Studies in the Directed Cyclopropanation of α-Allenic Alcohols

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Abstract: A highly regioselective cyclopropanation of α-allenic alcohols using samarium/dihalomethane provides a variety of methylene- and alkylidenecyclopropane carbinols in good yield. The nearby hydroxyl moiety and the samarium reagent are essential for this unique conversion. A comparison with the more traditional Simmons–Smith conditions and its variants is made. The diastereoselectivity varies from 1:1 to 50:1 and depends on the substituents on the carbinol side chain (R group) and on the substitution of the allene. Unequivocal assignment of the relative stereochemistry of the prepared methylenecyclopropanes has been made on the basis of NMR studies, independent synthesis, and X-ray crystallography. A facile one-pot, two-step enantioselective reduction of ynones with the chiral $LiAlH_4$/Darvon alcohol complex provides the starting allenic alcohols in 82–93% enantiomeric excess. Hydroboration of the methylenecyclopropane carbinols results in the formation of (*Z*)-substituted cyclopropyl dicarbinols, which were cyclized to 3-oxabicyclo[3.1.0]hexanes upon treatment with *p*-TsCl.

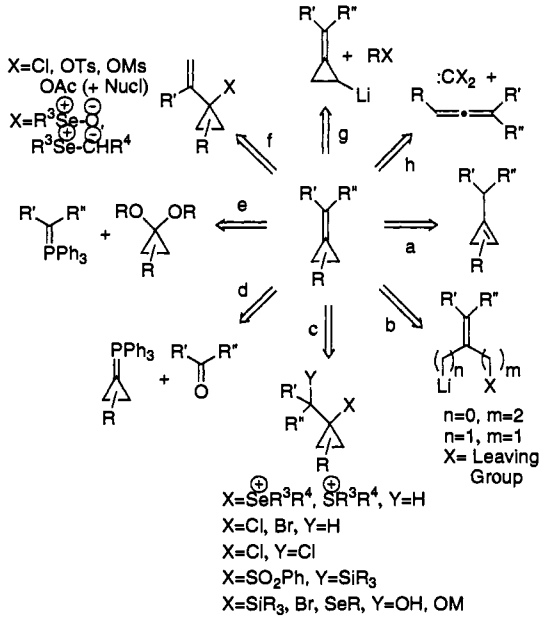
Introduction

Alkylidenecyclopropanes are highly strained carbocyclic molecules which have been shown to possess useful reactivity in organic synthesis.[2,3] A particularly interesting reaction of methylenecyclopropanes is the Ni(0)- or Pd(0)-catalyzed reaction with alkenes or alkynes which provides an efficient route for the synthesis of five-membered rings.[3a-e,4]

In addition, interest in methylenecyclopropanes from the mechanistic,[5] and biological,[6] perspective has emerged. Inactivation of the enzyme acyl-CoA dehydrogenase by a metabolite of the α-amino acid hypoglycin A is well-known, and its mechanism of action has been the focus of intense investigations.[6b-e,7] The diverse reactivity and utility of methylenecyclopropanes has led to an increased effort for the facile construction of more elaborate methylenecyclopropanes.

A number of strategies for the synthesis of alkylidene- and methylenecyclopropanes have been reported to date and are illustrated in Scheme 1. Base-catalyzed isomerization reactions of methylcyclopropene (route a)[8] have been described. Intramolecular nucleophilic displacement with a vinyl or allyl lithium

Scheme 1



(route b)[9] provides alkylidenecyclopropanes in moderate to good yield. Formation of the olefin by an elimination reaction of disubstituted cyclopropanes (route c)[10-13] is also well established. Wittig type olefination of an aldehyde or ketone with a phosphorane[14] or bis(cyclopropyl) titanocene[15] (route d) and olefination of cyclopropanone hemiacetals (route e)[16] have also been reported. Recently, alkylidenecyclopropanes have been

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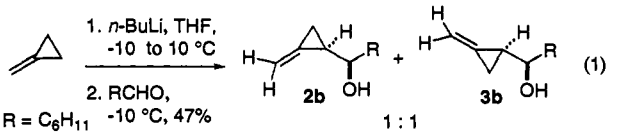
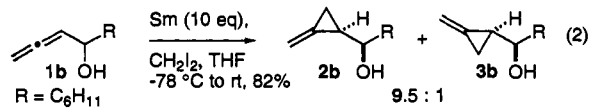
synthesized via a Pd(0)-catalyzed allylic transposition in the presence of a nucleophile (route f).[17] Intermolecular alkylation of the anion of methylenecyclopropane yields substituted methylenecyclopropanes (route g),[18] as does the addition of a carbene to an unsymmetrically substituted allene (route h).[19]

In spite of the studies reported to date, few of the methods are applicable to the convenient enantioselective preparation of the more functionalized methylenecyclopropyl carbinols.[20,21] Carbinol-substituted methylenecyclopropanes have been obtained in moderate yield as a 1:1 mixture of diastereomers by deprotonation of the parent methylenecyclopropane, followed by trapping of the allylic anion with an aldehyde,[18a] Scheme 1, route g, and eq 1.



In an earlier report, we have described our preliminary results on the selective cyclopropanation of α-allenic alchohols using samarium/diiodomethane as the carbenoid reagent,[22] eq 2.

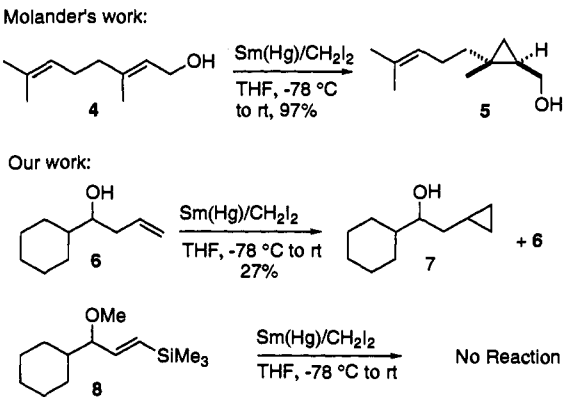


Methylenecyclopropane carbinols were obtained exclusively, with nearly complete chemoselectivity and very good levels of diastereoselectivity. We now wish to present a full account of our studies, including improved reaction conditions and absolute proof of the relative stereochemistry for all the methylenecyclopropanes synthesized.

Results and Discussion

Reactions in which a hydroxyl group directs a reagent to a nearby site represent a powerful method for regio- and stereocontrolled construction of complex molecules.[23-27] From Molander's seminal studies and our work, it is clear that the hydroxyl moiety is essential for an efficient samarium-mediated cyclopropanation. For example, the highly chemoselective cyclopropanation of the allylic double bond of geraniol **4** was reported,[27b] Scheme 2. The Simmons–Smith reagent and its variants yield products resulting from cyclopropanation of the isolated double bond, even when this double bond is remote from the hydroxyl moiety.[28] In contrast, not even trace amounts of these byproducts were observed using the samarium/diiodomethane procedure. To provide further evidence for the importance of the relative position of the hydroxyl group and olefin, treatment of the homoallylic substrate **6** with an excess of samarium/diiodomethane was studied. Only 27% of the cyclopropanated product **7**, along with recovered starting material, was obtained. Moreover, no reaction was observed when cyclopropanation of the allylic methyl ether **8** was attempted, indicating the importance of the *hydroxyl* moiety.

Scheme 2



We considered that the most efficient route to the target methylenecyclopropanes would be the regioselective cyclopropanation of an allenic alcohol, Scheme 1, route h. Cyclopropanation of α-allenic alcohols was first reported in 1967 by Bertrand and Maurin using the classical Simmons–Smith conditions.[19a,24] Equimolar mixtures of methylenecyclopropanes **2b** and **3b** and spiropentanes **9** and **10** were obtained, Table 1, entry 1. We reexamined this procedure along with several more recent modifications of the Simmons–Smith process. Allenic alcohol **1b** was chosen as the test substrate. The four possible products, **2b**, **3b**, **9**, and **10**, resulting from mono- and dimethylenation, respectively, are shown in Figure 1.[29]

Selective cyclopropanation of either double bond could not be achieved employing the Simmons–Smith and other zinc reagents, entries 3–11. Mixtures of regio- and stereoisomers were always obtained. However, it should be noted that the carbenoid did react preferentially with the proximal double bond, but the product is nearly as reactive as the starting material. That is, when reactions are stopped prematurely or when equimolar amounts of substrate and carbenoid are used, mono versus bis cyclopropanation ratios of 5:1 (entry 3) and 2.5:1 (entry 5) were obtained. However, when reactions were quenched when all the starting material had just been consumed, the spiropentane is produced

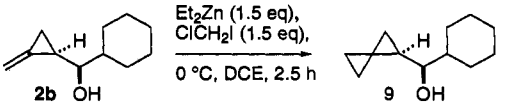


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Table 1. Comparison of Various Cyclopropanating Agents

entry	substrate	conditions: metal (equiv)	conditions: dihalomethane (equiv)	conditions: solv, temp	methylenecyclopropane diastereoselectivity (%): 2	methylenecyclopropane diastereoselectivity (%): 3	spiropentane diastereoselectivity (%): 9	spiropentane diastereoselectivity (%): 10	% conversion[a]
1	**1c**	Zn(Cu) (2.1)	CH_2I_2 (2)	Et_2O, reflux	40	10	35	15	(73)
2	**1c**	Sm(Hg) (7)	CH_2I_2 (7)	THF, −78 °C to rt[b]	80	20	0	0	(67)
3	**1b**	Zn(Cu) (2)	CH_2I_2 (2)	Et_2O, reflux	83		17		40
4	**1b**	Zn(Cu) (5)	CH_2I_2 (3.5)	Et_2O, reflux	27		54		100
5	**1b**	Et_2Zn (1)	$ClCH_2I$ (1)	CH_2Cl_2, 0 °C	67	3	20	10	69
6	**1b**	Et_2Zn (2.1)	CH_2I_2 (2.1)	toluene, 0 °C to rt	45		55		92
7	**1b**	Et_3Al (1.2)	CH_2I_2 (1.2)	CH_2Cl_2, 0 °C to rt					<5[c]
8	**1b**	1. *n*-BuLi (1), hexanes, °C 2. Et_2Zn (1), $ClCH_2I$ (1), CH_2Cl_2, 0 °C to rt			85	trace	13	3	37
9	**1b**	1. NaH (2), CH_2Cl_2, 0 °C 2. Et_2Zn (1), $ClCH_2I$ (1), CH_2Cl_2, 0 °C to rt			91	2	4	3	83
10	**1b**	1. NaH (1.2), CH_2Cl_2, 0 °C 2. Et_2Zn (2.4), $ClCH_2I$ (2.4), CH_2Cl_2, 0 °C to rt			72		22	6	100
11	**1b**	1. KHMDS (1), toluene, 0 °C 2. Et_2Zn (1), $ClCH_2I$ (1), CH_2Cl_2, 0 °C to rt			82		18	trace	20
12	**1b**	Sm (10)	$ClCH_2I$ (10)	THF, −78 °C to rt	90	10	0	0	(82)

[a] Isolated yields are shown in parentheses. [b] rt = room temperature. [c] When 3 equiv of Et_3Al and 2 equiv of CH_2I_2 were used, decomposition of the starting material occurred.

