IR ($CHCl_3$) 3040, 2930, 1660, 1540, 1350, 1270, 1075, 1020, 920, 845; ^1H NMR ($CDCl_3$) δ 8.49–8.40, 8.0–7.98 and 7.75–7.67 (4 H, m), 5.50–5.46 (1 H, ddd, J = 8.0, 2.2, 1.9). Anal. Calcd for $B_{10}C_{11}H_{18}N_4O_{11}$: C, 26.94; H, 3.70; N, 11.43; B, 22.04. Found: C, 26.59; H, 3.69; N, 11.24; B, 22.24.

(1*S*,2*R*)-1-[2-(*m*-Aminophenyl)-1,2-dicarbadodecaboran-(12)-1-yl]-1,2,3-propanetriol (10). A mixture of **9** (234 mg) in dioxane (3.5 mL), 95% EtOH (11 mL), water (1.1 mL), and 10% Pd/C (39 mg) was stirred under 4 atm of H_2 at 23 °C for 6 h. The catalyst was filtered off, and the filtrate evaporated. Flash column chromatography (MeOH:hexane:CH_2Cl_2 1:3:6) gave 112 mg (72%) of a white solid. Recrystallization in CH_2Cl_2 gave a white solid: mp 178 °C; $[\alpha]_D$ = +5.0 (c 10, EtOH); ^1H NMR ($CDCl_3$, meta isomer) δ 7.19–7.04 (2 H, m), 6.87–6.73 (2 H, m), 3.70–3.29 (4 H, br m); ^1H NMR ($CDCl_3$ + acetone-d_6, para isomer) δ 7.35 (2 H, d, J = 8.6), 6.57 (2 H, d, J = 8.6), 3.72 (2 H, br s), 3.40 (2 H, br s). Anal. Calcd for $B_{10}C_{11}H_{23}NO_3$ (meta isomer): C, 40.60; H, 7.12; N, 4.30; B, 33.22. Found: C, 40.63; H, 7.03; N, 4.11; B, 33.34.

(1*S*,2*R*)-1-[2-[3-(2-Hydroxy-1-napthyl)azo]phenyl]-1,2-dicarbadodecaboran(12)-1-yl]-1,2,3-propanetriol (11). An aqueous solution (7.7 M) of $NaNO_2$ (44.7 μL) was added to a solution of the amine **10** (193 mg) in 4.2 M HCl (490 μL) at 0 °C. The reaction was stirred at 0 C for 0.5 h and then added to a solution of β-naphthol (47.7 mg) in EtOH (33.5 mL) at 0 °C. The reaction was stirred at 0 °C for 1 h and warmed to ambient temperature. The solvent was evaporated, and the mixture purified by flash column chromatography (MeOH:CH_2Cl_2:hexane 1:4:5) to give 32 mg (21%) of a red solid: mp (dec) 216–218 °C; IR (KBr) 3501, 3376, 2649, 1599, 1245, 1211, 838, 762; λ_{max} 476 nm; ^1H NMR (acetone-d_6) δ 8.49 (1 H, d, J = 8.2), 8.15 (1 H, br s), 7.94 (1 H, dd, J = 1.2, 7.9), 7.83 (1 H, d, J = 9.4), 7.70 (1 H, dd, J = 1.1, 8.0), 7.66 (1 H, d, J = 7.9), 7.58–7.53 (2 H, apparent t, $J \simeq$ 8.0), 7.41 (1 H, apparent d of t, J = 1.1, 8.1), 6.81 (1 H, d, J = 9.4), 5.49 (1 H, d, J = 7.0), 4.25 (1 H, d, J = 5.9), 3.92–3.69 (3 H, m), 3.57 (1 H, m), 3.06 (1 H, br s). Anal. Calcd for $B_{10}C_{21}H_{28}N_2O_4$: C, 52.48; H, 5.87; B, 22.49. Found: C, 52.81; H, 5.86; B, 22.11.

Acknowledgment. Generous support from the National Institutes of Health (CA-31753) is gratefully acknowledged.

Registry No. **1e**, 123052-37-9; **1t**, 123074-11-3; **2e**, 123052-38-0; **2t**, 123052-39-1; **3e** isomer 1, 123052-40-4; **3e** isomer 2, 123052-53-9; **4e**, 123052-41-5; **4t**, 123052-42-6; **5e**, 123052-43-7; **5t**, 123052-44-8; **6**, 123052-45-9; **7**, 123052-46-0; **8**, 123052-47-1; *meta*-**9**, 123052-48-2; *para*-**9**, 123052-49-3; *meta*-**10**, 123052-50-6; *para*-**10**, 123052-51-7; **11**, 123052-52-8; phenylcarborane, 16390-61-7; 2,3-*O*-isopropylidene-D-glyceraldehyde, 15186-48-8; 1,2-dicarba-*closo*-dodecaborane, 16872-09-6; 1,2:3,4-di-*O*-isopropylidene-α-D-galactohexodialdo-1,5-pyranoside, 4933-77-1; 2,3:4,5-di-*O*-isopropylidene-L-arabinose, 23568-31-2; 1-(but-3-enyl)-1,2-dicarbadodecaborane, 17522-80-4; β-naphthol, 135-19-3.

Supplementary Material Available: Listings of crystallographic data collection, position and thermal parameters, interatomic distances, and angles, anisotropic thermal parameters for compound **1e** (14 pages). Ordering information is given on any current masthead page.

Rearrangement of Bicyclo[2.2.1]heptane Ring Systems by Titanocene Alkylidene Complexes to Bicyclo[3.2.0]heptane Enol Ethers. Total Synthesis of (±)-$\Delta^{9(12)}$-Capnellene†,‡

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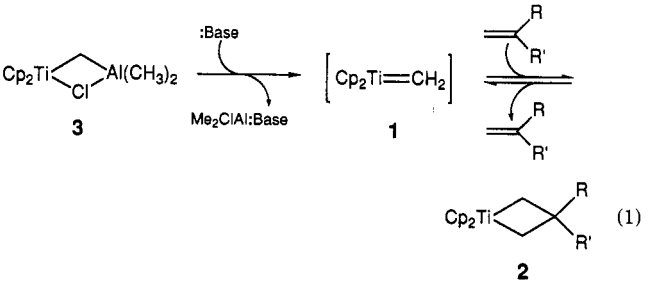
Received September 20, 1988

A variety of ester-substituted norbornenes react with titanamethylene complex (Tebbe's reagent) to yield stable titanacyclobutanes. Endo esters do not react with the reagent in competition with the norbornene double bond. The X-ray structure of the metallacycle formed from titanacene methylene complex and 1-methylbicyclo-[2.2.1]hept-5-ene-2,3-dicarboxylic acid diisopropyl ester was determined. On heating, the metallacycle rearranged to a carbene–olefin complex. The ratio of productive opening, cleavage of the bicycloheptane ring system, to nonproductive opening, regeneration of the starting materials, is controlled by a variety of steric factors that were studied and analyzed. The productive opening was detected by the formation of the product resulting from the intramolecular trapping of the intermediate titanium alkylidene by the endo ester functionality in a Wittig-like reaction to yield substituted bicyclo[3.2.0]heptenes. Rearrangement of the titanacycle formed from 4,4-dimethyltricyclo[5.2.1.0^{1,5}]dec-8-ene-6-carboxylic acid *tert*-butyl ester yielded 10,10-dimethyl-3-methoxy-7-vinyltricyclo[5.3.0.0^{2,5}]dec-2-ene, which was transformed into $\Delta^{9((12)}$-capnellene in good yield.

Introduction

In recent years, titanium-catalyzed olefin metathesis has become a very well understood process. Titanium complexes capable of generating the titanocene methylidene species (1, eq 1) have been shown to display catalytic metathesis activity. Initially, the dimethylaluminum chloride adduct **3** was isolated by Tebbe and co-workers and found to slowly catalyze the selective exchange of terminal methylene groups of isobutene and methylene cyclohexane.[1] Addition of a strong Lewis base cocatalyst



(1)

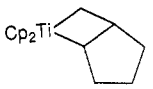
† Contribution no. 7849.

‡ Dedicated to the memory of John K. Stille, Distinguished Professor of Chemistry (Colorado State University). Deceased July 19, 1989.

0022-3263/90/1955-0843$02.50/0

to this titanium complex produced a rapid and efficient metathesis catalyst.[2] Intermediates in this process were isolated and structurally characterized as titanacyclobutanes.[3] These olefin adducts (2), which can regenerate the olefin and 1, also exhibited the ability to catalyze the degenerate metathesis of terminal olefins.[4] Even in the absence of a cocatalyst, the intermediate titanacyclobutanes were found to be efficient catalysts of methylene exchange.

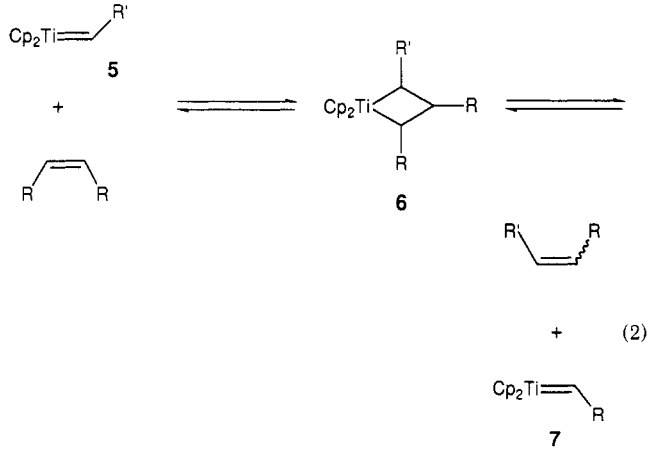
Despite the ability of 1 to catalyze degenerate metathesis, the productive metathesis of 1,2-disubstituted olefins was a very inefficient process.[5] Thermolysis of the α,β-disubstituted metallacycle 4 derived from the cycloaddition



4

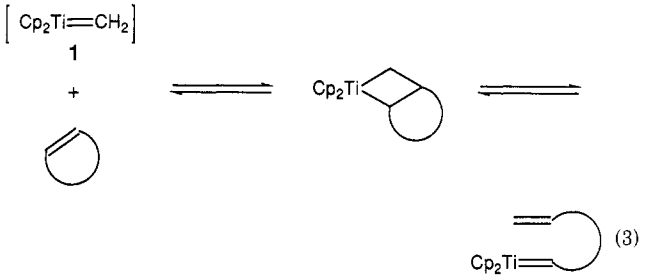
of 1 to cyclopentene quantitatively regenerated cyclopentene.[6] Thus the prevalent pathway for the dissociation of this intermediate α,β-disubstituted metallacycle was the reverse of its formation. Due to the orientation of available orbitals around the titanocene unit,[7] the bonding scheme of an alkylidene ligand is such that all four substituents on the titanium–carbon double bond, as on an organic olefin, lie in the same plane.[8] This arrangement of substituents results in severe steric interactions between the alkylidene substituent and the bulky cyclopentadienyl ligand. As the size of the substituent increases, these interactions become even less favorable. Thus, productive metathesis of 1,2-disubstituted olefins has been thwarted mostly by the lesser stability of the resulting alkyl-substituted titana olefin and, to a lesser extent, the greater stability of the more substituted organic olefin.

There are two methods that would be expected to enhance 1,2-disubstituted olefin metathesis. The first involves the generation of a substituted titanocene alkylidene 5 and subsequent olefin trapping to form the intermediate trisubstituted metallacyclobutane (6, eq 2). In these



(2)

systems where R′ is more sterically bulky than R, dissociation of the intermediate metallacycle would then favor the productive metathesis pathway and formation of alkylidene 7. Until recently, the major obstacle in this process was the lack of a way in which to cleanly generate an alkyl-substituted titanocene alkylidene. The need for a general, high-yield method of producing these species has received much attention.[9] A general process has not yet been discovered; however, the clean generation of a titanocene alkylidene has recently been reported.[9c] The second factor that will enhance 1,2-disubstituted olefin metathesis is ring strain. Metathesis of a strained, cyclic olefin would involve ring-opening with concomitant release of the intrinsic strain energy (eq 3). If the strain was large



(3)

enough, the energetics of the system would overcome the relative instability of the organometallic intermediate and favor the ring-opening product. In the process, the elusive substituted alkylidene is generated in a manner similar to that recently reported.[9c]

Norbornene is an extensively studied and readily available strained cyclic olefin. The compound itself has an inherent strain energy of 27.2 kcal/mol, whereas the saturated system, bicyclo[2.2.1]heptane, has a somewhat smaller value of 17.6 kcal/mol.[10] Metallacyclobutanes containing a bicyclo[2.2.1]heptane framework are possible intermediates in the structural rearrangement of tricyclo[3.2.1.$0^{2,4}$]oct-6-ene species,[11,12] though until recently they had not been observed. Waddington and Jennings were able to isolate several norbornene platinacyclobutanes and fully characterize these intermediates.[12] Investigation of an iridium-catalyzed system further suggested that ring-opening metathesis, through an iridium alkylidene, occurred in the rearrangement of a norbornene iridacyclobutane.[13]

Generation of 1 in the presence of this strained olefin was found to produce an unusually stable metallacycle.[14] Unstrained cis-1,2-disubstituted olefins form metallacycles that are normally stable only at temperatures below 0 °C.[5] With the formation of metallacycle 8, the strain due to the presence of the olefin in the bicyclic system (9.6 kcal/mol) was eliminated and not easily regenerated (Scheme I). In contrast to other α,β-disubstituted metallacyclobutanes, 8 showed no signs of thermal instability at temperatures

(1) (a) Tebbe, F. N.; Parshall, G. W.; Overall, D. W. *J. Am. Chem. Soc.* **1979**, *101*, 5074. (b) Klabunde, U.; Tebbe, F. N.; Parshall, G. W.; Harlow, R. L. *J. Mol. Catal.* **1980**, *8*, 37.

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(12) (a) Waddington, M. D.; Jennings, P. W. *Organometallics* **1982**, *1*, 385. (b) Waddington, M. D.; Jennings, P. W. *Organometallics* **1982**, *1*, 1370.

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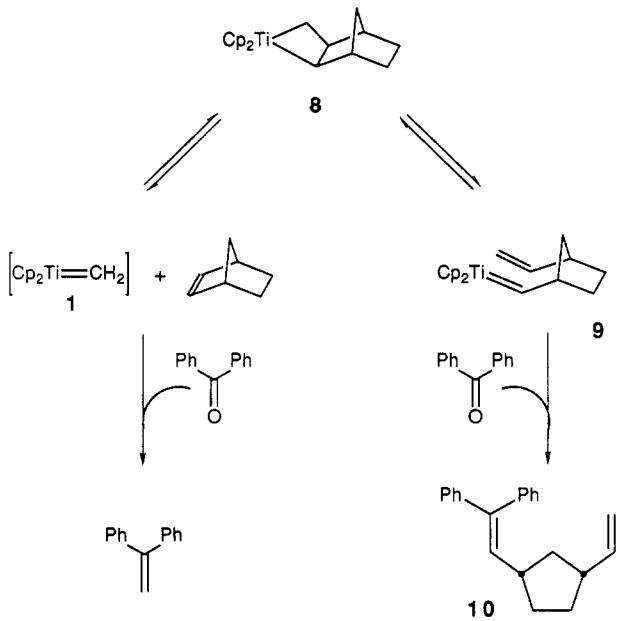
(14) (a) Marchand, A. P.; Grubbs, R. H., unpublished results. (b) Howard, T. H.; Grubbs, R. H.; Marchand, A. P. Southeast/Southwest Regional ACS Meeting, New Orleans, LA, Dec 1980, paper 262. (c) Hentges, S.; Grubbs, R. H., unpublished results.

Scheme I. Productive Metathesis of Norbornene by Thermolysis of 8



up to 55 °C. In the presence of benzophenone[15] at 65 °C, thermal decomposition gave rise to a product distribution containing 69% of the ring-opened product **10**, resulting from the substituted alkylidene **9**, and 29% 1,1-diphenylethylene.[16]

The achievement of a substantial amount of ring-opened product provided a means of studying the intricacies of the reaction. The focus of our attention was to further accentuate the ring-opening process and to develop the synthetic utility of the metathesis process. It became apparent that there existed a possibility for additional enhancement of the metathesis product. If the substituted alkylidene could be selectively removed from the equilibrium process illustrated in Scheme I, in preference to titanocene methylidene, the reaction would be drawn toward the ring-opened product. The most efficient way to attain selective trapping would be to involve a carbonyl on the norbornene. In such a system, trapping of the substituted alkylidene is an intramolecular process and entropically favored over the intermolecular reaction of the carbonyl with **1**. This intramolecular trapping process involves not only the formation of a carbon–carbon double bond but also has the added attraction of ring formation. The structural rearrangement by the ring-opening metathesis and subsequent ring forming processes has obvious synthetic interest.

The versatility of the titanium system, in addition to the metathesis activity, lies in the variety of carbonyl-trapping agents that can be employed.[15] Reaction of the ring-opened alkylidene with an attached ketone or aldehyde would give the same ring closure as an intramolecular Wittig reaction, which has found extensive application in organic synthesis.[17] The unique advantage of the titanium system is that alkylidene trapping can also be performed by esters[15] and amides,[15] producing the expected enol ethers and enamines, respectively. This "Wittig-type" alkylidene transfer chemistry has been performed only on esters by the transition-metal ylides of titanium,[15] zirconium,[18] niobium,[19] and tantalum,[19] and there have been no reports of an intramolecular process of this type. Our investigations focused on the ring-opening metathesis and intramolecular trapping of ester-substituted bicyclo[2.2.1]heptane substrates. Through the use of ^1H–^1H correlated NMR, the products of the structural rearrangement were unequivocally identified.[20]

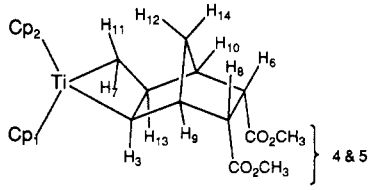
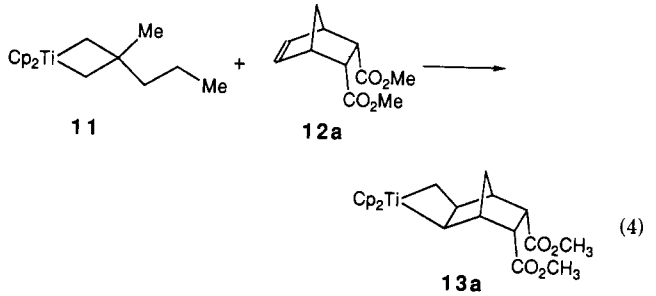


Figure 1. Proton resonance assignments of **13a** (protons are numbered as they occur from low field to high field).

Because titanocene methylidene (**1**), used in the formation of metallacycle **8**, also reacts readily with the esters to form enol ethers, the substrate had to be designed to yield selective initial reaction at the olefin. To accomplish this, the hindered endo ester was prepared, making the reaction of the ester with the sterically bulky titanocene unit highly unfavorable. An added advantage to the use of these endo ester substrates is their synthetic availability. A variety of endo-ester-substituted bicyclo[2.2.1]heptene compounds are easily prepared from readily accessible starting materials by using the Diels-Alder cycloaddition reaction.[21]

Results and Discussion

Synthesis and Thermolysis of 13. Initial investigation of the reaction between ester-substituted norbornene substrates and titanocene methylidene sources was performed with the dimethyl ester **12a**.[22] With **11** as the source of **1**, observation of the reaction by ^1H NMR revealed nearly quantitative conversion to a single metallacycle, as was evidenced by the appearance of two inequivalent cyclopentadienyl signals at 5.46 and 5.41 ppm (eq 4). On a preparative scale, the product was isolated in high yield (84%) as a deep red powder by using either **3** or **11** as the source of titanocene methylidene.



