Development of a Method for the Reductive Cyclization of Enones by a Titanium Catalyst

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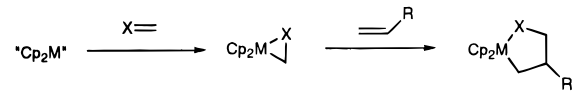
Abstract: An effective protocol in which bis(trimethylphosphine)titanocene is used to catalyze the reductive cyclization of enones to cyclopentanols via a metallacyclic intermediate has been developed. The key step in the process is the cleavage of the titanium−oxygen bond in the metallacycle by a silane to regenerate the catalyst. Mechanistic aspects of the reaction are discussed and the diastereoselectivity of the transformation is studied using both achiral and chiral substrates. The scope and limitations of the procedure are described. An *in situ* protocol for the generation of the air- and moisture-sensitive catalyst has also been developed. This work demonstrates, for the first time, the viability of using an early transition metal complex to catalyze the reductive cyclization of an alkene with a heteroatom-containing functional group.

Introduction

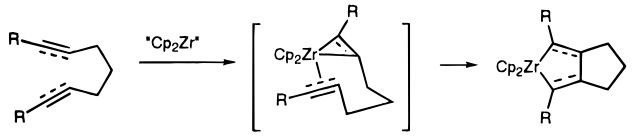
The early transition metal-mediated reductive cyclization of unsaturated organic fragments encompasses a well-documented class of reactions in which a metallacycle containing a new carbon−carbon bond is formed (Scheme 1).[1] In many cases, processes which employ these reactions represent interesting net organic transformations that are difficult or impossible to achieve using traditional methods of organic synthesis. The stoichiometric zirconocene-mediated reductive cyclizations of diynes,[2] dienes,[3] and enynes[4] were originally explored by Nugent and Negishi (Scheme 2). These methodologies have been extended to other group 4 metals[5] and to the reductive cyclization of heteroatom-containing unsaturated fragments including the intramolecular cyclizations of hydrazone/alkenes (or alkynes),[6] enones, and ynones.[7,8]

In order to make these methods more accessible to synthetic organic chemists, there is a need for the development of simpler, more efficient protocols for carrying out these reactions. A major improvement would be the development of catalytic procedures, which would not only decrease the amount of the metal required but also make use of more expensive chiral catalysts for enantioselective synthesis more practical.

Scheme 1



Scheme 2



Several groups have developed catalytic methods for the reductive cyclization of dienes and enynes. The initial formation of the metallacyclic intermediates of these reactions parallels that seen in the stoichiometric procedures. In order to develop a viable catalytic reaction, a number of strategies have been employed to liberate the organic product and regenerate an active form of the catalyst. For the catalytic reductive cyclization of dienes, Waymouth and co-workers employ *n*-butylmagnesium chloride to affect a transmetalation of the intermediate zirconacycle to generate the diGrignard organic product and dibutylzirconocene, which eliminates butane to reform the zirconocene−butene adduct (Scheme 3).[9] Mori and co-workers use a similar strategy for the catalytic formation of heterocycles from dienes.[10] In our laboratory, a catalytic technique for the reductive cyclization of enynes to bicyclic cyclopentenones was developed in which an isonitrile reacts with the intermediate metallacycle (Scheme 4). Reductive elimination of the iminocyclopentene reforms the Ti(II) catalyst.[11] In each case, the intermediate metallacycle is converted into a reactive metal complex which either is or can be converted to the active form of the catalyst.

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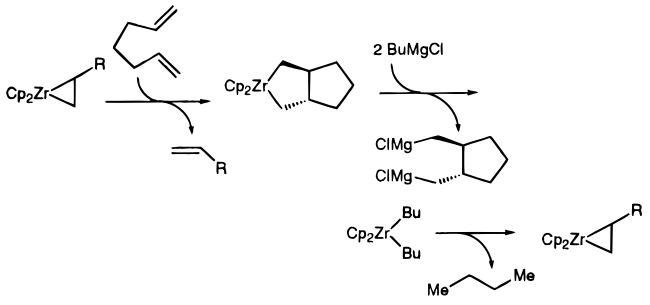
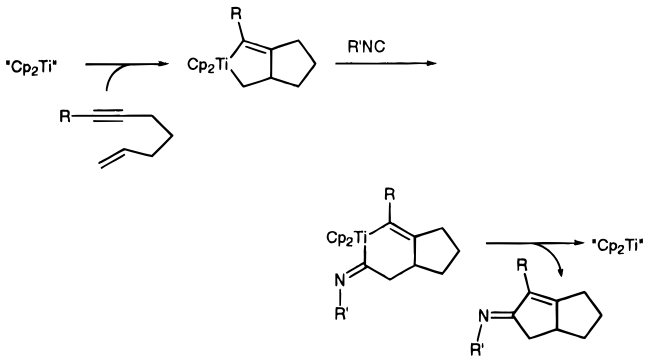
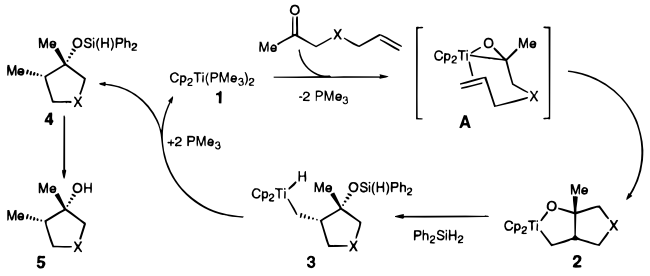
Scheme 3



Scheme 4

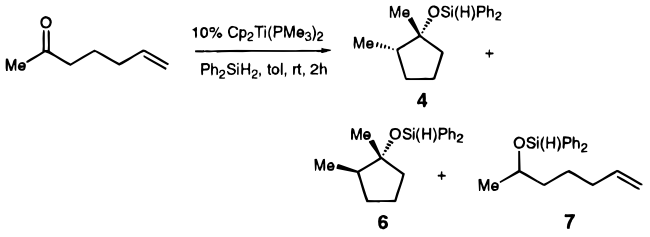


Scheme 5



Whitby and Hewlett have demonstrated that a stoichiometric quantity of $Cp_2Ti(PMe_3)_2$, **1**, can be used to convert 1,6-enones to oxatitanabicyclopentanes in good yields.[7] We became interested in developing a catalytic variant of this process. Cleaving the exceptionally strong titanium−oxygen bond in these metallacycles in such a way as to lead to the regeneration of a catalytically active species posed a significant challenge. Titanium−oxygen bond energies are approximately 104 kcal/mol and are significantly stronger than the 40 to 50 kcal/mol strength of the titanium− and zirconium−carbon bonds which are broken in the catalytic reactions mentioned earlier.[12] We have previously found that silanes will readily cleave titanium−oxygen bonds with concomitant formation of Ti−H and Si−O bonds[13] via a σ-bond metathesis process. Using this key reaction, we envisioned the catalytic process for the conversion of enones to cyclopentanols shown in Scheme 5. Formation of titanacycle **2** proceeds by insertion of the coordinated olefin into the Ti−C bond of the nascent titanocene−ketone complex **A**. The silane then cleaves the Ti−O bond to form the titanocene alkyl hydride **3**, which undergoes ligand-induced reductive elimination[14] to afford the silyl-protected cyclopentanol **4**, while regenerating the catalyst. Hydrolysis of the silyl ether produces the cyclopentanol **5**. We note that Crowe and Rachita independently developed a similar protocol based on the same key reactions; the initial work from both laboratories was recently communicated.[15]

Scheme 6



Results and Discussion

In initial experiments, the substrate, diphenylsilane, and 10 mol % **1** were combined in toluene under anhydrous conditions. While this protocol was found to work extremely well for aldehyde-containing substrates (Table 1, entry 4), the cyclization of ketone-containing substrates under these conditions resulted in the formation of a mixture of products (Scheme 6). In addition to the desired silylated *cis*-cyclopentanol **4**, a small quantity of the *trans* isomer **6** and a large amount of acyclic silyl ether **7**, resulting from the simple reduction of the carbonyl, were also produced. We first set out to determine the cause of the carbonyl reduction in an attempt to eliminate side product **7**.

When the reaction is monitored by gas chromatography, initially only cyclized isomers **4** and **6** are observed. As the reaction progresses, the relative amount of **7** is observed to increase rapidly. This suggests that the species responsible for the carbonyl reduction is different than the catalyst for the reductive cyclization; presumably, this species is generated by decomposition of the cyclization catalyst. We surmise that over the course of the reaction, some of the Ti(II) complex which acts as the cyclization catalyst is converted to a Ti(III) hydride, which merely reduces the carbonyl.[17] Other experimental observations support this hypothesis. For example, the addition of excess trimethylphosphine to the reaction mixture reduces the amount of **7** produced, possibly by stabilizing the Ti(II) complex. Additionally, running the reaction at lower temperatures also decreases the amount of **7** which is observed (see Table 2).