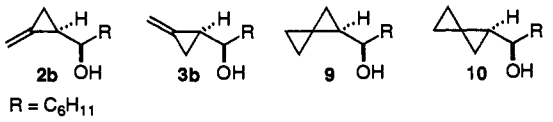


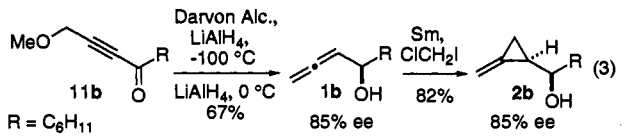
Figure 1.

in equimolar amounts or is the predominant product, entries 4 and 6. We also investigated whether an alkoxide would direct the carbenoid to the allene with higher regioselectivity than the free alcohol. Comparison of entries 6 with 9 and 10 shows that increased levels of selectivity are indeed observed. Under carefully optimized conditions, a 12:1 mixture favoring the methylenecyclopropane could be obtained with NaH deprotonation prior to treatment with 1 equiv of $Et_2Zn/ClCH_2I$ when conversion was 80% complete, entry 9. Unfortunately, a considerable erosion of the selectivity resulted when all the starting allenic alcohol had just been consumed, entry 10. Among the bases used for deprotonation, the best results were obtained with NaH. Deprotonation with *n*-BuLi or KHMDS, prior to treatment with the cyclopropanating agent, resulted in considerable amounts of spiropentane even at low percent conversion, entries 8 and 11. However, using the samarium/diiodomethane cyclopropanation conditions, a highly selective process (>70:1) ensued to yield only methylenecyclopropane products even without prior deprotonation, entries 2 and 12.

Enantiomerically Enriched Starting Materials

In keeping with the needs of modern synthetic methodology, an efficient route to enantiomerically pure allenic alcohols was needed.[30] We have developed a one-pot, two-step enantioselective reduction of substituted ynones, leading directly to enantiomerically enriched allenic alcohols as described below.

Many two-step, two-pot reaction sequences involving the highly enantioselective reduction of an ynone to an optically active propargylic alcohol (e.g. Noyori's Binal-H and chiral boron reagents),[31,32] followed by an S_N2' reduction with $LiAlH_4$, can be envisioned. The method of Mosher for the enantioselective reduction of ynones with the $LiAlH_4$/Darvon alcohol chiral complex was, however, considered to be ideal for a two-step, one-pot protocol.[33] Enantioselectivities of 85–95% are generally obtained when a propargyl ketone is added slowly to the preformed chiral aluminum hydride complex at low temperature.[34] It is also well established that treatment of 4-halo-, 4-(trialkylammonio)-, and 4-alkoxy-2-butyn-1-ols with $LiAlH_4$ provides α-allenic alcohols.[30a,35] Since $LiAlH_4$ is required in both steps, we were intrigued by the possibility of an operationally simple protocol to optically active α-allenic alcohols, eq 3.



In a typical experiment, an ethereal solution of $LiAlH_4$ and Darvon alcohol, premixed at 0 °C, was cooled to −100 °C, and a solution of the ynone **11b** in ether was added slowly at this temperature. When the addition was complete, stirring was continued until all the starting material was consumed. The mixture was allowed to warm to 0 °C, and another 1 equiv of $LiAlH_4$ was added portionwise. Allenic alcohol **1b** was obtained in 85% ee in good yield.[36] It should be noted that, despite the fact that hydridic species were still present (visualized by a vigorous reaction with gas evolution when water was added), no S_N2' displacement reaction would occur *unless* fresh $LiAlH_4$ was added.[37]

Enantioselectivities vary from 82% for *n*-alkyl-substituted ynones to 93% when the substitution is a *tert*-butyl group, Table 2.[38,39] When the methoxy leaving group is changed to a

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(35) For a recent review, see ref 26, p 1350.

(36) Similar observations were made by Mosher and Yamaguchi about unreactive aluminum hydride equivalents in other reactions; see ref 33a.

(37) For another strategy yielding moderately and highly enantiomerically enriched α-allenic alcohols, respectively, see: (a) Boldrini, G. P.; Lodi, L.; Tagliavini, E.; Tarasco, C.; Trombini, C.; Umani-Ronchi, A. *J. Org. Chem.* **1987**, *52*, 5447. (b) Corey, E. J.; Yu, C.-M.; Lee, D.-H. *J. Am. Chem. Soc.* **1990**, *112*, 878.

Table 2. Enantioselective Reduction of Propargylic Ketones

Entry	Substrate	Product	Enantioselectivity (%)	Yield (%)
1	**11a** R = *t*-Bu	**12a**	92	98
2	**b** *c*-hexyl	**b**	79	92
3	**11a** R' = Me R = *t*-Bu	**1a**	93	44
4	**b** *c*-hexyl	**b**	85	67
5	**c** *n*-heptyl	**c**	82	72
6	**d** R' = THP R = *t*-Bu	**d**	86	70

tetrahydropyranoxy group, enantioselectivities are slightly lower; compare entries 3 and 6. No loss of enantioselectivity was obtained in the second step of the procedure. If the reaction was quenched at −100 °C after the enantioselective reduction of the ketone was complete, propargyl alcohols with similar levels of selectivities were obtained, compare entries 1, 3 and 2, 4, respectively. Cyclopropanation of the enantiomerically enriched allenic alcohol **1b** showed that the enantiomeric purity was maintained in the formation of **2b**.

With the possibility of easy access to enantiomerically enriched starting materials in mind, the samarium/dihalomethane cyclopropane conditions were further investigated, and its scope was studied. As can be seen from Table 3, a variety of allenes can be cyclopropanated in moderate to good yields using diiodomethane as the methylene-transfer agent. For hindered substrates, e.g. tertiary alcohols and terminally substituted allenic alcohols, yields of approximately 40% were obtained and a considerable amount of starting material was recovered, entries 5–7. However, when the more reactive chloroiodomethane was used in the cyclopropanation, yields improved to 60–70% for these more hindered substrates, while an 82% yield was obtained for allenic alcohol **2b**, entry 2.[27b,c,40,41] Importantly, the reaction is applicable for the synthesis of simple and more functionalized alkylidenecyclopropanes, entries 8–11.

The diastereoselectivity for unsubstituted and terminally substituted allenic alcohols depends on the size of the carbinol side chain (R group). The selectivity increases in the series isopropyl (4.0:1), cyclohexyl (9.5:1), *tert*-butyl (50:1), leading to synthetically useful levels of selectivity; see entries 1–4. An *n*-alkyl group gave low and opposite selectivity, a trend which has previously been observed in samarium-mediated cyclopropanations.[27b,c,42] It is also interesting to observe that when the hydrogens on the terminal position are substituted for two alkyl chains, the selectivity drops from 9.5:1 to 1.7:1; compare entries 2 and 5. The detrimental effect of the propyl groups on the diastereoselectivity indicates that the propyl groups override the stereochemical preference set by the R group. The steric interaction between the propyl groups and the incoming carbenoid is also reflected in the lower yields of cyclopropanation for this substrate.

Diastereoselectivity was measured by ^{1}H (400 MHz) NMR and/or CGC on the crude reaction mixtures. When methylenation was very stereoselective, an authentic sample of the major

Table 3. Directed Cyclopropanation of α-Allenic Alcohols

Entry	Substrate	Product Diastereoselectivity[a]			Yield[b] (%)
		2	:	**3**	
1	**1a** R = *t*-Bu	50	:	1	57
2	**b** *c*-hexyl	9.5	:	1	82[d], 64
3	**c** *i*-Pr	4.0	:	1	67
4	**d** *n*-heptyl	1	:	2.1	73
		14	:	**15**	
5	**13** R = *c*-hexyl, R' = *n*-Pr	1.7	:	1	70[d], 43
		17			
6	**16** R, R' = -(CH$_2$)$_4$-				58[d], 30
7	**18** R = *i*-Pr, R' = Me			**19**	46
		21	:	**22**	
8	**20a** R = *c*-hexyl, R' = Me	7.9	:	1	66
9	**b** *n*-heptyl, R' = Me	1	:	2.1	52
10	**c** *c*-hexyl, R' = MeO	50	:	1	47[c]
11	**d** *n*-heptyl, R' = MeO	13	:	1	59[c]

[a] Diastereoselectivities determined by CGC, using a Carbowax HP-20M column, unless noted otherwise. [b] Isolated yield of pure product. [c] Diastereoselectivity determined by ^{1}H NMR (400 MHz). [d] $ClCH_2I$ was used in the cyclopropanation; see text.

diastereomer was subjected to an oxidation (PCC, NaOAc)/reduction ($LiAlH_4$) sequence to obtain, after chromatography, the minor diastereomer. Assignment of the relative stereochemistry of compounds **2a-d** and **3a-d** was achieved via independent synthesis from a compound with known stereochemistry and via derivatization to a conformationally locked 3-oxabicyclo[3.1.0]-hexane followed by NOE studies (*vide infra*). For the 1,1-disubstituted allenes **20c,d**, nonbonded steric interaction between R and R′ (1,2 interaction) appears to be less important than electronic effects. Comparison of the two series of entries 2, 8, 10 and 4, 9, 11 clearly supports this statement.

Transition structures with the hydroxyl group pointing "outside" can be used as a working model to explain the observed diastereoselectivities, Scheme 3. Pereyre, and later Molander, used this model to explain the diastereoselection for the respective zinc- and samarium-promoted cyclopropanations of allylic alcohols.[27] Ab initio calculations by Houk supported these models, and they are now often referred to as "the outside Houk model".[43]

In this model the hydroxyl, which delivers the carbenoid, and the olefin are at an angle of approximately 150°.[44] These transition structures are quite different from those frequently used to explain the diastereoselectivities for the hydroxyl-directed hydrogenation.[23] In the latter case the hydroxyl group is believed to be oriented perpendicularly to the olefin. One of the

(38) Either enantiomeric propargyl alcohol can be prepared in high ee via this reaction; see ref 33b. Approximately 20% of the allylic alcohol formed from a competing hydroalumination reaction was also observed when the allenic alcohol was prepared via the two-step, one-pot sequence.

(39) For $LiAlH_4$ reductions of optically active propargyl alcohols, see: (a) Claesson, A.; Olsson, L.-I.; Sullivan, G. R.; Mosher, H. S. *J. Am. Chem. Soc.* **1975**, *97*, 2919. (b) Claesson, A.; Olsson, L.-I. *J. Am. Chem. Soc.* **1979**, *101*, 7302. (c) Bertrand, M.; Gil, G.; Kumar, A. *Nouv. J. Chim.* **1980**, *4*, 69.

(40) Yields were also affected by the source of samarium; best yields were obtained when samarium from Rhône Poulenc (Shelton, CT) was employed.

(41) Denmark, S. E.; Edwards, J. P. *J. Org. Chem.* **1991**, *56*, 6974.

(42) Lautens, M.; Delanghe, P. H. M. *J. Org. Chem.* **1992**, *57*, 798.

(43) (a) Paddon-Row, M.; Rondan, N. G.; Houk, K. N. *J. Am. Chem. Soc.* **1982**, *104*, 7162. (b) Houk, K. N.; Rondan, N. G.; Wu, Y.-D.; Metz, J. T.; Paddon-Row, M. N. *Tetrahedron* **1984**, *40*, 2257. (c) Mareda, J.; Rondan, N. G.; Houk, K. N. *J. Am. Chem. Soc.* **1983**, *105*, 6997.

(44) It should be noted that in hydroxyl-directed cyclopropanation reaction involving dichlorocarbene, the transition structure contains a OCC=C dihedral angle of about 90°; Mohamadi, F.; Still, W. C. *Tetrahedron Lett.* **1986**, *27*, 893.

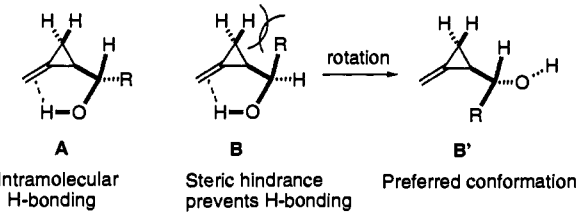
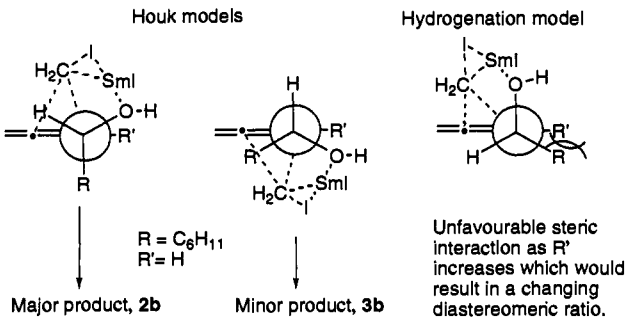


Figure 2.