(4)

The ^1H NMR assignments of this single isomer are shown in Figure 1. The presence of the two ester groups

(15) Organic carbonyls irreversibly trap titanocene alkylidenes producing the "Wittig-type" alkylidene transfer product. See: (a) Clawson, L.; Buchwald, S. L.; Grubbs, R. H. *Tetrahedron Lett.* **1984**, *25*, 5733. (b) Pine, S. H.; Zahler, R.; Evans, D. A.; Grubbs, R. H. *J. Am. Chem. Soc.* **1980**, *102*, 3270. (c) Pine, S. H.; Pettit, R. J.; Geib, G. D.; Cruz, S. G.; Gallego, C. H.; Tijerina, T.; Pine, R. D. *J. Org. Chem.* **1985**, *50*, 1212. (d) Cannizzo, L. F.; Grubbs, R. H. *J. Org. Chem.* **1985**, *50*, 2316.

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(17) For a review of the intramolecular Wittig reaction see: Becker, K. B. *Tetrahedron* **1980**, *36*, 1717.

(18) (a) Hartner, F. W., Jr.; Schwartz, J.; Clift, S. M. *J. Am. Chem. Soc.* **1983**, *105*, 640. (b) Clift, S. M.; Schwartz, J. *J. Am. Chem. Soc.* **1984**, *106*, 8300.

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(20) For information on two-dimensional NMR see: Bax, A. *Two-Dimensional Nuclear Magnetic Resonance in Liquids*; D. Reidel: Boston, 1982.

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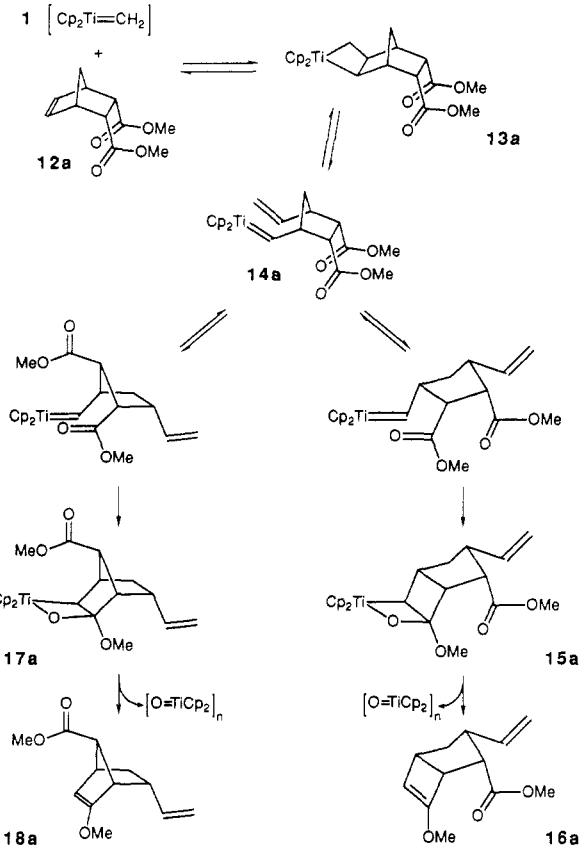
Scheme II. Pathways of Thermolysis Available to Metallacycle 13a



was evident from the methyl resonances at 3.46 and 3.40 ppm. Proton H_3 (Figure 1) had a chemical shift characteristic of a hydrogen on the tertiary carbon α to the titanium in the metallacycle ring. Signals due to protons H_9 and H_{10} had narrow peak shapes typical for bicyclo[2.2.1]heptene bridgehead hydrogen resonances, which normally exhibit very small coupling, if any, to vicinal protons.[23] Resonances H_{12} and H_{14} had the characteristic shape and pattern of protons on the methylene bridge of the norbornene substrate. From these distinctive patterns, partial assignment of proton resonances was made through the use of ^1H–^1H correlated two-dimensional NMR.[20] Difference nuclear Overhauser enhancement (NOE) experiments allowed the complete assignment of **13a**. Saturation of the downfield cyclopentadienyl resonance (Cp_1) produced enhancement of protons H_3, H_7, and H_{13}. The enhancement of protons H_9, H_{11}, and H_{12} resulted from the saturation of the upfield cyclopentadiene resonance (Cp_2). As a result of these experiments, proton H_9 was shown to be close to the metal center and thus vicinal to H_3. Another important feature of metallacycle **13a** was determined by the difference NOE experiments. The enhancement of H_{12}, upon saturation of the upfield cyclopentadienyl resonance, confirmed metallacycle **13a** as the isomer resulting from cycloaddition to the less hindered exo face of the strained olefin.

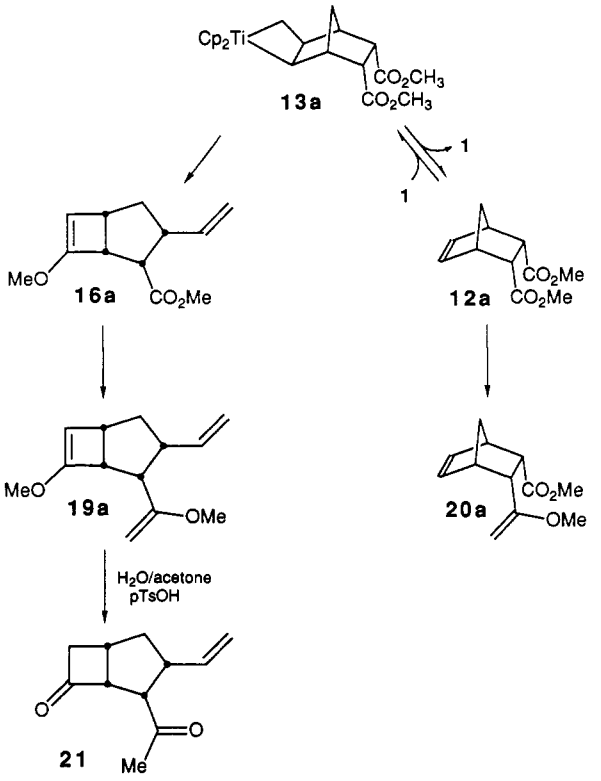
There were three conceivable routes of thermolysis available to the metallacycle (Scheme II). Because metallacycle formation is reversible, it was likely that starting olefin and **1** would be regenerated. If, on the other hand, ring-opening metathesis occurred to form intermediate **14a**, the substituted alkylidene would have two carbonyls with which it could react and, thus, two additional reaction pathways. Trapping of the alkylidene intermediate with the nearest carbonyl would result in the proposed intermediate oxametallacycle **15a**, which would then rapidly dissociate to the bicyclo[3.2.0]heptene ring system product **16a**. Alternately, the ester carbonyl across the cyclopentane could trap the alkylidene to produce **17a**, which would ultimately lead to the bicyclo[2.2.1]heptene ring system **18a**. This pathway would be less favorable due to the steric interaction between the ester substituent and the cyclopentadienyl ligands that would arise upon formation of **17a**. Due to the elevated reaction temperatures and the regeneration of **1**, products resulting from intermolecular methylenation of **12a**, **16a**, and **18a**, were possible as well.

Thermolysis of a benzene solution of **13a** for 11 h at 70 °C produced four distinct organic products (capillary gas chromatography). Disappearance of **13a** required temperatures of at least 65 °C to proceed at a reasonable rate; product distribution showed no change at reaction temperatures up to 90 °C. Varying the concentration of **13a** from 0.071 to 0.57 M similarly had no measurable effect on product distribution. Under the reaction conditions, there was no depletion of the products over an additional 5-day period at 85 °C.

Isolation of two products from the mixture of four was accomplished using flash chromatography. The least mobile compound was found to be identical in every respect with a sample of the starting olefin **12a**. The fraction with the highest R_f value was found to be a single compound that showed extensive structural rearrangement from the original norbornene substrate. This compound was very sensitive to hydrolysis and decomposed slowly upon contact with silica gel. The 500-MHz ^1H NMR spectrum revealed the presence of a terminal vinyl group by resonances at 6.30, 5.00, and 4.95 ppm, as well as a trisubstituted vinyl ether singlet at 4.45 ppm. This information suggested that ring-opening metathesis had occurred to produce a substituted alkylidene, which had then been intramolecularly trapped by an ester group. A terminal, monosubstituted vinyl ether functional group, resulting from methylenation of the second ester group, was also present by observation of the two proton resonances at 4.84 and 4.20 ppm. The absence of characteristic bicyclo[2.2.1]heptene peaks, such as those due to the bridgehead protons, suggested a methylenated derivative of **16a** (**19a**, Scheme III) rather than **18a**. The remaining elutant was examined by ^1H NMR and found to contain a 3:1 mixture of two compounds. The major component displayed two inequivalent norbornene olefin protons at 6.50 and 6.15 ppm, terminal vinyl ether protons at 3.95 and 3.82 ppm, and bridgehead protons at 2.93 and 2.78 ppm. This compound was methylenated product, **20a**, from the reaction of **12a** and **1**, which were both regenerated in the nonproductive dissociation of the metallacycle (Scheme III). This product could also have been formed from **13a** and **1** followed by metallacycle cycloreversion. The elevated temperature at which the cycloreversion took place allowed intermolecular trapping to be a much more favorable process than during the formation of **13a**. The spectra of the minor component of the binary mixture resembled that of the other ring-opened product **19a** in every way except for one—the terminal vinyl ether resonances were absent and a downfield methyl ester singlet at 3.43 ppm was observed instead of the methyl ether singlet at 3.27 ppm. From this information, the minor component of this mixture was determined to be a product

(23) For ^1H NMR information on bicyclo[2.2.1]heptene compounds see: (a) Mellor, J. M.; Webb, C. F. *J. Chem. Soc., Perkin Trans 2* **1974**, 26. (b) Davis, J. C.; Van Auken, T. *J. Am. Chem. Soc.* **1965**, *87*, 3900.

Scheme III. Product Map of the Thermolysis of Metallacycle 13a



that resulted from ring opening and subsequent intramolecular trapping consistent with the structure of **16a**. Compound **16a** was also very sensitive to hydrolytic conditions such as extended contact with silica gel. Acid-catalyzed hydrolysis of the methylenated, ring-opened compound **19a** with acetone/water produced the corresponding dione **21**, which was then characterized. Carbonyl stretching frequencies of 1777 and 1710 cm^{-1} suggested the presence of both a cyclobutanone and an unstrained ketone, respectively.[24] The structural skeleton of this derivative was confirmed by the decoupling of each individual proton resonance.

The preference for the formation of **16a**, over that of **18a** was the direct result of the intermediates involved in their formation. Intermediate **15a**, although never observed, was favored with respect to **17a**. The origin of this preference was mostly the result of the unfavorable syn ester substituent on **17a**. The severe steric interaction of the ester with the titanocene unit is demonstrated by the absence of **18a** in the product mixture. The effect of similar interactions on metallacycle formation has been observed by Gilliom using a *syn*-7-methylnorbornene substrate.[25] Due to the interactions between the methyl substituent and the cyclopentadienyl ligands of **1**, metallacycle formation does not occur.

Once the products had been identified and their specific proton resonances assigned, the products were quantified by ^1H NMR integration against an internal standard of mesitylene. Results of this quantification are shown in Table I. Ring opening of the norbornene unit by the metallacycle accounted for 19% of the products—12% due to the methylenation of **16a**. Nonproductive metallacycle decomposition was responsible for 62% of the products;

(24) Silverstein, R. M.; Bassler, G. C.; Morrill, T. C. *Spectrometric Identification of Organic Compounds*, 4th ed.; Wiley: New York, 1981.
(25) Gilliom, L. R. Ph.D Thesis, California Institute of Technology, 1986.

Table I. Dependence of Product Distribution on the Steric Properties of the Ester Group

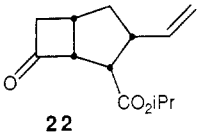
substrate		product yield, %				conversion % (16 + 19)/(12 + 20 + 16 + 19)
	R	19	16	12	20	
a	Me	12	7	40	22	23
b	Et	7	22	42	11	35
c	iPr		39	46		46

22% was due to the side product produced from methylenation of **12b**. It became apparent from the product analysis that side products resulting from intermolecular methylenation by **1** must be minimized to selectively generate a single product.

The effect of increasing the steric bulk of the ester group, thereby reducing the accessibility of the carbonyl, was investigated by using the diethyl ester substrate **12b**.[22] After formation and isolation of the diethyl ester norbornene metallacycle, it was allowed to thermally rearrange under conditions similar to those used for **13a**. Products that resulted from the reaction were analyzed by capillary gas chromatography and ^1H NMR and quantified as shown in Table I. By changing the ester groups from methyl to ethyl, dramatic changes in the product distribution were observed. Side products, resulting from the methylenation of both **16** and the norbornene diester, were both markedly reduced, and the yield of the desired product **16** was increased. Further steric bulk at the ester groups was anticipated to continue this trend.

The ester carbonyl groups were made even less accessible through the synthesis of the more hindered diisopropyl ester **12c**. Reaction of the isopropyl ester substrate with **11** formed the expected metallacycle, which was isolated in 58% yield. The reduced yield with respect to **13a** was due to the high solubility of **13c** in nonprotic solvents. Heating a benzene solution of the metallacycle at 80 °C for 12 h produced only two organic products. Quantification of these products using ^1H NMR integration, versus the internal standard mesitylene, revealed 39% of the rearranged product **16c** and 46% of the regenerated diester **12c**. Side products that resulted from methylene transfer to the carbonyls of the products were not observed. On a preparative scale, the product and diester were easily separated through the use of flash chromatography, although recovery of **16c** was greatly reduced due to the sensitivity of this compound toward silica gel. The product of productive metathesis, **16c**, was isolated as a clear, colorless liquid. The terminal olefin resonances at 6.36, 5.05, and 4.97 ppm were quite diagnostic of the ring-opening metathesis process. Subsequent intramolecular trapping of the ring-opened alkylidene was evident by the cyclobutene enol ether formation. The presence of this functional group was verified by the olefinic enol ether singlet at 4.33 ppm and the isopropyl ether proton resonance at 3.94 ppm, which differed substantially from the isopropyl ester proton signal at 5.05 ppm. The individual decoupling of each proton resonance allowed the assignment of all proton resonances, but verification of the bicyclo[3.2.0]heptene ring system analogous to **16**, as opposed to the bicyclo[2.2.1]heptene system such as **18**, could not be made for this molecule. Absence of coupling to the enol ether proton prevented the distinction between the two different carbon skeletons.

Hydrolysis of **16c** with a catalytic amount of *p*-toluenesulfonic acid produced the corresponding cyclobutanone **22**, confirming the bicyclo[3.2.0]heptane ring system. Carbonyl stretches characteristic of a cyclobutanone and an ester were observed by infrared spec-



22

troscopy at 1780 and 1724 cm^{-1}, respectively. Assignment of each individual ^1H NMR proton resonance was made through the use of ^1H–^1H correlated NMR. Analysis of the spectrum cross peaks that resulted from vicinal J coupling verified the bicyclo[3.2.0]heptane ring skeleton.

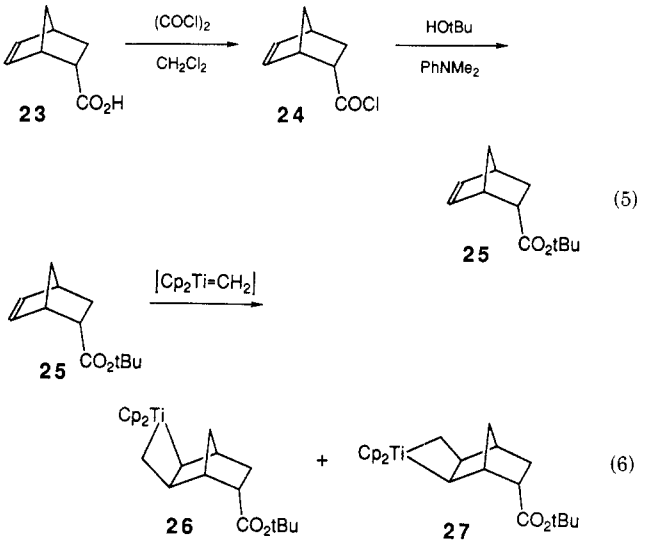
The effect of increasing the size of the ester alkyl group was apparent from the data in Table I. As the substituent became more bulky, two important changes occurred. The most obvious change was the reduction and ultimate elimination of the side products due to intermolecular methylenation. A more subtle change was the effect of the delicate metathesis equilibrium of this system. As the ester group changed from methyl to isopropyl, the ratio of ring-opened products to nonproductive metathesis products doubled. This was observed by examining the conversion of **12** to the rearranged products **16** and **19**. With the methyl ester, only a 23% conversion was obtained. Besides reducing the quantities of side products, the ethyl group enhanced the conversion of the ring-opening process to 35%. Through the use of the bulky isopropyl ester, the side products were finally eliminated and conversion was further enhanced to a value of 46%.

From the diester series of substrates, it was learned that the product distribution was highly dependent upon the steric properties of the ester group. The size of the *O*-alkyl substituent on the ester had two effects on the homologation process that altered the composition of the product mixture. Because ester substituents adopt the greatly favored s-cis conformation,[26] in which the substituent eclipses the carbonyl, an increase in size of the alkyl group had a dramatic effect on the steric protection of the carbonyl. In addition to the shelter provided by the alkyl substituents, the less bulky carbonyl oxygens were directed under the norbornene framework. As a result, the carbonyl groups were further sheltered by the bicyclic skeleton from the intermolecular attack of **1**. Although the increased size of ester substituents affected both homologation processes, intermolecular methylenation was reduced and ultimately eliminated with respect to the intramolecular cyclization process. The observed increase in selectivity was also due, in part, to the promotion of the ring-opening process. Because of the increased size of the ester substituents, the vicinal steric interactions of the ester groups became accentuated. The only way in which these eclipsing interactions could be reduced was through the metathesis of the norbornene ring system.

Metathesis of Unsymmetrical Norbornene Substrates. In the absence of one of the ester groups, it was anticipated that the bulk of the ester would still direct the carbonyl toward the norbornene framework, though the single carbonyl would be more subject to the intermolecular attack. In this case, however, a problem concerning the regiochemical cycloaddition of **1** to the unsymmetrical olefin substrate arose. An unsymmetrical strained olefin was prepared through the Diels–Alder reaction of acrylic acid and cyclopentadiene. The resulting acid was obtained as pure endo-bicyclo[2.2.1]hep-5-ene-2-carboxylic acid (**23**) and was easily transformed to the *tert*-butyl ester through the synthesis of the intermediate acid chloride (**24**, eq 5).

(26) For methyl acetate, the ΔH(s-cis–s-trans) is 4.20 kcal/mol. For a review on the conformations of esters see: Jones, G. I. L.; Owen, N. L. *J. Mol. Struct.* **1973**, *18*, 1.