Experimentally it was found that 10 mol % **1**, 60 mol % trimethylphosphine, and 1.0 equiv of diphenylsiliane at −20 °C will convert an enone to the cyclopentanol silyl ethers **4** and **6**, while virtually eliminating the production of the acyclic silyl ether **7**. The results of the reaction under these conditions are shown in Table 1. It should be noted that under conditions employing excess PMe_3, reduction is the main pathway for aldehyde substrates. This contrasting behavior can be explained if the reduction can also occur through a second pathway as shown in Scheme 7. Here, the silane cleaves the titanium−oxygen bond in titanocene−carbonyl complexes **B** or **C**, followed by reductive elimination of the acyclic reduced product. The addition of excess trimethylphosphine will favor the formation of the PMe_3 adducts of **B** and **C**. In both instances, as is shown in Scheme 7a, two geometric isomers of the adducts

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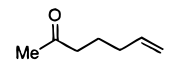
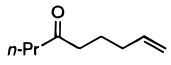
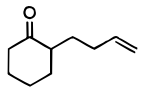
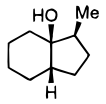
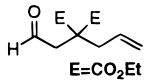
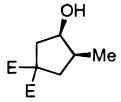
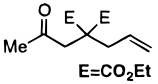
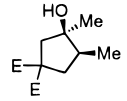
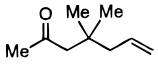
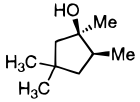
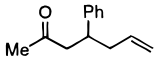
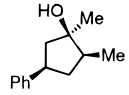
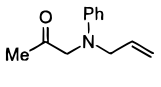
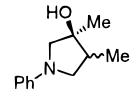
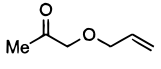
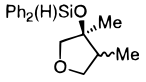
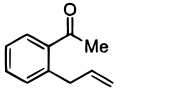
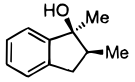
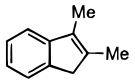
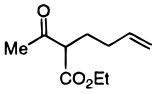
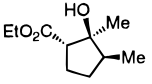
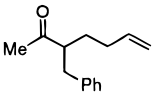
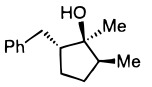
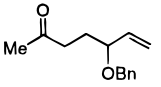
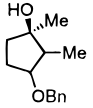
(17) (a) Aitken, C. T.; Harrod, J. F.; Samuel, E. *J. Am. Chem. Soc.* **1986**, *108*, 4059. (b) Harrod, J. F.; Yun, S. S. *Organometallics* **1987**, *6*, 1381. (c) Harrod, J. F. In *Inorganic and Organometallic Polymers*; Zeldin, M., Wayne, K. J., Allcock, H. R., Eds.; ACS Symposium Series 360; American Chemical Society: Washington, DC, 1988; Chapter 7. Titanium hydrides have been previously postulated as carbonyl reduction catalysts in ref 13 and in: (d) Nakamo, T.; Nagai, Y. *Chem. Lett.* **1988**, 481.

Table 1

Entry	Enone	Product[a]	Workup[b]	Temp(°C)	Cyc./Red. (3+5):6[c]	*cis*/*trans* 3:5[c]	Yield (%)[d]
1			A	-20	17:1	43:1	64
2			A	-20	23:1	22:1	64
3[e]			A	-20	6:1	70:1	72[f]
4[g]			B	21	99:1	99:1	65
5			B	-20	99:1	10:1	68
6			A	-20	16:1	13:1	56
7			A	-20	99:1	2.5:1[k]	63[h]
8			A	-20	99:1	1:1	75[i]
9			C	-20	80:1	3:2	72[j]
10			D	-20	99:1	99:1	86
			A	-20	99:1	99:1	71
11			B	21	99:1	90:1[k]	78
12			A	21	99:1	20:1[k]	71
13			B	21	3:1	3:2[k]	50[l]
				-20	8.5:1	4:1.6:1[k]	45[m]

[a] Major isomer. [b] Workup A: HCl/acetone, 3 h. Workup B: TFA/H_2O/THF/CH_2Cl_2 0 °C, 12 h. Workup C: silyl ether purified by distillation. Workup D: TBAF/THF, 15 min. [c] As determined by GC. [d] Isolated yield of major isomer analytically pure except for entries 1, 2, and 6 which are of >95% purity as judged by GC and ^{1}H NMR analyses. The reported yields are an average of two or more runs. [e] $PhMeSiH_2$ was used instead of Ph_2SiH_2. [f] Isolated as a 9/1 mixture of **4** and **6** (see text). [g] No excess PMe_3 used with this substrate. [h] Yield of single isomer. [i] Total yield is 75%, but isomers were separated chromatographically in 37% and 38% yields. [j] Isolated as a mixture of **4** and **5** (see text). [k] Ratio refers to the two (or three) major isomers observed (see text). The major isomer is shown. [l] Total yield is 50%, but isomers were separated chromatographically in 30% and 20% yields. [m] Total yield of the major two of the three isomers detected, which were also separated chromatographically in 32% and 13% yields. The third isomer coelutes with the reduced products and was not isolated.

Scheme 7

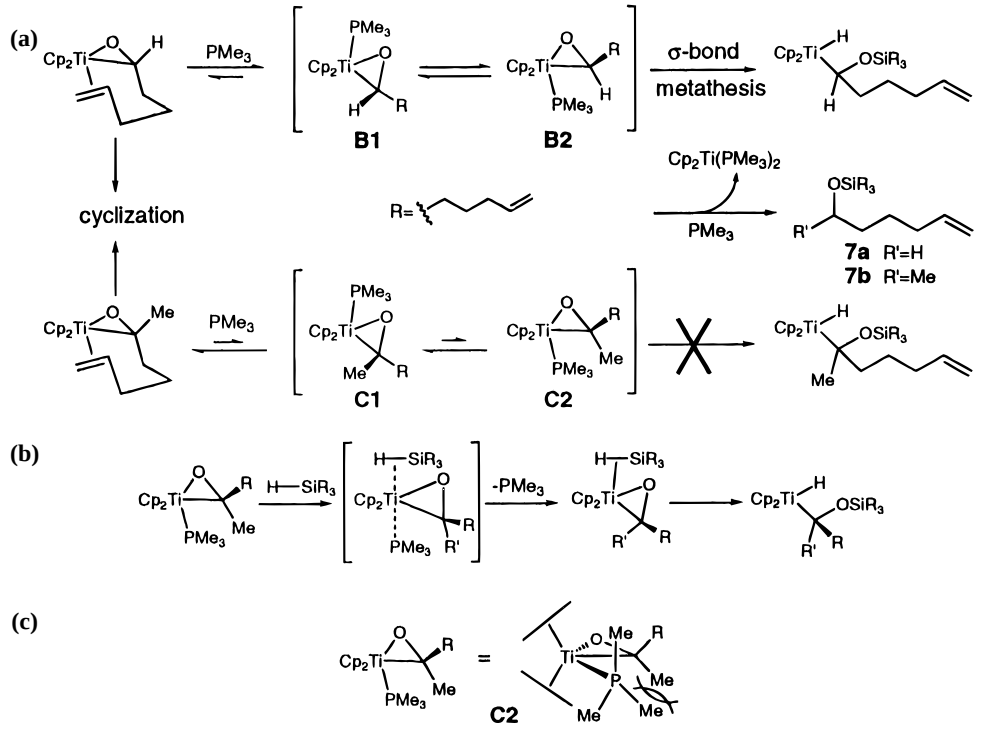
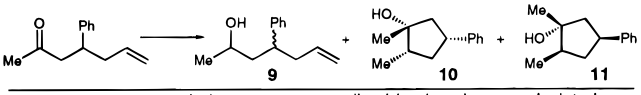
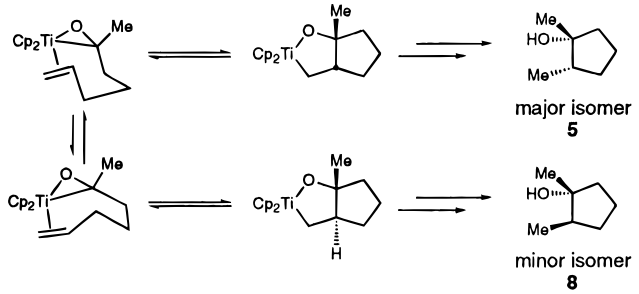


Table 2



temperature °C	cis / trans [9:10]	cyclized / reduced [(9+10):8]	isolated yield of 9 (%)
-20	2.2:1	99:1	63
-5	3:1	65:1	59
0	3.5:1	46:1	50
21	5:1	10:1	63
50	6:1	10:1	55

Scheme 8



are possible. We speculate that only the isomer with the PMe_3 group coordinated anti to the oxygen can undergo the σ-bond metathesis reaction. A possible explanation for this is that the silane precoordinates with the complex syn to the oxygen before σ-bond metathesis occurs (see Scheme 7b).[16] For enal complexes, both **B1** and **B2** are viable and the reaction may proceed via a σ-bond metathesis process through **B2**, leading to side product **7a**. For enones, **C2** is destabilized for steric reasons (see Scheme 7c) and the quantity of **7b** produced is minimal.

Diastereoselectivity of Cyclization—Effect of Substituents. In addition to exploring the mechanism of this cyclization reaction, we have also investigated the cyclization of a wide range of substrates in order to study the diastereoselectivity of the transformation. Two aspects of the diastereoselectivity will be discussed: the formation of new chiral centers at the ring junction of the intermediate metallacycles, and the effect of preexisting chiral centers on the diastereoselectivity of the cyclization.

