1H), 2.60−2.30 (m, 4H), 1.93−1.72 (m, 3H), 1.51 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.69, 132.58, 118.50, 79.73, 39.92, 29.34, 27.06, 18.30.

(3*R,5*S**)-Dihydro-3-(3-chloropropyl)-5-(2-propenyl)furan-2(3*H*)-one (27a)** was prepared from dihydro-5-(2-propenyl)furan-2(3*H*)one[18] by alkylation with 1-chloro-3-iodopropane according to the general procedure for the preparation of **6a** to afford a 20:1 mixture of diastereomeric products (major diastereomer **27a**) in 69% yield after flash chromatography with 11% EtOAc/hexanes: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.74 (m, 1H), 5.15 (m, 2H), 4.56 (m, 1H), 3.53 (dt, J = 2.69, 5.86 Hz, 2H), 2.59 (m, 1H), 2.39 (m, 2H), 2.14 (m, 1H), 1.92 (m, 4H), 1.65 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.53, 131.98, 119.07, 77.47, 44.36, 39.42, 38.39, 32.56, 30.08, 28.52; IR (neat) 1769.2, 1642.4 cm^{-1}.

Tetrahydro-3-(3-chloropropyl)-6-(2-propenyl)pyran-2(2*H*)-one (27b) was prepared from **26b** according to the general procedure for the preparation of **6a** by alkylation of **26b** with 1-chloro-3-iodopropane to afford **27b** as a 1.3:1 mixture of diastereomers in 65% yield after flash chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.77 (m, 1H), 5.10 (m, 2H), 4.30 (m, 1H), 3.53 (m, 2H), 2.49−2.23 (m, 3H), 2.13−1.45 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.91, 173.09, 132.70, 132.51, 118.59, 118.45, 80.55, 77.26, 44.80, 44.68, 40.31, 40.27, 39.40, 37.62, 30.06, 29.90, 29.34, 28.29, 28.18, 26.07, 25.64, 23.44.

(3*R,5*R**)-Dihydro-3-(3-chloropropyl)-3-methyl-5-(2-propenyl)-furan-2(3*H*)-one (28a)** was prepared according the general procedure for the preparation of **6a** by alkylation of **27a** with methyl iodide to afford **28a** in 80% yield after flash chromatography with 6−7% EtOAc/hexanes: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.76 (m, 1H), 5.16 (m, 2H), 4.48 (m, 1H), 3.53 (m, 2H), 2.49 (m, 1H), 2.39 (m, 1H), 2.01 (dd, J = 12.79, 5.79 Hz, 1H), 1.78 (m, 5H), 1.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.77, 132.00, 118.92, 76.12, 44.85, 43.61, 39.82, 39.45, 34.93, 27.69, 22.67; IR (neat) 1765.9, 1643.2 cm^{-1}.

(3*R,6*S**)/(3*R**,6*R**)-Tetrahydro-3-(3-chloropropyl)-3-methyl-6-(2-propenyl)pyran-2(2*H*)-one (28b and 28c)** was prepared according to the general procedure for **6a** by alkylation of **27b** with methyl iodide. Purification of the crude product, a 2.5:1 mixture of diastereomeric products separable by flash chromatography, afforded **28b** (high R_f, major diastereomer) in 75% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.79 (m, 1H), 5.14 (m, 2H), 4.29 (m, 1H), 3.52 (m, 2H), 2.41 (m, 2H), 1.82 (m, 4H), 1.68 (m, 4H), 1.27 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.31, 132.52, 118.62, 80.64, 44.95, 41.45, 40.29, 37.80, 31.40, 27.80, 26.61, 25.27; (**28c**, minor diastereomer): ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.80 (m, 1H), 5.14 (m, 2H), 4.32 (m, 1H), 3.52 (m, 2H), 2.41 (m, 2H), 1.74 (m, 8H), 1.26 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.38, 132.44, 118.64, 80.31, 45.03, 40.73, 40.06, 36.87, 31.21, 27.30, 25.72, 25.02.