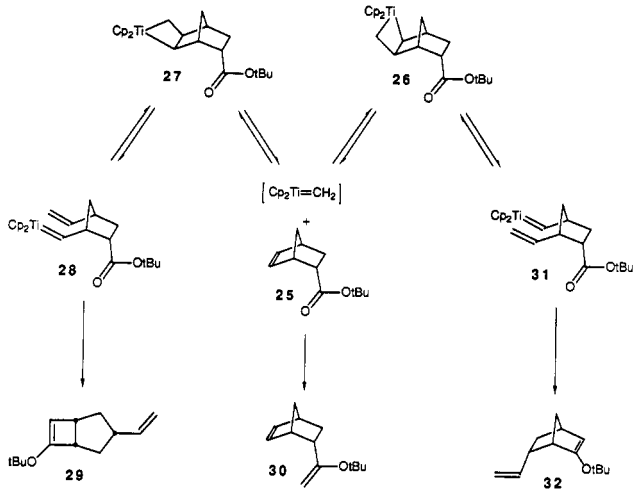
The reaction of **1** with **25** produced a nearly statistical mixture of regiochemical metallacycle isomers (eq 6). By



^1H NMR of a crude reaction mixture, the ratio of **26** to **27** was determined to be 53:47. There was no evidence for products resulting from methylene transfer to the carbonyl of **25**. Thus, the *tert*-butyl ester had sufficient steric bulk to prevent intermolecular methylenation from occurring but did not regiochemically direct the metallacycle formation to any appreciable extent. On a larger reaction scale, each of the regioisomers could be isolated for characterization by repeated fractional crystallization. The structures of the two isomers were determined through the use of ^1H–^1H correlated NMR and difference NOE studies on isomerically pure samples. The regiochemistry of **26** was found to be that shown in eq 6 by the skeletal mapping of those protons displaying cross peaks in the ^1H–^1H correlated spectrum. Crosspeaks that resulted from J coupling to the bridgehead protons made possible the detection of vicinal coupling which, in the normal proton spectrum, could not be extracted from the broad bridgehead proton resonances. In addition, difference NOE studies confirmed this regioisomer as that which was formed from the exo face of the strained olefin. Difference NOE experiments on the other regioisomer **27** allowed confirmation of its structure.

Exposure of each separate isomer to a temperature of 80 °C for 12 h resulted in two very different product distributions. Regioisomer **27** generated a mixture of two organic products, which was determined by capillary gas chromatography, ^1H NMR, and ^{13}C NMR to be an 86:14 combination of **29** and **25**, respectively (Scheme IV). The abundance of the terminal vinyl group confirmed that the ring-opening process had occurred to a large extent, and the proton singlet at 4.34 ppm verified the subsequent intramolecular trapping of the alkylidene and formation of **29**. Upon thermolysis of the other metallacycle isomer, **26**, an organic product mixture of five compounds was generated. Of this mixture, **25** contributed to 9% of the products, and 33% was due to the presence of **29**. Two more major products accounted for 29% and 22% of the mixture. Although separation and full characterization of these two compounds was not achieved, it was suggested by ^1H NMR that 29% of the product mixture resulted from the intermolecular trapping of **1** by **25** to form **30**. The other product was thought to have arisen from the intramolecular trapping of the productive metathesis intermediate **31** to form the norbornene enol ether **32**. The fifth compound detected constituted only 7% of the

Scheme IV. Metathesis Equilibrium and Product Distribution of 25 at 80 °C



product mixture; its structure and nature of origin were undetermined.

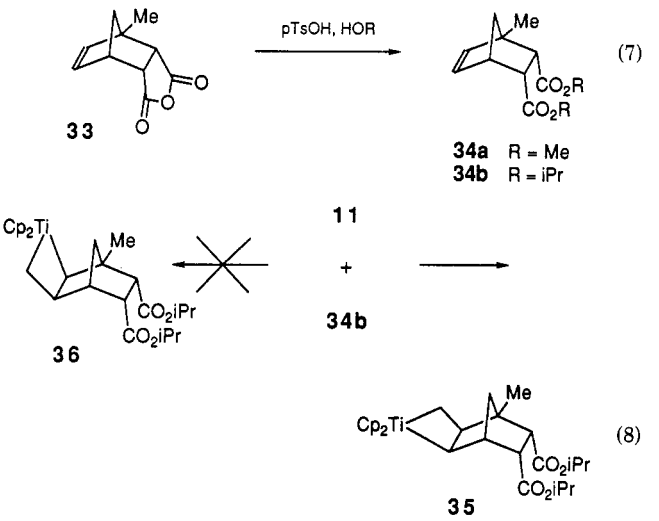
From the product distributions observed for these two monosubstituted ester metallacycle regioisomers (**26** and **27**), as well as for that of the diisopropyl ester metallacycle (**13c**), a greater understanding of the metathesis process was acquired. Efforts to enhance the ring-opening were somewhat successful compared to the parent metallacycle of norbornene (Scheme I). As a result of the intramolecular process, the amount of the ring-opened product was increased from 67% to 86% of the product mixture. This enhancement occurred only when there was a single carbonyl in the position required to form the cyclobutene enol ether. If the carbonyl was situated in the adjacent position, such as in **26**, the ring-opening to **31** would occur, but the trapping process to form **32** was less favorable than the cyclobutene enol ether formation. Because of the less favorable pathway, the reversible recombination of the olefin to form **26** became competitive with the intramolecular carbonyl trapping of **31**. Thus, the equilibrium between **25** and **31** was shifted toward the intermolecular dissociation process and to the regeneration of **1** and **25**. (The ratio (**25** + **30**):**32** was 38:22). These two species accounted for the presence of the other two major products by intermolecular reaction at the carbonyl to produce **30** and through the regioisomeric recombination with the strained olefin to form **27** and, ultimately, **29**.

In the metathesis process where an unsymmetrical substrate was involved and more than one metallacycle intermediate was possible, such as the case observed for **26** and **27**, the path of entry into the equilibrium was crucial to the resulting product distribution. The initial metallacycle formation became important because the transformation of **26** and **27** required the dissociation to **1** and substrate. At the temperature required for this intermolecular isomerization to occur, the lifetime of the uncomplexed **1** was relatively short, and if recombination with the norbornene olefin did not occur, the titanocene methylidene irreversibly decomposed. This instability limited the equilibrium between **26** and **27** from being completely established and thus product formation was under kinetic control.

In the presence of a second, nonparticipating ester substituent, the ratio of the ring-opened product to the nonproductive product was greatly reduced. The effect of the spectator ester substituent was believed to arise from restricting the freedom of movement of the trapping ester into a correct orientation for trapping. With the intramolecular carbonyl trapping process less favorable, the delicate metathesis equilibrium was tipped back toward intramolecular metallacycle formation and nonproductive dissociation to **1** and the norbornene substrate.

It became apparent that a method of directing the methylidene addition with the olefin, to selectively form one of the regioisomeric metallacycles, had to be established. With the ability to regioselectively form the metallacycle, the orientation of a single ester substituent could be controlled. The most effective place to position a substituent was thought to be on a site as close as possible to the olefin, without actually being on the double bond. With a substituent on the olefin itself, the thermal stability of the metallacycle would be greatly reduced. From earlier work with 1-methylnorbornene, it was found that placing a methyl group at the bridgehead position of the norbornene framework was an effective way in which to direct metallacycle formation in these systems.[25]

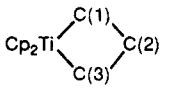
Synthesis of the norbornene diesters with a 1-methyl substituent was accomplished from the corresponding anhydride **33** as shown in eq 7. To prepare the anhydride, 1-methylcyclopentadiene was selectively prepared by using a slight modification of the procedure of Mironov and co-workers[27] and was subsequently trapped with maleic anhydride to form the Diels–Alder adduct **33**. The resulting anhydride was then used to prepare the desired ester substrates by acid-catalyzed esterification (eq 7). Reaction of **34b** with **11** was observed by 500-MHz ^{1}H NMR to form only one metallacycle isomer (eq 8). Isolation of this product was achieved on a larger scale by crystallization from ether to produce a 72% yield of red crystals. Through a difference NOE experiment, the single isomer was found to have the configuration of **35**. Saturation of the upfield cyclopentadienyl ligand produced enhancement of the metallacycle ring proton cis to the norbornene skeleton, and the norbornene bridge proton syn to the metallacycle was also enhanced as expected. In addition to these two protons, the bridgehead proton was enhanced in these studies. The effect upon the bridgehead proton verified the proximity of the bridgehead proton to the Cp ligand as in isomer **35**.

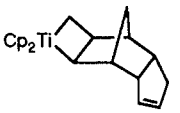
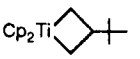
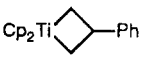


Slow crystallization of **35** from an ether/toluene mixture produced single crystals satisfactory for X-ray crystallographic analysis. Refinement of the structure led to a final R value of 0.058. Information acquired from the resulting

(27) Mironov, V. A.; Sobolev, E. V.; Elizarova, A. N. *Tetrahedron* **1963**, *19*, 1939.

Table II. Selected Structural Parameters of Titanacyclobutanes



	35			
		Bond Lengths[a]		
Ti–C(1)	2.130 (40)	2.124 (2)	2.16	2.127 (3)
Ti–C(3)	2.133 (4)	2.141 (2)	2.14	2.113 (4)
C(1)–C(2)	1.560 (6)	1.555 (3)	1.55	1.546 (5)
C(2)–C(3)	1.596 (6)	1.607 (3)	1.53	1.579 (5)
		Bond Angles[b]		
C(1)–Ti–C(3)	75.1 (2)	76.9 (1)	75	75.3 (1)
C(1)–C(2)–C(3)	110.8 (3)	113.9 (2)	116	112.0 (3)
Ti–C(1)–C(2)	85.2 (2)	84.2 (1)	84	86.0 (2)
Ti–C(3)–C(2)	84.3 (2)	82.5 (1)	85	85.7 (2)
displacement[c]	0.37	0.27	0.09	0.05
pucker angle[d]	25	18	6	3
reference		25	3	3

[a] In angstroms. [b] In degrees. [c] The displacement of C(2) from the plane defined by C(1)–Ti–C(3), in angstroms. [d] The angle between the plane containing C(1)–Ti–C(2) and the plane containing C(1)–C(2)–C(3), in degrees.

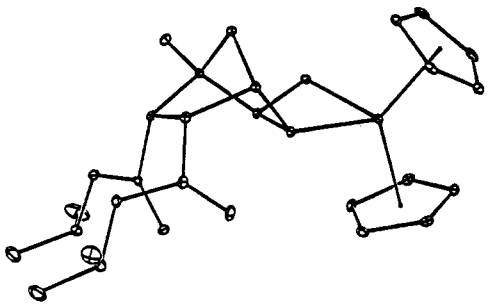


Figure 2. ORTEP drawing of the molecular structure of metallacycle **35**.

crystal structure revealed many interesting features of this norbornene metallacycle. The most obvious feature was the confirmation of the structure **35**, in which the metallacycle had formed on the exo face of the olefin with the regiochemical addition of the titanocene unit away from the methyl substituent (Figure 2). A summary of important bond distances and angles, compared with previously reported titanacyclobutane structures, is shown in Table II.[28] Compared with reported titanacyclobutanes,[3,25] this norbornene metallacycle displayed some unique characteristics. In addition to being a disubstituted metallacycle, the norbornene framework locked both ring substituents in place and forced the bridge carbon toward the cyclopentadienyl ligand. As a result, the syn bridge proton interacted directly with the cyclopentadienyl hydrogens. To relieve these steric interactions, the norbornene skeleton twisted away from the titanium ligand, causing a puckering of the normally planar metallacyclobutane ring. The metallacycle settled into a conformation where the C(1)–Ti–C(3) plane puckered from the C(1)–C(2)–C(3) plane to an extent of 25° (0.37-Å displacement of C(2) from the C(1)–Ti–C(3) plane). The twisting of the norbornene framework and puckering of the metallacycle allowed the syn hydrogen on the norbornene bridge to maintain an interatomic distance of 2.02 Å from the closest cyclopentadienyl hydrogen. This value is well within the sum of the van der Waals radii (2.40 Å) and is smaller than the 2.2-Å value found in the metallacycle of dicyclopentadiene. The inability of metallacyclobutanes such as **8** to accommodate a syn ester substituent, such as intermediate **17**, or a syn methyl group[25] was quite evident from this structure.

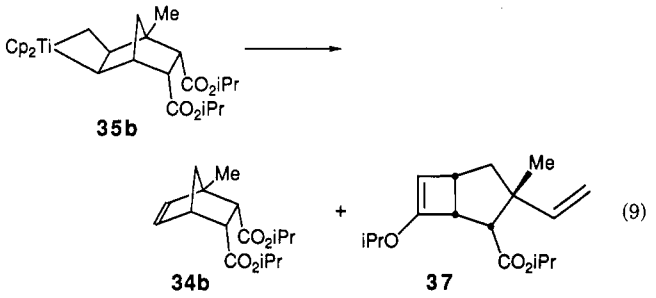
With regard to the metathesis process, there was no apparent distortion of the metallacycle toward a metal alkylidene–olefin complex analogous to **14** (Table II). Both metal–carbon bonds were equal within the limits of their error. The only metallacycle distortion that was observed was the greater length of C(2)–C(3) (1.596 Å) than that of the C(1)–C(2) bond (1.560 Å). This difference in bond lengths was not significantly greater than those previously reported for the β-substituted metallacycles.

As had been expected, the carbonyl of the ester was directed under the norbornene skeleton due to the steric bulk of the *O*-alkyl substituents. As viewed from the ORTEP projection, the effect of these two substituents on each other resulted in an orientation in which the ester groups aligned to minimize steric interactions. Alignment of the carbonyl that would ultimately trap the alkylidene resulted in the correct reorientation for the trapping process. The *O*-alkyl substituents were also observed in the more stable s-cis conformation in which the carbonyl eclipses *O*-alkyl group. The O(2)–C(10)–O(1)–C(11) and O(4)–C(14)–O(3)–C(15) torsion angles were found to be 4.2° and 0.4°, respectively. The preference for this conformation, as previously discussed, helped accentuate the effect of varying the bulk of the ester substituent with respect to the intermolecular side reactions.

The methyl-substituted norbornene metallacycle **35** showed greater resistance to thermolysis than did **13c**. For complete reaction within 12 h, temperatures of 90 °C were required. The product distribution showed no difference to that of a sample exposed to temperatures of 80 °C for 24 h. With the methyl group present on the norbornene framework, the ring-opening was significantly reduced compared to the thermolysis of **13c**. Quantification of the products by comparison to a ^{1}H NMR internal standard revealed that only 13% of the productive metathesis product **37** was formed while 52% of the diester was regenerated (eq 9). By incorporation of a methyl group at

(28) A more complete tabulation of structural information is available on request.

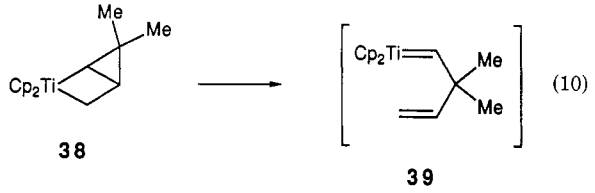
the bridgehead position of the norbornene, the regiochemistry could be completely controlled; however, the presence of the substituent caused the ring-opening pathway to become less favorable for substrates with two vicinal endo ester substituents.



(9)

The effect that the methyl group had on this process did not appear to arise from the hindered intramolecular trapping of the ring-opened product as a result of conformational effects. Instead, it was believed that the inhibition of the rearrangement process was caused by the intramolecular recombination of the alkylidene intermediate with the terminal olefin, thus shifting the metathesis equilibrium toward the more favorable nonproductive intermolecular dissociation of the norbornene substrate. The prominence of diester regeneration was thought to have arisen from steric interaction of the methyl group with the metallacycle ring. From these results, it became apparent that the inherent strain in the norbornene ring was not enough to enhance productive metathesis in the presence of the spectator carbonyl and was even less effective with a 1-methyl substituent present. As previously discussed, there was a second means by which the ring-opened goal could be enhanced—the use of a substituted alkylidene (eq 2).

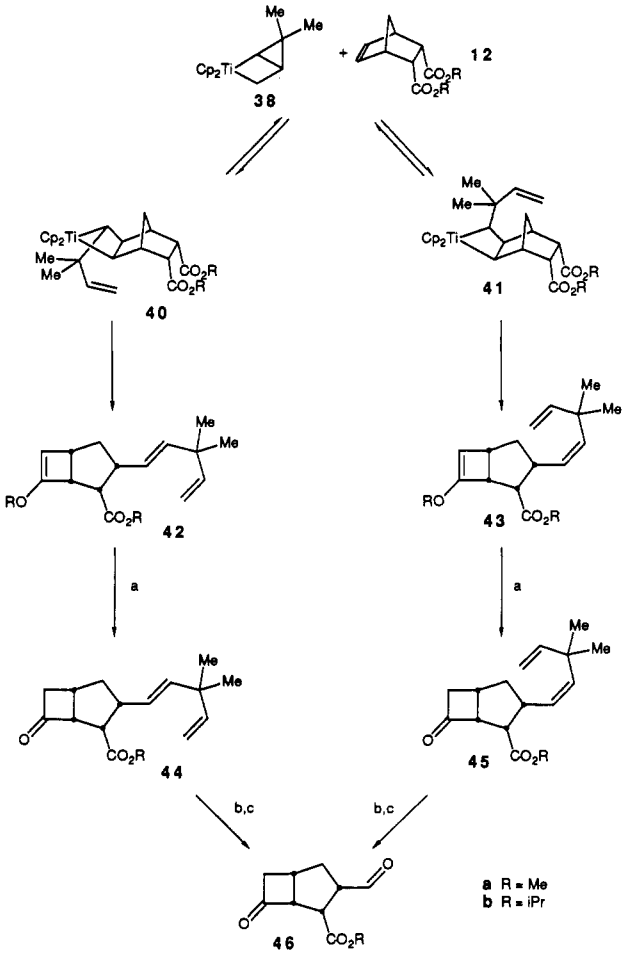
Formation and Thermolysis of Trisubstituted Metallacycles. A high-yield means of generating a substituted titanocene alkylidene was recently reported.[9c] Similar to the strategy employed to ring-open strained norbornene olefins, this method used the strain of a cyclopropane ring to induce complete metathesis of a cyclopropene substrate. The thermal decay of metallacycle **38** at room temperature, formed by cycloaddition of **1** to 3,3-dimethylcyclopropene, has been shown to cleanly generate the titanocene alkylidene fragment **39** (eq 10). Through the use of the substituted alkylidene **39** in the formation of an α,β,α'-trisubstituted norbornene metallacycle (**6**), ring strain was expected to increase the productive metathesis pathway.



(10)

With the use of the dimethyl ester **12a** as a trapping agent, **38** was completely consumed within 1 h. Observation of the reaction mixture by ^{1}H NMR at ambient temperature revealed the formation of a new metallacycle with inequivalent cyclopentadienyl ligands at 5.66 and 5.49 ppm and a single cyclobutene enol ether product resonance at 4.57 ppm. Complete metallacycle thermolysis was accomplished by heating the mixture at 55 °C for 15 h to produce a second cyclobutene enol ether peak which was generated in 3 times the amount of the initial enol ether peak. On a larger scale, the two organic thermolysis products could

Scheme V. Product Map of the Reaction between 38 and 12



be isolated as a mixture. Examination of the product mixture by 500-MHz ^{1}H NMR showed extensive similarities in the two compounds with the major differences arising in the olefinic region. It was evident that both products were the result of the ring-opening process and subsequent ring closure to the cyclobutene enol ether **42a** and **43a** (Scheme V). The differences in the olefinic region resulted from the formation of two different isomers of the intermediate metallacyclobutanes. Two exo metallacycle isomers resulted from the reaction of the substituted alkylidene with the strained olefin. The cycloaddition of the titanocene alkylidene to the strained olefin resulted in formation of metallacycle **40a** with the alkylidene substituent in a trans orientation to the norbornene substrate and, to a lesser extent, a titanacyclobutane with the substituent cis to the norbornene substrate (**41a**). Assuming that this stereochemistry was retained during the ring-opening process, two product isomers would be formed differing only in their *E* (**42a**) or *Z* (**43a**) configuration of the disubstituted olefin. This postulate was easily substantiated by the chemical severing of the carbon–carbon double bonds. Hydrolysis of the two enol ether products generated the two respective ketones, **44a** and **45a**, with an unchanged product ratio (Scheme V). Ozonolysis, followed by a reductive workup, produced a single aldehyde product, **46a**. Characterization of this compound was achieved through the use of two-dimensional ^{1}H–^{1}H correlated NMR, which also confirmed the bicyclo[3.2.0]-heptanone skeletal framework for aldehyde **46a**. This assignment supported in infrared carbonyl stretches at 1718 (aldehyde), 1728 (ester), and 1777 cm^{-1} (cyclobutanone).