Whitby found that the stoichiometric reaction of achiral substrates is completely diastereoselective; only the thermodynamically favored *cis*-fused metallacycle is formed.[7] The diastereoselectivity of the catalytic reaction for achiral substrates, while not complete, is generally very good (Table 1, entries 1−4 and 10). Though *cis*-cyclopentanol **5**, which is formed via a *cis*-fused metallacycle, is the major product formed in the catalytic reaction, small amounts of isomer **8**, formed via a *trans*-fused metallacycle, are also detected in most cases (Scheme 8). In the stoichiometric reaction, the steps leading to metallacycle formation are reversible, so only the thermodynamically favored product is formed. During the catalytic process, the organic fragment can be cleaved from the intermediate titanium complex by the silane before complete equilibration to the thermodynamic product can occur, and a mixture of isomers is produced.[18] For substrates containing a heteroatom in the backbone (Table 1, entries 8 and 9), little or no diastereoselectivity is observed. The reactions of these substrates showed no kinetic selectivity when transformed to the metallacycles stoichiometrically but equilibrated to the more stable *cis*-isomer over several days (Scheme 9).[19,20] Hence, the catalytic reactions employing these substrates would not be expected to be diastereoselective

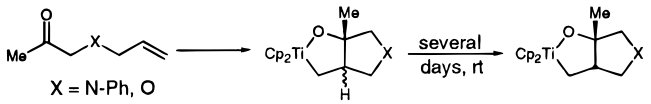
The interplay of kinetic and thermodynamic factors also contributes to the slight decrease in diastereoselectivity for the cyclization of enones that are disubstituted in the β-position

(18) Poor diastereoselectivity in catalytic transformations compared to the corresponding stoichiometric processes has previously been observed, see ref 10.

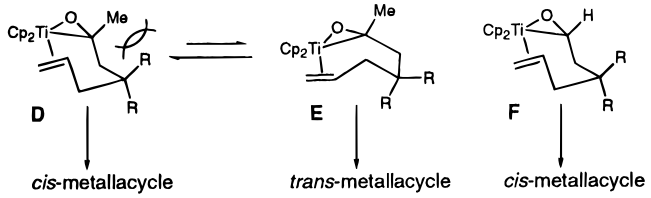
(19) A similar effect upon heteroatom substitution has been noted: (a) Davis, J. M.; Whitby, R. J.; Jaxa-Chamiec, A. *Tetrahedron Lett.* **1992**, *33*, 5655. (b) Taber, D. F.; Louey, J. P.; Wang, Y.; Nugent, W. A.; Dixon, D. A.; Harlow, R. L. *J. Am. Chem. Soc.* **1994**, *116*, 9457.

(20) The equilibration of these substrates to the *cis* isomer was monitored using ^{1}H NMR verses an internal standard, and the stereochemistry was determined by nOe analysis of the resulting silyl ether of entry 9, Table 1.

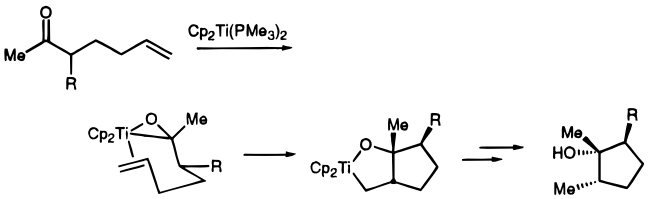
Scheme 9



Scheme 10



Scheme 11



(Table 1, entries 5 and 6). Scheme 10 shows that the "chair-like" intermediate **D** which leads to the *cis*-fused metallacycle contains a destabilizing pseudo-1,3-diaxial interaction between the substituent on the β-position and the methyl group. This decreases the energy difference between **D** and the "boat-like" intermediate **E**, leading to increased formation of the *trans*-product. For an aldehyde that is disubstituted in the β-position (Table 1, entry 4), there is a significantly less severe pseudo-1,3-diaxial interaction in intermediate **F**, and excellent selectivity is observed.

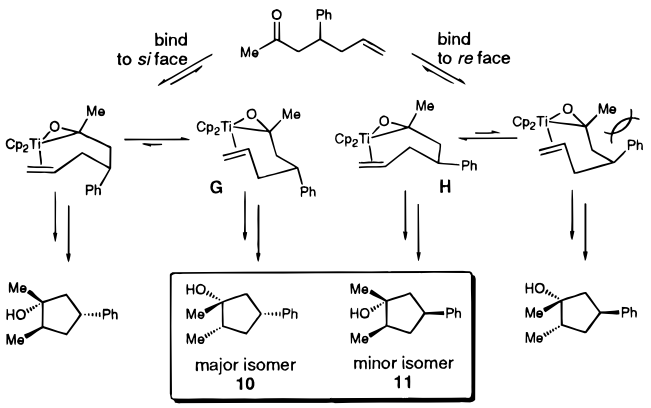
The acetophenone derivative (Table 1, entry 10) is interesting in that it is cyclized by this protocol very selectively to give only one observable silyl ether product. Depending on the method of workup employed, either the bicyclic cyclopentanol or the dimethylindene can be produced in good yield.

Chiral substrates with single substituents on the backbone (Table 1, entries 7, 11, 12, and 13) can form four isomers. Substrates with substituents α, β, and γ to the carbonyl were studied. In these cases, modest to excellent diastereoselectivity is observed.

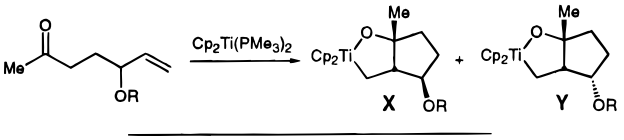
Substrates with a single substituent in the position α to the carbonyl (Table 1, entries 11 and 12) proceed with good to excellent diasteroselectivity, and one isomeric product is primarily observed. As shown in Scheme 11, the substituent is placed preferentially in the equatorial position of the chair-like intermediate. Cleavage of the organic fragment from the resulting metallacycle followed by hydrodesilylation provides the observed cyclopentanol. If the α substituent is an ethyl ester (Table 1, entry 11), cyclization occurs with a 90:1 diastereo-selectiviy; if it is a benzyl group (Table 1, entry 12), the diastereoselectivity is 20:1. Crowe and Rachita reported the cyclization of an aldehyde with a methyl group α to the carbonyl proceeded with the formation of two diastereomers with a 4:1 selectivity.[15b]

Scheme 12 shows that in the reaction of 4-phenyl-6-hepten-2-one (Table 1, entry 7), which has a phenyl group in the β-position, two of the four possible isomers are formed (assignment by nOe analysis). Additionally, as shown in Table 2, the ratio of the isomers which are observed is temperature dependent. A possible explanation for these findings is that the titanocene moiety can initially bind to either of the two diastereotopic faces of the carbonyl. If the titanium binds to

Scheme 12



Scheme 13



R =		
	Ac	X / Y= 1.4:1
	Bn	1.3:1
	TIPS	1:1.4

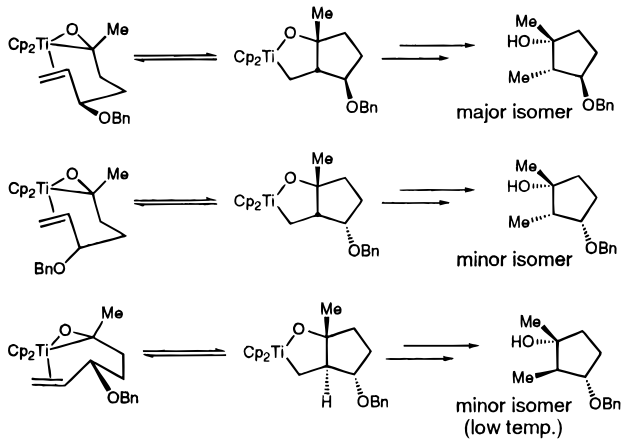
the *si* face, reaction via the chair-like intermediate **G** is favored, and the major isomer **10** is formed. If the titanium binds to the *re* face, reaction via the boat-like intermediate **H** is favored, and the minor isomer **11** is formed. The temperature dependence of the isomeric ratio may result from the sensitivity of the rate of the equilibration between the *re* and *si* faces on temperature. At higher temperatures, the equilibration between the diastereomeric complexes is fast, so that the proportion of the isomer formed via the thermodynamically favored intermediate increases.[21] At lower temperatures, the organic fragment is cleaved from the metal before equilibration is complete, so that a mixture of isomers is produced.

Cyclizations of substrates which have γ substituents proceeded with very low levels of diastereoselectivity. Several substrates were cyclized using a stiochiometric quantity of **1**; in each case an *ca.* 1:1 mixture of *cis*-metallacycles was observed. For substrates with smaller γ substituents, such as OAc and OBn, the product with the substituent on the *exo*-face was slightly favored. When the substituent was the larger triisopropylsilyl group, the metallacycle with the *endo* substituent was slightly favored (Scheme 13). The benzyl-substituted substrate (Table 1, entry 13) was cyclized under catalytic conditions, and at room temperature two products were produced which corresponded to the intermediate *cis*-metallacycles (Scheme 14). When the reaction was run at -20 °C, a third isomer could be identified as shown in Scheme 14.