Scheme 3



consequences of the cyclopropanation and hydrogenation models is apparent when considering the effect on diastereoselectivities upon increasing size of the R′ groups. In the hydrogenation model, an increase in the size of R′ results in a reversal of diastereoselectivities in order to minimize interaction between R and R′. We, however, do not observe any significant change in selectivities when a methyl group (R′) is introduced in the allenic position, Table 3; compare entries 2, 8 and 4, 9, respectively. Since the R and R′ groups are too far apart to cause any interaction in both reactive rotamers, no change in selectivity is expected when R′ increases from H to Me. However, the observations do fit the transition-state structures based on the Houk model.

In contrast, introduction of the methoxy substituents has a profound effect on the diastereoselectivities as increasing levels of selectivities are observed (compare entries 2, 8, 10 (R = cyclohexyl) and 4, 9, 11 (R = *n*-heptyl)). Although it is not yet clear why improved diastereoselectivities are observed for the α-methoxy-substituted allenes, these selectivities are routinely very high, irrespective of the R group.

Determination of Relative Stereochemistry

We are also able to make an unequivocal assignment of the relative stereochemistry of the diastereomeric methylenecyclopropanes. Earlier, Bertrand and Maurin considered the behavior of the two diastereomers using gas and thin-layer chromatography and concluded that the population of the conformers was responsible for the difference in behavior. Their assignment was based on the weak intramolecular hydrogen bonding between the hydroxyl and the alkene portion of the methylenecyclopropyl carbinol.[45,46] Due to steric interactions, this hydrogen bonding is only possible in one of the two diastereomers, Figure 2. While diastereomer A has the possibility of intramolecular hydrogen bonding, this is not favored for conformer B because of a nonbonded interaction between the cis proton and the carbinol R group. Diastereomer B will therefore prefer a conformation like that shown in B′. Diastereomer A, having intramolecular hydrogen bonding, will display a hydrogen-bonding peak in the IR spectrum and decreased polarity, compared with the non-hydrogen-bonded diastereomer B′. The decreased polarity of A versus B′ arises from the unavailability of the hydroxyl functionality of A to interact intermolecularly and is reflected in the smaller retention times and R_f values in gas and thin-layer chromatography, respectively. Although these observations may be of assistance, a more secure method was necessary. Moreover, this tool would not be reliable for more substituted methylenecyclopropanes **21** and **22**, as the methyl and methoxy substituents provide additional steric hindrance.

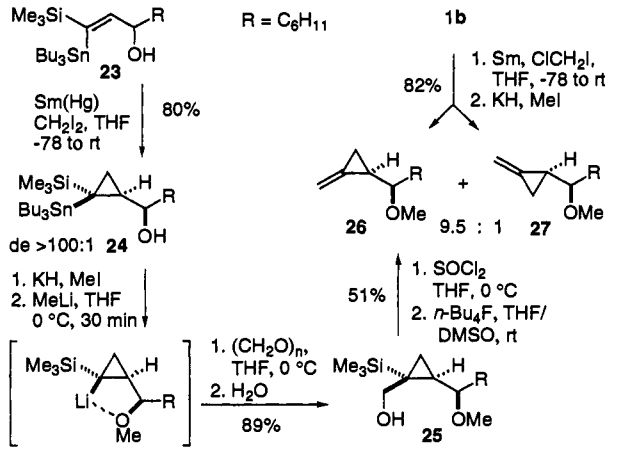


Figure 3.

We have shown in an earlier report that the cyclopropanation of a silylstannyl-substituted allylic alcohol **23** (using samarium/CH_2I_2) yields the corresponding cyclopropane **24** with extremely high diastereoselectivity, Figure 3.[42] The (*Z*)-tributyltin group acts as the diastereoselective controller group via an allylic strain dominated process.[47] After protection of the hydroxyl functionality as a methyl ether, smooth transmetalation can be achieved by treatment with MeLi (THF, 0 °C, 30 min). When the resulting lithiocyclopropane was trapped with paraformaldehyde, the cyclopropyl carbinol **25** was isolated in 89% yield. Treatment of this compound with $SOCl_2$ (THF, 0 °C), followed by tetrabutylammonium fluoride, gave the methylenecyclopropane **26** in an overall yield of 45% from the silylstannyl cyclopropane. The ^{13}C NMR spectra (100 MHz) of **26** and of both methylated diastereomers, obtained from the direct regioselective methylenation of the α-allenic alcohol **1b**, were compared. The chemical shift differences between **26** and **27** (typically >3 ppm) clearly show that the major product from the cyclopropanation was **26**.

Spectroscopic Stereochemical Assignment. Stereochemical assignment of **2a,c,d** (and their diastereomers **3a,c,d**) was initially made by analogy with the GC and TLC retention times for each set of diastereomers. In addition, a striking trend in the ^1H NMR for the chemical shift of the methylene protons was observed. Within one diastereomeric series the difference in chemical shift of each methylene proton ($\Delta\delta$) was considerably larger than in the other series,[48] Table 4. The observed NMR trend holds for compounds **21c** and **22a**, for which the relative stereochemistry was unambiguously confirmed via X-ray structure determination,[49] and for **2b**, which was synthesized via an independent route. This tool therefore further supports the preliminary assignment of relative stereochemistry made, based on CGC retention times and TLC R_f values, and more importantly can be used as a guide to the assignment of new methylenecyclopropane carbinols, provided both diastereomers are available.

Assignment Using Locked Derivatives. Further confirmation of the relative stereochemistry for the diastereomeric products **2d** and **3d** was obtained by NMR studies of conformationally locked derivatives.

Derivatization of both diastereomeric isomers of the methylenecyclopropanes **2b,d** and **3b,d** into the more rigid 3-oxabicyclo-

(45) Maurin, R.; Bertrand, M. *Bull. Soc. Chim. Fr.* **1970**, 2261.
(46) (a) Wiberley, S. E.; Bunce, S. E. *Anal. Chem.* **1952**, *24*, 623. (b) Joris, L.; Schleyer, P. v. R.; Gleiter, P. *J. Am. Chem. Soc.* **1968**, *90*, 327 and references therein.
(47) For a recent review on allylic strain, see: Hoffmann, R. W. *Chem. Rev.* **1989**, *89*, 1841.
(48) For a detailed study of coupling constants and chemical shifts in some methyl-substituted methylenecyclopropanes, see: Saal, W. von der; Risler, W.; Stawitz, J.; Quast, H. *J. Org. Chem.* **1983**, *48*, 2374 and references therein.
(49) Details of the crystal structure investigation are available on request from the Director of the Cambridge Crystallographic Data Centre, 12 Union Road, GB-Cambridge CB2 1EZ (U.K.), on quoting the full journal citation.

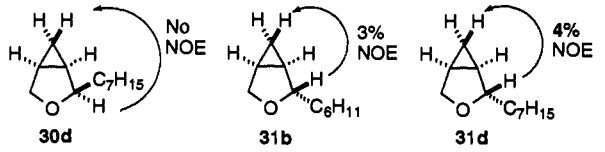
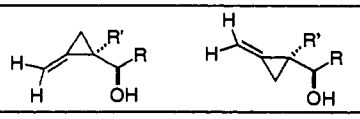


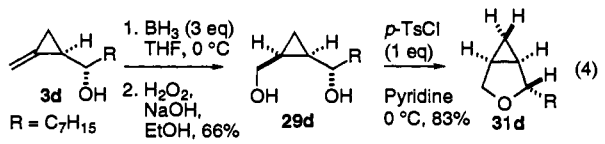
Figure 4.

Table 4. Chemical Shifts of Methylene Protons



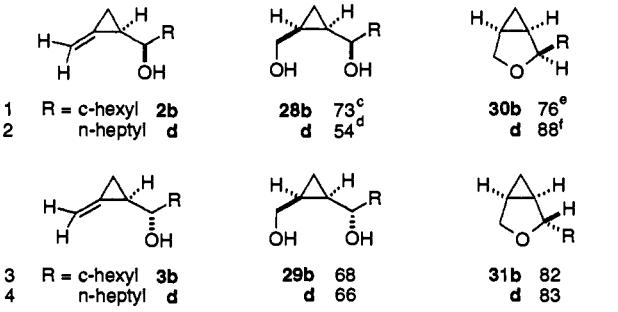
Entry	Substrate		Chemical Shifts δ (ppm)	(Δδ) (Small)	Chemical Shifts δ (ppm)	(Δδ) (Large)
		R' = H,				
1	**2, 3a**	R = *t*-Bu	5.40, 5.35	(0.05)	--	--
2	**b**	*c*-hexyl	5.40, 5.37	(0.03)	5.50, 5.44	(0.06)
3	**c**	*i*-Pr	5.41, 5.37	(0.04)	--	--
4	**d**	*n*-heptyl	5.39, 5.39	(0.00)	5.49, 5.42	(0.07)
		R' = Me,				
5	**19, 20a**	R = *c*-hexyl	5.35, 5.31	(0.04)	5.47, 5.34	(0.13)
6	**b**	*n*-heptyl	5.35, 5.34	(0.01)	5.43, 5.31	(0.12)
		R' = OMe,				
7	**19, 20c**	R = *c*-hexyl	5.56, 5.53	(0.03)	5.76, 5.57	(0.19)
8	**d**	*n*-heptyl	5.63, 5.54	(0.09)	5.69, 5.53	(0.16)

[3.1.0]hexanes **30** and **31** made it possible to obtain stereochemical assignment based on NOE difference spectroscopy, Figure 4. An NOE between one of the clearly distinguishable cyclopropyl protons and the furan ring protons is only possible in one of the isomers. Conversion to the 3-oxabicyclo[3.1.0]hexanes was attempted under various conditions. However, $AgNO_3/CaCO_3$,[50] phenylselenyl chloride,[50b,51] Br_2,[52] NIS, and KOtBu[53] all failed to induce ring closure.[54] Instead, a two-step procedure to the target 3-oxabicyclo[3.1.0]hexanes was used, eq 4. As expected, hydroboration with BH_3·SMe_2, followed by basic oxidation with H_2O_2 of either diastereomer, occurred with high regioselectivity and in good yields, Table 5.



Moreover, high facial selectivity, from the stereochemically less hindered side of the double bond, was observed to give the desired cis-substituted cyclopropane diols **28** and **29**. Treatment of the diols with 1 equiv of *p*-TsCl in pyridine led to the 3-oxabicyclo[3.1.0]hexanes **30** and **31** in one step in good yields.[55] The ring closure reaction involves selective tosylation of the primary alcohol, followed by intramolecular displacement of the tosylate leaving group by the secondary alcohol.[56] In the tosylation/cyclization of **28b,d**, the desired products **30b,d** were contaminated with 10% of the epimeric products **31b,d**. These byproducts arise from tosylation of the secondary alcohol followed by intramolecular S_N2 displacement by the primary alcohol, with inversion of stereochemistry at the secondary carbinol center. NMR irradiation experiments showed small NOE enhancements for the 3-oxabicyclo[3.1.0]hexanes **31b,d**, Figure 4.