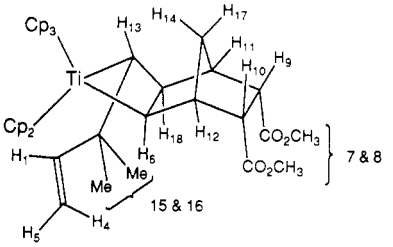


Figure 3. Proton resonance assignments of **40a** (protons are numbered as they occur from low field to high field).

On a preparative scale, a single metallacycle product was isolated from the reaction of **38** and **12a**. In addition to the normal resonances observed for the dimethyl ester metallacycle **13a**, a ^{1}H NMR spectrum of this compound revealed the presence of a terminal olefin group and two methyl groups. Assignment of proton resonances was possible through coupling constants, chemical shifts, and resonance patterns analogous to those found for compound **13a** (Figure 3). Difference NOE experiments were then used to determine the configuration of the substituents on the metallacycle ring. Saturation of the upfield cyclopentadienyl ligand resulted in the enhancement of the nearest bridge proton H_{14}, the closest bridgehead proton H_{12}, and one metallacycle ring proton (H_{13}). This cyclopentadienyl ligand was therefore cis to the norbornene framework on the metallacyclobutane ring. Enhancement of two metallacycle ring protons, as well as the slight enhancement of the internal vinyl proton H_1 was observed by the saturation of the downfield cyclopentadienyl ligand. This series of spectroscopic experiments allowed the metallacycle to be assigned as the trans isomer **40a**. Decomposition of this single isomer at 55 °C in C_6D_6 produced only the (*E*)-cyclobutene enol ether product **42a** and regenerated **12a** in an 86:14 ratio. The assignment as the *E* isomer was substantiated by the magnitude of the coupling between the two protons on the disubstituted olefin (15 Hz). This product was found to be the major isomer produced from the thermolysis of the mixture of **40a** and **41a**.

Reflecting upon the information acquired from the reaction outlined in Scheme V, several important features of this process were noted. Addition of the substituted alkylidene **39a** to the norbornene substrate proceeded with two different orientations. These different reaction pathways resulted in the formation of the two diastereomeric trisubstituted metallacyclobutanes **40a** and **41a**. The metallacycle with the substituent cis to the norbornene framework (**41a**) rapidly regenerated **12a**, produced the cis cyclobutene enol ether **43a** at room temperature, and was not observed as an intermediate in the reaction. The relative instability of this intermediate was undoubtedly due to the steric interactions that resulted from the bulky substituent in a configuration cis to the norbornene. Models showed highly unfavorable interactions between the substituent and both the bridge and bridgehead protons of the norbornene skeleton. Relief of this strain was accomplished only by formation of metallacycle **40a** and the organic product **43a**, resulting from the cis metallacycle, were observed. Upon heating to 55 °C, thermolysis of the less sterically strained **40a** occurred, producing the second and major product of the reaction (**42a**). It was also observed that, in spite of the use of the dimethyl ester, side products resulting from intermolecular trapping were not detected.

To determine the amounts of products that were formed from the intermediate trisubstituted metallacycles **40** and **41**, ^{1}H NMR integration versus an internal standard was used. ^{1}H NMR integration was the method of choice due to the sensitivity of the cyclobutene enol ether functionality during the process of isolation. The use of 1.30 equiv of metallacycle **38** ensured complete metallacycle formation with the diester substrate **12**. After thermolysis, the products were compared to an internal standard of mesitylene. The results can be seen in Table III. The separate reaction of both the dimethyl and diisopropyl esters produced similar overall product yields, but the distribution of the products differed for the two substrates. The conversion of the norbornene substrate to ring-opened metathesis products for **12c** (89%) was much higher than that for **12a** (67%). This trend was similar to that observed for the ring-opening metathesis by the titanocene methylidene fragment. As previously discussed, the cis substituent interactions of the ester groups are relieved somewhat upon ring-opening to a substituted cyclopentane moiety. The increased size of the isopropyl groups could have caused an increase in these steric interactions by inducing a less favorable orientation of these carbonyl substituents. As a result, ring opening became enhanced for the diisopropyl ester substrate.

Table III. Product Distribution upon Reaction of 12 with 38

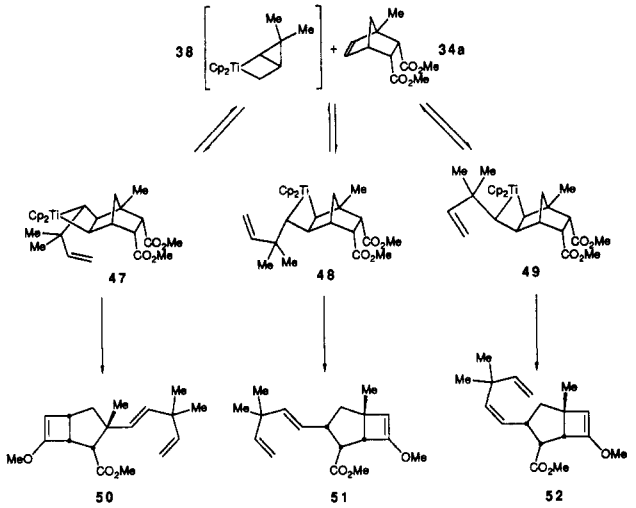
	substrate R	product yield, % 42	43	12	42/43	conversion (42 + 43)/(12 + 42 + 43)	overall yield, %
a	Me	46	15	30	3.1	67	91
b	iPr	57	23	10	2.5	89	90

From the observation that the isolated trans-substituted metallacycle **40a** decomposed to produce an 86% conversion of **12a**, it was deduced that productive metathesis was more prevalent for the trans metallacycle **40** than the cis metallacycle **41**. Added steric interactions between the cis quaternary substituent and the norbornene framework were thought to cause the increased intermolecular dissociation of the titanocene methylidene fragment from **12a**. Also of note from Table III were the differing ratios of trans to cis products. The origin of the larger ratio of 3.1:1.0 for **12a**, in comparison to that of 2.5:1.0 for **12c**, was undetermined.

With the use of the substituted alkylidene, the ring-opening of the strained olefin was greatly enhanced with respect to the metathesis induced by titanocene methylidene. In spite of the fact that minor complications had occurred by the formation of both cis and trans product isomers, the development and utility of this process began to show promise. As previously noted, it was observed that ring-opening metathesis was further enhanced by the absence of the second, nonparticipating ester group. The increase in substrate conversion was observed only for the metallacycle regioisomer with the correct orientation for intramolecular trapping to occur. Similar results were obtained for the reaction of **38** with **25**. Thermolysis of this metallacycle mixture produced six organic products, as determined by capillary gas chromatography, of which the major isomer contributed only 40% toward the total product mixture. The need for a substrate substituent to direct the regiochemical addition of the alkylidene to the strained olefin was obvious. Although difficult to predict, it was thought that the presence of a 1-methyl substituent would again direct the regiochemical addition of the substituted alkylidene. Due to increased steric interaction with the alkylidene substituent, the methyl directing group was also expected to reduce, if not eliminate, the amount of cis metallacycle formed.

Reaction of **38** with the 1-methyl dimethyl ester **34a** at

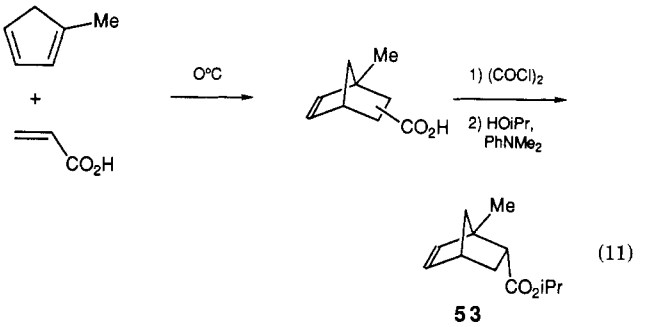
Scheme VI. Product Map of the Reaction between 38 and 34a



room temperature, followed by heating at 65 °C for 12 h, produced three cyclobutene enol ether peaks in a ratio of 65:32:4 as observed by ^{1}H NMR. Thin-layer silica gel chromatography produced two distinct spots upon elution with petroleum ether/ether (9:1). The products of R_f 0.19 and 0.25 were separated by flash chromatography and spectroscopically characterized. The more rapidly eluted compound was found to be **50**, the expected product of the ring-opening process, and was the major product of the reaction (Scheme VI). The remaining elutant was shown to be an 8:1 mixture of inseparable isomers that both resulted from the ring-opening process. Confirmation of the structure of the major isomer was accomplished by two-dimensional NMR. Due to the large vicinal coupling between olefinic protons (16 Hz), the major isomer (**51**) was found to have a trans geometry about the disubstituted olefin. The minor isomer was determined to be the cis isomer (**52**) of the same methyl-substituted bicyclo[3.2.0]heptane skeleton, due to spectroscopic similarities and negligible differences in elutant polarity. This 8:1 ratio of trans to cis isomers, in which the titanium metal center added to the strained olefin on the same side as the methyl directing groups, was the result of the opposite regiochemical addition that produced **50**. Of the observed organic products, the expected product **50** accounted for 44% of the mixture. The products resulting from the opposite regiochemical addition were found to be 22% (**51**) and roughly 2% (**52**) of the reaction mixture. The remaining 32% was accounted for by the regeneration of **34a**. Thus, with this substrate, 68% conversion was achieved.

In the cycloaddition of the substituted alkylidene with **34a**, the 1-methyl substituent on the norbornene had a lesser directing effect on the regiochemical metallacycle formation. The inability of the methyl substituent to direct the cycloaddition of **39** as efficiently as observed for the addition of **1** was due to the increased steric interaction between the added alkylidene substituent and the methyl group. Because this interaction had reached a magnitude comparable to that of the cyclopentadienyl ligand interactions with the methyl substituent, both pathways resulted in product formation. The effects of the increased alkylidene substituent interactions with the methyl substituent were also evident by the absence of the corresponding *Z* isomer of **50**. The larger ratio of the trans:cis products **51** and **52**, 8:1, as compared to 3:1 for the titanocene methylidene source, was most likely due to the differing conformational preferences of this metallacycle ring for a trans substituent as a result of the methyl group. Unlike the relationship between **34b** and **12c**, conversion of **12c** was not dramatically different than that for the methyl-substituted **34a**.

As observed through the thermolysis of **26**, formation of bicyclo[2.2.1]heptene products was not favored. The extent to which this process would occur was examined by reaction of the titanocene alkylidene species with a substrate containing a single ester group vicinal to the methyl directing group. The synthesis of substrate **53** was accomplished through the Diels–Alder reaction of 1-methylcyclopentadiene and acrylic acid, followed by the formation of the isopropyl ester **53** from the corresponding acid chloride (eq 11). This isomer was isolated in 92% isomeric purity through the use of silica gel chromatography in 48% yield.

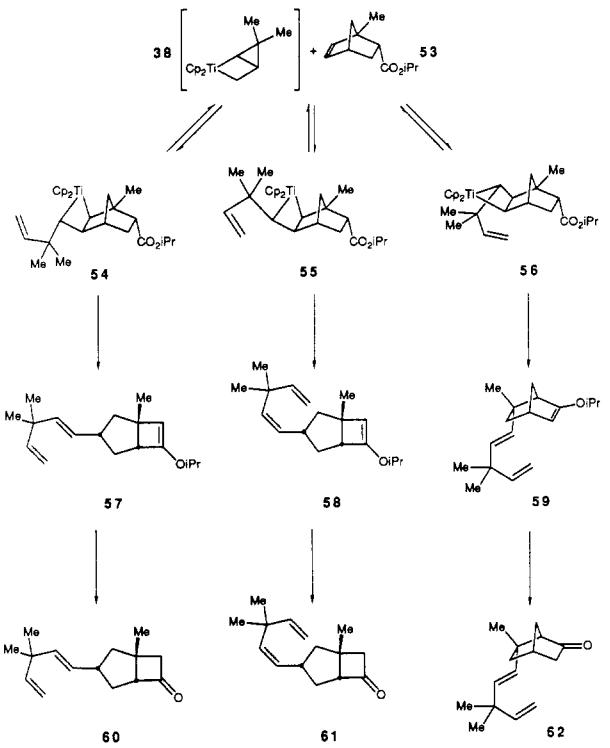


(11)

Allowing the substituted alkylidene **39** to react with **53** gave three productive organic products in the ratio 2.6:1.1:1.0, and **53** was regenerated to an extent of only 6%. This mixture of products was inseparable by silica gel chromatography and was hydrolyzed. The resulting mixture of ketones produced two eluants of R_f = 0.48 and 0.32 in petroleum ether/ether (4:1). The faster moving material was a mixture of two isomeric compounds, and a single product was obtained from the band with the lower R_f. By 400-MHz ^{1}H NMR, the mixture of compounds was a 2.5:1.0 ratio of *trans*- to *cis*-cyclobutanones that did not contain isolated disubstituted double bonds. Thus, it was assumed that this mixture had resulted from the regiochemical addition of the titanium on the same side as the methyl substituent to form **54** and **55**, followed by the ring-opening and alkylidene-trapping process to produce **57** and **58** (Scheme VII). By ^{1}H NMR, the remaining product was found to have the isolated disubstituted double bond of the expected product **62**, as well as the very characteristic bridgehead protons of the bicyclo[2.2.1]-heptane ring system. ^{1}H–^{1}H correlated NMR confirmed the skeleton and found the regiochemistry of the substituents consistent with the structure **62**. This molecule exhibited a carbonyl stretching frequency of 1750 cm^{-1} and a ^{13}C NMR resonance of 212 ppm, which supported this structural assignment.

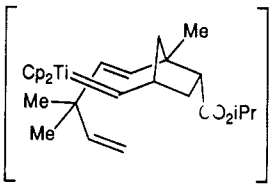
The product distributions shown in Scheme VII differed significantly from those observed for the other 1-methyl directing system investigated (Scheme VI). In the system involving the diester **34a**, it was found that the methyl substituent had a somewhat reduced directing effect on the regiochemical addition of the substituted alkylidene. Nevertheless, it did display a positive directing effect, 65:35, in favor of metallacycle formation with the titanocene unit directed away from the methyl substituent. A different distribution was found by using the ester **53**. In this case, products resulting from metallacycle formation with the titanocene unit closes to the methyl substituent accounted for the major portion of the ring-opened product mixture. In fact, **62**, the product expected from the directing effect of the methyl group, contributed only 22%

Scheme VII. Products of the Reaction between 38 and 53



to the productive metathesis mixture.

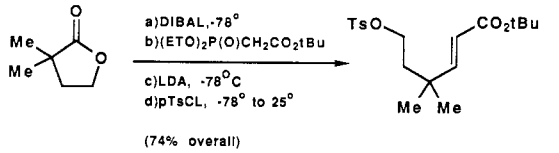
The delicate balance of the metathesis equilibrium again comes into effect. It was unlikely that the addition of a single methyl ester substituent had a large enough effect to completely reverse the kinetic regiochemical addition of the substituted alkylidene to the two substrates **34a** and **53**—especially in light of the negligible regiochemical preference for kinetic metallacycle formation observed with **25**. Instead, it was more probable that the metallacycle **56**, leading to the formation of **59**, was actually formed to a greater extent than indicated by the product distribution. The low conversion of this metallacycle to **59** could result from a number of factors. This metallacycle could have a much greater propensity than that of **34a** to nonproductively dissociate, but this difference was unlikely since all previous observations indicate that the ring-opening of the monomer substituted norbornene substrates occurred to an equal or greater extent than the diester substrates. The fate of metallacycle **56** was thus believed to involve ring-opening to the substituted alkylidene **63**. From this



63

intermediate, two intramolecular reactions could occur. The productive trapping of the alkylidene to form **59** appeared to be unfavorable relative to other available pathways, and **59** was formed to only a small extent. Intramolecular cycloaddition to the olefin again regenerated the same metallacycle intermediate **56**. Intermolecular dissociation to **53** and **39**, followed by recombination to form the opposite regioisomers, **54** and **55**, allowed the more favorable cyclobutene enol ether formation. Thus, the unfavorable trapping process to form the bicyclo[2.2.1]-heptene enol ether allowed the equilibrium to be drawn against the directing effect of the methyl substituent toward the more facile formation of **58** and **59**. Again, as in the separate thermolysis of **26** and **27**, evidence for the equilibrium of metallacycles through the intermediate titanocene alkylidene was observed. During the regeneration of **39**, which appeared to be less subject to decomposition than **1**, conversion to productive metathesis products was high (94%), and products resulting from the intermolecular olefination of the ester group were not observed. The increased stability of alkylidene **39**, during the dissociation of **56** and the recombination to **54** and **55**, was expected to result from intramolecular formation of the intermediate metallacycle **38**.

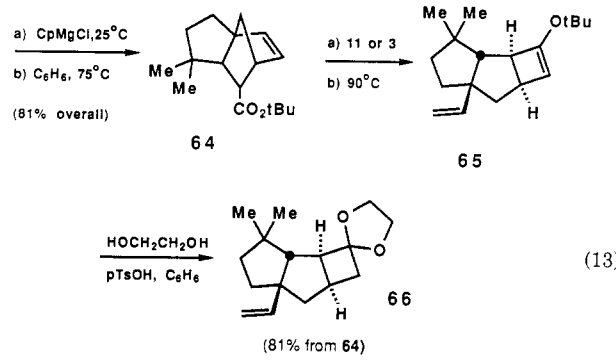
Total Synthesis of $\Delta^{9(12)}$-Capnellene. From the results that were obtained from the variety of substrates and metallacycles studied, the optimal substrate for this synthetic transformation was determined. The substrate had to possess a single endo ester substituent such as **25** but also required a bridgehead substituent to regiochemically direct metallacycle formation. The relationship between the alkyl directing group and the ester was required to be "meta". Such a substrate was expected to specifically form the isomer analogous to **27** upon reaction with titanocene methylidene. Of particular interest in our efforts was the bridged tricyclic substrate **64**. This strained olefin has been prepared in 60% overall yield from α,α-dimethyl-γ-butyrolactone (eq 12).[29] Rearrangement of **64** would then



(12)

produce a cis–anti–cis linear tricyclic framework as a precursor to naturally occurring compounds. A representative triquinane, $\Delta^{9(12)}$-capnellene (**75**), which was isolated from the soft coral *Capnella imbricata*[30] and has received substantial synthetic interest recently,[31] was chosen as the target of this synthetic effort.[32]

Reaction of **64** with 1.15 equiv of **11** was found to proceed as expected (eq 13). Thermolysis of the mixture



(13)

produced the desired tricyclic product **65** and regenerated **64** in a 84:16 ratio, respectively. ^{1}H NMR comparison of the products with an internal standard revealed a total

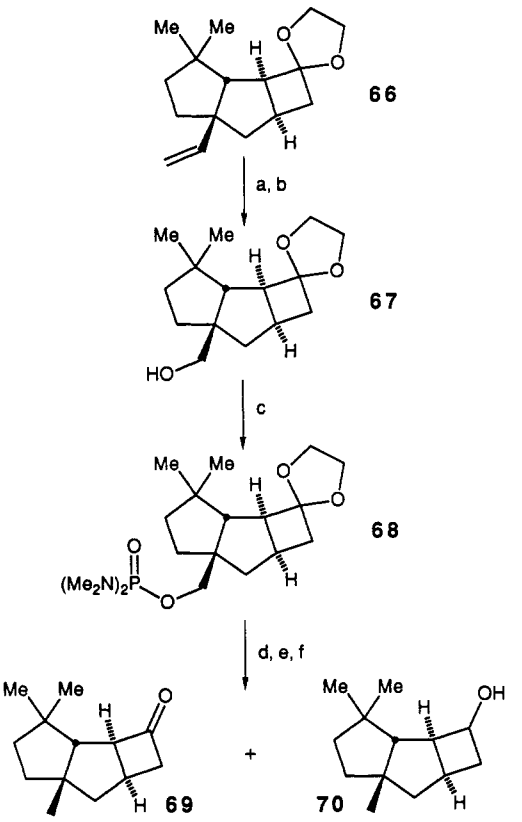
(29) Stille, J. R.; Grubbs, R. H. *J. Org. Chem.* **1989**, *54*, 434.
(30) Ayanoglu, E.; Gebreyesus, T.; Beechan, C. M.; Djerassi, C.; Kaisin, M. *Tetrahedron Lett.* **1978**, 1671.
(31) For previous total syntheses of **75**, see: (a) Curran, D. P.; Chen, M.-H. *Tetrahedron Lett.* **1985**, 4991. (b) Liu, H. J.; Kulkarni, M. G. *Tetrahedron Lett.* **1985**, 4847. (c) Mehta, G.; Murthy, A. N.; Reddy, D. S.; Reddy, A. V. *J. Am. Chem. Soc.* **1986**, *108*, 3443. (d) Iyoda, M.; Kuchida, T.; Kitami, S.; Oda, M. *J. Chem. Soc., Chem. Commun.* **1987**, 1607. (e) Piers, E.; Karunaratne, V. *Tetrahedron* **1989**, *45*, 1089, and references cited in these articles.
(32) A preliminary account of this synthesis has been reported: Stille, J. R.; Grubbs, R. H. *J. Am. Chem. Soc.* **1986**, *108*, 855.

quantitative yield (100%) of the two products. Conversion of this substrate showed essentially no difference from the 86% conversion of the non-bridgehead-substituted metallacycle **27**. Unlike the relationship between the thermolysis of **12c** and **34b**, the methyl directing group did not substantially reduce conversion. The reaction of **64** with **38**, on the other hand, did not produce the expected results. Instead of reacting in a selective manner, as with **53**, thermolysis of the mixture produced six products. These results were similar to those observed for the reaction of **38** with **25**, which also contained the sterically forbidding *tert*-butyl ester carbonyl.