(3*R,5*R**)-Dihydro-3-(3-chloropropyl)-5-(3-iodopropyl)-3-methylfuran-2(3*H*)-one (29a)** was prepared from **28a** according to the general procedure for the preparation of **8a** to afford **29a** as a single

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diastereomeric product in 50% yield after flash chromatography with 5% EtOAc/hexanes: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.42 (m, 1H), 3.53 (m, 2H), 3.21 (m, 2H), 2.04 (m, 2H), 1.90 (m, 2H), 1.54 (m, 6H), 1.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.68, 76.06, 44.82, 43.61, 40.56, 36.52, 34.88, 29.34, 27.65, 22.55, 5.84.

Tetrahydro-3-(3-chloropropyl)-6-(3-iodopropyl)-3-methylpyran-2(2*H*)-one (29b and 29c) was prepared from a mixture of **28b** and **28c** according to the general procedure for **8a**. Purification of the crude product (a 3:1 mixture of diastereomers, high R_f component was the major diastereomer **29b**) by flash chromatography afforded a mixture of **29b** and **29c** in 45% yield: (major diastereomer, **29b**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.25 (m, 1H), 3.51 (m, 2H), 3.20 (dt, J = 3.45, 6.67, 2H), 2.05 (m, 1H), 1.95−1.79 (m, 5H), 1.78−1.66 (m, 4H), 1.63 (m, 2H), 1.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.18, 80.28, 44.98, 41.48, 37.77, 37.00, 31.44, 28.65, 27.79, 26.70, 26.06, 6.16; ^{1}H NMR (300 MHz, $CDCl_3$) (minor diastereomer, **29c**): δ 4.31 (m, 1H), 3.50 (m, 2H), 3.19 (m, 2H), 2.00 (m, 2H), 1.91−1.62 (m, 10H), 1.24 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.29, 79.97, 45.04, 40.80, 36.92, 36.79, 31.71, 28.65, 27.31, 28.65, 27.31, 25.94, 25.76, 6.23.

(1*R,5*R**,7*RS**)-7-Methylbicyclo[5.3.0]decan-1,5-diol (30a). General Procedure for Sequenced Reactions of Dihalide Substrates.** The same general procedures were used as for the preparation of **9a**, except addition of the substrate **29a** took place over 5−6 h to afford **30a** and a minor diastereomer (stereochemistry unassigned) as a 5:1 mixture of products in 58% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.10 (m, 1H), 2.19 (s, 2H), 1.91 (m, 3H), 1.67 (m, 10H), 1.47 (m, 1H), 1.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 83.13, 69.68, 46.60, 46.45, 42.07, 41.88, 38.83, 38.13, 26.19, 19.36, 18.09; HRMS calcd for $C_{11}H_{20}O_2$ 184.1463, found 184.1472; LRMS (EI$^+$) *m/z* 184 (10), 166 (98), 151 (100), 148 (40), 141 (60), 41 (98).

(1*R,5*R**,8*R**)-8-Methylbicyclo[6.3.0]undecan-1,5-diol (30b)** was prepared from a 53:1 mixture of **29b** and its diastereomer according to the general procedure for the preparation of **30a**. Product **30b** and a diastereomer (stereochemistry unassigned) were isolated in a 10:1 ratio (white solid) in 68% yield after flash chromatography and Kugelrohr distillation: mp 83.0−84.5 °C; (major diastereomer, **30b**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.03 (m, 1H), 1.98 (m, 1H), 1.88−1.34 (m, 17H), 1.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 82.26, 70.90, 45.50, 45.05, 41.77, 38.06, 36.18, 32.14, 31.88, 21.44, 20.58, 18.20; ^{1}H NMR (400 MHz, $CDCl_3$) (minor diastereomer of unassigned stereochemistry, high R_f) δ 4.10 (t, J = 8.57 Hz, 1H), 2.45 (bs, 1H), 2.12 (m, 1H), 2.01 (m, 1H), 1.91 (m, 3H), 1.76−1.47 (m, 7H), 1.46−1.34 (m, 3H), 1.22 (m, 2H), 0.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 81.63, 66.22, 45.90, 44.71, 44.26, 35.87, 34.65, 31.89, 29.06, 22.62, 17.67, 17.08; IR ($CHCl_3$) 3606.4, 3450.8, 2944.1, 2862.3, 1110.8, 1082.9 cm^{-1} (CCl_4, dilute) 3621.4 cm^{-1}; LRMS (EI$^+$) *m/z* 180 (100), 165 (98), 155 (80), 147 (50); (CI−) *m/z* 197 (100), 179 (60), 148 (18). Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18. Found: C, 72.75; H, 11.10.