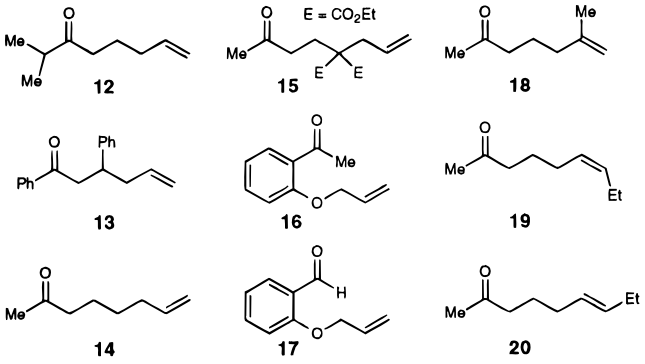
Scope and Limitations. The scope of this cyclization methodology was explored, and it was found that these reactions are in general very sensitive to the steric bulk of the substrates. While methyl and *n*-propyl ketones (Table 1, entries 1 and 2) cyclized smoothly under the conditions outlined above, more sterically congested ketones such as entry 3 required a smaller silane for catalysis. However, small silanes such as methylphenylsilane also reacted faster with the catalyst to form Ti(III) complexes,[17a] resulting in an increase in the production of acyclic reduction products. Enones with isopropyl and phenyl

(21) It is assumed that the rate of the σ-bond metathesis is relatively insensitive to temperature changes.

Scheme 14



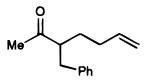
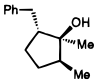
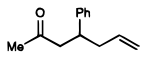
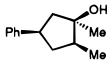
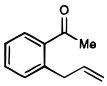
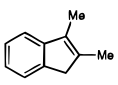
Scheme 15



substituents on the ketone (**12** and **13**) formed metallacycles stoichiometrically, but they were too large to undergo facile σ-bond metathesis without significant carbonyl reduction under catalytic conditions. Both Whitby and Crowe found that substrates that would give rise to cyclohexanols do not cyclize at all, even stoichiometrically; we found that 7-hexen-2-one, **14**, failed to cyclize. We attempted to favor ring closure by incorporating substituents on the backbone; however, compounds **15**, **16**, and **17** also failed to form metallacycles when treated with a stoichiometric amount of **1**. Furthermore, substitution on the alkene was not tolerated by this protocol; enones **18**, **19**, and **20** did not form metallacycles when treated with a stoichiometric quantity of **1**. The moderate degree of functional group tolerance of this methodology should be noted. Often early transition metal catalysts are incompatible with polar functional groups; however, in the transformation reported here, enones containing esters and allyl ethers are tolerated (Table 1, entries 4, 5, and 9).[5a] Additionally, the cyclization of the β-keto ester (Table 1, entry 11) shows that the acidic proton is not detrimental to cyclization. In related studies of McMurry couplings, Fürstner has shown that functional group compatibility is extremely sensitive to the exact nature of the low-valent titanium species employed; he has described very good functional group compatibility using both Ti(I) and Ti(II) complexes.[22]

***In Situ* Generation of the Catalyst.** A limitation to the use of this methodology is that the catalyst, **1**, is a pyrophoric, air- and moisture-sensitive complex that must be stored and handled in a glovebox under argon. In order to make this methodology more practical, a protocol for the *in situ* generation of the catalyst utilizing the inexpensive, air- and moisture-stable Cp_2TiCl_2 was developed. Whitby originally synthesized the oxatitanacycles from $Cp_2Ti(PMe_3)_2$ formed *in situ* from Cp_2TiCl_2 and PMe_3. We found that a variation of this method, which is experimentally less complicated, forms a viable catalyst that is active at 15 mol %.[23] Treating finely ground Cp_2TiCl_2 with *n*-BuLi and excess PMe_3 in toluene produced $Cp_2Ti(PMe_3)_2$, which was then cannula filtered into a separate vessel containing 7.5 equiv of the enone. This solution was then cooled to the desired temperature and the silane was added. Because the formation of $Cp_2Ti(PMe_3)_2$ is not quantitative (upon filtration, some titanium residue is left behind), a slightly higher catalyst loading is necessary. Without the filtration step, products resulting from carbonyl reduction are observed. Attempts to form the oxametallacycles directly from Cp_2TiCl_2 and *n*-BuLi were unsuccessful. Table 3 compares the results obtained using the two methods for catalyst generation with several substrates.

Table 3

enone	isolated product	*cis*/*trans* (see Table I)	yield (%) using *in situ* method	yield using $Cp_2Ti(PMe_3)_2$
		17:1	74	75
		2.5:1	60	63
		99:1 for silyl ether intermediate	72	71

Conclusion

In summary, we have developed a titanium-catalyzed reductive cyclization of enones. We have explored the scope, limitations, and the diastereoselectivity of the catalytic cyclization, and we have developed a method for the *in situ* generation of an active catalyst. The net transformation described here resembles the conversion of enones to cyclopentanols by techniques which proceed *via* radical pathways,[24] but several differences should be noted. The titanium-catalyzed method is complementary, in that it affords the opposite isomer than that obtained in the radical cyclizations. Furthermore, the intermediacy of titanacycle **1** provides the opportunity for further elaboration of the method, such as the use of a chiral titanocene catalyst or functionalization of the Ti−C bond.

It is instructive to compare the two recent independent studies of this type of reaction. The protocol of Crowe and co-workers, although it uses twice the catalyst loading (20 mol %), works well for aldehyde-containing substrates. The use of triethoxysilane[25] lends itself to ease in isolation of the products, since the resulting silyl ethers are stable to silica gel chromatography. Diphenylsilyl ethers produced by the method described here are

(22) (a) Fürstner, A.; Hupperts, A.; Ptock, A.; Janssen, E. *J. Org. Chem.* **1994**, *59*, 5215. (b) Fürstner, A.; Hupperts, A. *J. Am. Chem. Soc.* **1995**, *117*, 4468. (c) Fürstner, A.; Jumbam, D. N.; Shi, N. *Z. Nacturforsch.* **1995**, *55b*, 326.

(23) A similar protocol was also developed for catalytic enyne cyclizations in: Hicks, F. A.; Berk, S. C.; Buchwald, S. L. *J. Org. Chem.* In press.

(24) For leading references see: (a) Shono, T.; Nishiguchi, I.; Ohmizu, H.; Mitani, M. *J. Am. Chem. Soc.* **1978**, *100*, 545. (b) Lee, G. H.; Choi, E. B.; Lee, E.; Pak, C. S. *J. Org. Chem.* **1994**, *59*, 1428. (c) Shono, T.; Kise, N.; Fujimoto, T.; Yamanami, A.; Nomura, R. *J. Org. Chem.* **1994**, *59*, 1730. For related samarium-mediated cyclizations that also give *trans* selectivity, see: (d) Molander, G. A.; Kenny, C. *Tetrahedron Lett.* **1987**, *28*, 4367.

(25) Safety note: Triethoxysilane vapors can cause blindness. *Silicon Compounds Register and Review*; Anderson, R., Larson, G. L, Smith, C., Eds.; Hüls America, Inc.; Piscataway, NJ, 1991; p 5, 190. Additionally, under inert atmosphere, triethoxysilane is disproportionated by titanium reagents to form SiH_4, a pyrophoric gas. See: Xin, S.; Aitken, C.; Harrod, J. F.; Mu, Y.; Samuel, E. *Can. J. Chem.* **1990**, *68*, 471.

not stable to silica gel and must be hydrodesilylated before analytically pure products can be isolated. The protocol described here is preferred for the cyclization of ketone-containing substrates, since excessive carbonyl reduction is avoided. We have also shown that aldehydes can be cyclized under similar conditions using only a 10 mol % catalyst loading.

This methodology is the first example of an early transition metal-catalyzed reductive cyclization of an alkene with a heteroatom-containing functional group. Efforts toward the development of other synthetically useful transformations based on this and related catalytic processes are in progress.

Experimental Section

General Considerations. All manipulations involving air-sensitive materials were conducted in a Vacuum Atmospheres glovebox under an atmosphere of argon or using standard Schlenk techniques under argon. THF was distilled under argon from sodium/benzophenone ketyl before use. Toluene was distilled under argon from molten sodium, and CH_2Cl_2 was distilled under nitrogen from CaH_2. Bis(trimethylphosphine)titanocene, $Cp_2Ti(PMe_3)_2$, **1**, was prepared from titanocene dichloride (obtained from Boulder Scientific, Boulder, CO) by the procedure of Binger et al.,[26] and was stored in a glovebox under argon. The enone ethyl 2-oxo-6-heptene-3-carboxylate (Table 1, entry 11)[27] was prepared from ethyl acetoacetate and 4-bromobutene (NaOEt, HOEt, reflux), and the enones 6-hepten-2-one,[28] 8-nonen-4-one,[29] and 2-homoallylcyclohexanone[28] (Table 1, entries 1, 2, and 3) were prepared using the same procedure with the appropriate ethyl acetate followed by decarboxylation. Enones 4,4-dimethyl-6-hepten-2-one and 4-phenyl-6-hepten-2-one (Table 1, entries 6 and 7) were prepared from the allylation of the appropriate α,β-unsaturated ketone with allyltrimethylsilane and $TiCl_4$.[30] Enone diethyl 1-oxo-5-hexene-3,3-dicarboxylate (Table 1, entry 4) was prepared by the procedure of Bernard et al.[31] Allyl acetonyl ether (Table 1, entry 9) was prepared according to the procedure of Kachinsky and Salomon[32] (NaH, allyl alcohol, and propylene oxide, followed by PCC oxidation). *o*-Allylacetophenone (Table 1, entry 10) was prepared by a Stille coupling of allyltributyltin and *o*-bromoacetophenone.[33] Syntheses of previously unreported enone substrates are described below. All other reagents were available from commercial sources and were used without further purification, unless otherwise noted.