For the generation of **1** on a larger scale, the use of the commercially available Tebbe reagent **3** was preferable to the use of **11**. Metallacycle formation using **3** as the source, followed by removal of the aluminum adduct, produced results similar to the reaction with **11** upon thermolysis. The drawback to this procedure was the need to remove the Me_2AlCl·DMAP adduct from the metallacycle solution. The removal process not only required special inert atmosphere techniques but also was very costly to overall product yield. In an attempt to avoid this purification step, the reaction mixture containing the aluminum adduct was heated. In the presence of the aluminum adduct, complete conversion of the substrate to **65** was achieved. The ability of the aluminum adduct to produce complete conversion of the substrate was believed to have arisen from an ability to stabilize **1** and prevent its decomposition in solution, to promote ring-opening of the intermediate metallacycle through interaction with the metallacycle itself, and/or to activate the ester carbonyl toward intramolecular olefination. Because **1** was not removed from the equilibrium mixture by decomposition, the equilibrium was driven toward the formation of **65**. Due to the sensitive nature of the cyclobutene enol ether, as previously discussed, **65** was transformed into the corresponding 1,3-dioxolane **66**. As **66**, the product was isolated in 81% yield based on substrate **64** (eq 13).

From **66**, the synthesis of capnellene required the modification of two separate parts of the molecule. The vinyl substituent at C(4) had to be trimmed to a methyl group, a ring expansion of the cyclobutanone to a cyclopentanone was also necessary. Removal of the excess carbon on the C(4) substituent was accomplished through ozonolysis (Scheme VIII). Reductive workup of the methoxy hydroperoxide with sodium borohydride produced the alcohol **67** in 91% isolated yield. Further reduction of the neopentyl-like alcohol was accomplished by reported methods.[33] Following established procedure,[34] the bis(dimethylamino)phosphorodiamidate ester **68** was prepared and could be isolated in 88% yield; however, use of crude **68** proved more efficient in the overall transformation of **67** to **69**. Reductive cleavage of **68** was accomplished with 20 equiv of lithium in ethylamine. Under normal conditions (0 °C), the deep-blue solvated lithium solution became colorless within 30 min, signifying the unusual consumption of all solvated electrons. After standard workup, the protecting group was removed by acid-catalyzed exchange dioxolanation to acetone with acid catalyst. Analysis of the mixture revealed the presence of two compounds. Separation of these products revealed the desired cyclobutanone **69** (30%) and a single cyclobutanol isomer **70** (51%). At −78 °C, the reaction proceeded very slowly with very little conversion occurring over a 4-h period. Analysis of products that were formed after 4 h at −78 °C showed mostly the ketal of **69**, but reduction to the alcohol **70** was also observed to an extent of about 5%. Because the formation of **70** could not be eliminated, the reduction was performed at −50 to −40 °C and followed closely by thin-layer chromatography. After 1 h, the reaction was quenched and, following removal of the ketal protecting group, produced ≈ 9:1 mixture of **69**:**70**. The slight overreduction of **69** was easily remedied by the addition of 0.15 equiv of pyridinium dichromate. This procedure completely oxidized **70** to **69**. Isolation of the cyclobutanone **69** from this solution was achieved in 68% overall yield from the alcohol **67**.

Scheme VIII.[a] **Synthetic Modification of the Angular C(4) Substituent**

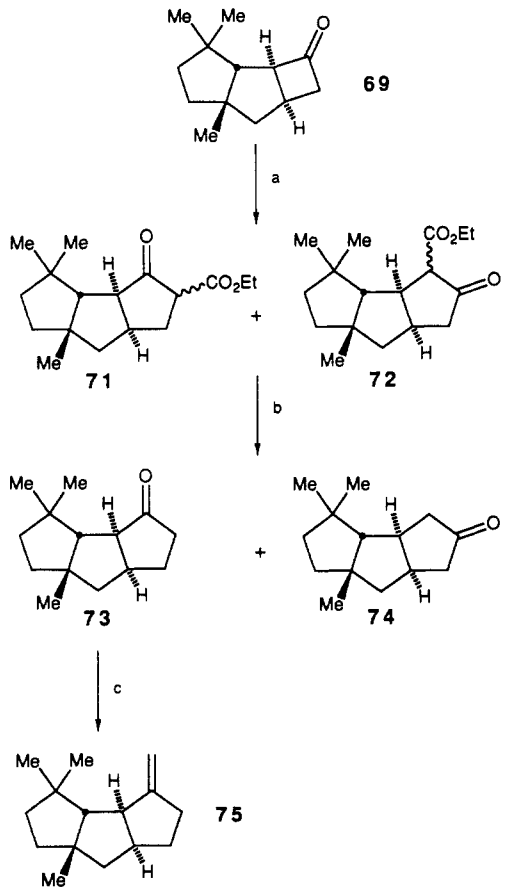


[a] (a) O_3, $MeOH/CH_2Cl_2$, −78 °C; (b) $NaBH_4$ −78 to 25 °C (91%); (c) nBuLi, $(Me_2N)_2POCl$, NEt_3, DME, 25 °C; (d) Li, tBuOH, $EtNH_2$, THF, −50 to −40 °C; (e) H_2O/acetone, *p*-TsOH·H_2O, benzene, reflux; (f) 0.15 equiv of PDC, CH_2Cl_2, 25 °C (68%).

Once the transformation of the vinyl substituent to the methyl group had been accomplished, the ring expansion of the cyclobutanone to the cyclopentanone was examined. A similar system, a cyclobutanone fused to a six-membered ring, showed complete regiospecificity of the boron trifluoride etherate catalyzed ring expansion with ethyl diazoacetate at room temperature.[35a] The expansion of **69** proved somewhat different. At room temperature, the reaction produced a mixture of four isomeric β-keto esters **71** and **72** (Scheme IX). Decarboxylation of the β-keto esters, according to established procedure,[36] produced a 2.9:1.0 ratio of ketones **73** and **74**. At −28 °C, the boron trifluoride etherate catalyzed ring expansion of **69** with ethyl diazoacetate produced a mixture of β-keto esters

(33) Ireland, R. E.; Muchmore, D. C.; Hengartner, J. *J. Am. Chem. Soc.* **1972**, *94*, 5098.
(34) Muchmore, D. C., Ph.D. Thesis, California Institute of Technology, 1971.
(35) (a) Liu, H. J.; Ogino, T. *Tetrahedron Lett.* **1973**, 4937. (b) Greene, A. E.; Luche, M.-J.; Serra, A. A. *J. Org. Chem.* **1985**, *50*, 3957.
(36) (a) Krapcho, A. P.; Lovey, A. J. *Tetrahedron Lett.* **1973**, 957. (b) Krapcho, A. P.; Jahngen, E. G. E.; Lovey, A. *Tetrahedron Lett.* **1974**, 1091.

Scheme IX.[a] Ring Expansion of 69



[a] (a) $BF_3{\cdot}Et_2O$, N_2CHCO_2Et, Et_2O, −28 °C; (b) NaCl, DMSO, H_2O, 150 °C (73%); (c) **3**, pyridine, Et_2O, −40 to 25 °C (93%).

which, after decarboxylation, gave a 5.0:1.0 ratio of **73**:**74**. Separation of these isomers was achieved through flash chromatography to give a single ketone in 73% isolated yield. By comparison to spectra of independently synthesized **73**,[37] the major ketone product was verified as **73** by NMR and IR. Following completion of this project, the ring expansion of a cyclobutanone fused to a five-membered ring was obtained with 98:2 regioselectivity using ethyl diazoacetate and $SbCl_5$.[35b]

The final transformation of **73** to the natural product **75** has been reported for most syntheses of capnellene.[31] Usually, the α,β-unsaturated analogue of **73** is hydrogenated in high yield and then taken on to **75** without isolated. The yields of this two-step process have been reported to vary from 36% to 84% due to the sensitive nature of the methylene Wittig reagent. The use of Tebbe reagent (**3**) for the methylenation process proved to be a highly efficient method for the transformation of **75** to $\Delta^{9(12)}$-capnellene. Workup of the reaction mixture required only dilution with pentane and filtration through silica gel. The only eluting product was isolated in 93% yield. Compared to spectra of $\Delta^{9(12)}$-capnellene isolated from *Capnella imbricata*,[38] the product was confirmed by spectroscopic analysis to be **75**.

This synthesis of $\Delta^{9(12)}$-capnellene is the first to achieve the formation of all four asymmetric centers in a single step. By using the intramolecular cycloaddition for this purpose, a promising route to enantiomerically pure **75** has been opened. Through the use of chiral auxiliaries,[21] asymmetric induction in the cycloaddition process appears encouraging. Use of the versatile Tebbe reagent has provided a novel way in which to rearrange the bridged cycloaddition product to the required linear skeleton. This rearrangement was achieved through the ring-opening metathesis of the strained olefin and subsequent intramolecular trapping of the substituted alkylidene. After functional group modification using established methods, the ketone precursor to **75** was obtained. Final methylenation using **3** proved to very efficient in the transformation of the ketone to **75**. Overall, the yield of capnellene obtained through this synthetic route was 20% from α,α-dimethyl-γ-butyrolactone.

The above description demonstrates the subtle features required for successful application of "metathesis-like" reactions to the synthesis of natural product ring systems. Numerous other related applications can be considered.[39-41]

Experimental Section

General Procedures. All manipulations of air- and/or moisture-sensitive compounds were carried out with use of standard Schlenk or vacuum line techniques. Argon was purified by passage through columns of BASF RS-11 (Chemalog) and Linde 4-Å molecular sieves. Solids were transferred in a nitrogen-filled Vacuum Atmospheres Dri-Lab equipped with an MO-40-1 purification train and a DK-3E Dri-Kool. Measurement of weight was conducted after minimizing static interference through the use of a Staticmaster ionizing unit (Nuclear Products Co.). Flash chromatography was performed according to general procedure of Still and co-workers[42] employing Silica Woelm 32–63 (32–63 μm). Analytical thin-layer chromatography (TLC) was performed using EM Reagents 0.25-mm silica gel 60-F plates and visualized by iodine vapor or phosphomolybdic acid dip.[43] All reaction temperatures were measured externally.

Materials. *tert*-Butyl alcohol was distilled from CaH_2 before use. Mesitylene (MCB Reagents) was stored over 4-Å molecular sieves under argon. Acrylic acid was distilled immediately prior to use. Preparation of metallacycle reagents **11**[3] and **38**[9c] was performed according to reported procedures. Tebbe reagent (**3**) was prepared according to literature procedure.[4] The norbornene substrates *endo*-bicyclo[2.2.1]hept-5-ene-2-carboxylic acid[44] and the dimethyl and diethyl esters of *endo,endo*-bicyclo[2.2.1]-hept-5-ene-2,3-dicarboxylic acid[22] were prepared by using reported methods. 4-(Dimethylamino)pyridine (DMAP) was obtained from Aldrich Chemical Co., decolorized with activated charcoal, and recrystallized from hot toluene. Boron trifluoride etherate (Aldrich Chemical Co.) was treated with small amounts of diethyl ether and then distilled at reduced pressure (10 mmHg, 46 °C). Bis-(dimethylamino)phosphorochloridate (Aldrich Chemical Co.) was distilled prior to use. Ethylamine ($EtNH_2$, Matheson) was passed through a tower of KOH immediately before use. Triethylamine (MCB Reagents) was distilled from CaH_2 under argon. *tert*-Butyl alcohol (Aldrich Chemical Co.) was dried over $MgSO_4$, filtered, and degassed through two freeze–pump–thaw cycles. Lithium wire was cleaned by washing with pentane, methanol, and then pentane.

$CDCl_3$ was stored over 4-Å molecular sieves and filtered through Activity I alumina immediately prior to use. Dichloromethane (CH_2Cl_2) was dried over P_2O_5 and degassed on a vacuum line. Pentane was stirred over H_2SO_4, dried over CaH_2, and vacuum-transferred onto sodium–benzophenone ketyl. Benzene and

(37) Copies of spectra were generously provided by Professor J. K. Stille (Colorado State University).
(38) Copies of spectra obtained from Professor C. Djerassi (Stanford University) were generously provided by Professor J. K. Stille (Colorado State University).
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tetrahydrofuran (THF) were dried over CaH_2 and vacuum-transferred onto sodium–benzophenone ketyl. Diethyl ether (ether), dimethoxyethane (DME), toluene, benzene-d_6 (Cambridge Isotope Laboratories), and toluene-d_8 (Cambridge Isotope Laboratories) were degassed and stirred over sodium–benzophenone ketyl. The dried and degassed solvents were vacuum-transferred into dry vessels equipped with Teflon valve closures and stored under argon. Reagent grade petroleum ether (35–60 °C) was used without further purification. In the cases where the rigid exclusion of oxygen was not required, anhydrous ether was used without further purification.

Instrumentation. NMR spectra were recorded on a JEOL FX-90Q (89.60 MHz ^1H; 22.53 MHz ^{13}C), a JEOL GX-400 (399.65 MHz ^1H; 100.40 MHz ^{13}C), or a Bruker WM-500 (500.13 MHz ^1H). Chemical shifts are reported versus residual solvent signals on the δ scale. Data were reported as follows: chemical shift (multiplicity [s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and br = broad], coupling constant [hertz], integration). Difference NOE experiments were performed according to published procedures.[45] Analytical gas chromatographic analyses (VPC) were performed on a Shimadzu GE-Mini 2 flame ionization instrument modified for capillary use and equipped with a Hewlett-Packard Model 339A integrator (column: 0.24 mm × 15 m DB1). The detector and injector temperatures were 250 °C. Column temperature and retention times (t_r) are reported. Preparative gas chromatography was performed on a Varian Aerograph Model 920 instrument using a 5ft × $^1/_4$in. Hallcomid M-18-01 60/80 on Chromosorb W (column b). Infrared analyses utilized a Beckman 4210 spectrophotometer and are reported in reciprocal centimeters (cm^{-1}). Melting points were determined on a Thomas-Hoover Unimelt capillary melting point apparatus and are uncorrected. Ozone was obtained by using a Welsbach generator.

Combustion analyses were performed by Galbraith Laboratories, Inc. (Knoxville, TN) or by Lawrence Henling at the California Institute of Technology Microanalytical Laboratory.

Two-Dimensional ^1H–^1H Correlated NMR Spectra.[20] The data were acquired by using a JEOL GX-400 NMR spectrometer operating at 399.65 MHz proton frequency. The pulse sequence was 90°–t_1–45°–acquisition–relaxation delay, and the phases of the pulses and receiver were cycled to provide quadrature detection in f_1 and selection of "P-type" peaks. The 90° ^1H pulse width on the 5-mm $^1H/^{13}C$ probe was 15.0 μs. The f_2 spectral width was 3201.0 Hz, and the pulse delay (PD) was 3.0 s. Two dummy scans were taken before each slice to eliminate non-equilibrium magnetization. Eight transients of 1K data points were collected for 384 increments of t_1. The total acquisition time was 3.5 h. The data were zero-filled to 512 points in t_1, apodized with a sine-ball window function in both dimensions, and Fourier transformed in both dimensions. The absolute value spectrum was calculated, and the entire data set symmetrized.

General Procedure for NMR Tube Reactions. An NMR tube was first weighed under static-free conditions in a nitrogen atmosphere. Solids were loaded into the tube, static was removed, and weight was recorded. A latex septum was fitted onto the NMR tube and sealed with Parafilm. Solvent (400 μL) and liquid substrates were added via syringe. Reactions were conducted following the same conditions as described for preparative reactions. To quantify the resulting products, mesitylene was added via syringe and the compounds assayed by integration of peak areas. Paramagnetic titanium products were quenched by exposure to oxygen so that NMR spectra could be obtained. Results of these reactions are described fully in the text of this paper.

Preparation of 13a from 11. To a solution of **11** (1.14 g, 4.13 mmol) in 8 mL of toluene at −50 °C was added a precooled solution of **12a** (1.48 g, 7.1 mmol) in 7 mL of toluene. The mixture was warmed to −10 °C and then slowly allowed to reach ambient temperature over 1 h. After being stirred at room temperature for 30 min, the mixture was concentrated to a red slush in vacuo. The reaction mixture was suspended in 50 mL of pentane and stirred for 30 min. The precipitate was removed by filtration, washed with 2 × 10 mL of pentane, and dried in vacuo. After dissolving this solid in a minimum amount of CH_2Cl_2 at −40 °C, the product was slowly precipitated from solution with 20 mL of pentane, and stirred at −40 °C for 15 min. The precipitate was isolated by filtration and residual solvent was removed in vacuo to produce 1.41 g (85% yield) of a red powder: ^1H NMR (400 MHz, C_6D_6), proton assignments as shown in Figure 1, δ 5.46 (s, 5 H, Cp_1), 5.41 (s, 5 H, Cp_2), 4.48 (d, J = 8.3 Hz, 1 H, H_3), 3.46 (s, 3 H, CH_3), 3.40 (s, 3 H, CH_3), 3.09 (dd, J = 4.4, 11.4 Hz, 1 H, H_6), 2.94 (dd, J = 9.0, 10.8 Hz, 1 H, H_7), 2.72 (dd, J = 3.0, 11.4 Hz, 1 H, H_8), 2.53 (br s, 1 H, H_9), 2.49 (br s, 1 H, H_{10}), 1.67 (dd, J = 9.0, 9.4 Hz, 1 H, H_{11}), 1.12 (d, J = 10.1 Hz, 1 H, H_{12}), 0.83 (ddd, J = 8.3, 9.4, 10.8 Hz, 1 H, H_{13}), 0.68 (d, J = 10.1 Hz, 1 H, H_{14}); ^{13}C NMR (22.5 MHz, C_6D_6) δ 173.1, 172.4, 109.9, 108.8, 96.3, 73.0, 51.8, 51.0, 50.7, 49.8, 47.1, 46.2, 35.9, 15.8; IR (CH_2Cl_2) 2950, 1740, 1433, 1200, 1170, 815 cm^{-1}.