Table 5. Hydroboration of Methylenecyclopropanes and Cyclization to 3-Oxabicyclo[3.1.0]hexanes



Entry	Substrate		Diol[a] (% yield)	3-Oxabicyclo[3.1.0] hexane (% yield)[b]
1	R = *c*-hexyl	**2b**	**28b** 73[c]	**30b** 76[e]
2	*n*-heptyl	**d**	**d** 54[d]	**d** 88[f]
3	R = *c*-hexyl	**3b**	**29b** 68	**31b** 82
4	*n*-heptyl	**d**	**d** 66	**d** 83

[a] Conditions for the hydroboration/oxidation: (1) BH_3·SMe_2 (3 equiv), THF, 0 °C, 2 h; (2) H_2O_2, NaOH, EtOH. [b] Conditions for the cyclization; *p*-TsCl (1 equiv), pyridine, 0 °C, 3 h. [c] The product was isolated as an inseparable 13:1 mixture of **28b** and its trans-substituted cyclopropyl epimer. [d] The product was isolated as an inseparable 16:1 mixture of **28d** and its trans-substituted cyclopropyl epimer. [e] The product was contaminated with 10% of the epimeric 3-oxabicyclo[3.1.0]hexane **31b**. [f] The product was contaminated with 19% of the epimeric 3-oxabicyclo[3.1.0]-hexane **31d**.

Thus, we have used a combination of X-ray crystallography, independent synthesis from a stereochemically defined compound, and NMR experiments of the conformationally rigid 3-oxabicyclo-[3.1.0]hexanes **30** and **31** to unambiguously prove the relative stereochemistry for several of the substituted methylenecyclopropanes we prepared. This allows us to confirm the early stereochemical assignment made by Bertrand and Maurin, which was based on the assumption of selective intramolecular H-bonding between the hydroxyl moiety and the exocyclic double bond for the two diastereomeric compounds.[45]

Summary

We have shown that substituted, enantiomerically enriched methylenecyclopropanes carbinols are available in three steps, starting from racemic ynones via a two-step, one-pot asymmetric reduction, followed by a highly chemoselective cyclopropanation of the α-allenic alcohol. Moderate to excellent diastereoselectivity is obtained for a variety of allenic alcohols, depending on the size of the carbinol side chain and (R group) and the substitution on the allene. Currently, we are exploring these more functionalized methylenecyclopropane in inter- and intramolecular Ni(0)- and Pd(0)-catalyzed [3+2] cycloadditions for the synthesis of highly substituted five-membered-ring systems.

Experimental Section

General. Analytical thin-layer chromatography (TLC) was performed on precoated aluminum-backed silica gel (Merck 60F-254). Standard column chromatography was performed using 230–400 mesh silica gel.[57] Melting points were obtained on a Fisher-Johns melting point apparatus and are uncorrected. Infrared spectra were taken on a Nicolet 8210E FTIR spectrophotometer. ^1H and ^{13}C NMR spectra were recorded on a Varian Gemini-200 or VXR-400 spectrometer. ^{19}F and ^{119}Sn NMR were recorded on a Varian Gemini-300 spectrometer. Chemical shifts for ^1H NMR spectra are reported in parts per million from tetramethylsilane with the solvent resonance as the internal standard (chloroform: δ 7.24 ppm). Chemical shifts for ^{13}C NMR spectra are reported in parts per million from tetramethylsilane with the solvent as the internal standard (deuteriochloroform: δ 77.00 ppm). Chemical shifts for ^{119}Sn NMR are

(50) (a) Olson, L.-I.; Claesson, A. *Synthesis* **1979**, 743. (b) Marshall, J. A.; Wang, X. *J. Org. Chem.* **1991**, *56*, 4913.

(51) (a) Beaulieu, P. L.; Morisset, V. M.; Garrat, D. G. *Tetrahedron Lett.* **1980**, *21*, 129. (b) Marshall, J. A.; Wang, X. *J. Org. Chem.* **1990**, *55*, 2995.

(52) Bridges, A. J.; Thomas, R. D. *J. Chem. Soc., Chem. Commun.* **1984**, 694.

(53) Magnus, P.; Albaugh-Robertson, P. *J. Chem. Soc., Chem. Commun.* **1984**, 804.

(54) Ring closure reactions of α-allenic alcohols have, however, been reported under many of the examined conditions; see refs 50–53.

(55) For other approaches toward 3-oxabicyclo[3.1.0]hexanes, see for example: (a) Grandjean, D.; Pale, P.; Chuche, J. *Tetrahedron Lett.* **1992**, *33*, 4905. (b) Harvey, D. F.; Brown, M. F. *J. Org. Chem.* **1992**, *57*, 5559. (c) Weng, W.-W.; Luh, T.-Y. *J. Org. Chem.* **1993**, *58*, 5574.

(56) Selective tosylations of primary alcohols in the presence of secondary alcohols are well-established reactions. For two recent examples, see: (a) Ishihara, K.; Kurihara, H.; Yamamoto, H. *J. Org. Chem.* **1993**, *58*, 3791. (b) Boons, G.-J.; Castle, G. H.; Clase, J. A.; Grice, P.; Ley, S. V.; Pinel, C. *Synlett* **1993**, 913.

(57) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

reported in parts per million using tetramethyltin as the external reference (0.00 ppm). High-resolution mass spectra were recorded with a VG 70-250S spectrometer. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, TN. Optical rotations were taken with a Perkin-Elmer 243B polarimeter. Capillary GC analyses were obtained from a Hewlett-Packard Model 5890A gas–liquid chromatograph, using a HP 20M Carbowax column, equipped with a Hewlett-Packard Model 3396A digital integrator. All glassware was flame dried under an inert atmosphere of dry nitrogen or argon.

Reagents. Unless stated otherwise commercial reagents were used without purification. Tetrahydrofuran and diethyl ether were distilled immediately prior to use from sodium wire/benzophenone. Pyridine and dichloromethane were distilled immediately prior to use from calcium hydride. Diiodomethane was distilled from copper powder at reduced pressure. Samarium metal (<40 mesh) was purchased from Rhône-Poulenc, Shelton, CT. *p*-Toluenesulfonyl chloride was purified via washing of an ethereal solution with 10% aqueous NaOH and crystallized by cooling on dry ice.

Starting Materials. The allenic alcohols **1a-d**, **13**, and **16** were prepared via treatment of the corresponding 4-methoxy- or 4-pyranoxybutyn-1-ol with $LiAlH_4$.[30a] The ynones **11a-d** were obtained via additions of methyl propargyl ether or tetrahydro-2-(2-propynyloxy)-2*H*-pyran to the appropriate aldehyde, followed by NaOAc-buffered PCC oxidation. The 1-methoxy-substituted allenic alcohols **20b,d** were prepared via addition of 1-methoxy-1-lithioallene to the aldehyde.[30b] The 1-methyl-substituted allenic alcohols **20a,c** were prepared via the procedure of Yamamoto.[30c]

General Procedure for the Enantioselective Reduction of Ynones. To a dry round-bottomed flask equipped with a stirbar and capped with a rubber septum was added a suspension of $LiAlH_4$ (1.0 M solution in diethyl ether) followed by diethyl ether. To this suspension was added dropwise via cannula a solution of (*R*)-Chirald in diethyl ether at 0 °C. A white precipitate was formed immediately after the Chirald addition was complete. The flask was cooled to −100 °C, and an ethereal solution of the ynone was added over 1–2 h at this temperature. After the addition was complete stirring was usually continued for an additional 2–6 h. The reaction was quenched at this temperature by addition of either 5% HCl or Rochelle's salt, followed by extraction with diethyl ether. The combined organic layer was washed two times with 5% HCl or Rochelle's salt, washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by Kugelrohr distillation or flash chromatography on silica gel. Alternatively, to obtain the allenic alcohol in one pot, the reaction mixture was allowed to warm to 0 °C and an additional 0.6–1.0 equiv of solid $LiAlH_4$ was added portionwise at this temperature. The reaction was followed by TLC, and when no propargyl alcohol was present anymore, the same aqueous workup and purification was done as above.

(*R*)-(−)-1-Cyclohexyl-2,3-butadienol (1b).[37] According to the general procedure a solution of (*R*)-Chirald (1.76 g, 6.22 mmol) in 17 mL of diethyl ether was added over 5 min to a solution of $LiAlH_4$ (2.64 mL, 1.0 M solution in diethyl ether, 2.64 mmol) in 65 mL of diethyl ether at 0 °C. After stirring for an additional 2 min, a solution of the ynone **11b** (400 mg, 2.22 mmol) in 13 mL of diethyl ether was added over 75 min (2 × 1.0-mL rinse). After stirring for another 2 h at −100 °C, the reaction mixture was treated with $LiAlH_4$ (1.3 mL, 1 M solution in diethyl ether, 1.3 mmol) at 0 °C and stirred for 90 min at this temperature. After purification by flash chromatography on silica gel, eluting with 20:1 to 10:1 hexanes:diethyl ether, **1b** (230 mg, 67%) was obtained as a colorless oil. The ee of this alcohol was found to be 85% by ^1H and ^{19}F NMR analysis of the Mosher ester derivative: R_f = 0.46 on silica gel (hexanes:diethyl ether 2:1); $[\alpha]_D$ = −10.2° (*c* = 2.1 in benzene); IR (cm^{-1}, neat) 3360 (br, s), 2924 (s), 2854 (s), 1954 (m), 1715 (m), 1448 (m), 1082 (m), 1054 (m), 1026 (m), 843 (m); ^1H NMR (200 MHz, $CDCl_3$) δ 5.21 (1H, q, *J* = 6.6 Hz), 4.82 (2H, dd, *J* = 6.6, 2.3 Hz), 3.91 (1H, dtt, *J* = 6.6, 4.7, 2.3 Hz), 1.90–0.90 (11H, m), 1.58 (1H, d, *J* = 4.7 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 207.3, 93.3, 77.0, 74.2, 44.2, 28.7, 28.4, 26.6, 26.2, 26.1. The ee of this alcohol was found to be 85% by ^{19}F NMR analysis of the (*R*)-Mosher ester derivative: ^1H NMR (200 MHz, $CDCl_3$) δ 7.40 (5H, m), 5.20 (1H, m), 4.80 (1H, m), 3.53 (3H, s), 1.82–0.80 (11H, m); ^{19}F NMR (282 MHz, $CDCl_3$) δ −71.70, −71.88.

(*R*)-5,5-Dimethyl-1,2-hexadien-4-ol (1a).[37b] According to the general procedure, a solution of (*R*)-Chirald (285 mg, 1.00 mmol) in 2 mL of diethyl ether was added to a solution of $LiAlH_4$ (0.43 mL, 1.0 M solution in diethyl ether, 0.43 mmol) at 0 °C over 2 min. After stirring for an additional 2 min, a solution of the ynone **11a** (55 mg, 0.36 mmol) in 1.6 mL of diethyl ether was added over 1 h (0.3-mL rinse). After stirring for another 6 h at −100 °C, the reaction mixture was treated with $LiAlH_4$ (0.43 mL, 1 M solution in diethyl ether, 0.43 mmol) at 0 °C and stirred for 1 h at this temperature. After purification by flash chromatography on silica gel, eluting with hexanes:diethyl ether 20:1 to 10:1, **1a** (20 mg, 44%) was obtained as a colorless oil. The ee of this alcohol was found to be 93% by ^{19}F NMR analysis of the (*R*)-Mosher ester derivative.