(1*R,5*S**,8*R**)-8-Methylbicyclo[6.3.0]undecan-1,5-diol (30c)** was prepared from a 20:1 mixture of **29c** and **29b** according to the general procedure outlined for the preparation of **30a**. The cyclization products **30c** and a minor diastereomer (stereochemistry unassigned) were isolated as white solids in an 8:1 ratio in 65% yield after flash chromatography and Kugelrohr distillation: major diastereomer; mp 101−102 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.00 (m, 1H), 2.64 (s, 2H), 1.97−1.23 (m, 16H), 1.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 82.17, 69.49, 45.44, 45.00, 42.92, 38.21, 33.84, 32.40, 32.08, 21.36, 18.19, 18.08; IR (CCl_4, dilute) 3613.5, 3420.2 cm^{-1}; LRMS (EI+) *m/z* 180 (12), 109 (27), 98 (38), 81 (39), 67 (41), 55 (66), 41 (99); HRMS calcd for $C_{12}H_{22}O_2$ 198.1620, found 198.1635. Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18. Found: C, 72.21; H, 11.33.

Ethyl 2-Oxycyclopentaneacetate (31c). Cyclopentanone (1.68 g, 20.0 mmol) in 10 mL THF was added slowly dropwise over approximately 30 min to a stirred solution of LDA (22.0 mmol) at −78 °C. After the substrate addition was complete, the reaction mixture was stirred for an additional 30 min at −78 °C. Then, ethyl bromoacetate (3.67 g, 22.0 mmol) in 4.2 mL of HMPA was added slowly dropwise and the reaction mixture was allowed to come slowly to rt overnight. The reaction mixture was quenched with saturated aqueous NH_4Cl. Aqueous workup followed by flash chromatography with 5% EtOAc/hexanes and Kugelrohr distillation (ot 120 °C at 8 mm Hg) afforded **31a** in 44% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.08 (q, J = 7.08 Hz, 2H), 2.68 (m, 1H), 2.39 (m, 2H), 2.25 (m, 2H), 2.07 (m, 2H), 1.80 (m, 1H), 1.60 (m, 1H), 1.24 (t, J = 6.77 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 218.84, 172.02, 60.52, 45.55, 37.37, 33.95, 29.24, 20.54, 14.11.

Ethyl 2-oxocyclohexaneacetate (31d) was prepared from cyclohexanone according to the general procedure for the preparation of **31c** to afford **31d**, 68% yield, after shortpath distillation, bp 65 °C at 0.05 mm Hg: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.11 (q, J = 7.17 Hz, 2H), 2.85 (m, 1H), 2.74 (dd, J = 7.17, 16.40 Hz, 1H), 2.36 (m, 2H), 2.10 (m, 3H), 1.86 (m, 1H), 1.65 (m, 2H), 1.39 (dq, J = 3.68, 12.78 Hz, 1H), 1.23 (t, J = 7.15 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.03, 172.58, 60.40, 47.09, 41.80, 34.42, 33.85, 27.76, 25.17, 14.16.

***cis*-2-Oxa-1-(2-propenyl)bicyclo[4.3.0]nonan-3-one (32a)** was prepared from **31a** (n = 1, m = 1)[31] according to the general procedure for the preparation of **21a** to afford a 9:1 mixture of **32a** and the trans hydroxy ester in 87% yield after flash chromatography with 10% EtOAc/hexanes: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.80 (m, 1H), 5.04 (m, 2H), 2.39 (m, 4H), 2.08 (m, 1H), 1.86 (m, 4H), 1.62 (m, 4H); ^{1}13C NMR (75 MHz, $CDCl_3$) δ 172.21, 132.52, 93.26, 44.85, 39.28, 38.58, 32.00, 29.52, 23.92, 22.80, 22.17.