Flash chromatography was performed on E. M. Science Kieselgel 60 (230−400 mesh). Yields, unless otherwise stated, refer to isolated yields of compounds of greater than 95% purity as estimated by capillary GC and ^{1}H NMR analysis, and in the cases of unknown compounds, elemental analysis. Yields indicated in this section refer to a single experiment, while those reported in the tables are an average of two or more runs, so the numbers may differ slightly. All compounds were characterized by ^{1}H NMR, ^{13}C NMR, and IR spectroscopies. Previously unreported compounds were also characterized by elemental analysis (E & R Analytical Laboratory, Inc.). Nuclear magnetic resonance (NMR) spectra were recorded on a Varian XL-300, a Varian XL-500, or a Varian Unity 300. Splitting patterns are designated as follows: s, singlet; d, doublet; dd, doublet of doublets; t, triplet; q, quartet; qd, quartet of doublets; m, multiplet. All ^{1}H NMR spectra are reported in δ units, parts per million (ppm) downfield from tetramethylsilane. All ^{13}C NMR spectra are reported in ppm relative to deuteriochloroform. Infrared (IR) spectra were recorded on a Perkin-Elmer 1600 Series Fourier transform spectrometer. Gas chromatography (GC) analyses were performed on a Hewlet-Packard 5890 gas chromatograph with a 3392A integrator and FID detector using a 25-m capillary column with cross-linked SE-30 as a stationary phase.

Preparation of Enone Starting Materials. Diethyl 2-Oxo-6-heptene-4,4-dicarboxylate (Table 1, Entry 5). Using a modified Wacker oxidation,[34] palladium(II) chloride (1.06 g, 6 mmol), copper(I) chloride (2.97 g, 30 mmol), dimethylformamide (15 mL), and water (2.1 mL) were added to a flask and stirred under a balloon of oxygen for 2 h (until the solution turned green in color). Diethyl allylmalonate (6 mL, 30 mmol) was added and the solution was stirred for 18 h. Following the addition of H_2O (30 mL), the mixture was extracted with 3×30 mL Et_2O, the combined organic layers were washed with brine and dried over $MgSO_4$, and the solvent was removed *in vacuo*. Purification of the resulting yellow oil by flash chromatography (hexane−ethyl acetate 4:1) yielded 3.7 g (56% yield) of a clear oil. Of this, 2 g (9 mmol) was added to an oven-dried Schlenk flask containing a slurry of NaH (0.5 g, 14 mmol) and toluene (50 mL) and the mixture was heated to 65 °C for 0.5 h. The mixture was cooled to room temperature and allyl bromide (0.66 mL, 11 mmol) was added. The solution was stirred at 85 °C for 12 h. After cooling the solution to room temperature, *p*-toluenesulfonic acid (0.6 g, 3 mmol) was added and the mixture was stirred for 10 min and then filtered through Celite. The solvent was removed *in vacuo* and purification by flash chromatography (hexane−ethyl acetate 9:1) afforded 0.7 g (34% yield) of a colorless oil. ^{1}H NMR (300 MHz, C_6D_6): δ 5.71 (m, 1 H); 4.92 (m, 2 H); 3.99 (q, $J = 7.2$ Hz, 4 H); 3.05 (s, 2 H); 3.03 (d, $J = 7.3$ Hz, 2 H); 1.64 (s, 3 H); 0.94 (t, $J = 7.2$ Hz, 6 H). ^{13}C NMR (75 MHz, C_6D_6): δ 203.8, 170.2, 133.8, 118.9, 61.4, 55.5, 45.8, 38.1, 29.8, 14.0. IR (neat): 2892, 2938, 1732, 1640, 1466, 1407, 1366, 1287, 1200, 1095, 925. Anal. Calcd for $C_{13}H_{20}O_5$: C, 60.91; H, 7.87. Found: C, 61.06; H, 8.13.

***N*-Allyl-*N*-acetonylaniline (Table 1, Entry 8).** A modified version of Watanabe's procedure[35] was used. Under an argon atmosphere, *N*-allylaniline (4,4 mL, 25 mmol), propargyl alcohol (1.5 mL, 25 mmol), cadmium acetate dihydrate (12 mg, 0.04 mmol), and zinc acetate dihydrate (12 mg, 0.05 mmol) were added to a Schlenk flask fitted with a reflux condenser and heated to 80 °C for 3 days. The reaction products were first purified by vacuum distillation, then the fraction containing the title compound was further purified by flash chromatography (hexane−ethyl acetate 9:1), which afforded 0.95 g (20% yield) of a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.19 (dd, $J = 8.9$ Hz, $J = 7.3$ Hz, 2 H); 6.73 (t, $J = 7.3$ Hz, 1 H); 6.58 (d, $J = 8.9$ Hz, 2 H); 5.85 (m, 1 H); 5.17 (m, 2 H); 3.99 (d, $J = 4.2$ Hz, 2 H); 3.98 (s 2 H); 2.15 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 203.2, 148.0, 133.4, 129.2, 117.3, 116.7, 112.2, 60.7, 54.3, 26.9. IR (neat): 3040, 2917, 1726, 1675, 1599, 1506, 1383, 1354, 1233, 1165, 994, 692, 748. Anal. Calcd for $C_{12}H_{15}NO$: C, 76.14; H, 7.99. Found: C, 76.32; H, 8.03.

3-Benzyl-6-hepten-2-one (Table 1, Entry 12). To a flame-dried Schlenk flask containing NaH (0.26g, 11 mmol) and THF (20 mL), *tert*-butyl 2-acetyl-5-hexenoate[36] (2.3g, 11 mmol) was added. The mixture was stirred at room temperature for 1 h, then benzyl bromide (1.3 mL, 11 mmol) was added and the flask was fitted with a reflux condenser and refluxed for 15 h. The mixture was cooled, quenched with H_2O (50 mL), and extracted with 3×30 mL of ethyl acetate. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated, and the 3 benzyl-3-(*tert*-butoxycarbonyl)-6-heptenoate was purified by Kugelrohr distillation. A solution of *p*-toluenesulfonic acid monohydrate (65 mg, 0.34 mmol) in toluene (30 mL) under argon in a 50-mL round-bottom flask equipped with a Dean-Stark trap and reflux condenser was heated at reflux for 1.5 h. The solution was cooled to room temperature and all of the 3 benzyl-3-(*tert*-butoxycarbonyl)-6-heptenoate from the previous step was added. The mixture was heated at reflux for 5 h, then it was cooled to room temperature overnight. The solution was diluted with 30 mL of diethyl ether, washed with 30 mL of saturated $NaHCO_3$ solution, and dried over $MgSO_4$. The solvent was removed *in vacuo*, and the crude material was purified by flash chromatography (hexane−ethyl acetate

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19:1) to yield 1.1 g (50% yield) of a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.2 (m, 5 H); 5.72 (m, 1 H); 4.99 (m, 2 H); 2.74 (m, 2 H); 2.69 (m, 1 H); 2.03 (m, 2 H); 1.98 (s, 3 H); 1.75 (m, 1 H); 1.51 (m, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 212.2, 139.4, 137.8, 128.8, 128.5, 126.3, 115.3, 53.8, 38.0, 31.4, 30.5, 30.4. IR (neat): 3027, 2926, 1713, 1496, 1453, 1351, 1162, 914, 753, 700. Anal. Calcd for $C_{14}H_{18}O$: C, 83.11; H, 8.97. Found: C, 83.35; H, 8.92.