The allenic alcohol **1a** was also prepared via enantioselective reduction of ynone **11d**. As in the general procedure, a solution of (*R*)-Chirald (176 mg, 0.62 mmol) in 1.5 mL of diethyl ether was added over 2 min to a solution of $LiAlH_4$ (0.27 mL, 1.0 M solution in diethyl ether, 0.27 mmol) in 0.75 mL of diethyl ether at 0 °C. After stirring for an additional 2 min, a solution of the ynone **11d** (50 mg, 0.22 mmol) in 1.2 mL of diethyl ether was added over 1 h (0.3-mL rinse). After stirring for another 6 h at −100 °C, the reaction mixture was treated with $LiAlH_4$ (10.2 mg, 0.27 mmol) at 0 °C and stirred for 2 h at this temperature. After purification by flash chromatography on silica gel, eluting with 10:1 pentane:diethyl ether, **1a** (19.4 mg, 70%) was obtained as a colorless oil. The ee of this alcohol was found to be 86% by ^1H and ^{19}F NMR analysis of the Mosher ester derivative: R_f = 0.68 on silica gel (hexanes:diethyl ether 1:1); IR (cm^{-1}, neat) 3429 (br, m), 2956 (s), 2869 (m), 1955 (m), 1478 (m), 1363 (m), 1051 (m), 1005 (m), 839 (m); ^1H NMR (400 MHz, $CDCl_3$) δ 5.26 (1H, dt, *J* = 6.6, 6.6 Hz), 4.84 (2H, dd, *J* = 6.6, 2.2 Hz), 3.81 (1H, dt, *J* = 6.6, 2.2 Hz), 1.22 (1H, br s), 0.92 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.32, 91.78, 77.33, 77.22, 35.57, 25.39.

(*R*)-Undecadien-4-ol (1d).[37b] According to the general procedure, a solution of (*R*)-Chirald (198 mg, 0.70 mmol) in 2.0 mL of diethyl ether was added over 2 min to a solution of $LiAlH_4$ (0.3 mL, 1.0 M solution in diethyl ether, 0.3 mmol) in 1.0 mL of diethyl ether at 0 °C. After stirring for an additional 2 min, a solution of the ynone **11c** (50 mg, 0.25 mmol) in 1.6 mL of diethyl ether was added over 1 h (0.3-mL rinse). After stirring for another 6 h at −100 °C, the reaction mixture was treated with $LiAlH_4$ (0.3 mL, 1.0 M solution in diethyl ether, 0.3 mmol) at 0 °C and stirred for 2 h at this temperature. After purification by flash chromatography on silica gel and eluting with 10:1 hexanes:diethyl ether, **1d** (31 mg, 72%) was obtained as a colorless oil. The ee of this alcohol was found to be 82% by ^1H and ^{19}F NMR analysis of the Mosher ester derivative: R_f = 0.55 on silica gel (hexanes:diethyl ether 1:1); IR (cm^{-1}, neat) 3346 (br, s), 2959 (s), 2931 (s), 2854 (s), 1954 (s), 1462 (m), 1054 (m), 1026 (m), 843 (s); ^1H NMR (200 MHz, $CDCl_3$) δ 5.21 (1H, q, *J* = 6.6 Hz), 4.82 (2H, d, *J* = 6.6, 2.4 Hz), 4.14 (1H, dddd, *J* = 6.3, 4.8, 2.4, 2.4 Hz), 1.80 (1H, br s), 1.52 (2H, m), 1.24 (10H, m), 0.85 (3H, t, *J* = 6.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.9, 94.9, 77.5, 69.7, 37.5, 31.8, 29.4, 29.2, 25.4, 22.6, 14.1.

(*R*)-(+)-5,5-Dimethyl-1-methoxy-2-hexyn-4-ol (12a). According to the general procedure, a solution of (*R*)-Chirald (300 mg, 1.06 mmol) in 2 mL of diethyl ether was added to a solution of $LiAlH_4$ (0.45 mL, 1.0 M solution in diethyl ether, 0.45 mmol) at 0 °C over 2 min. After stirring for an additional 2 min, a solution of the ynone **11a** (58 mg, 0.38 mmol) in 1.6 mL of diethyl ether was added over 1 h (0.3-mL rinse). After stirring for another 6 h at −100 °C, the reaction was quenched and purified by flash chromatography on silica gel, eluting with 10:1 hexanes:diethyl ether, to yield 58 mg (98%) of **12a**. The ee of this alcohol was found to be 93% by ^1H and ^{19}F NMR analysis of the Mosher ester derivative: $[\alpha]_D$ +4.0° (*c* = 1.8, benzene); IR (cm^{-1}, neat) 3388 (br, s), 2961 (s), 2908 (s), 2871 (s), 2213 (w), 1720 (w), 1676 (s), 1482 (s), 1464 (s), 1365 (s), 1192 (s), 1135 (s), 1094 (s), 1010 (s); ^1H NMR (200 MHz, $CDCl_3$) δ 4.13 (2H, d, *J* = 1.7 Hz), 4.05 (1H, m), 3.37 (3H, s), 1.73 (1H, d, *J* = 5.8 Hz), 0.98 (9H, s); ^{13}C NMR (50 MHz, $CDCl_3$) δ 86.40, 81.30, 71.34, 59.97, 57.61, 35.97, 25.50.

(*R*)-(+)-1-Cyclohexyl-4-methoxy-2-butynol (12b). According to the general procedure, a solution of (*R*)-Chirald (218 mg, 0.77 mmol) in 1 mL of diethyl ether was added to a solution of $LiAlH_4$ (0.34 mL, 1.0 M solution in diethyl ether, 0.34 mmol) at 0 °C over 2 min. After stirring for an additional 2 min, a solution of the ynone **11b** (50 mg, 0.28 mmol) in 1.6 mL of diethyl ether was added over 75 min (2 × 0.3-mL rinse). After stirring for another 6 h at −100 °C, the reaction was quenched and purified by Kugelrohr distillation (95 °C/0.15 mmHg) to yield 47 mg (92%) of **12b**. The ee of this alcohol was found to be 79% by ^1H and ^{19}F NMR analysis of the Mosher ester derivative: $[\alpha]_D$ +7.0° (c = 1.8, benzene); IR (cm^{-1}, neat) 3416 (br, s), 2931 (s), 2854 (s), 1672 (w), 1447 (m), 1448 (s), 1188 (s), 1096 (s), 1012 (s); ^1H NMR (200 MHz, $CDCl_3$) δ 4.19 (1H, m), 4.12 (2H, d, *J* = 1.6 Hz), 3.36 (3H, s), 1.90–1.45 (6H, m), 1.69 (1H, d, *J* = 5.8 Hz), 1.30–1.00 (5H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 86.75, 81.10, 67.10, 59.97, 57.58(2), 44.16, 28.73, 28.29, 26.54, 26.05.

General Procedure for the Synthesis of Methylenecyclopropane with Samarium/Diiodomethane. To a dry round-bottomed flask equipped with a stirbar and capped with a rubber septum was added 5–10 equiv of samarium metal. The flask was flame dried, while flushing with nitrogen.

After the flask was allowed to cool to room temperature, mercuric chloride (10 mol % based on samarium) was added quickly, followed by half of the total volume of THF. The gray suspension was stirred for 10 min. The α-allenic alcohol (1 equiv) was dissolved in an equal volume of THF and transferred via cannula to the flask. The flask was cooled to −78 °C, and diiodomethane was added dropwise. The mixture was allowed to warm to room temperature over 2 h and stirred for an additional 2–4 h. The viscous dark blue reaction mixture was quenched with a saturated aqueous K_2CO_3 solution and extracted three times with diethyl ether. The organic layers were collected, washed three times with brine, dried over anhydrous Na_2SO_4, and filtered. After concentration of the crude product purification was executed by flash chromatography on silica gel.

Cyclopropanation of 5,5-Dimethyl-1,2-hexadien-4-ol (1a). According to the general procedure, using 50 mg (0.40 mmol) of **1a** and 601 mg (4.0 mmol) of samarium in 4 mL of THF, 31.8 mg (57%) of a colorless oil was obtained as a 50:1 mixture of two diastereomers, as determined by GC analysis. After flash chromatography on silica gel, eluting with 20:1 pentane:diethyl ether, the solvent was very carefully removed by distillation and Kugelrohr distillation to yield the pure major diastereomer.

(*R,*S**)-α-(1,1-Dimethylethyl)-2-methylenecyclopropanemethanol (2a, major diastereomer):** R_f = 0.55 on silica gel (hexanes:diethyl ether 1:1); IR (cm^{-1}, neat) 3416 (br, m), 3072 (w), 3051 (w), 2959 (s), 2910 (m), 2868 (m), 1483 (m), 1363 (m), 1124 (m), 1047 (m), 1005 (s), 885 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.40 (1H, m), 5.35 (1H, m), 2.72 (1H, dd, J = 8.9, 3.6 Hz), 1.65 (1H, m), 1.49 (1H, d, J = 3.6 Hz), 1.25 (2H, m), 0.97 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.95, 104.32, 82.04, 35.28, 26.04, 19.27, 6.96; HRMS calcd for $C_9H_{15}O$ $(M-H)^+$ 139.1123, found 139.1124.

A 2.8:1 mixture of the minor and the major diastereomer, respectively, was obtained by NaOAc-buffered PCC oxidation of the pure major diastereomeric methylenecyclopropyl alcohol (**2a**), followed by nonselective reduction of the resulting ketone with $LiAlH_4$. R_f (minor diastereomer) = 0.55 on silica gel (hexanes:diethyl ether 1:1).

Cyclopropanation of (*R*)-(−)-1-Cyclohexyl-2,3-butadienol (1b). According to the general procedure, using 100 mg (0.65 mmol) of (*R*)-**1b** and 977 mg (6.5 mmol) of samarium in 6 mL of THF, 69.2 mg (64%) of a colorless oil was obtained as a 9.5:1 mixture of two diastereomers, as determined by GC analysis. After flash chromatography on silica gel, eluting with 20:1 to 10:1 pentane:diethyl ether, the pure major diastereomer was obtained.

(*R*,*S*)-(−)-α-(Methylenecyclopropyl)cyclohexanemethanol (2b, major diastereomer): $[\alpha]_D$ = −23.1° (c = 1.1 in chloroform); R_f = 0.28 on silica gel (hexanes:diethyl ether 2:1); IR (cm^{-1}, neat) 3381 (br, s), 3072 (w), 3051 (w), 2924 (s), 2854 (s), 1743 (w), 1448 (s), 1406 (m), 1124 (m), 1089 (m), 1019 (s), 885 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.40 (1H, m), 5.37 (1H, m), 2.83 (1H, ddd, J = 8.4, 6.2, 3.4 Hz (J = 3.4 Hz disappears with D_2O)), 1.87–1.58 (6H, m), 1.50 (1H, d, J = 3.4 Hz), 1.46 (1H, m), 1.30–0.99 (6H, m), 0.95 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.28, 104.36, 78.69, 44.04, 28.94, 28.89, 26.52, 26.27, 26.12, 20.82, 7.19; HRMS calcd for $C_{11}H_{17}O$ $(M-H)^+$ 165.1279, found 165.1289. The ee of this alcohol was found to be 84% by ^{19}F NMR analysis of the (*R*)-Mosher ester derivative: ^{19}F NMR (282 MHz, $CDCl_3$) δ −71.54, −71.73.

The minor diastereomer was obtained by NaOAc-buffered PCC oxidation of the pure major diastereomeric methylenecyclopropyl alcohol **2b**, followed by nonselective reduction of the resulting ketone with $LiAlH_4$. The resulting mixture of diastereomers was separated and purified by flash chromatography on silica gel, eluting with 20:1 to 10:1 hexanes: diethyl ether, yielding the minor diastereomer.

(*R,*R**)-α-(Methylenecyclopropyl)cyclohexanemethanol (3b, minor diastereomer):** R_f = 0.47 on silica gel (hexanes:diethyl ether 2:1); IR (cm^{-1}, neat) 3402 (br, s), 3072 (w), 3044 (w), 2924 (s), 2854 (s), 1743 (w), 1448 (s), 1398 (m), 1131 (m), 1103 (m), 1012 (s), 892 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.50 (1H, m), 5.44 (1H, m), 2.94 (1H, ddd, J = 7.0, 6.2, 5.7 Hz (J = 5.7 Hz disappears with D_2O)), 1.92–1.58 (6H, m), 1.48 (1H, m), 1.37 (1H, m), 1.30–1.05 (6H, m), 0.97 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.26, 104.25, 78.54, 44.49, 28.95, 28.63, 26.53, 26.26, 14.12, 19.61, 8.23.