***cis*-2-Oxa-1-(2-propenyl)bicyclo[3.3.0]octan-3-one (32c)** was prepared from **31c** according to the general procedure for the preparation of **21a** to afford a 5:1 mixture of **32c** and the trans hydroxy ester in 75% yield after flash chromatography with 9−10% EtOAc/hexanes and Kugelrohr distillation (ot 120−130 °C at 8 mm Hg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.77 (m, 1H), 5.14 (m, 2H), 2.79 (dd, J = 10.0, 18.3 Hz, 1H), 2.52 (m, 2H), 2.25 (dd, J = 2.69, 18.6 Hz, 1H), 1.99 (m, 1H), 1.85 (m, 1H), 1.82 (m, 1H), 1.65 (m, 3H), 1.50 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.24, 132.14, 119.54, 97.04, 43.16, 41.28, 38.16, 36.94, 34.37, 23.91; IR (neat) 1766.5, 1640.7 cm^{-1}.

***cis*-9-Oxa-1-(2-propenyl)bicyclo[4.3.0]nonan-8-one (32d)** was prepared from **31d** according to the general procedure for the preparation of **21a** to afford a 5.3:1 mixture of **32d** and the trans hydroxy ester in 94% yield after shortpath distillation, bp 81−83 °C at 0.05 mm Hg: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.81 (m, 1H), 5.12 (m, 2H), 2.55 (m, 1H), 2.41 (m, 4H), 2.19 (m, 1H), 1.73 (m, 2H), 1.43 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.54, 132.34, 119.22, 86.31, 41.93, 37.73, 34.67, 32.38, 25.99, 21.52, 20.67, (hydroxy ester) δ 176.30, 132.00, 118.91, 86.95, 47.15, 34.23, 33.42, 33.29, 25.26, 34.39, 22.06.

(1*R,4*S**,6*S**)/(1*R**,4*R**,6*S**)-4-(3-Chloropropyl)-2-oxa-1-(2-propenyl)bicyclo[4.3.0]nonan-3-one (33a and 33b)** was prepared from **32a** according to the general procedure for the preparation of **6a** to afford a 2.5:1 mixture of **33a** and **33b** in 70% yield. The two isomers were separable by flash chromatography with 6% EtOAc/hexanes. High R_f diastereomer, **33b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.79 (m, 1H), 5.13 (m, 2H), 3.53 (t, J = 6.35 Hz, 2H), 2.39 (m, 2H), 2.21 (m, 2H), 1.85 (m, 8H), 1.54 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.68, 132.42, 119.61, 92.01, 46.20, 44.95, 40.85, 39.64, 39.02, 32.56, 31.68, 30.01, 28.09, 22.38. Low R_f diastereomer, **33a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.80 (m, 1H), 5.10 (m, 2H), 3.53 (t, J = 6.35 Hz, 2H), 2.38 (m, 2H), 2.17 (m, 2H), 1.89 (m, 8H), 1.59 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.67, 132.57, 119.11, 93.18, 44.85, 44.44, 39.74, 37.97, 34.77, 29.95 (2), 28.49, 27.88, 22.41.

(1*R,4*S**,5*S**)-4-(3-Chloropropyl)-2-oxa-1-(2-propenyl)bicyclo[3.3.0]octan-3-one (33c)** was prepared according to the general procedure for the preparation of **6a** by alkylation of **32c** with 1-chloro-3-iodopropane to afford **33c** as a single diastereomer in 70% yield after flash chromatography with 5% EtOAc/hexanes: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.76 (m, 1H), 5.13 (m, 2H), 3.52 (m, 2H), 2.44 (m, 2H), 2.24 (m, 2H), 1.86 (m, 5H), 1.64 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.78, 132.39, 119.60, 95.07, 47.98, 47.90, 44.40, 44.24, 38.01, 34.21, 30.27, 29.56, 23.88; IR (neat) 1760.2, 1641.0 cm^{-1}.