5-(Benzyloxy)-6-hepten-2-one (Table 1, Entry 13). 1,6-Heptadien-3-ol was prepared by a method adapted from that of Ireland[37] by the addition of vinylmagnesium bromide to the crude aldehyde product generated by the Swern oxidation of 4-penten-1-ol. The 1,6-heptadien-3-ol (1.6 g, 14 mmol) was added to a flame-dried Schlenk flask under argon containing a slurry of NaH (0.5 g, 20 mmol) and THF (20 mL) and fitted with a reflux condenser. The mixture was heated to reflux for 20 min, benzyl bromide (1.62 mL, 14 mmol) was added, and the solution was heated at reflux for 10 h. The mixture was quenched with 20 mL of H_2O, acidified with several drops of 4 N HCl solution, and extracted with 3 × 50 mL of diethyl ether. The combined organic layers were washed with 30 mL of saturated $NaHCO_3$ solution and 30 mL of brine, then dried over $MgSO_4$. The solvent was removed *in vacuo* and the resulting oil was purified to 90% purity by flash chromatography (hexane−ethyl acetate 48:1) to afford 1.2 g (6 mmol) of material. Without further purification, this material was added to a suspension of palladium(II) chloride (0.1 g, 0.6 mmol), copper(I) chloride (0.6 g, 6 mmol), dimethylformamide (5 mL), and H_2O (0.6 mL) that had stirred under a balloon of oxygen for 1 h.[34] The mixture was stirred for 4 h and then quenched with water and extracted with 3 × 20 mL of diethyl ether. The combined organic layers were washed with 20 mL of brine and dried over $MgSO_4$. The solvent was removed *in vacuo*, and the resulting oil was purified by flash chromatography (hexane−ethyl acetate 9:1) to afford 0.6 g (10% yield from 4-penten-1-ol) of a colorless oil.^{1}H NMR (300 MHz, $CDCl_3$): δ 7.28 (d, J = 8.1 Hz, 2 H); 7.18 (t, J = 7.2 Hz, 2 H); 7.10 (t, J = 7.2 Hz, 1 H); 5.58 (m, 1 H); 5.08 (m, 2 H); 4.47 (d, J = 11.9 Hz, 1 H); 4.18 (d, J = 11.9 Hz, 1 H); 3.61 (q, J = 7.3 Hz, 1 H); 2.13 (t, J = 6.5 Hz, 2 H); 1.83 (q, J = 7.0 Hz, 2 H); 1.61 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 208.5, 138.3, 128.3, 127.7, 127.6, 127.4, 117.4, 79.3, 70.0, 39.2, 29.9, 29.2. IR (neat): 3030, 2926, 1717, 1452, 1422, 1356, 1166, 1071, 1028, 993, 928, 736, 699. Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 76.97; H, 8.40.

Conversion of Enones to Cyclopentanones. General Procedure A. $Cp_2Ti(PMe_3)_2$ (0.1 equiv), toluene (2−3 mL), PMe_3 (0.6 equiv), and enone (1.0 equiv, thoroughly dried by passage through a column of activated alumina) were added to a dry Schlenk tube in a glovebox under argon. The solution was cooled at −40 °C for 20 min, then Ph_2SiH_2 (1.0 equiv, also thoroughly dried by passage through a column of activated alumina) was added. The flask was then sealed, removed from the glovebox, and placed in a −20 °C bath to be stirred for 16−48 h. After this time, the solution was allowed to warm to room temperature. The toluene was removed *in vacuo* and acetone (10 mL) and 1 N HCl (1 mL) were added. The mixture was stirred for 1−4 h and then was diluted with 30 mL of ether and 30 mL of saturated NH_4-Cl solution. The organic layer was washed with brine and dried over $MgSO_4$ to afford the crude product.

General Procedure B. $Cp_2Ti(PMe_3)_2$ (0.1 equiv), toluene (2−3 mL), PMe_3 (0.6 equiv), and enone (1.0 equiv, thoroughly dried by passage through a column of activated alumina) were added to a dry Schlenk tube in a glovebox under argon. The solution was cooled at −40 °C for 20 min, then Ph_2SiH_2 (1.0 equiv, also thoroughly dried by passage through a column of activated alumina) was added. The flask was then sealed, removed from the glovebox, and placed in a −20 °C bath to be stirred for 16−48 h. After this time, the solution was allowed to warm to room temperature. The toluene was removed *in vacuo* and the residue was put under an atmosphere of argon. THF (10 mL) and CH_2Cl_2 (10 mL) were added and the solution was cooled to 0 °C. Trifluoroacetic acid (3 mL) and H_2O (0.3 mL) were added, and the reaction was stirred vigorously as the ice bath warmed to room temperature. After 16 h, saturated $NaHCO_3$ solution (30 mL) was added *slowly*, and after bubbling ceased, the reaction mixture was poured into a seperatory funnel containing 30 mL each of ethyl ether and H_2O. The aqueous layer was extracted with 30-mL portions of ethyl ether and ethyl acetate, then the combined organic layers were washed with brine and dried over $MgSO_4$ to afford the crude product.

General Procedure C. $Cp_2Ti(PMe_3)_2$ (0.1 equiv), toluene (2−3 mL), PMe_3 (0.6 equiv), and enone (1.0 equiv, thoroughly dried by passage through a column of activated alumina) were added to a dry Schlenk tube in a glovebox under argon. The solution was cooled at −40 °C for 20 min, then Ph_2SiH_2 (1.0 equiv, also thoroughly dried by passage through a column of activated alumina) was added. The flask was then sealed, removed from the glovebox, and placed in a −20 °C bath to be stirred for 16−48 h. After this time, the solution was allowed to warm to room temperature. The toluene was removed *in vacuo* to afford the crude product.

General Procedure D. $Cp_2Ti(PMe_3)_2$ (0.1 equiv), toluene (2−3 mL), PMe_3 (0.6 equiv), and enone (1.0 equiv, thoroughly dried by passage through a column of activated alumina) were added to a dry Schlenk tube in a glovebox under argon. The solution was cooled at −40 °C for 20 min, then Ph_2SiH_2 (1.0 equiv, also thoroughly dried by passage through a column of activated alumina) was added. The flask was then sealed, removed from the glovebox, and placed in a −20 °C bath to be stirred for 16−48 h. After this time, the solution was allowed to warm to room temperature. The toluene was removed *in vacuo* and the residue was put under an atmosphere of argon. THF (5 mL) and then 1 N TBAF in THF (5 mL) were added and the reaction was stirred for 15 min. The THF was removed *in vacuo* and residue was taken up in ether and water (30 mL each). The organic layer was washed with brine and dried over $MgSO_4$ to afford the crude product.

***In Situ* Generation of the Catalyst. General Procedure E.** Finely crushed Cp_2TiCl_2 (0.15 equiv) was added to a dry Schlenk flask under argon. The flask was evacuated and backfilled three times with argon, then 2 mL of toluene was added. The suspension was cooled to −78 °C and 0.3 equiv *n*-BuLi added, then after 10 min, 1 equiv of PMe_3 was added. The red-colored mixture was stirred for 1 h at −78 °C and then for 1 h at 0 °C, during which time the solution turned brown. The reaction mixture was then cannula filtered into a dry Schlenk tube containing 1 equiv of enone. The resulting red solution was cooled to −20 °C, Ph_2SiH_2 was added, and the reaction was stirred at low temperature for 16−48 h. After this time, the solution was allowed to warm to room temperature. The toluene was removed *in vacuo* and acetone (10 mL) and 1 N HCl (1 mL) were added. The mixture was stirred for 1−4 h and then diluted with 30 mL of ether and 30 mL of saturated NH_4Cl solution. The organic layer was washed with brine and dried over $MgSO_4$ to afford the crude product.

1,2-Dimethylcyclopentanol (Table 1, Entry 1).[38] Procedure A was used to convert 6-hepten-2-one (0.230 g, 2.34 mmol) to the desired product. Purification by Kugelrohr distillation followed by flash chromatography (pentane−ethyl ether 4:1) afforded 0.150 g (65% yield) of a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.8−1.3 (m, 7 H), 1.25 (s, 3 H), 1.13 (s, 1 H), 0.94 (d, J = 6.7 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 79.8, 43.8, 41.0, 32.1, 25.9, 20.8, 12.4. IR (neat): 3418, 2959, 2873, 1454, 1374, 1292, 1213, 1151, 1088, 1030, 916, 875, 841, 734.

1,2-Dimethyl-1-*n*-propylcyclopentanone (Table 1, Entry 2).[39] Procedure A was used to convert 8-nonen-4-one (0.254 g, 1.8 mmol) to the desired product. Purification by Kugelrohr distillation followed by flash chromatography (ethyl ether−pentane 1:6) afforded 0.170 g (67% yield) of the desired compound as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.85−1.25 (m, 11 H), 0.96 (t, J = 7.9 Hz, 3 H), 0.92 (d, J = 7.0 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 82.2, 42.9, 41.9, 38.3, 32.1, 21.0, 18.0, 14.8, 12.5. IR (neat): 3478, 2956, 2872, 1456, 1378, 942, 735.

9-Methylbicyclo[4.3.0]nonan-1-ol (Table 1, Entry 3). Procedure A was used to convert 2-homoallylcyclohexanone (0.138 g, 0.9 mmol) to the desired product. Purification by Kugelrohr distillation followed by flash chromatography afforded 0.10 g (72% yield) of a 9:1 mixture of cyclized product and the carbonyl reduction product as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) mixture: δ 2.1−1.0 (m, 15 H), 0.90 (d, J = 6.8 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 81.0, 47.1, 36.2, 33.7, 31.1, 29.6, 27.8, 25.0, 23.2, 12.8. IR (neat) mixture: 3443, 2928,

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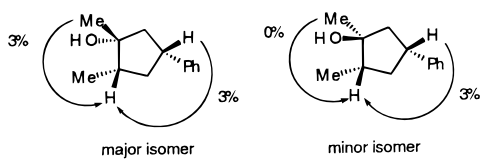
2856, 1448, 1120, 1076, 997, 952, 939. Anal. Calcd for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 77.77; H, 11.73.