Cyclopropanation of 5-Methyl-1,2-hexadien-4-ol (1c). According to the general procedure, using 700 mg (6.24 mmol) of **1c** and 6.6 g (43.7 mmol) of samarium in 40 mL of THF, 314 mg (40%) of a colorless oil was obtained as a 4.0:1 mixture of two diastereomers, as determined by GC analysis. After flash chromatography on silica gel, eluting with 20:1 pentane:diethyl ether, the solvent was very carefully removed by distillation and Kugelrohr distillation to yield the pure major diastereomer.

(*R,*S**)-2-Methylene-α-(1-methylethyl)cyclopropanemethanol (2c, major diastereomer):** R_f = 0.47 on silica gel (hexanes:diethyl ether 2:1); IR (cm^{-1}, neat) 3381 (br, s), 3072 (w), 2959 (s), 2931 (s), 2875 (s), 1469 (m), 1384 (m), 1026 (s), 885 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.41 (1H, m), 5.37 (1H, m), 2.83 (1H, t, J = 7.1 Hz), 1.80 (1H, oct, J = 6.7 Hz), 1.54 (1H, br, s), 1.26 (2H, m), 0.98 (3H, d, J = 6.8 Hz), 0.97 (3H, d, J = 6.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.28, 104.32, 79.30, 34.10, 20.68, 18.60, 18.24, 7.24.

R_f (minor diastereomer) = 0.61 on silica gel (hexanes:diethyl ether 2:1).

Cyclopropanation of 1,2-Undecadien-4-ol (1d). According to the general procedure, using 500 mg (2.97 mmol) of **1d** and 3.13 g (20.8 mmol) of samarium in 24 mL of THF, 395 mg (73%) of a colorless oil was obtained as a 2.1:1 mixture of two diastereomers, as determined by GC analysis. Both diastereomers were obtained after flash chromatography on silica gel, eluting with hexanes to 20:1 hexanes:diethyl ether.

(*R,*R**)-α-Heptyl-2-methylenecyclopropanemethanol (3d, major diastereomer):** R_f = 0.26 on silica gel (hexanes:diethyl ether 3:1); IR (cm^{-1}, neat) 3374 (br, m), 3072 (w), 3044 (w), 2959 (s), 2924 (s), 2854 (s), 1462 (m), 1068 (m), 1019 (m), 892 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.49 (1H, m), 5.42 (1H, m), 3.21 (1H, tt, J = 7.1, 5.0 Hz), 1.64–1.50 (3H, m), 1.40 (1H, m), 1.40 (1H, d, J = 5.0 Hz), 1.32–1.21 (10H, m), 0.97 (1H, m), 0.86 (3H, t, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.30, 103.97, 74.28, 37.14, 31.83, 29.64, 29.28, 25.64, 22.65, 21.82, 14.09, 7.53; HRMS calcd for $C_{12}H_{21}O$ $(M-H)^+$ 181.1592, found 181.1595, calcd for $C_{11}H_{19}O$ $(M-CH_3)^+$ 167.1440, found 167.1436.

(*R,*S**)-α-Heptyl-2-methylenecyclopropanemethanol (2d, minor diastereomer):** R_f = 0.39 on silica gel (hexanes:diethyl ether 3:1); IR (cm^{-1}, neat) 3395 (br, s), 3072 (w), 2959 (s), 2931 (s), 2854 (s), 1645 (w), 1462 (m), 1019 (m), 885 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.39 (2H, m), 3.12 (1H, dt, J = 7.5, 5.6 Hz), 1.61 (1H, br s), 1.61–1.50 (3H, m), 1.47–1.32 (2H, m), 1.31–1.20 (9H, m), 0.90 (1H, m), 0.85 (3H, t, J = 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.89, 104.10, 74.26, 37.07, 31.81, 29.60, 29.25, 25.54, 22.64, 22.59, 14.08, 7.50.

Cyclopropanation of 1-Cyclohexyl-4-propyl-2,3-heptadienol (13). According to the general procedure, using 250 mg (1.05 mmol) of **13** and 1.58 g (10.5 mmol) of samarium in 7 mL of THF, 111 mg (43%) of a viscous colorless liquid was obtained as a 1.7:1 mixture of two diastereomers, as determined by GC analysis. Both diastereomers were obtained after flash chromatography on silica gel, eluting with hexanes to 20:1 hexanes:diethyl ether.

(*R,*S**)-α-(1-Propylbutylidenecyclopropyl)cyclohexanemethanol (14, major diastereomer):** R_f = 0.50 on silica gel (hexanes:diethyl ether 3:1); IR (cm^{-1}, neat) 3345 (br, m), 2959 (s), 2931 (s), 2868 (s), 2854 (s), 1469 (m), 1455 (m), 1082 (m), 906 (s), 738 (s); ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.24 (1H, m), 2.09 (4H, m), 2.00–0.95 (19H, m), 0.87 (3H, t, J = 7.4 Hz), 0.85 (3H, t, J = 7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 130.99, 116.92, 76.05, 43.61, 37.06, 36.62, 29.74, 27.38, 26.57, 26.53, 26.31, 21.47, 20.91, 19.47, 14.13, 14.02, 5.60.

(*R,*R**)-α-(1-Propylbutylidenecyclopropyl)cyclohexanemethanol (15, minor diastereomer):** R_f = 0.75 on silica gel (hexanes:diethyl ether 3:1); IR (cm^{-1}, neat) 3459 (br, m), 3030 (w), 2966 (s), 2924 (s), 2854 (s), 1448 (s), 1384 (m), 1082 (m), 1012 (s), 892 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.78 (1H, ddd, J = 8.1, 6.5, 4.3 Hz), 2.18 (2H, m), 2.11 (2H, m), 1.96–1.00 (18H, m), 1.34 (1H, d, J = 4.3 Hz), 0.87 (3H, t, J = 7.4 Hz), 0.86 (3H, t, J = 7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 130.19, 117.80, 80.27, 44.65, 37.51, 36.25, 29.34, 28.88, 26.59, 26.35, 26.19, 21.64, 20.88, 19.51, 14.05, 8.22; HRMS calcd for $C_{17}H_{30}O$ $(M)^+$ 250.2297, found 250.2297.

Cyclopropanation of 1-Hydroxy-1-(1,2-propadienyl)cyclohexane (16). According to the general procedure, using 185 mg (1.34 mmol) of **16** and 1.0 g (6.70 mmol) of samarium in 8 mL of THF, 61 mg (30%) of a colorless oil was obtained after flash chromatography on silica gel, eluting with 20:1 hexanes:diethyl ether.

1-(Methylenecyclopropyl)cyclohexanol (17): R_f = 0.44 on silica gel (hexanes:diethyl ether 2:1); IR (cm^{-1}, neat) 3445 (br, s), 3065 (m), 2981 (s), 2938 (s), 2861 (s), 1743 (w), 1448 (m), 1152 (m), 970 (m), 885 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.44 (1H, m), 5.40 (1H, m), 1.68–1.36 (10H, m), 1.22 (1H, m), 1.10 (2H, m), 0.99 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.15, 104.06, 69.54, 37.67, 36.36, 26.12, 25.67, 22.02, 21.88, 4.76; HRMS calcd for $C_{10}H_{15}O$ $(M-H)^+$ 151.1123, found 151.1129.

Cyclopropanation of 4,5-Dimethyl-1,2-hexadien-4-ol (18). According to the general procedure, using 250 mg (1.98 mmol) of **18** and 2.98 g (19.8 mmol) of samarium in 12 mL of THF, 127 mg (46%) of a colorless oil was obtained. After flash chromatography on silica gel, eluting with 20:1 to 10:1 hexanes:diethyl ether, one diastereomer was obtained.

(*R,*S**)-α-Methyl-2-methylene-α'-(1-methylethyl)cyclopropanemethanol (19, major diastereomer):** R_f = 0.30 on silica gel (hexanes:diethyl

ether 2:1); IR (cm^{-1}, neat) 3445 (br, s), 3072 (w), 2988 (s), 2966 (s), 2875 (s), 1743 (w), 1469 (m), 1370 (s), 1131 (m), 1082 (m), 906 (m), 885 (s); ^1H NMR (200 MHz, $CDCl_3$) δ 5.44 (1H, m), 5.39 (1H, m), 1.80 (1H, septet, J = 6.9 Hz), 1.65 (1H, m), 1.14 (2H, m), 1.11 (1H, s), 1.03 (3H, s), 0.97 (6H, d, J = 6.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.52, 104.02, 73.20, 37.99, 23.99, 22.67, 17.69, 17.42, 5.19; HRMS calcd for $C_9H_{16}O$ $(M)^+$ 140.1201, found 140.1212.

Cyclopropanation of 1-Cyclohexyl-2-methyl-2,3-butadienol (20a). According to the general procedure, using 500 mg (3.01 mmol) of **20a** and 4.52 g (30.1 mmol) of samarium in 30 mL of THF, 361 mg (66%) of a colorless oil was obtained as a 7.9:1 mixture of two diastereomers, as determined by GC analysis. After flash chromatography on silica gel, eluting with hexanes to 10:1 hexanes:diethyl ether, both diastereomers were obtained.

(R^*,S^*)-α-(1-Methyl-2-methylenecyclopropyl)cyclohexanemethanol (21a, major diastereomer): R_f = 0.33 on silica gel (hexanes:diethyl ether 2:1); IR (cm^{-1}, neat) 3409 (br, m), 3072 (w), 3044 (w), 2924 (s), 2854 (s), 1448 (s), 1377 (m), 1019 (s), 990 (s), 885 (s), 738 (m); ^1H NMR (400 MHz, $CDCl_3$) δ 5.35 (1H, br s), 5.31 (1H, dt, J = 2.6, 0.8 Hz), 2.62 (1H, dd, J = 9.1, 2.5 Hz (J = 2.5 Hz disappears with D_2O)), 2.05 (1H, m), 1.78–1.15 (11H, m), 1.10 (3H, s), 0.99 (1H, ddd, J = 8.5, 2.4, 2.1 Hz), 0.92 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.09, 103.88, 81.10, 41.32, 30.20, 29.08, 26.44, 26.20, 25.90, 24.81, 16.31, 15.51; HRMS calcd for $C_{12}H_{19}O$ $(M - H)^+$ 179.1436, found 179.1440.

(R^*,R^*)-α-(1-Methyl-2-methylenecyclopropyl)cyclohexanemethanol (22a, Minor Diastereomer). Recrystallization from diethyl ether gave colorless crystals: R_f = 0.53 on silica gel (hexanes:diethyl ether 2:1); mp = 59–61 °C; IR (cm^{-1}, neat) 3452 (br, m), 3065 (w), 3044 (w), 2924 (s), 2854 (s), 1729 (m), 1448 (m), 1265 (m), 1026 (m), 892 (m); ^1H NMR (200 MHz, $CDCl_3$) δ 5.47 (1H, dt, J = 2.5, 0.7 Hz), 5.34 (1H, m), 2.74 (1H, dd, J = 8.5, 4.3 Hz), 2.05–0.80 (13H, m), 1.33 (1H, d, J = 4.3 Hz), 1.12 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.20, 102.66, 81.12, 41.32, 29.69, 29.35, 26.50, 26.23, 25.97, 23.33, 16.27, 16.18; HRMS calcd for $C_{12}H_{19}O$ $(M - H)^+$ 179.1436, found 179.1430.