Anal. Calcd for $C_{22}H_{26}O_4Ti$: C, 65.68; H, 6.51. Found: C, 65.53; H, 6.46.

Preparation of 13a from 3. To a solution of **3** (2.27 g, 8 mmol) in 15 mL of THF at −50 °C was added a precooled solution of **12a** (2.10 g, 10 mmol) in 15 mL of THF. The reaction mixture was allowed to warm to ambient temperature over the period of 5 min and then was stirred at room temperature for 15 min. After concentration of the mixture in vacuo to a thick oil, the products were suspended in 50 mL of pentane. The solid was isolated by filtration and washed with 2 × 15 mL of ether and finally with 1 × 20 mL of pentane. Residual solvent was removed in vacuo to give 2.70 g of **13a** (84%) as a red powder. This powder was identical with the product obtained from the reaction of **12a** with **11**.

Thermolysis of 13a. A solution of **13a** (1.00 g, 2.49 mmol) in 7 mL of benzene was heated at 80 °C for 22 h. The reaction mixture was then cooled to room temperature and quenched by pouring into 100 mL of vigorously stirring pentane. After being stirred for 1 h, the solution was filtered and concentrated to an oil. The oil was redissolved in pentane and stirred for 1 day. Following removal of insoluble products by filtration, the solution was concentrated to an oil. Partial separation of this mixture was achieved through flash chromatography using petroleum ether/ether (1:1). The eluant of R_f = 0.77 (28 mg, 1.4%) was found to be **19a**. The next elutant was identified as a mixture of **16a** and **20a** of R_f = 0.56 (74 mg, 14%). Isolation of **16a** was achieved by preparative gas chromatography (column b). Compound **18a** was unstable to the conditions of preparative gas chromatography. The remaining organic product had R_f = 0.41 (168 mg, 32%) and was spectroscopically identical with **12a**.

19a: ^1H NMR (500 MHz, C_6D_6) δ 6.30 (ddd, J = 9.0, 10.5, 17.5 Hz, 1 H), 5.00 (ddd, J = 1.5, 2.0, 17.5 Hz, 1 H), 4.95 (ddd, J = 1.5, 2.0, 10.5 Hz, 1 H), 4.84 (dd, J = 1.5, 2.0, Hz, 1 H), 4.45 (s, 1 H), 4.20 (d, J = 2.0 Hz, 1 H), 3.55 (dd, J = 3.8, 6.5 Hz, 1 H), 3.28 (s, 3 H), 3.18 (s, 3 H), 3.10–3.20 (m, 1 H), 2.85 (dd, J = 7.0, 3.5 Hz, 1 H), 2.75 (dd, J = 6.8, 6.8 Hz, 1 H), 1.85 (d, J = 13.5 Hz, 1 H), 1.75 (ddd, J = 7.5, 7.5, 13.5, Hz, 1 H); ^{13}C NMR (22.5 MHz, C_6D_6) δ 162.4, 155.9, 143.3, 113.1, 100.8, 83.2, 55.0, 54.1, 51.1, 50.0, 46.6, 38.1, 35.5.

16a: ^1H NMR (500 MHz, C_6D_6) δ 6.30 (ddd, J = 8.8, 10.5, 17.0 Hz, 1 H), 4.99 (dd, J = 2.0, 17.0 Hz, 1 H), 4.96 (dd, J = 2.0, 10.5 Hz, 1 H), 4.40 (s, 1 H), 3.45 (dd, J = 3.6, 7.5 Hz, 1 H), 2.95 (br ddd, J = 3.2, 7.5, 15.5 Hz, 1 H), 2.68–2.72 (m, 1 H), 2.55 (dd, J = 7.5, 7.5 Hz, 1 H), 1.80 (ddd, J = 2.8, 2.8, 13.0 Hz, 1 H), 1.55 (ddd, J = 7.5, 7.5, 13.0 Hz, 1 H); ^{13}C NMR (100.4 MHz, C_6D_6) δ 171.4, 155.6, 142.1, 114.0, 100.9, 55.4, 51.1, 51.0, 48.6, 48.5, 38.9, 35.7.

20a: ^1H NMR (500 MHz, C_6D_6) δ 6.51 (dd, J = 3.0, 5.5 Hz, 1 H), 6.15 (dd, J = 3.0, 5.5 Hz, 1 H), 3.94 (d, J = 2.0 Hz, 1 H), 3.81 (d, J = 2.0 Hz, 1 H), 3.34 (s, 3 H), 3.09 (s, 3 H), 3.05 (dd, J = 3.1, 10.5 Hz, 1 H), 2.98 (dd, J = 3.3, 10.5 Hz, 1 H), 2.91 (br s, 1 H), 2.76 (br s, 1 H), 1.27 (ddd, J = 2.0, 2.0, 8.3 Hz, 1 H), 0.92 (ddd, J = 0.6, 0.6, 8.3 Hz, 1 H); ^{13}C NMR (100.4 MHz, C_6D_6) δ 172.6, 163.6, 135.7, 134.2, 82.3, 54.4, 51.5, 44.94, 49.91, 48.9, 48.8, 46.6.

Hydrolysis of 19a. To a solution of **19a** (28 mg, 0.14 mmol) in 5 mL of acetone was added a solution of 5 mg of p-toluenesulfonic acid in 3 mL of H_2O. The reaction mixture was first allowed to be stirred for 24 h at room temperature, and then the acetone was removed at reduced pressure. The aqueous layer was extracted with 3 × 10 mL of ether, and the combined organics

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were washed with 1 × 5 mL of saturated aqueous $NaHCO_3$ and dried ($MgSO_4$). Concentration in vacuo produced **21**: ^1H NMR (500 MHz, C_6D_6) δ 5.65 (ddd, J = 8.0, 10.5, 17.0 Hz, 1 H), 4.88 (ddd, J = 2.0, 3.0, 17.0 Hz, 1 H), 4.83 (ddd, J = 1.0, 2.0, 10.5 Hz, 1 H), 3.18 (dddd, J = 3.0, 3.5, 9.0, 9.5 1 H), 2.75 (ddd, J = 3.0, 4.8, 18.0 Hz, 1 H), 2.66 (ddd, J = 3.5, 8.5, 18.0 Hz, 1 H), 2.57 (dd, J = 7.5, 9.5 Hz, 1 H), 2.38–2.45 (m, 1 H), 2.18 (ddddd, J = 4.8, 6.5, 8.5, 8.5, 9.0 Hz, 1 H), 1.80 (s, 3 H, CH_3), 1.71–1.82 (m, 2 H, CH_2); ^{13}C NMR (22.5 MHz, C_6D_6) δ 207.9, 207.2, 137.6, 116.2, 67.1, 58.7, 52.4, 52.2, 38.2, 32.3, 29.3; IR (neat) 1778, 1710, 1640, 1364, 1172 cm^{-1}.

Preparation and Thermolysis of 13b. To a solution of **11** (276 mg, 1 mmol) in 2 mL of toluene at −50 °C, was added a precooled solution of **12b** (238 mg, 1 mmol) in 2 mL of toluene. The mixture was warmed to −10 °C and then slowly allowed to reach ambient temperature over 1 h. After being stirred at room temperature for 20 min, the mixture was concentrated in vacuo to an oil. The oil was taken up in a minimum amount of pentane and then cooled to −50 °C. The resulting precipitate was isolated by filtration, and residual solvent was removed in vacuo. After the red powder was dissolved in 2 mL of benzene, the solution was heated at 80 °C for 12 h. The reaction mixture was cooled to room temperature, diluted with petroleum ether, and allowed to stir in contact with air for 1 h. Filtration of this mixture produced a clear solution of products, which was analyzed by capillary gas chromatography. Analysis at 120 °C revealed four products with t_r = 9.18 (**19b**, 7%), 10.10 (**20b**, 11%), 10.26 (**16b**, 22%), and 11.42 min (**12b**, 42%).

Preparation of 12c. A solution of 10.00 g of bicyclo[2.2.1]-hept-5-ene-2,3-dicarboxylic anhydride and 0.20 g of *p*-toluenesulfonic acid monohydrate in 30 mL of dry isopropyl alcohol was heated to reflux. The mixture was maintained at reflux for 16 h, and then the condenser was removed to allow 20 mL of isopropyl alcohol to boil off. An additional 20 mL of isopropyl alcohol was added and subsequently allowed to boil from the reaction vessel. This procedure was repeated two times with a total of 40 mL of isopropyl alcohol. Next, the reaction mixture was redissolved in 20 mL of isopropyl alcohol and heated at reflux for an additional 22 h. After cooling to room temperature, the mixture was concentrated in vacuo. The resulting oil was taken up in 150 mL of diethyl ether, washed with 6 × 50 mL of saturated aqueous $NaHCO_3$, 3 × 50 mL of H_2O, 1 × 50 mL of saturated NaCl solution, and dried over $MgSO_4$. After concentration of the product, it was redissolved in petroleum ether/ether (4:1) and filtered through a pad of silica gel. Concentration of the elutant gave 12.3 g of **12c** (76% yield): ^1H NMR (90 MHz, C_6D_6) δ 6.22 (dd, J = 1.5, 1.5 Hz, 2 H), 4.89 (qq, J = 6.3, 6.3 Hz, 2 H), 2.80–3.05 (m, 4 H), 1.06 (d, J = 6.3 Hz, 6 H), 1.04 (d, J = 6.3 Hz, 6 H), 0.70–1.30 (m, 2 H); ^{13}C NMR (22.5 MHz, C_6D_6) δ 171.2, 135.0, 67.1, 48.5, 46.7, 22.0, 21.9; IR (neat) 2980, 2940, 1740, 1375, 1255, 1200, 1175, 1110 cm^{-1}.

Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.65; H, 8.33. Found: C, 67.59; H, 8.37.

Preparation of 13c from 11. To a solution of **11** (276 mg, 1 mmol) in 2 mL of toluene at −50 °C was added a precooled solution of **12c** (266 mg, 1 mmol) in 2 mL of toluene. The mixture was warmed to −10 °C and then slowly allowed to reach ambient temperature over 1 h. After stirring at room temperature for 1 h, the reaction mixture was concentrated in vacuo to a red oil. This oil was taken up in a minimum amount of pentane and filtered, and the mother liquor slowly cooled to produce red crystals. Isolation of the crystalline solid by filtration and removal of the residual solvent in vacuo produced 353 mg (76% yield) of **13c**: ^1H NMR (500 MHz, C_6D_6), proton assignments as in analogous compound **12a**. **12a**: δ 5.48 (s, 5 H, Cp_1), 5.41 (s, 5 H, Cp_2), 5.18 (qq, J = 6.2, 6.2 Hz, 1 H, $CH(CH_3)_2$), 5.06 (qq, J = 6.2, 6.2 Hz, 1 H, $CH(CH_3)_2$), 4.60 (d, J = 9.0 Hz, 1 H, H_3), 3.09 (dd, J = 4.2, 11.4 Hz, 1 H, H_6), 3.02 (dd, J = 9.3, 9.3 Hz, 1 H, H_6), 2.72 (dd, J = 2.3, 11.4 Hz, 1 H, H_8), 2.56 (br s, 1 H, H_9), 2.54 (br s, 1 H, H_{10}), 1.72 (dd, J = 9.3, 9.3 Hz, 1 H, H_{11}), 1.17 (d, J = 6.2 Hz, 3 H, CH_3), 1.15 (d, J = 6.2 Hz, 3 H, CH_3), 1.14 (d, J = 6.2 Hz, 3 H, CH_3), 1.12 (d, J = 6.2 Hz, 3 H, CH_3), 1.0–1.2 (m, 1 H, H_{12}), 0.91 (ddd, J = 9.0, 9.3, 9.3 Hz, 1 H, H_{13}), 0.69 (d, J = 10.0 Hz, 1 H, H_{14}); ^{13}C NMR (22.5 MHz, C_6D_6) δ 172.0, 171.5, 109.8, 108.7, 97.4, 73.2, 67.1, 66.7, 52.0, 50.1, 47.3, 46.3, 35.9, 22.2, 22.0, 15.6.

Anal. Calcd for $C_{26}H_{34}O_4Ti$: C, 68.12; H, 7.48. Found: C, 68.24; H, 7.07.

Thermolysis of 13c. To a solution of **3** (5.00 g, 17.6 mmol) in 15 mL of CH_2Cl_2 at −40 °C was added a solution of **12c** (3.98 g, 14.9 mmol) in 15 mL of CH_2Cl_2. Under a strong flow of argon, DMAP was added to the mixture through the top of the reaction vessel. The reaction mixture was allowed to warm to room temperature over 10 min and stirred at room temperature for 15 min. Slow transfer of this solution into 250 mL of pentane −30 °C resulted in the precipitation of DMAP·Me_2AlCl from solution. The solid was removed by filtration, and the solution was concentrated to a red oil in vacuo. The mixture was dissolved in 35 mL of C_6H_6 and heated at 80 °C for 15 h. After the solution cooled, it was transferred into 600 mL of oxygenated pentane. The mixture was stirred for 1 h, filtered, and then concentrated to an oil. This oil was dissolved in 300 mL of pentane and stirred for 1 h. After filtration, the solution was concentrated to an oil. Separation of **16c** and **12c** was achieved through silica gel flash chromatography with petroleum ether/ether (8:1). The cyclobutene enol ether **16c** (625 mg, 16%) was the more mobile (R_f = 0.30) and was isolated as a colorless liquid. The diester **12c** (1.59 g, 40%), with R_f = 0.12, was also recovered.

16c: ^1H NMR (500 MHz, C_6D_6) δ 6.36 (dd, J = 8.2, 10.2, 17.2 Hz, 1 H), 5.05 (qq, J = 6.3, 6.3 Hz, 1 H), 4.97 (ddd, J = 1.3, 2.0, 17.2 Hz, 1 H), 4.94 (ddd, J = 1.3, 2.0, 10.2 Hz, 1 H), 4.33 (s, 1 H), 3.94 (qq, J = 6.1, 6.1 Hz, 1 H), 3.44 (dd, J = 3.8, 7.5 Hz, 1 H), 2.97 (dddddd, J = 1.3, 1.3, 3.3, 7.2, 7.4, 8.2 Hz, 1 H), 2.75 (ddd, J = 2.0, 3.8, 7.2 Hz, 1 H), 2.57 (dd, J = 7.4, 7.5 Hz, 1 H), 1.79 (ddd, J = 2.0, 3.3, 12.9 Hz), 1.58 (ddd, J = 7.2, 7.2, 12.9 Hz, 1 H), 1.14 (d, J = 6.3 Hz, 3 H, CH_3), 1.11 (d, J = 6.1 Hz, 3 H, CH_3), 1.10 (d, J = 6.3 Hz, 3 H, CH_3), 1.06 (d, J = 6.1 Hz, 3 H, CH_3); ^{13}C NMR (22.5 MHz, C_6D_6) δ 170.8, 153.7, 142.6, 113.4, 100.4, 70.7, 66.9, 51.3, 48.3, 48.1, 38.7, 35.7, 22.1, 21.8; IR (neat) 3060, 2980, 2940, 1730, 1628, 1375, 1260, 1110 cm^{-1}.

Anal. Calcd for $C_{16}H_{24}O_3$: C, 72.69; H, 9.15. Found: C, 72.28; H, 9.03.

Hydrolysis of 16c. To a solution of **16c** (430 mg, 1.63 mmol) in 12 mL of acetone was added a solution of 30 mg of *p*-toluenesulfonic acid in 6 mL of H_2O. The reaction mixture was stirred for 5.5 h at room temperature. After removal of the acetone in vacuo, the aqueous layer was extracted with 3 × 30 mL of ether. The combined organic extractions were washed with 2 × 25 mL of saturated aqueous $NaHCO_3$ and 1 × 20 mL of saturated aqueous NaCl and dried ($MgSO_4$). Concentration of the solution produced a colorless oil, which was purified by flash chromatography. Elution on silica gel with petroleum ether/ether (1:1) produced a single compound. Distillation of this product at reduced pressure (Kugelrohr, 10 mmHg, 65 °C) produced 340 mg of **22** (94%).

22: ^1H NMR (500 MHz, C_6D_6) δ 5.88 (ddd, J = 7.4, 10.4, 17.2 Hz, 1 H), 4.99 (qq, J = 6.3, 6.3 Hz, 1 H), 4.97 (ddd, J = 1.4, 1.9, 17.2 Hz, 1 H), 4.94 (ddd, J = 1.0, 1.9, 10.4 Hz, 1 H), 3.28 (dddd, J = 2.9, 3.4, 9.5, 9.7 Hz, 1 H), 2.76 (dd, J = 7.7, 9.7 Hz, 1 H), 2.74 (ddd, J = 2.9, 4.7, 17.9 Hz, 1 H), 2.66 (ddd, J = 3.4, 8.5, 17.9 Hz, 1 H), 2.40 (dddddd, J = 1.0, 1.4, 7.4, 7.4, 7.7, 11.5 Hz, 1 H), 2.15 (ddddd, J = 4.7, 7.2, 7.4, 8.5, 9.5 Hz, 1 H), 1.99 (ddd, J = 7.2, 11.5, 12.9 Hz, 1 H), 1.83 (ddd, J = 7.4, 7.4, 12.9 Hz, 1 H), 1.08 (d, J = 6.3 Hz, 3 H), 1.03 (d, J = 6.3 Hz, 3 H); ^{13}C NMR (22.5 MHz, C_6D_6) δ 207.2, 171.5, 137.1, 116.3, 68.2, 67.6, 53.0, 52.4, 51.6, 38.4, 29.5, 21.9; IR (neat) 3080, 2980, 2940, 1780, 1725, 1640, 1380, 1190, 1110 cm^{-1}.

Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.25, H, 8.16. Found: C, 70.07; H, 7.90.

Preparation of 25. To a solution of *endo*-bicyclo[2.2.1]-hept-5-ene-2-carboxylic acid (4.44 g, 32.1 mmol) in 55 mL of CH_2Cl_2 at 0 °C was added oxalyl chloride (20.4 g, 16.1 mmol) via syringe. The reaction mixture was stirred at 0 °C for 9 h until gas evolution had ceased. After concentration of this mixture to an oil in vacuo, the acid chloride was distilled (Kugelrohr, 5 mmHg, 80 °C). The distillate was diluted with 10 mL of $CHCl_3$ and added over 45 min to a mixture of *N,N*-dimethylaniline (5.83 g, 48.2 mmol) and *tert*-butyl alcohol (6.00 g, 80.9 mmol) at 0 °C. Once addition was complete, the mixture was stirred at room temperature for 1 h and was then heated to reflux and stirred at reflux for 4 h. The reaction mixture was cooled to 0 °C and quenched by the addition of 25 mL of 6 N H_2SO_4. After the aqueous layer

was extracted with 3 × 45 mL of ether, the organic extractions were combined. The organics were washed with 25 mL of 6 N H_2SO_4, 2 × 30 mL of H_2O, 2 × 30 mL of 10% K_2CO_3, and 1 × 15 mL of saturated aqueous NaCl and then dried (Na_2SO_4, K_2CO_3). After concentration of the mixture, the product was distilled from MgO under reduced pressure (Kugelrohr, 5 mmHg, 85 °C). Distillation produced 4.44 g of **25** (71%) as a colorless oil.