(1*R,6*S**,7*S**)-7-(3-Chloropropyl)-9-oxa-1-(2-propenyl)bicyclo[4.3.0]nonan-8-one (33d)** was prepared according to the general procedure for the preparation of **6a** by alkylation of **32d** with 1-chloro-3-iodopropane to afford a 20:1 mixture of **33d** and a diastereomer epimeric at C-7 in 85% yield after flash chromatography with 8% EtOAc/hexanes: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.81 (m, 1H), 5.12 (m, 2H), 3.56 (t, J = 6.49 Hz, 2H), 2.57 (m, 2H), 2.40 (dd, J = 7.17, 14.68 Hz, 1H), 2.09 (m, 2H), 1.98 (m, 1H), 1.87 (m, 1H), 1.73 (m, 4H), 1.58 (m, 2H), 1.33 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ

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177.94, 132.28, 119.27, 84.24, 44.95, 43.51, 41.12, 40.57, 33.21, 29.34, 26.14, 23.27, 22.25, 19.70.

(1*R,4*S**,6*S**)-4-(3-Chloropropyl)-1-(4-iodopropyl)-2-oxabicyclo-[4.3.0]nonan-3-one (34a)** was prepared from **33a** according to the general procedure for the preparation of **8a** to afford **34a** in 50% yield after flash chromatography with 5−6% EtOAc/hexanes: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.53 (t, J = 6.35 Hz, 2H), 3.17 (m, 2H), 2.39 (m, 1H), 2.11 (m, 1H), 2.00 (m, 2H), 1.71 (m, 14H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.54, 93.26, 44.81, 41.28, 39.51, 39.38, 34.68, 29.93, 29.64, 28.56, 27.92, 27.84, 22.50, 6.98.

(1*R,4*R**,6*S**)-4-(3-Chloropropyl)-1-(4-iodopropyl)-2-oxabicyclo-[4.3.0]nonan-3-one (34b)** was prepared from **33b** according to the general procedure for the preparation of **8a** to afford **34b** in 51% yield after flash chromatography with 5−6% EtOAc/hexanes: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.56 (t, J = 6.52 Hz, 2H), 3.17 (m, 2H), 2.25 (m, 1H), 2.13 (m, 1H), 2.00 (m, 4H), 1.88 (m, 5H), 1.73 (m, 4H), 1.59 (m, 2H), 1.49 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.62, 92.18, 44.94, 43.00, 42.54, 39.39, 38.73, 32.52, 31.65, 30.03, 28.12, 27.90, 22.54, 6.94.

(1*R,4*S**,5*S**)-4-(3-Chloropropyl)-1-(3-iodopropyl)-2-oxabicyclo-[3.3.0]octan-3-one (34c)** was prepared from **33c** according to the general procedure for the preparation of **8a** to afford **34c** in 72% yield after flash chromatography (3−4% EtOAc/hexanes): ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.55 (m, 2H), 3.18 (m, 2H), 2.25 (m, 2H), 1.76 (m, 14H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.62, 95.15, 49.49, 47.82, 44.35, 41.55, 37.83, 34.04, 30.22, 29.95, 28.36, 23.90, 6.49; IR (neat) 1754.5 cm^{-1}.

(1*R,6*S**,7*S**)-7-(3-Chloropropyl)-1-(3-iodopropyl)-9-oxabicyclo-[4.3.0]nonan-8-one (34d)** was prepared from **33d** according to the general procedure for the preparation of **8a** to afford **34d** in 50% yield after flash chromatography with 7% EtOAc/hexanes: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.57 (t, J = 6.50 Hz, 2H), 3.20 (m, 2H), 2.60 (m, 1H), 2.11 (m, 1H), 1.95 (m, 6H), 1.75 (m, 5H), 1.61 (m, 2H), 1.32 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.88, 84.33, 44.93 (2), 41.13, 37.15, 32.80, 29.40, 27.37, 26.24, 23.45, 22.36, 19.92, 6.70.

(1*R,5*R**,9*R**,11*R**)-Tricyclo[9.3.0.0^{5,9}]tetradecane-1,5-diol (35a)** was prepared from **34a** according to the general procedure for the preparation of **30a** to afford **35a** as a single diastereomer in 67% yield after flash chromatography with 14−15% EtOAc/hexanes: mp 92−93 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.24 (m, 2H), 1.76 (m, 9H), 1.59 (m, 4H), 1.42 (m, 8H), 1.13 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 82.22 (2), 44.95 (2), 42.18 (2), 41.72 (2), 33.75 (2), 31.60, 21.40 (2), 19.22; IR ($CHCl_3$) 3601.0 (CCl_4) 3615.7 cm^{-1}; LRMS (EI) *m/z* 224 (10), 206 (35), 188 (100), 94 (90), 79 (85), 41 (85). Anal. Calcd for $C_{14}H_{24}O_2$: C, 74.95; H, 10.79. Found: C, 74.61; H, 10.78.