Cyclopropanation of 1-Cyclohexyl-2-methoxy-2,3-butadienol (20c). According to the general procedure, using 300 mg (1.65 mmol) of **20c** and 1.73 g (11.6 mmol) of samarium in 15 mL of THF, 151 mg (47%) of a white solid was obtained after flash chromatography on silica gel, eluting with 10:1 hexanes:diethyl ether. Recrystallization from diethyl ether gave colorless crystals.

(R^*,R^*)-α-(1-Methoxy-2-methylenecyclopropyl)cyclohexanemethanol (21c, major diastereomer): R_f = 0.35 on silica gel (hexanes:diethyl ether 1:1); mp = 44–45 °C; IR (cm^{-1}, neat) 3445 (br, m), 3072 (w), 3044 (w), 2924 (s), 2854 (s), 1448 (m), 1237 (m), 1110 (m), 1033 (m), 892 (m); ^1H NMR (500 MHz, $CDCl_3$) δ 5.56 (1H, dd, J = 2.9, 2.4 Hz), 5.53 (1H, dd, J = 2.4, 2.3 Hz), 3.31 (3H, s), 2.97 (1H, dd, J = 8.3, 5.4 Hz), 2.04 (1H, m), 1.82 (1H, m), 1.73 (3H, m), 1.65 (1H, m), 1.45 (1H, ddd, J = 10.8, 2.9, 2.4 Hz), 1.27 (4H, m), 1.13 (1H, m), 0.99 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.02, 107.38, 79.77, 63.78, 55.78, 41.13, 29.56, 29.48, 26.48, 26.19, 26.01, 13.84. Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.33; H, 10.30.

Cyclopropanation of 3-Methyl-1,2-undecadien-4-ol (20b). According to the general procedure, using 170 mg (0.93 mmol) of **20b** and 1.40 g (9.3 mmol) of samarium in 9 mL of THF, 95.2 mg (52%) of a colorless oil was obtained as a 2.1:1 mixture of two diastereomers, as determined by GC analysis. After flash chromatography on silica gel, eluting with 90:9.5:0.5 hexanes:diethyl ether:triethyl amine, both diastereomers were obtained.

(R^*,S^*)-α-Heptyl-1-methyl-2-methylenecyclopropanemethanol (21b, minor diastereomer): R_f = 0.50 on silica gel (hexanes:diethyl ether 1:1); IR (cm^{-1}, neat) 3391 (br, s), 3069 (w), 2959 (s), 2932 (s), 2860 (s), 1459 (s), 1380 (m), 1022 (m), 886 (m); ^1H NMR (400 MHz, $CDCl_3$) δ 5.35 (1H, m), 5.34 (1H, m), 3.09 (1H, ddd, J = 8.1, 5.2, 3.0 Hz), 1.56–1.38 (4H, m), 1.46 (1H, d, J = 3.0 Hz), 1.27 (8H, m), 1.12 (3H, s), 1.08 (1H, dt, J = 8.8, 2.2 Hz), 0.94 (1H, dt, J = 8.8, 2.2 Hz), 0.86 (3H, t, J = 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.77, 103.10, 76.37, 34.14, 31.88, 29.67, 29.30, 26.19, 25.35, 22.69, 16.44, 15.72, 14.14; HRMS calcd for $C_{13}H_{23}O$ $(M - H)^+$ 195.1750, found 195.1745.

(R^*,R^*)-α-Heptyl-1-methyl-2-methylenecyclopropanemethanol (22b, major diastereomer): R_f = 0.63 on silica gel (hexanes:diethyl ether 1:1); IR (cm^{-1}, neat) 3391 (br, s), 3068 (w), 2964 (s), 2931 (s), 2860 (s), 1461 (s), 1382 (m), 1072 (m), 888 (s); ^1H NMR (400 MHz, $CDCl_3$) δ 5.44 (1H, dt, J = 2.2, 0.7 Hz), 5.32 (1H, br s), 3.13 (1H, ddd, J = 8.4, 4.4, 4.4 Hz), 1.59–1.38 (4H, m), 1.35 (1H, d, J = 4.4 Hz), 1.28 (8H, m), 1.13 (3H, s), 1.10 (1H, dt, J = 8.8, 2.2 Hz), 0.93 (1H, dt, J = 8.8, 2.2 Hz), 0.86 (3H, t, J = 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.69, 102.27, 76.74, 33.85, 31.88, 29.72, 29.32, 26.26, 24.69, 22.69, 16.85, 14.86, 14.13; HRMS calcd for $C_{13}H_{23}O$ $(M - H)^+$ 195.1750, found 195.1738.

Cyclopropanation of 3-Methoxy-1,2-undecadien-4-ol (20d). According to the general procedure, 500 mg (2.52 mmol) of **20d** and 2.65 g (17.6 mmol) of samarium in 22 mL of THF was used to obtain a 13:1 mixture of diastereomers. A colorless oil, 272 mg (51%) was obtained as an inseparable mixture after flash chromatography on silica gel, eluting with 90:9.5:0.5 hexanes:diethyl ether:triethyl amine.

(R^*,R^*)-α-Heptyl-1-methoxy-2-methylenecyclopropanemethanol (21d, major diastereomer): R_f = 0.29 on silica gel (hexanes:diethyl ether 3:1); IR (cm^{-1}, neat) 3445 (br, s), 3079 (w), 2924 (s), 2854 (s), 1645 (w), 1462 (m), 1230 (m), 1110 (m), 1040 (m), 899 (m); ^1H NMR (400 MHz, $CDCl_3$) δ 5.60 (1H, t, J = 2.9 Hz), 5.50 (1H, t, J = 2.3 Hz), 3.48 (1H, m), 3.31 (3H, s), 2.10 (1H, br s), 1.54 (2H, m), 1.40 (1H, ddd, J = 10.4, 2.9, 2.3 Hz), 1.31 (1H, ddd, J = 10.4, 2.9, 2.3 Hz), 1.24 (10H, m), 0.83 (3H, t, J = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.59, 113.37, 80.08, 70.79, 62.21, 39.70, 38.10, 35.87, 35.53, 32.34, 28.90, 20.70, 20.34; HRMS calcd for $C_{13}H_{25}O$ $(M + H)^+$ 213.1855, found 213.1847.

(R^*,S^*)-(Methylenecyclopropyl)cyclohexylmethyl Methyl Ether (26). To a dry round-bottomed flask, equipped with a stirbar and capped with a rubber septum, was added the cyclopropane carbinol **25**, followed by 2 mL of CH_2Cl_2. The flask was cooled to 0 °C, and Et_3N (12.2 μL, 0.09 mmol) and $SOCl_2$ (6.4 μL, 0.09 mmol) were added successively. The reaction was stirred at 0 °C for 5 min. The reaction mixture was concentrated by removal of the solvent *in vacuo*.

Tetrabutylammonium fluoride (0.3 mL, 1.0 M solution in THF, 0.3 mmol) was added, followed by 2 mL of DMSO, and the reaction mixture was stirred for 24 h at room temperature. The reaction mixture was diluted with diethyl ether, washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash chromatography, eluting with hexanes to 20:1 hexanes:diethyl ether, yielded 5.9 mg (44%) of a colorless oil. The methyl ether **26** was also prepared in 93% yield, by treatment of the methylenecyclopropane carbinol **2b** with 2 equiv of KH in THF, followed by 2.1 equiv of MeI.

(R^*,S^*)-(Methylenecyclopropyl)cyclohexylmethyl methyl ether (26): IR (cm^{-1}, neat) 3072 (w), 3051 (w), 2973 (m), 2924 (s), 2854 (s), 2819 (m), 1743 (w), 1448 (m), 1152 (m), 1110 (s), 1089 (s), 885 (s); ^1H NMR (500 MHz, $CDCl_3$) δ 5.40 (1H, m), 5.37 (1H, m), 3.40 (3H, s), 2.45 (1H, dd, J = 8.8, 5.4 Hz), 1.74 (4H, m), 1.64 (1H, m), 1.52 (2H, m), 1.35 (1H, m), 1.12 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.77, 104.36, 87.89, 57.66, 42.69, 29.01, 28.56, 26.63, 26.47, 26.46, 17.92, 8.80; HRMS calcd for $C_{12}H_{19}O$ $(M - H)^+$ 179.1436, found 179.1440.

(R^*,R^*)-(Methylenecyclopropyl)cyclohexylmethyl Methyl Ether (27). To a dry round-bottomed flask, equipped with a stirbar and capped with a rubber septum, was added KH (27.6 mg, 0.24 mmol, 35 wt % in mineral oil) which was washed three times with pentane. After addition of 18-crown-6 (3 mg, 0.012 mmol) the flask was cooled to 0 °C and half of the total amount of THF added. The substrate **3b** was transferred to the reaction flask via a cannula in the remaining THF. The reaction mixture was stirred for 10 min at 0 °C. MeI (15.6 μL, 0.25 mmol) was added to the reaction and stirred for 15 min at 0 °C. The reaction mixture was quenched with aqueous NH_4Cl and extracted three times with diethyl ether. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash chromatography, eluting with hexanes to 20:1 hexanes:diethyl ether, gave 19.6 mg (90%) of **27** as a colorless oil.

(R^*,R^*)-(Methylenecyclopropyl)cyclohexylmethyl methyl ether (27): IR (cm^{-1}, neat) 3072 (w), 3051 (w), 2931 (s), 2854 (s), 2826 (m), 1743 (w), 1448 (m), 1110 (m), 885 (m); ^1H NMR (500 MHz, $CDCl_3$) δ 5.44 (2H, m), 3.36 (3H, s), 2.40 (1H, dd, J = 8.8, 4.9 Hz), 1.83 (1H, m), 1.74 (2H, m), 1.64 (1H, m), 1.55 (1H, m), 1.49 (m), 1.18 (7H, m), 0.82 (1H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 129.78, 99.71, 83.70, 53.25, 38.87, 24.91, 24.09, 22.17, 22.03, 22.00, 13.11, 2.92.

General Procedure for the Hydroboration/Oxidation. To a dry round-bottomed flask, equipped with a stirbar and capped with a rubber septum, was added the methylenecyclopropane quickly, followed by THF. The flask was cooled to 0 °C and BH_3·SMe_3 (3 equiv, 2.0 M solution in THF) was added slowly. The reaction mixture was stirred at 0 °C and followed by TLC. When no starting material was present (usually after 2–3 h), EtOH (30 equiv), aqueous NaOH (5 equiv), and H_2O_2 (13 equiv) was added successively. The reaction mixture was heated to 60 °C for 1 h and stirred at room temperature for an additional 12–16 h. The reaction mixture was extracted three times with ethyl acetate. The combined organic layers were washed three times with saturated aqueous $Na_2S_2O_3$ and three times with brine, dried over $MgSO_4$, and filtered *in*

vacuo. Purification by flash chromatography on silica gel, eluting with a hexanes:diethyl ether gradient, yielded the desired product.

1,2-Cyclopropyldicarbinol 28b. According to the general procedure, **2b** (250 mg, 1.50 mmol) in 12 mL of THF was treated with BH_3·SMe_3 (2.25 mL, 2.0 M solution in THF, 4.5 mmol) at 0 °C. After successive treatment with EtOH (2.6 mL, 45 mmol), NaOH (1.5 mL, 5.0 M aqueous solution, 7.5 mmol), and H_2O_2 (2.0 mL, 30 wt % in H_2O, 19.7 mmol) the crude product was purified by flash chromatography on silica gel, eluting with 10:1 hexanes:diethyl ether to pure ether. The product (201 mg, 73%) was isolated as a white solid as a 13:1 inseparable mixture of **28b** and its trans-substituted epimer: IR (cm^{-1}, neat) 3343 (br, s), 3004 (w), 2924 (s), 2850 (s), 1451 (m), 1030 (m), 1009 (m); ^1H NMR (400 MHz, $CDCl_3$) δ 3.71 (1H, dd, J = 11.0, 6.6 Hz), 3.53 (1H, dd, J = 11.0, 7.7 Hz), 3.07 (1H, dd, J = 8.8, 5.9 Hz), 1.89 (1H, m), 1.75 (2H, m), 1.65 (1H, m), 1.49 (1H, m), 1.41 (1H, m), 1.29–0.99 (9H, m), 0.77 (1H, ddd, J = 8.4, 8.1, 4.8 Hz), 0.30 (1H, ddd, J = 5.9, 5.5, 4.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 75.33, 63.08, 44.75, 29.30, 28.10, 26.47, 26.35, 26.14, 21.27, 19.53, 6.95. Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.70; H, 10.94. Found: C, 71.65; H, 11.35.