Diethyl 1-Hydroxy-2-methylcyclopentane-4,4-dicarboxylate (Table 1, Entry 4). Procedure B was used to convert diethyl 1-oxo-5-hexene-3,3-dicarboxylate (0.183 g, 0.75 mmol) to the desired product. Purification by Kugelrohr distillation followed by flash chromatography (pentane−ethyl ether 7:3) afforded 0.121 g (66% yield) of a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.22 (m, 4 H), 4.08 (m, 1 H), 2.48 (m, 1 H), 2.45 (dd, J = 14.9 Hz, J = 16.1 Hz, 1 H), 2.34 (dd, J = 4.4 Hz, J = 14.9 Hz, 1 H), 2.03 (m, 1 H), 2.01 (s, 1 H), 1.98 (m, 1 H), 1.24 (td, J = 7.1 Hz, J = 2.5 Hz, 6 H), 1.06 (d, J = 6.4 Hz, 3 H). ^{13}C NMR (75 MHz, C_6D_6): δ 173.7, 173.0, 75.8, 61.9, 61.6, 59.5, 44.1, 40.7, 39.9, 14.34, 14.30, 13.6. IR (neat): 3534, 2979, 1731, 1446, 1367, 1259, 1181, 1146, 1096, 1038, 961, 862, 756. Anal. Calcd for $C_{12}H_{20}O_5$: C, 59.0; H, 8.25. Found: C, 59.23; H, 8.19.

Diethyl 1-Hydroxy-1,2-dimethylcyclopentane-4,4-dicarboxylate (Table 1, Entry 5). Procedure B was used to convert diethyl 2-oxo-6-heptene-4,4-dicarboxylate (0.232 g, 0.75 mmol) to the desired product. Purification by Kugelrohr distillation followed by flash chromatography (hexane−ethyl acetate 9:1) afforded 0.161 g (69% yield) of a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.19 (m, 4 H), 2.54 (dd, J = 8.0 Hz, J = 13.8 Hz, 1 H), 2.50 (d, J = 14.8 Hz, 1 H), 2.21 (d, J = 14.8 Hz, 1 H), 2.11 (s, 1 H), 2.03 (dd, J = 12.2 Hz, 1 H), 1.82 (m, 1 H), 1.259 (m, 9 H), 0.97 (d, J = 7.1 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.1, 172.6, 79.5, 61.8, 61.5, 57.1, 48.9, 43.9, 40.5, 24.5, 14.0, 13.9, 11.4. IR (neat): 3533, 2976, 1731, 1447, 1368, 1259, 1153, 1061, 930, 867. Anal. Calcd for $C_{13}H_{22}O_5$: C, 60.45; H, 8.58. Found: C, 60.58; H, 8.38.

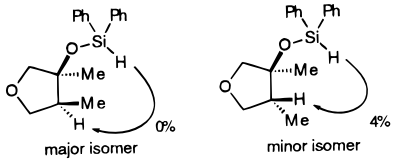
1,2,4,4-Tetramethylcyclopentanol (Table 1, Entry 6).[40] Procedure A was used to convert 4,4-dimethyl-6-hepten-2-one (0.140 g, 1.0 mmol) to the desired product. Purification by Kugelrohr distillation followed by flash chromatography (pentane−ethyl ether 4:1) afforded 85 mg (61% yield) of a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.84 (m, 1 H), 1.7−1.4 (m, 4 H), 1.22 (s, 3 H), 1.10 (s, 3 H), 1.03 (s, 1 H), 1.00 (s, 3 H), 0.92 (d, J = 6.6 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 81.1, 56.6, 48.5, 43.4, 35.2, 31.9, 31.8, 26.8, 11.8. IR (neat): 3472, 2953, 2866, 2361, 1456, 1372, 1303, 1236, 1210, 1079, 1009, 933, 910, 847.

1,2-Dimethyl-4-phenylcyclopentanol (Table 1, Entry 7). Procedure A was used to convert 4-phenyl-6-hepten-2-one (0.188 g, 1.0 mmol) to the desired product. Purification by Kugelrohr distillation followed by flash chromatography (hexane−ethyl acetate 5.7: 1) afforded 0.117 g (62% yield) of a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.28 (m, 4 H), 7.15 (m, 1 H), 3.09 (m, 1H), 2.30 (dd, J = 10.2 Hz, J = 14.1 Hz, 1 H), 2.12 (m, 1 H), 1.90 (dd, J = 7.1 Hz, J = 15.0 Hz, 1 H), 1.78 (m, 1 H), 1.69 (m, 1 H), 1.32 (s, 3 H), 1.20 (s, 1 H), 1.01 (d, J = 6.2 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 146.6, 128.3, 127.3, 125.7, 79.6, 49.7, 45.2, 42.7, 42.2, 27.3, 12.1. IR (neat): 3576, 3461, 2958, 2931, 2871, 1945, 1871, 1804, 1602, 1493, 1455, 1373, 1121, 1031, 922, 847, 759, 700. Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.53. Found: C, 81.84; H, 9.70. A nuclear Overhauser enhancement study was undertaken to determine the relative configuration of the two isomers. For the major isomer, irradiation of the C-3 hydrogen at δ 3.09 gave a 3% enhancement at the C-4 hydrogen, and irradiation of the C-1 methyl at δ 1.32 gave a 3% enhancement at the C-4 hydrogen. For the minor isomer, irradiation of the C-3 hydrogen at δ 3.36 also gave a 3% enhancement at the C-4 hydrogen, while irradiation of the C-1 methyl at δ 1.01 gave no enhancement at the C-4 hydrogen. Based on these observations, the configuration of the isomers were assigned as shown:



1,2-Dimethyl-4-phenyl-4-azacyclopentanol (Table 1, Entry 8). Procedure A was used to convert *N*-allyl-*N*-acetonylaniline (0.177 g, 9.3 mmol) to the mixture of desired products. Purification by Kugelrohr distillation followed by separation on a chromatatron (hexane−ethyl acetate 9:1) afforded 61 mg of isomer A and 69 mg of isomer B (36% and 40% yields, respectively) as colorless oils which turn to a blue color over time if not stored at low temperature. ^{1}H NMR (300 MHz, $CDCl_3$): Isomer A: δ 7.21 (t, J = 8.8 Hz, 2 H), 6.65 (t, J = 8.3 Hz, 1 H), 6.50 (d, J = 8.8 Hz, 2 H), 3.42 (dd, J = 8.7 Hz, 1 H), 3.29 (dd, J = 10.3 Hz, J = 17.1 Hz, 1 H), 3.07 (dd, J = 9.5 Hz, 1 H), 2.09 (m, 1 H), 1.68 (s, 1 H), 1.34 (s, 3 H), 1.05 (d, J = 6.7 Hz, 3 H). Isomer B: δ 7.22 (t, J = 7.7 Hz, 2 H), 6.66 (t, J = 7.3 Hz, 1 H), 6.50 (d, J = 7.8 Hz, 2 H), 3.63 (dd, J = 7.2 Hz, J = 9.3 Hz, 1 H), 3.28 (dd, J = 9.8 Hz, J = 21.0 Hz, 2 H), 2.94 (dd, J = 5.5 Hz, J = 9.3 Hz, 1 H), 2.22 (m, 1 H), 1.94 (s, 1 H), 1.29 (s, 3 H), 1.0 (d, J = 7.0 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): Isomer A: δ 129.1, 115.8, 111.4, 102.2, 77.4, 61.6, 53.7, 42.2, 23.0, 10.1. Isomer B: δ 129.1, 115.8, 111.3, 102.2, 78.6, 59.9, 54.0, 43.4, 21.3, 14.5. IR (neat): Isomer A: 3433, 2965, 2833, 1919, 1810, 1599, 1509, 1472, 1386, 1194, 1120, 938, 873, 750, 691. Isomer B: 3396, 2967, 2841, 1912, 1711, 1662, 1599, 1505, 1481, 1372, 1184, 1141, 999, 747, 692. Anal. Calcd for $C_{12}H_{17}NO$ (A): C, 75.35; H, 8.96. Found: C, 75.32; H, 8.86.