(1*R,5*R**,9*S**,11*S**)-Tricyclo[9.3.0.0^{5,9}]tetradecane-1,5-diol (35b)** was prepared from **34b** according to the general procedure for the preparation of **30a** to afford **35b** as a single diastereomer in 72% yield after flash chromatography with 14−15% EtOAc/hexanes: mp 85.0−86.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.64 (s, 2H), 2.05 (dq, J = 2.49, 6.98 Hz, 2H), 1.91 (m, 3H), 1.72 (m, 4H), 1.62 (m, 5H), 1.45 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 78.70, 50.46, 46.85, 41.60, 36.08, 30.79, 21.05, 19.09; IR (CCl_4, 0.03 M) 3607.6, 3471.3 cm^{-1}; HRMS calcd for $C_{14}H_{24}O_2$ 224.1776, found 224.1792; LRMS (EI+) *m/z* 224 (10), 206 (71), 188 (97), 122 (49), 110 (65), 94 (85), 79 (70), 67 (55), 55 (61), 41 (99). Anal. Calcd for $C_{14}H_{24}O_2$: C, 74.95; H, 10.79. Found: C, 75.09; H, 11.03.

(1*R,5*R**,9*R**,10*R**)-Tricyclo[8.3.0.0^{5,9}]tridecane-1,5-diol (35c)** was prepared from **34c** according to the general procedure for the preparation of **30a** to afford **35c** as a single diastereomer in 91% yield after flash chromatography with 18% EtOAc/hexanes: mp 118.5−119 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.46 (s, 2H), 1.83 (m, 10H), 1.48 (m, 9H), 1.12 (dq, J = 6.84, 11.72 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 82.44, 81.90, 54.39, 52.39, 45.45, 43.47, 42.10, 39.05, 34.97, 33.31, 24.52, 22.80, 18.39; IR ($CHCl_3$) 3275.6 cm^{-1}; HRMS calcd for $C_{13}H_{22}O_2$ 210.1620, found 210.1623; LRMS (EI$^+$) *m/z* 210 (25), 192 (100), 174 (98), 131 (85).

(1*R,5*R**,9*S**,10*R**)-Tricyclo[9.4.0.0^{5,9}]tetradecane-1,5-diol (35d)** was prepared from **34d** according to the general procedure for the preparation of **30a** to afford **35d** as a single product in 83% yield after flash chromatography with 21% EtOAc/hexanes: mp 92.5−93.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.08 (m, 1H), 1.97 (m, 1H), 1.84 (m, 1H), 1.75 (bs, 1H), 1.95 (m, 3H), 1.62 (m, 10H), 1.33 (m, 8H), 1.09 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 81.20, 73.40, 56.67, 49.08, 46.31, 44.62, 42.04, 38.33, 33.64, 32.04, 26.05, 21.80, 21.63, 18.62; IR ($CHCl_3$) 3583.8, 3441.1 cm^{-1}; HRMS calcd for $C_{14}H_{24}O_2$ 224.1776, found 224.1774; LRMS (EI+) *m/z* 224 (19), 206 (100), 135 (61), 122 (82), 94 (83), 79 (60), 67 (64), 55 (54), 41 (98). Anal. Calcd for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78. Found: C, 75.09; H, 10.65.

(1*R,6*S**,7*S**)-7-Methyl-9-oxa-1-(2-propenyl)bicyclo[4.3.0]nonan-8-one (36)** was prepared according to the general procedure for the preparation of **6a** by alkylation of **32d** with methyl iodide to afford a 20:1 mixture of **36** and a diastereomer epimeric at C-7 in 73% yield after flash chromatography with 10% EtOAc/hexanes and Kugelrohr distillation (ot 100−110 °C): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.82 (m, 1H), 5.12 (m, 2H), 2.58 (m, 2H), 2.40 (dd, J = 7.45, 14.88 Hz, 1H), 1.97 (m, 2H), 1.71 (m, 2H), 1.56 (m, 2H), 1.33 (m, 3H), 1.18 (d, J = 6.94 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.91, 132.46, 119.06, 84.38, 46.10, 40.57, 37.20, 33.08, 23.16, 22.40, 19.74, 13.48.