1,2-Cyclopropyldicarbinol 28d. According to the general procedure, **2d** (100 mg, 0.55 mmol) in 5 mL of THF was treated with BH_3·SMe_3 (0.82 mL, 2.0 M solution in THF, 1.65 mmol) at 0 °C. After successive treatment with EtOH (1.0 mL, 17 mmol), NaOH (0.9 mL, 3.0 M aqueous solution, 2.7 mmol), and H_2O_2 (0.7 mL, 30 wt % in H_2O, 7.1 mmol) the crude product was purified by flash chromatography on silica gel, eluting with 10:1 hexanes:diethyl ether to pure ether. The product (59 mg, 54%) was isolated as a colorless oil as a 16:1 inseparable mixture of **28d** and its trans-substituted epimer: IR (cm^{-1}, neat) 3337 (br, s), 3070 (w), 3002 (m), 2955 (s), 2926 (s), 2857 (s), 1468 (m), 1025 (m); ^1H NMR (400 MHz, $CDCl_3$) δ 3.61 (2H, d, J = 7.3 Hz), 3.33 (1H, dt, J = 8.4, 7.0 Hz), 1.94 (1H, br s), 1.87 (1H, br s), 1.55 (2H, m), 1.44–1.18 (11H, m), 1.02 (1H, dddd, J = 8.8, 8.4, 8.4, 5.7 Hz), 0.84 (3H, t, J = 7.0 Hz), 0.74 (1H, ddd, J = 8.4, 8.4, 4.9 Hz), 0.31 (1H, ddd, J = 5.7, 5.5, 4.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 71.64, 62.85, 38.07, 31.81, 29.62, 29.27, 25.66, 23.11, 22.63, 18.80, 14.07, 7.60; HRMS calcd for $C_{12}H_{23}O_2$ $(M - H)^-$ 199.1698, found 199.1690. Anal. Calcd for $C_{12}H_{24}O_2$: C, 71.95; H, 12.08. Found: C, 72.21; H, 12.16.

1,2-Cyclopropyldicarbinol 29b. According to the general procedure, **3b** (45 mg, 0.27 mmol) in 2.5 mL of THF was treated with BH_3·SMe_3 (0.41 mL, 2.0 M solution in THF, 0.81 mmol) at 0 °C. After successive treatment with EtOH (0.5 mL, 8.2 mmol), NaOH (0.3 mL, 5.0 M aqueous solution, 1.5 mmol), and H_2O_2 (0.4 mL, 30 wt % in H_2O, 3.7 mmol) the crude product was purified by flash chromatography on silica gel, eluting with 10:1 to 2:1 hexanes:diethyl ether, to yield 34 mg, 68%, of a colorless oil: IR (cm^{-1}, neat) 3391 (br, m), 2931 (s), 2851 (s), 1450 (m), 1033 (m); ^1H NMR (400 MHz, $CDCl_3$) δ 4.07 (1H, dd, J = 11.5, 5.1 Hz), 3.21 (1H, dd, J = 11.5, 11.5 Hz), 3.14 (2H, br s), 2.98 (1H, dd, J = 10.1, 6.8 Hz), 1.88 (2H, m), 1.74 (2H, m), 1.65 (1H, m), 1.48 (1H, m), 1.29–0.90 (7H, m), 0.81 (1H, ddd, J = 8.4, 8.1, 5.1 Hz), 0.20 (1H, ddd, J = 5.5, 5.1, 5.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 77.52, 63.56, 44.77, 29.22, 29.09, 26.54, 26.22, 26.09, 20.24, 16.63, 9.62; HRMS calcd for $C_{11}H_{19}O_2$ $(M - H)^-$ 183.1385, found 183.1380. Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.70; H, 10.94. Found: C, 71.66; H, 10.95.

1,2-Cyclopropyldicarbinol 29d. According to the general procedure, **3d** (150 mg, 0.82 mmol) in 8.0 mL of THF was treated with BH_3·SMe_3 (1.23 mL, 2.0 M solution in THF, 2.5 mmol) at 0 °C. After successive treatment with EtOH (1.5 mL, 25.0 mmol), NaOH (1.4 mL, 3.0 M aqueous solution, 4.1 mmol), and H_2O_2 (1.1 mL, 30 wt % in H_2O, 10.7 mmol) the crude product was purified by flash chromatography on silica gel, eluting with 10:1 to 1:2 hexanes:diethyl ether, to yield 109 mg, 66%, of a colorless oil: IR (cm^{-1}, neat) 3328 (br, s), 3071 (m), 3002 (m), 2955 (s), 2926 (s), 2858 (s), 1463 (m), 1035 (m); ^1H NMR (400 MHz, $CDCl_3$) δ 4.09 (1H, dd, J = 11.5, 5.5 Hz), 3.25 (1H, m), 3.22, (1H, m), 2.10 (2H, br s), 1.76 (1H, m), 1.63 (2H, m), 1.44–1.20 (10H, m), 1.00 (1H, dddd, J = 10.0, 8.4, 8.1, 5.5 Hz), 0.86 (3H, t, J = 7.0 Hz), 0.79 (1H, ddd J = 8.4, 8.1, 5.1 Hz), 0.18 (1H, ddd, J = 5.5, 5.1, 5.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 73.18, 63.49, 37.72, 31.81, 29.69, 29.27, 25.84, 22.64, 22.46, 17.11, 14.07, 8.96. Anal. Calcd for $C_{12}H_{24}O_2$: C, 71.95; H, 12.08. Found: C, 71.49; H, 11.85.

General Procedure for the Tosylation/Cyclization. To a dry round-bottomed flask, equipped with a stirbar and capped with a rubber septum, was quickly added the diol, followed by pyridine. The flask was cooled to 0 °C, and *p*-toluenesulfonyl chloride was added quickly. The reaction was followed by TLC, until all the starting material had reacted. The reaction mixture was diluted with diethyl ether and washed with saturated aqueous $CuSO_4$ to remove the pyridine, washed three times with brine, dried over $MgSO_4$, and filtered *in vacuo*. Purification by flash chromatography on silica gel, eluting with a pentane:diethyl ether or a hexanes:diethyl ether gradient, yielded the desired product.

3-Oxabicyclo[3.1.0]hexane 30b. According to the general procedure, **28b** (20 mg, 0.11 mmol) in 2 mL of pyridine was treated with *p*-TsCl (21 mg, 0.11 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 3 h. After purification by flash chromatography on silica gel, eluting with pentane to 20:1 pentane:diethyl ether, the product (13.8 mg, 76%) was isolated as a colorless oil of an inseparable 8.5:1 mixture of **30b** and its epimer, **31b**: IR (cm^{-1}, neat) 2927 (s), 2854 (s), 1451 (m), 1250 (m), 1093 (m), 1029 (m), 837 (s); ^1H NMR (400 MHz, $CDCl_3$) δ 3.79 (1H, d, J = 8.1 Hz), 3.69 (1H, dd, J = 8.1, 2.6 Hz), 3.51 (1H, dd, J = 8.6, 2.4 Hz), 1.93–0.96 (13H, m), 0.38 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 84.37, 69.57, 40.72, 30.85, 29.88, 26.54, 26.09, 25.84, 18.78, 16.10, 4.04. Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.04; H, 11.21.

3-Oxabicyclo[3.1.0]hexane 30d. According to the general procedure, **28d** (50 mg, 0.25 mmol) in 2 mL of pyridine was treated with *p*-TsCl (47 mg, 0.25 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 3 h. After purification by flash chromatography on silica gel, eluting with pentane to 20:1 pentane:diethyl ether, the product (40 mg, 88%) was isolated as a colorless oil of an inseparable 4.4:1 mixture of **30d** and its epimer, **31d**: IR (cm^{-1}, neat) 3077 (w), 3045 (w), 2996 (w), 2959 (s), 2931 (s), 2858 (s), 1462 (m), 1377 (m), 1104 (m), 971 (m); ^1H NMR (400 MHz, $CDCl_3$) δ 3.85 (1H, m), 3.78 (1H, d, J = 8.2 Hz), 3.70 (1H, dd, J = 8.2, 1.8 Hz), 1.59–1.20 (14H, m), 0.86 (3H, t, J = 6.9 Hz), 0.36 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 79.49, 69.56, 32.51, 31.85, 29.84, 29.31, 26.76, 22.69, 20.23, 16.44, 14.13, 3.77; HRMS calcd for $C_{12}H_{21}O$ $(M - H)^-$ 181.1592, found 181.1590.

3-Oxabicyclo[3.1.0]hexane 31b. According to the general procedure, **29b** (20 mg, 0.11 mmol) in 2 mL of pyridine was treated with *p*-TsCl (21 mg, 0.11 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 5 h, followed by 16 h at room temperature. After purification by flash chromatography on silica gel, eluting with pentane to 20:1 pentane:diethyl ether, the product **31b** (14.9 mg, 82%) was isolated as a colorless oil: IR (cm^{-1}, neat) 2926 (s), 2852 (s), 1731 (m), 1249 (m), 837 (m); ^1H NMR (400 MHz, $CDCl_3$) δ 3.75 (1H, dd, J = 7.9, 2.9 Hz), 3.70 (1H, d, J = 7.9 Hz), 3.54 (1H, d, J = 7.3 Hz), 1.95–0.84 (13H, m), 0.58 (1H, ddd, J = 7.7, 7.7, 4.4 Hz), 0.24 (1H, ddd, J = 4.4, 4.4, 4.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 85.34, 68.84, 42.28, 29.36, 28.90, 26.58, 26.19, 26.12, 19.35, 17.50, 8.85; HRMS calcd for $C_{11}H_{18}O$ $(M)^+$ 166.1358, found 166.1358.

3-Oxabicyclo[3.1.0]hexane 31d. According to the general procedure, **29d** (55 mg, 0.27 mmol) in 5 mL of pyridine was treated with *p*-TsCl (52 mg, 0.27 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 7 h, followed by 20 h at room temperature. After purification by flash chromatography on silica gel, eluting with 20:1 pentane to pentane:diethyl ether, the product **31d** (41 mg, 83%) was isolated as a colorless oil: IR (cm^{-1}, neat) 3074 (w), 3050 (w), 2994 (w), 2958 (m), 2925 (s), 2858 (s), 1467 (m), 1100 (m), 1086 (m), 967(m); ^1H NMR (400 MHz, $CDCl_3$) δ 3.81 (1H, m), 3.73 (1H, dd, J = 8.1, 2.9 Hz), 3.69 (1H, d, J = 8.1 Hz), 1.49 (1H, dddd, J = 7.7, 7.0, 4.4, 2.9 Hz), 1.42–1.20 (12H, m), 1.37 (1H, ddd, J = 7.7, 7.0, 4.0 Hz), 0.86 (3H, t, J = 6.9 Hz), 0.52 (1H, ddd J = 7.7, 7.7, 4.4 Hz), 0.27 (1H, ddd, J = 4.4, 4.4, 4.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 80.46, 67.51, 34.55, 31.80, 29.61, 29.25, 25.73, 22.62, 21.22, 16.62, 14.04, 8.04; HRMS calcd for $C_{12}H_{21}O$ $(M - H)^-$ 181.1592, found 181.1595.

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