1,2-Dimethyl-4-oxacyclopentyl Diphenylsilyl Ether (Table 1, Entry 9). Procedure D was used to convert allyl acetonyl ether (0.103 g, 0.9 mmol) to the desired product. Purification by Kugelrohr distillation afforded 0.210 g (77% yield) of a 3:2 mixture of the desired compounds as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) mixture: Isomer A: δ 7.62 (m, 4 H), 7.39 (m, 6 H), 5.55 (s, 1 H), 4.03 (dd, J = 7.8 Hz, J = 15.8 Hz, 2 H), 3.62 (dd, J = 10.2 Hz, J = 20.0 Hz, 2 H), 2.01 (m, 1 H), 1.34 (s, 3 H), 1.03 (d, J = 6.9, 3 H). Isomer B: δ 7.62 (m, 4 H), 7.39 (m, 6 H), 5.55 (s, 1 H), 4.17 (t, J = 8.1 Hz, 1 H), 3.88 (d, J = 9.0 Hz, 1 H), 3.66 (d, J = 10.4 Hz, 1 H), 3.43 (t, J = 7.8 Hz, 1 H), 2.32 (m, 1 H), 1.33 (s, 3 H), 0.92 (d, J = 7.5 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) mixture: δ 134.4 (2), 130.0, 130.1, 127.9 (4), 83.6, 82.1, 79.3, 78.3, 74.9, 74.2, 49.7, 44.8, 22.3, 20.6, 14.2, 9.0. IR (neat) mixture: 3135, 3068, 3049, 3000, 2969, 2930, 2867, 2123, 1959, 1889, 1823, 1589, 1455, 1428, 1383, 1324, 1241, 1154, 1112, 1058, 1036, 1012, 926, 890, 824, 734, 699. Anal. Calcd for $C_{18}H_{22}O_2Si$ (mixture): C, 72.44; H, 7.43. Found: C, 72.68; H, 7.55. A nuclear Overhauser enhancement study was undertaken to determine the relative configurations of the two isomers observed. For the major isomer, irradiation of the Si hydrogen at δ 5.55 gave no enhancement at the C-2 hydrogen, while for the minor isomer, irradiation of the Si hydrogen at δ 5.55 gave a 4% enhancement at the C-2 hydrogen. Based on this observation, the relative configurations of the two isomers were assigned as shown:



1,2-Dimethyl-1-hydroxy-2,3-dihydroindene (Table 1, Entry 10a). Procedure B was used to convert *o*-allylacetophenone (0.160 g, 1.0 mmol) to the desired product. Purification by flash chromatography (ethyl acetate−hexane 1:4) followed by Kugelrohr distillation afforded 0.144 g (89% yield) of the desired compound as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.38 (m, 1 H), 7.24 (m, 3 H), 2.96 (dd, J = 7.2 Hz, J = 15.6 Hz, 1 H), 2.66 (dd, J = 9.0 Hz, J = 15.6 Hz, 1 H), 2.25 (m, 1 H), 1.56 (s, 3 H), 1.38 (s, 1 H), 1.16 (d, J = 7.7 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 148.1, 142.6, 128.3, 126.7, 124.9, 122.6, 80.7, 45.0, 37.9, 25.1, 12.9. IR (neat): 3422, 3068, 2967, 1913, 1707, 1606, 1477, 1375, 1290, 1215, 1183, 1076, 912, 841, 761, cm^{-1}. Anal. Calcd for $C_{11}H_{14}O$: C, 81.4; H, 8.7. Found: C, 81.19; H, 8.66.

1,2-Dimethylindene (Table 1, Entry 10b).[41] Procedure A was used to convert *o*-allylacetophenone (0.146 g, 0.91 mmol) to the desired product. Purification by Kugelrohr distillation followed by flash chromatography (hexane) afforded 93 mg (71% yield) of the desired compound as a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36 (d, J = 8.3 Hz, 1 H), 7.23 (m, 2 H), 7.10 (t, J = 6.5 Hz, 1 H), 3.25 (s, 2 H), 2.05 (s, 3 H), 2.02 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.5, 142.3, 137.9, 132.4, 126.0, 123.6, 123.0, 117.9, 42.4, 13.8, 10.1.

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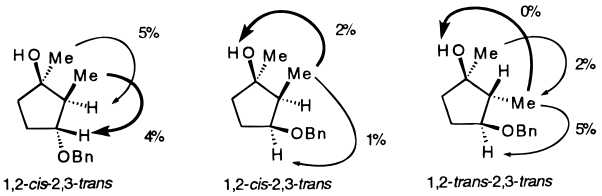
IR (neat): 3066, 3042, 2911, 1933, 1897, 1782, 1636, 1607, 1467, 1458, 1395, 1226, 1205, 1015, 757, 717. Anal. Calcd for $C_{11}H_{12}$: C, 91.61; H, 8.39. Found: C, 91.49; H, 8.64.

Ethyl 1-Hydroxy-1,2-dimethylcyclopentanol-5-carboxylate (Table 1, Entry 11). Procedure B was used to convert ethyl 2-oxo-6-heptene-3-carboxylate (0.166 g, 0.9 mmol) to the title compound. Purification by Kugelrohr distillation followed by flash chromatography (pentane−ethyl acetate 3:1) afforded 0.132 g (79% yield) of a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.14 (qd, $J = 7.0$ Hz, $J = 2.1$ Hz, 2 H); 2.83 (t, $J = 6.5$ Hz, 1 H); 1.91 (m, 4 H); 1.66 (s, 1 H); 1.21 (m, 1 H); 1.28 (t, $J = 7.1$ Hz, 3 H); 1.21 (s, 3 H); 0.96 (d, $J = 6.7$ Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.9, 81.6, 60.3, 55.8, 43.1, 30.9, 24.9, 23.7, 14.3, 13.0. IR (neat): 3508, 2966, 2906, 2875, 1784, 1716, 1455, 1373, 1342, 1299, 1253, 1188, 1096, 1039, 917, 857. Anal. Calcd for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74. Found: C, 64.36; H, 9.86.

5-Benzyl-1,2-dimethylcyclopentanol (Table 1, Entry 12). Procedure A was used to convert 3-benzyl-6-hepten-2-one (0.153 g, 0.76 mmol) to the title compound. Purification by Kugelrohr distillation followed by flash chromatography (hexane−ethyl acetate 12:1) afforded 0.120 g (77% yield) of a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.27 (m, 2 H); 7.24 (m, 3 H); 2.93 (dd, $J = 3.4$ Hz, $J = 12.6$ Hz, 1 H); 2.23 (t, $J = 11.7$ Hz, 1 H); 2.15 (m, 1 H); 1.75 (m, 3 H); 1.23 (s, 3 H); 1.22 (m, 2 H); 1.19 (s, 1 H); 0.96 (d, $J = 6.5$ Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 141.5, 128.9, 128.3, 125.7, 81.1, 51.4, 42.9, 37.8, 30.3, 27.6, 23.4, 14.0. IR (neat): 3449, 3028, 2956, 2871, 1583, 1495, 1452, 1372, 910, 698. Anal. Calcd for $C_{14}H_{20}O$: C, 82.29; H, 9.87. Found: C, 82.50; H, 9.82.

3-(Benzyloxy)-1,2-dimethylcyclopentanol (1,2-*cis*-2,3-*trans* and 1,2-*cis*-2,3-*cis*) (Table 1, Entry 13). Procedure B was used to convert 5-(benzyloxy)-6-hepten-2-one (99 mg, 0.45 mmol) to the title compound. Purification by Kugelrohr distillation followed by flash chromatography (hexane−ethyl acetate 9:1 (200 mL), 2.5:1 (100 mL)) afforded 38 mg of 1,2-*cis*-2,3-*trans* title compound and 14 mg of 1,2-*cis*-2,3-*trans* title compound (52% combined yield) as colorless oils. **1,2-*cis*-2,3-*trans*:** ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.30 (m, 5 H); 4.58 (d, $J = 11.7$ Hz, 1 H); 4.45 (d, $J = 11.7$ Hz, 1 H); 3.72 (m, 1 H); 2.13 (m, 1 H); 1.89 (m, 1 H); 1.70 (m, 3 H); 1.27 (s, 3 H); 1.10 (s 1 H); 1.04 (d, $J = 7.0$ Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.8, 128.3, 127.7, 127.4, 86.2, 79.1, 71.7, 50.1, 38.5, 28.3, 26.7, 10.6. IR (neat): 3528, 2965, 1453, 1406, 1061, 1028, 734, 696. Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.31; H, 9.16. Found: C, 76.04; H, 9.30. **1,2-*cis*-2,3-*cis*:** ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32 (m, 5 H); 4.64 (d, $J = 12.2$ Hz, 1 H); 4.38 (d, $J = 12.2$ Hz, 1 H); 3.90 (t, $J = 4.9$ Hz, 1 H); 3.19 (s, 1 H); 2.01 (m, 2 H); 1.78 (m, 2 H); 1.60 (m, 1 H); 1.23 (s, 3 H); 1.10 (d, $J = 6.8$ Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 134.3, 128.3, 127.5, 127.3, 84.3, 79.6, 70.8, 48.2, 40.0, 28.1, 24.7, 7.5. IR (neat): 3448, 2962, 2871, 1453, 1207, 1091, 1027, 917, 734, 697. Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.31; H, 9.16. Found: C, 76.30; H, 9.28. A nuclear Overhauser enhancement study was undertaken to determine the relative configuration of the three isomers observed. For the 1,2-*cis*-2,3-*trans* isomer (major isomer), irradiation of the C-1 methyl at δ 1.27 gave a 5% enhancement at the C-2 hydrogen, and irradiation of the C-2 methyl at δ 1.04 gave a 4% enhancement at the C-3 hydrogen. For the 1,2-*cis*-2,3-*cis* isomer (minor isomer), irradiation of the C-2 methyl at δ 1.10 gave a 2% enhancement at the C-1 hydroxyl, but only a 1% enhancement of the C-3 hydrogen. For the 1,2-*trans*-2,3-*cis* isomer (not isolated, but observed when reaction run at −20 °C), irradiation of the C-1 methyl at δ 1.21 gave a 2% enhancement of the C-2 methyl, but only a 1% enhancement at the C-2 hydrogen. Irradiation of the C-1 methyl at δ 0.87 gave a 5% enhancement at the C-3 hydrogen and no enhancement at the C-1 hydroxyl. Based on these observations, the configurations of the three isomers were assigned as shown:



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