(1*R,6*S**,7*S**)-7-(4-Chlorobutyl)-7-methyl-9-oxa-1-(2-propenyl)-bicyclo[4.3.0]nonan-8-one (37)** was prepared according to the general procedure for the preparation of **6a** by alkylation with a 20:1 mixture of **36** and its diastereomer with 1-chloro-4-iodobutane to afford **37** as a single diasteromer in 82% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.82 (m, 1H), 5.13 (m, 2H), 3.51 (m, 2H), 2.53 (dd, J = 6.98, 14.58 Hz, 1H), 2.41 (dd, J = 7.42, 14.62 Hz, 1H), 2.25 (d, J = 6.73 Hz, 1H), 2.02 (d, J = 13.50 Hz, 1H), 1.72 (m, 5H), 1.49 (m, 8H), 1.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.47, 132.70, 119.46, 84.19, 46.80, 44.73, 42.62, 42.49, 39.43, 34.20, 32.73, 22.37, 21.76, 21.68, 21.62, 21.57.

(1*R,6*S**,7*S**)-7-(4-Chlorobutyl)-1-(3-iodoethyl)-7-methyl-9-oxa-bicyclo[4.3.0]nonan-8-one (38)** was prepared from **37** according to the general procedure for the preparation of (1*R**,2*S**)-ethyl 2-((*tert*-butyldimethylsilyl)oxy)-2-(2-hydroxyethyl)-1-(3-hydroxypropyl)cyclopentanecarboxylate to afford the crude hydroxy ester which was subjected directly to iodination according to the following general procedure.[32] To the crude hydroxy ester (1.44 g, 5.0 mmol) in 5 mL of dry CH_2Cl_2 under argon at rt was added TMSI (1.50 g, 7.5 mmol) and the resultant colored solution was stirred at rt for 24−36 h. After this period of time, the reaction mixture was quenched carefully with saturated aqueous $NaHSO_3$. Aqueous workup followed by flash chromatography with 9% EtOAc/hexanes afforded the desired product in 40% yield from the starting olefin, **37**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.53 (dt, J = 6.49, 2.39 Hz, 2H), 3.20 (m, 2H), 2.48 (m, 1H), 2.25 (m, 1H), 2.14 (m, 1H), 2.09 (m, 1H), 1.68 (m, 7H), 1.42 (m, 6H), 1.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.89, 85.30, 46.61, 44.55, 44.08, 43.58, 39.63, 32.67, 32.63, 22.40 (2), 21.61, 21.56, 21.47, 21.40.

(1*R,4*S**,9*S**)-9-Methyltricyclo[9.4.0^{4,9}]tetradecane-1,4-diol (39)** was prepared from **38** according to the general procedure for the preparation of **30a** to afford a 40:1 mixture of **39** and a diastereomer (stereochemistry unassigned) in 80% yield after flash chromatography with 17% EtOAc/hexanes. **39**: mp 125−126 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.07 (dt, J = 5.74, 13.10 Hz, 1H), 1.98 (dt, J = 4.95, 13.43 Hz, 1H), 1.79 (m, 1H), 1.54 (m, 10H), 1.24 (m, 10H), 0.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 73.64, 71.35, 43.52, 42.05, 40.16, 37.79, 32.71, 32.28, 26.74, 21.68, 21.47, 21.09, 20.89, 19.04; IR ($CHCl_3$) 3611.6 cm^{-1}; HRMS calcd for $C_{15}H_{26}O_2$ 238.1933, found 238.1922; LRMS (EI+) *m/z* 238 (29), 220 (17), 205 (100), 125 (99), 67 (48), 55 (65), 41 (85). Anal. Calcd for $C_{15}H_{26}O_2$: C, 75.58; H, 10.99. Found: C, 75.16; H, 10.98.

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