25: ^{1}H NMR (400 MHz, C_6D_6) δ 6.08 (dd, J = 3.1, 5.5 Hz, 1 H), 6.03 (dd, J = 2.7, 5.6 Hz, 1 H), 3.10 (br s, 1 H), 2.69 (ddd, J = 4.3, 4.3, 8.6 Hz, 1 H), 2.61 (br s, 1 H), 1.55–1.66 (m, 2 H), 1.34 (s, 9 H), 1.28–1.36 (m, 1 H), 0.95 (d, J = 8.3 Hz, 1 H); ^{13}C NMR (22.5 MHz, C_6D_6) δ 173.0, 137.6, 132.5, 79.0, 49.8, 46.1, 44.4, 42.9, 29.2, 28.2.

Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.04; H, 9.21.

Preparation and Isolation of 26 and 27. To a solution of **3** (1.17 g, 4.12 mmol) in 4 mL of CH_2Cl_2 at −40 °C was added a precooled solution of **25** in 4 mL of CH_2Cl_2. To this mixture was added DMAP (0.74 g, 6.1 mmol) through a rapid flow of argon. The reaction mixture was allowed to warm to ambient temperature over 15 min and then stirred for 3 h at room temperature. This mixture was then slowly added to 75 mL of vigorously stirred pentane at −30 °C. After the resulting precipitate (DMAP·Me_2AlCl) was removed by filtration, the solution was concentrated in vacuo to an oil. Repeated fractional crystallization from pentane/toluene (3:1) produced 250 mg of **26** (16%) as the least soluble isomer and 250 mg of **27** (16%) as the more soluble isomer. Although further crystallization of remaining fractions would have produced increased yields of **26** and **27**, a sufficient amount had been isolated to examine the properties of each individual isomer.

26: ^{1}H NMR (400 MHz, C_6D_6) δ 5.43 (s, 5 H), 5.41 (s, 5 H), 3.77 (d, J = 9.0 Hz, 1 H), 3.10 (dd, J = 8.8, 11.0 Hz, 1 H), 2.78 (ddd, J = 3.6, 4.0, 11.0 Hz, 1 H), 2.64 (d, J = 4.0 Hz, 1 H), 2.20 (br s, 1 H), 1.97 (ddd, J = 1.4, 3.2, 3.6 Hz, 1 H), 1.82 (dd, J = 8.8, 8.8 Hz, 1 H), 1.64 (ddd, J = 3.7, 11.0, 11.4 Hz, 1 H), 1.43 (s, 9 H), 1.14 (dd, J = 1.2, 9.5 Hz, 1 H), 0.87 (dd, J = 2.4, 9.5 Hz, 1 H), 0.61 (ddd, J = 8.8, 9.0, 11.0 Hz, 1 H); ^{13}C NMR (100.4 MHz, C_6D_6) δ 174.0, 109.7, 108.8, 105.2, 79.3, 74.2, 48.7, 47.1, 46.5, 37.7, 37.0, 28.8, 16.6.

27: ^{1}H NMR (400 MHz, C_6D_6), δ 5.39 (s, 5 H), 5.36 (s, 5 H), 3.85 (d, J = 9.3 Hz, 1 H), 3.11 (dd, J = 9.3, 11.2 Hz, 1 H), 2.73 (ddd, J = 3.9, 5.1, 12.5 Hz, 1 H), 2.67 (br s, 1 H), 2.18 (br d, J = 3.9 Hz, 1 H), 1.90 (ddd, J = 2.2, 5.1, 10.8 Hz, 1 H), 1.85 (dd, J = 8.8, 9.3 Hz, 1 H), 1.70 (ddd, J = 4.5, 10.8, 12.5 Hz, 1 H), 1.45 (s, 9 H), 1.10 (d, J = 9.9 Hz, 1 H), 0.86 (d, J = 9.9 Hz, 1 H), 0.29 (ddd, J = 8.8, 9.3, 11.2 Hz, 1 H); ^{13}C NMR (100.4 MHz, C_6D_6) δ 173.5, 109.5, 108.6, 98.4, 79.0, 77.0, 51.5, 43.5, 36.7, 32.6, 28.8, 20.8.

Anal. Calcd for $C_{23}H_{30}O_2Ti$: C, 71.50; H, 7.83. Found: C, 71.84; H, 7.82.

Preparation of 1-Methylcyclopentadiene. A 2.8 M solution of MeMgBr in ether (97 mL, 271 mmol) was concentrated in vacuo to a white solid and then redissolved in 100 mL of THF. After this solution was cooled to 0 °C, freshly distilled cyclopentadiene (12.4 g, 187 mmol) was added via syringe. The mixture was allowed to stir at 0 °C for 30 min and then at room temperature for 2 h. At this time, the gas evolution had slowed, and the reaction mixture was heated to 85 °C for 3 h until gas evolution had ceased. After the mixture was cooled to room temperature, all volatiles were removed in vacuo. The resulting mixture was dissolved in 550 mL of THF and cooled to 0 °C. As methyl iodide (53.1 g, 374 mmol) was slowly added over 20 min, the internal temperature of the exothermic reaction mixture was carefully maintained between 15 and 30 °C through the use of an ice bath. Once addition was complete, the solution was stirred for 1 h. The reaction mixture was degassed by two freeze–pump–thaw cycles, and the volatiles were subsequently vacuum-transferred into a 78 K flask. The solution containing volatile products was stirred for 4 h at room temperature. This solution was used for the preparation of **34** and **53** without further purification.

Preparation of 33. To a solution of 1-methylcyclopentadiene at 0 °C, prepared from 290 mmol of cyclopentadiene, was added maleic anhydride (17.06 g, 174 mmol). The reaction was stirred at 0 °C for 1 h and then for 12 h at room temperature. Concentration of the mixture in vacuo produced a white solid. Crystallization from ether produced 21.7 g (70%) of the isomerically pure anhydride **33**: mp 87.5–88.5 °C (lit.[27] mp 88.5–89.0 °C).

Preparation of 34a. A solution of anhydride **33** (3.0 g, 16.8 mmol) and 30 mg of *p*-toluenesulfonic acid monohydrate in 10 mL of methanol was heated at reflux for 15 h. The reaction mixture was concentrated to 4 mL by allowing methanol to boil off in the absence of a reflux condenser. An additional 10 mL of methanol was added, and the reaction was heated at reflux for 12 h. The reaction mixture was again concentrated to 4 mL, 10 mL of methanol was added, and the reaction was heated at reflux for 3 h. After the mixture was cooled to room temperature, the solvent was removed in vacuo. The resulting liquid was taken up in 50 mL of ether, washed with 3 × 50 mL of saturated aqueous $NaHCO_3$ and 1 × 10 mL of saturated aqueous NaCl, and then dried ($MgSO_4$). The solution was concentrated to a liquid in vacuo and subsequently distilled at reduced pressure (Kugelrohr, 0.1 mmHg, 80 °C) to give 3.27 g of **34a** (87%) as a colorless liquid. Cooling of this liquid induced solidification. Recrystallization from ether/pentane gave white crystalline **34a**: mp 34.8–35.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.19 (dd, J = 3.2, 5.6 Hz, 1 H), 6.04 (d, J = 5.6, 1 H), 3.61 (s, 3 H), 3.58 (s, 3 H), 3.44 (dd, J = 3.5, 10.3 Hz, 1 H), 3.09 (br s 1 H), 3.05 (d, J = 10.3 Hz, 1 H), 1.37 (s, 3 H), 1.31–1.43 (m, 1 H), 1.29 (d, J = 8.6 Hz, 1 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 171.61, 171.58, 138.5, 133.8, 54.6, 53.7, 53.0, 51.0, 50.94, 50.91, 49.9, 17.4.

Preparation of 34b. A flask containing a solution of anhydride **33** (5.00 g, 28.1 mmol) and 0.50 g of *p*-toluenesulfonic acid monohydrate in isopropyl alcohol was equipped with a Soxhlet extraction apparatus. The extraction thimble was filled with 4-Å molecular sieves for the purpose of removing water from the esterification process. The volume of isopropyl was adjusted so that the minimum volume of the mixture of the reaction vessel was 10–15 mL, and then the mixture was heated to reflux for 4 days. After cooling to room temperature, the isopropyl alcohol was removed in vacuo. The resulting liquid was purified by flash chromatography. Eluting with petroleum ether/ether (4:1) on silica gel, followed by distillation at reduced pressure (Kugelrohr, 0.1 mmHg, 90 °C), produced 4.83 g of **34b** (62%) as a colorless oil.

34b: ^{1}H NMR (90 MHz, C_6D_6) δ 6.40 (dd, J = 3.0, 5.4 Hz, 1 H), 6.16 (d, J = 5.4 Hz, 1 H), 5.05 (qq, J = 6.3, 6.3 Hz, 1 H), 5.00 (qq, J = 6.3, 6.3 Hz, 1 H), 3.11 (dd, J = 3.5, 10.2 Hz, 1 H), 2.91 (br s, 1 H), 2.77 (d, J = 10.2 Hz, 1 H), 1.29 (s, 3 H), 1.16 (dd, J = 1.7, 8.3 Hz, 1 H), 1.15 (d, J = 6.3 Hz, 3 H), 1.09 (d, J = 6.3 Hz, 3 H), 1.08 (d, J = 6.3 Hz, 3 H), 1.06 (d, J = 6.3 Hz, 3 H), 0.79 (d, J = 8.3 Hz, 1 H); ^{13}C NMR (22.5 MHz, C_6D_6) δ 171.0, 139.0, 135.1, 67.2, 54.8, 54.4, 53.8, 51.9, 46.6, 22.1, 21.9, 17.8.

Anal. Calcd for $C_{16}H_{24}O_4$: C, 68.55; H, 8.63. Found: C, 68.31; H, 8.42.

Preparation of 35. To a solution of metallacycle **11** (382 mg, 1.38 mmol) in 4 mL of toluene at −50 °C was added a precooled solution of **34b** (507 mg, 1.81 mmol) in 4 mL of toluene. The mixture was then placed in a −10 °C bath and allowed to slowly warm to room temperature over 45 min. After removal of solvent from the reaction mixture in vacuo, the metallacycle product was taken up in a minimal amount of ether, filtered, and then slowly cooled to −50 °C. Crystallization from ether produced 470 mg of **35** (72%) as red crystals: ^{1}H NMR (500 MHz, C_6D_6) δ 5.53 (s, 5 H), 5.47 (s, 5 H), 5.20 (qq, J = 6.3, 6.3 Hz, 1 H), 5.07 (qq, J = 6.3, 6.3 Hz, 1 H), 4.64 (d, J = 8.7 Hz, 1 H), 2.95 (d, J = 11.3 Hz, 1 H), 2.76 (dd, J = 2.8, 11.3 Hz, 1 H), 2.66 (dd, J = 9.3, 9.3 Hz, 1 H), 2.51 (br s, 1 H), 1.67 (dd, J = 9.3, 9.3 Hz, 1 H), 1.40 (s, 3 H), 1.18 (d, J = 6.3 Hz, 3 H), 1.15 (d, J = 6.3 Hz, 3 H), 1.14 (d, J = 6.3 Hz, 3 H), 1.10 (d, J = 6.3 Hz, 3 H), 1.05–1.20 (m, 1 H), 0.67 (ddd, J = 8.7, 9.3, 9.3 Hz, 1 H), 0.59 (d, J = 10.0 Hz, 1 H); ^{13}C NMR (22.5 MHz, C_6D_6) δ 171.7, 171.5, 110.0, 109.1, 9.77, 68.3, 67.0, 66.5, 53.9, 53.5, 51.4, 49.7, 42.5, 22.3, 22.1, 21.9, 21.0, 20.8.

Anal. Calcd for $C_{27}H_{36}O_4Ti$: C, 68.64; H, 7.68. Found: C, 68.89; H, 7.73.

Isolation of 40a. To a solution of **38** (260 mg, 1.00 mmol) in 1 mL of toluene at −20 °C was added **12a** (210 mg, 1.00 mmol) via syringe. The reaction mixture was warmed to −5 °C and then allowed to warm slowly to ambient temperature over 1 h. After being stirred at room temperature for 3 h, the reaction mixture was diluted with 10 mL of pentane and cooled to −40 °C. The

solution was filtered, warmed to room temperature, and then concentrated in vacuo to an oil. This oil was dissolved in 5 mL of pentane/ether (4:1) and slowly cooled to −50 °C. The mixture was filtered, and the solution concentrated to 1 mL in vacuo. After the solution was allowed to cool slowly to −50 °C, the resulting solid was isolated by filtration and washed with 3 × 4 mL of cold pentane. Removal of residual solvent in vacuo produced 201 mg of **40a** (43%) as a purple powder: ^{1}H NMR (400 MHz, C_6D_6), assignments are shown in Figure 3, δ 6.19 (dd, J = 10.8, 17.6 Hz, 1 H, H_1), 5.66 (s, 5 H, Cp_2), 5.39 (s, 5 H, Cp_3), 5.03 (dd, J = 1.4, 17.6 Hz, 1 H, H_4), 4.95 (dd, J = 1.4, 10.8 Hz, 1 H, H_5), 4.77 (d, J = 9.2 Hz, 1 H, H_6), 3.49 (s, 3 H, H_7), 3.43 (s, 3 H, H_8), 3.09 (dd, J = 4.6, 11.3 Hz, 1 H, H_9), 2.72 (dd, J = 3.0, 11.3 Hz, 1 H, H_{10}), 2.65 (br d, J = 3.7 Hz, 1 H, H_{11}), 2.60 (br s, 1 H, H_{12}), 2.53 (d, J = 11.6 Hz, 1 H, H_{13}), 1.29 (br d, J = 10.3 Hz, 1 H, H_{14}), 1.19 (s, 3 H, H_{15}), 1.11 (s, 3 H, H_{16}), 0.71 (br d, J = 10.3 Hz, 1 H, H_{17}), 0.60 (dd, J = 9.2, 11.6 Hz, 1 H, H_{18}); ^{13}C NMR (22.5 MHz, C_6D_6) δ 173.0, 172.5, 149.8, 109.2, 108.7, 101.6, 99.9, 51.4, 50.9, 50.7, 49.9, 47.2, 45.9, 45.7, 35.5, 32.5, 30.2, 18.9.

Anal. Calcd for $C_{27}H_{34}O_4Ti$: C, 68.93; H, 7.28. Found: C, 68.78; H, 7.28.

Preparation of 42a and 43a. To a solution of **12a** (210 mg, 1.0 mmol) in 2 mL of toluene at room temperature was added a solution of **38** (416 mg, 1.6 mmol) in 2 mL of toluene. After being stirred for 4 h at room temperature, the reaction mixture was heated to 55 °C and maintained at that temperature for 15 h. Upon cooling to ambient temperature, the reaction mixture was added to 125 mL of petroleum ether. This mixture was stirred for 4 h with exposure to oxygen and then filtered. The solution was concentrated to an oil and purified by silica gel flash chromatography. An inseparable mixture of **42a** and **43a** (R_f = 0.44) could be isolated by elution on silica gel with petroleum ether/ether (3:1). Separation from **12a** (R_f = 0.22) was accomplished to give 146 mg of a 3.9:1.0 mixture of **42** and **43** (53%).

Preparation of 46. A 3.9:1.0 mixture of **42**:**43** (100 mg, 0.362 mmol) was dissolved in 4 mL of acetone/water (4:1), and 5 mg of *p*-toluenesulfonic acid monohydrate was added. After the mixture was stirred for 4 h at 25 °C, the acetone was removed in vacuo and the aqueous solution extracted with 5 mL of ether. The ether solution was washed with 2 × 1 mL of saturated aqueous $NaHCO_3$ and dried ($MgSO_4$). Concentration of this solution gave 95 mg of an oil. This oil was dissolved in 3 mL of methanol/CH_2Cl_2 (5:1). A solution of Sudan IV indicator[46] in CH_2Cl_2 was added until the reaction mixture became a detectable tint of red. The mixture was cooled to −78 °C and treated with ozone until the red tint of indicator was absent. After the reaction vessel was flushed with nitrogen for 20 min at −78 °C, methyl sulfide (3 mL) was added. Over 8 h, the reaction mixture was allowed to warm to ambient temperature. The mixture was then concentrated to an oil in vacuo and purified by flash chromatography. Elution on silica gel with ether produced 61 mg of **46** (86%) as a colorless oil with R_f = 0.26: ^{1}H NMR (400 MHz, C_6D_6) δ 9.67 (d, J = 1.5 Hz, 1 H), 3.41 (s, 3 H), 3.38 (dddd, J = 3.4, 3.5, 8.2, 9.5 Hz, 1 H), 2.73 (dd, J = 7.9, 9.5 Hz, 1 H), 2.63 (ddd, J = 3.4, 9.2, 18.3, Hz, 1 H), 2.54 (dddd, J = 1.5, 8.2, 7.9, 8.2 Hz, 1 H), 2.38 (ddd, J = 3.5, 3.5, 18.3 Hz, 1 H), 2.13 (ddddd, J = 3.5, 3.7, 8.2, 8.2, 9.2 Hz, 1 H), 1.85 (ddd, J = 3.7, 5.2, 13.7 Hz, 1 H), 1.61 (ddd, J = 8.2, 8.2, 13.7 Hz, 1 H); ^{13}C NMR (100.4 MHz, C_6D_6) δ 206.3, 200.3, 170.9, 66.5, 56.3, 52.8, 52.0, 49.0, 33.5, 29.6; IR (neat) 2950, 2865, 2840, 2730, 1777, 1728, 1718, 1435, 1200 cm^{-1}.

Anal. Calcd for $C_{10}H_{12}O_4$: C, 61.22; H, 6.16. Found: C, 60.84; H, 6.29.

Reaction of 34a with 38. A solution of **34a** (224 mg, 1 mmol) and **38** (286 mg, 1.1 mmol) in 3 mL of toluene was stirred at room temperature for 30 min and then heated at 65 °C for 18 h. Upon cooling, the reaction mixture was diluted with petroleum ether and exposed to oxygen. After being stirred for 1 h, the mixture was filtered, and the resulting solution was concentrated in vacuo. The product mixture was purified by flash chromatography. Elution on silica gel with petroleum ether/ether (9:1) produced two separate fractions containing products of the metathesis rearrangement. The more mobile fraction, R_f = 0.38, contained 64 mg of **50** (22%) as a colorless oil. The fraction of R_f = 0.33 contained 41 mg (14%) of an inseparable mixture of **51** and **52** (9.3:1.0).

50: ^{1}H NMR (500 MHz, C_6D_6) δ 6.07 (d, J = 16.1 Hz, 1 H), 5.87 (dd, J = 10.5, 17.5 Hz, 1 H), 5.41 (d, J = 16.1 Hz, 1 H), 5.01 (dd, J = 15, 17.5 Hz, 1 H), 4.92 (dd, J = 1.5, 10.5 Hz, 1 H), 4.40 (s, 1 H), 3.56 (dd, J = 3.7, 7.6 Hz, 1 H), 3.42 (s, 3 H), 3.27 (s, 3 H), 2.76 (ddd, J = 2.1, 3.7, 7.2 Hz, 1 H), 2.30 (d, J = 7.6 Hz, 1 H), 1.98 (dd, J = 2.1, 12.8 Hz, 1 H), 1.32 (dd, J = 7.2, 12.8 Hz, 1 H), 1.22 (s, 3 H), 1.11 (s, 3 H), 1.10 (s, 3 H); ^{13}C NMR (22.5 MHz, C_6D_6) δ 171.8, 155.0, 148.1, 134.9, 134.8, 110.5, 100.3, 55.0, 54.2, 52.0, 50.6, 49.1, 42.9, 39.2, 37.5, 29.3, 27.5, 27.3.

51: ^{1}H NMR (500 MHz, C_6D_6) δ 5.89 (dd, J = 8.6, 15.6 Hz, 1 H), 5.87 (dd, J = 10.5, 17.3 Hz, 1 H), 5.43 (d, J = 15.6 Hz, 1 H), 5.04 (dd, J = 1.5, 17.3 Hz, 1 H), 4.94 (dd, J = 1.5, 10.5 Hz, 1 H), 4.42 (s, 1 H), 3.43 (s, 3 H), 3.28 (s, 3 H), 3.07 (dddd, J = 3.2, 7.2, 7.3, 8.6 Hz, 1 H), 2.96 (d, J = 7.1 Hz, 1 H), 2.73 (dd, J = 7.1, 7.2 Hz, 1 H), 1.83 (dd, J = 3.2, 12.7 Hz, 1 H), 1.45 (dd, J = 7.3, 12.7 Hz, 1 H), 1.16 (s, 3 H), 1.12 (s, 3 H), 1.11 (s, 3 H); ^{13}C NMR (22.5 MHz, C_6D_6) δ 171.6, 155.0, 147.9, 138.5, 130.0, 110.6, 104.3, 56.7, 55.1, 50.6, 48.8, 47.7, 45.5, 41.9, 39.2, 27.5, 27.3, 24.5.

Preparation of 53. A solution of 1-methylcyclopentadiene, prepared from 72.4 mmol of cyclopentadiene, was diluted to 45 mL with ether. Acrylic acid (5.22 g, 72.4 mmol) was added to this solution, and the reaction allowed to stir for 48 h. After concentration of the mixture in vacuo, the cycloaddition products were distilled at reduced pressure (Kugelrohr, 2 mmHg, 100 °C) to give 5.65 g (37.1 mmol, 51%) of a colorless oil. The oil was dissolved in 20 mL of CH_2Cl_2 and cooled to 0 °C, and oxalyl chloride (14.15 g, 111.4 mmol) was added via syringe. After being stirred for 5 h at 0 °C, the mixture was concentrated in vacuo at 0 °C. The residual oil was distilled at reduced pressure (Kugelrohr, 5 mmHg, 90 °C) to produce 4.30 g (23.0 mmol, 62% from acid) of the mixture of acid chlorides. A solution of the acid chloride mixture in 5.0 mL of $CHCl_3$ was slowly added to a mixture of *N*,*N*-dimethylaniline (4.19 g, 34.5 mmol) and 35 mL of isopropyl alcohol. After the mixture had been stirred for 1 h at 0 °C, the reaction mixture was heated to 65 °C and then sitrred for 5 h at that temperature. Removal of the isopropyl alcohol was achieved in vacuo, and then the reaction quenched with 25 mL of 6 N H_2SO_4. The aqueous solution was extracted with 3 × 40 mL ether. The combined organics were subsequently washed with 1 × 25 mL of 6 N H_2SO_4, 2 × 50 mL of H_2O, 2 × 50 mL of 10% aqueous K_2CO_3, and 1 × 20 mL of saturated aqueous NaCl and then dried (Na_2SO_4). Concentration of the mixture in vacuo followed by distillation at reduced pressure (Kugelrohr, 10 mmHg, 100 °C) produced 3.23 g (16.6 mmol, 72% from acid chloride) of a mixture of esters. The mixture was purified by flash chromatography with petroleum ether/ether (25:1). Concentration of the R_f = 0.23 elutant gave 1.55 g of an inseparable mixture of two isomeric esters. The mixture was shown to consist of **53** (92%) and an isomeric impurity (8%).

53: ^{1}H NMR (400 MHz, C_6H_6) δ 6.09 (dd, J = 3.1, 5.6 Hz, 1 H), 5.87 (d, J = 5.6 Hz, 1 H), 4.97 (qq, J = 6.1, 6.4 Hz, 1 H), 2.55 (br s, 1 H), 2.47 (dd, J = 4.4, 9.3 Hz, 1 H), 1.85 (ddd, J = 3.7, 9.3, 11.7 Hz, 1 H), 1.70 (ddd, J = 3.1, 3.5, 11.7 Hz, 1 H), 1.48 (s, 3 H), 1.23 (ddd, J = 2.0, 2.7, 8.1 Hz, 1 H), 1.02 (d, J = 6.1 Hz, 3 H), 1.01 (d, J = 6.1 Hz, 3 H), 0.96 (br d, J v 8.1 Hz, 1 H); ^{13}C NMR (22.5 MHz, C_6D_6) δ 173.2, 137.4, 137.0, 66.9, 56.6, 55.5, 53.8, 48.7, 42.9, 31.2, 21.9, 18.4.

Reaction of 53 with 38. To a solution of **38** (265 mg, 1.02 mmol) in 1.0 mL of benzene was added a solution of **53** (152 mg, 0.78 mmol) in 1.5 mL of benzene. The mixture was allowed to stir for 2 h at ambient temperature and was then heated at 60 °C for 26 h. Once the reaction mixture had cooled to room temperature, the mixture was added to 100 mL of petroleum ether and stirred for 1 h. The mixture was filtered and the resulting solution concentrated to an oil. This oil was dissolved in 15 mL of acetone/water (5:1), and 5 mg of *p*-toluenesulfone acid monohydrate was added. After the mixture was stirred for 5 h, the acetone was removed in vacuo, and the aqueous layer washed with 3 × 5 mL of ether. The combined organic extractions were washed with 1 × 5 mL of saturated aqueous $NaHCO_3$ and 1 × 5 mL of saturated aqueous NaCl and dried ($MgSO_4$). Concentration in vacuo produced an oil. Flash chromatography allowed the separation of two eluting fractions of R_f = 0.48 and R_f = 0.32. The more mobile elutant was found by ^{1}H NMR to be an inseparable

(46) Veysoglu, T.; Mitscher, L. A.; Swaze, J. K. *Synthesis* **1980**, 807.

2.3:1.0 mixture of **60** and **61** (90 mg, 53%), respectively. The major isomer **60** was identified by the olefin region of the ^{1}H NMR [(400 MHz, C_6D_6) δ 5.81 (dd, J = 10.6, 17.2 Hz, 1 H), 5.40 (d, J = 16.5 Hz, 1 H), 5.27 (dd, J = 6.6, 16.5 Hz, 1 H), 4.98 (d, J = 17.2 Hz, 1 H), 4.94 (d, J = 10.6 Hz, 1 H)]. Identification of the cis minor isomer **61** was also accomplished by ^{1}H NMR [(400 MHz, C_6D_6) δ 5.91 (dd, J = 10.5, 17.3 Hz, 1 H), 5.22 (d, J = 10.4 Hz, 1 H), 5.05 (dd, J = 10.4, 10.4 Hz, 1 H), 4.97 (d, J = 17.3 Hz, 1 H), 4.87 (d, J = 10.5 Hz, 1 H)]. Not only were the resonances at 5.27 and 5.05 ppm coupled to the resonances at 5.40 and 5.22 ppm, respectively, but each was also coupled to a vicinal allyl proton. This information confirmed the position of the methyl group as that of isomers **60** and **61**. The elutant of R_f = 0.32 was further purified by preparative chromatography to give 24 mg of **62** (14%): ^{1}H NMR (400 MHz, C_6D_6) δ 5.85 (dd, J = 10.6, 17.5 Hz, 1 H), 5.51 (d, J = 16.0 Hz, 1 H), 5.43 (d, J = 16.0 Hz, 1 H), 5.01 (dd, J = 1.3, 17.5 Hz, 1 H), 4.95 (dd, J = 1.3, 10.6 Hz, 1 H), 2.09 (s, 1 H), 2.04 (br s, 1 H), 1.64 (ddd, J = 2.9, 4.8, 17.3 Hz, 1 H), 1.44 (dd, J = 4.4, 17.3 Hz, 1 H), 1.40 (dd, J = 2.0, 12.2 Hz, 1 H), 1.18 (ddd, J = 2.9, 4.3, 12.2 Hz, 1 H), 1.05–1.40 (m, 2 H), 1.09 (s, 0.89 (s, 3 H); ^{13}C NMR (100.4 MHz, C_6D_6) δ 212.1, 147.4, 136.5, 134.3, 111.0, 62.2, 44.1, 41.9, 41.7, 39.6, 36.4, 36.3, 28.6, 27.8, 27.7; IR (CCl_4) 2860, 1750, 1640, 1410 cm^{-1}.

Spiro-(1*S,2*S**,5*R**,7*S**)-10,10-dimethyl-7-vinyltricyclo-[5.3.0.0^{2,5}]decane-3,2′-[1,3]dioxolane (66).** To a solution of DMAP (1.56 g, 12.8 mmol) and **64** (1.68 g, 6.4 mmol) in 13 mL of benzene was slowly added a solution of **3** (92.73 g, 9.6 mmol) in 6 mL of benzene. The reaction temperature was maintained below 30 °C through the use of an ice bath. Once addition was complete, the reaction mixture was stirred for 1.5 h at room temperature. The solvent volume was reduced in vacuo by 1 mL, and the reaction vessel sealed and then placed in a 90 °C oil bath for 4 h. After the reaction was allowed to cool to room temperature, the mixture was slowly added to 1 L of petroleum ether. The mixture was allowed to stir in contact with oxygen for 72 h at room temperature. The mixture was cooled to −30 °C, the precipitate was removed by filtration, and the solution was concentrated to a slushy solid. The precipitate that was removed from the solution was further extracted by suspension in 20 mL of benzene and stirring for 3 h and was subsequently diluted with 1 L of petroleum ether. This mixture was cooled to −30 °C and filtered, and the resulting solution was combined with the previously obtained slushy solid. After concentration of the mixture, the solid was brought up in 800 mL of petroleum ether, and the mixture was cooled to −30 °C and filtered. The resulting solution was concentrated in vacuo to an oil and then dissolved in 150 mL of benzene and 20 mL of ethylene glycol. To this mixture was added *p*-toluenesulfonic acid monohydrate (500 mg). The reaction flask was equipped with a Dean–Stark trap containing 4-Å molecular sieves and heated to reflux for 20 h. Once the reaction mixture had cooled to room temperature, the reaction mixture was poured into saturated aqueous 100 mL of $NaHCO_3$, diluted with 150 mL of benzene, and separated. The aqueous layer was extracted with 2 × 100 mL of benzene. The organic extractions were combined, washed with saturated aqueous $NaHCO_3$, and then dried ($MgSO_4$). After filtration through a silica gel pad, which was washed thoroughly with benzene, the solution was concentrated to give 1.30 g of **66** (81%) as an oil: ^{1}H NMR (400 MHz, C_6D_6) δ 6.41 (dd, J = 10.7, 17.3 Hz, 1 H), 5.18 (dd, J = 1.2, 17.3 Hz, 1 H), 4.98 (dd, J = 1.2, 10.7 Hz, 1 H), 3.38–3.48 (m, 4 H), 2.94–2.99 (m, 1 H), 2.44–2.54 (m, 2 H), 2.44 (d, J = 2.4 Hz, 1 H), 2.20–2.28 (m, 1 H), 1.88–1.98 (m, 2 H), 1.72 (dd, J = 7.7, 13.6 Hz, 1 H), 1.34–1.56 (m, 4 H), 1.02 (s, 3 H), 0.87 (s, 3 H); ^{13}C NMR (100.4 MHz, C_6D_6) δ 150.2, 109.2, 108.6, 64.5, 63.5, 62.9, 61.8, 55.9, 48.0, 42.4, 42.1, 40.6, 38.9, 33.7, 30.9, 26.6. IR (neat) 3080, 2940, 2860, 1630, 1460, 1365, 1280, 1145, 1040 cm^{-1}.

Anal. Calcd for $C_{16}H_{24}O_2$: C, 77.38; H, 9.74. Found: C, 77.26; H, 9.72.

(1*S,2*S**,5*R**,7*R**)-10,10-Dimethyl-7-(hydroxymethyl)-tricyclo[5.3.0.0^{2,5}]decane-3,3′-[1,3]dioxolane (67).** Olefin **66** (1.37 g, 5.48 mmol) was dissolved in 85 mL of CH_2Cl_2/methanol (3:1), and a solution of indicator Sudan IV in CH_2Cl_2 was added until a faint red tint to the solution was detectable.[46] The solution was cooled to −78 °C, and O_3 was bubbled through the mixture until the color of the indicator was replaced with a blue tint. After dry nitrogen was bubbled through the solution for 20 min, the mixture was treated with sodium borohydride (0.622 g, 16.4 mmol) and stirred an additional 3 h at −78 °C. The reaction mixture was warmed to room temperature, stirred 15 min, and then quenched by the addition of 50 mL of water. After separation of the mixture, the aqueous layer was extracted with 3 × 50 mL ether. The combined organic fractions were combined and dried ($MgSO_4$). Concentration of the solution produced an oil that was purified by flash chromatography. Elution on silica gel with ether/petroleum ether (3:1) gave 1.25 g of **67** (91%) with R_f = 0.36: ^{1}H NMR (400 MHz, C_6D_6) δ 3.72 (d, J = 10.7 Hz, 1 H), 3.64 (br d, J = 10.7 Hz, 1 H, pattern sharpens upon addition of D_2O), 3.23–3.40 (m, 4 H), 2.92–2.96 (br m, 1 H), 2.48–2.63 (m, 2 H), 2.46 (br s, 1 H, exchanged with D_2O), 2.29 (dd, J = 2.8, 12.5 Hz, 1 H), 2.11 (d, J = 1.0 Hz, 1 H), 1.98 (dd, J = 2.3, 14.0 Hz, 1 H), 1.59–1.74 (m, 2 H), 1.32–1.48 (m, 3 H), 0.93 (s, 3 H), 0.75 (s, 3 H); ^{13}C NMR (100.4 MHz, C_6D_6) δ 108.7, 71.4, 64.4, 63.4, 63.1, 59.7, 55.3, 45.6, 43.2, 42.7, 41.8, 38.6, 34.1, 30.1, 25.1; IR (neat) 3420, 2940, 2860, 1460, 1040, 1010 cm^{-1}.

Anal. Calcd for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59. Found: C, 71.07; H, 9.46.

Esterification of Bis(dimethylamino)phosphinic Chloride with 67. To a solution of alcohol **67** (1.17 g, 4.64 mmol) in 48 mL of DME at room temperature was added a solution of 1.6 M *n*-butyllithium in hexanes (3.3 mL, 5.3 mmol). After stirring for 1 h, a solution of bis(dimethylamino)phosphinic chloride (2.5 mL, ≈14 mmol) in 4.8 mL of triethylamine was added, and the reaction mixture stirred for 5 h at room temperature. The mixture was treated with 100 mL of water and separated, and the aqueous layer extracted with 3 × 100 mL of ether. The combined organics were washed with 2 × 50 mL of water and 1 × 30 mL of saturated aqueous NaCl and dried over $MgSO_4$. Following removal of solvent, the crude ester was isolated by flash chromatography. Elution down a short silica gel column with ethyl acetate produced 1.58 g of ester **68** (88%) with R_f = 0.11: ^{1}H NMR (400 MHz, C_6D_6) δ 4.34 (dd, J = 5.1, 9.8 Hz, 1 H), 4.17 (dd, J = 4.4, 9.5 Hz, 1 H), 3.32–3.45 (m, 4 H), 2.93–2.99 (m, 1 H), 2.55 (d, J = 9.3 Hz, 6 H), 2.53 (d, J = 9.3 Hz, 6 H), 2.44–2.66 (m, 2 H), 2.10–2.22 (m, 3 H), 1.96–2.00 (m, 1 H), 1.63 (d, J = 8.7, 14.3 Hz, 1 H), 1.41–1.58 (m, 3 H), 0.95 (s, 3 H), 0.75 (s, 3 H); ^{13}C NMR (100.4 MHz, C_6D_6) δ 108.3, 72.1 (d, J = 5.1 Hz), 64.5, 63.5, 61.5 (d, J = 7.3 Hz), 59.3, 55.0, 45.3, 43.2, 42.3, 42.2, 38.1, 37.1 (d, J = 3.7 Hz), 34.0, 30.1, 25.0.

Reduction of 68 at 0 °C. To a 0 °C solution of lithium (0.54 g, 78 mmol) in 200 mL of $EtNH_2$ was slowly added a solution of **68** (1.51 g, 3.90 mmol) and *tert*-butyl alcohol (0.39 g, 5.3 mmol) in 60 mL of THF. After stirring for 30 min at 0 °C, the reaction mixture became clear and colorless. The reaction was quenched after 1 h by the addition of saturated aqueous NH_4Cl. Following concentration of the solution at reduced pressure and temperature (aspirator, 0 °C), saturated aqueous $NaHCO_3$ was added. The aqueous solution was extracted with 3 × 200 mL of pentane; the combined organic fractions were dried ($MgSO_4$) and concentrated to an oil. The oil was dissolved in 50 mL of acetone/water (20:1), and *p*-toluenesulfonic acid monohydrate (100 mg) was added. After the mixture was heated at reflux for 20 h, the solution was cooled and quenched with saturated aqueous $NaHCO_3$, and the acetone was removed in vacuo. The aqueous solution was extracted with 3 × 50 mL of pentane, and the combined organics were dried ($MgSO_4$). TLC revealed two compounds with R_f = 0.38 and 0.06 upon elution with petroleum ether/ether (9:1). Separation of these compounds was achieved through the use of flash chromatography. Elution with petroleum ether/ether (9:1) produced 225 mg of **69** (30%) as a colorless oil. Subsequent elution with ether produced an oil that was crystallized from pentane to give 387 mg of **70** (51%) as a white crystalline solid.

69: ^{1}H NMR (400 MHz, C_6D_6) δ 3.15–3.20 (m, 1 H), 2.78–2.90 (m, 1 H), 2.33–2.45 (m, 2 H), 1.95 (s, 1 H), 1.73 (dd, J = 8.9, 14.1 Hz, 1 H), 1.28–1.48 (m, 5 H), 1.06 (s, 3 H), 0.84 (s, 3 H), 0.61 (s, 3 H); ^{13}C NMR (100.4 MHz, C_6D_6) δ 211.8, 68.7, 66.7, 55.5, 54.3, 48.9, 42.3, 42.1, 41.1, 33.5, 31.8, 30.6, 25.4; IR (neat) 2950, 2830, 1780, 1470, 1460, 1075 cm^{-1}.

Anal. Calcd for $C_{13}H_{20}O$: C, 81.20; H, 10.48 Found: C, 81.12; H, 10.47.

70: mp 66.0–67.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.09 (dd, J = 6.6, 12.2 Hz, 1 H), 2.55–2.65 (m, 1 H), 2.45 (dd, J = 5.4, 8.1 Hz, 1 H), 1.84–2.05 (m, 4 H), 1.61 (s, 1 H), 1.49–1.54 (m, 2 H),

1.30–1.45 (m, 2 H), 1.30–1.45 (m, 3 H), 1.25 (s, 3 H), 0.96 (s, 3 H), 0.80 (s, 3 H); ^{13}C NMR (100.4 MHz, C_6D_6) δ 73.2, 68.5, 56.9, 55.9, 50.7, 42.8, 42.5, 42.2, 38.0, 35.0, 31.9, 31.1, 25.7; IR (CCl_4) 3620, 2950, 2870, 1460, 1110 cm^{-1}.

Anal. Calcd for $C_{13}H_{22}O$: C, 80.35; H, 11.41. Found: C, 80.15; H, 11.25.

(1*R,2*S**,5*R**,7*S**)-7,10,10-Trimethyltricyclo[5.3.0^{2,5}]decan-3-one (69).** To a solution of **67** (1.08 g, 4.27 mmol) in 48 mL of DME at room temperature was added a solution of 2.5 M *n*-butyllithium in hexanes (2.0 mL, 4.9 mmol). After this stirred for 1 h, a solution of bis(dimethylamino)phosphorochloridate (2.5 mL, ≈14 mmol) in 4.8 mL of triethylamine was added, and the reaction mixture stirred for 10 h at room temperature. The mixture was treated with 100 mL of water and separated, and the aqueous layer extracted with 3 × 100 mL of ether. The combined organics were washed with 2 × 50 mL of water and 1 × 30 mL of saturated aqueous NaCl and dried ($MgSO_4$). Concentration of this solution produced 1.56 g of crude **68** (95% mass balance). A −78 °C mixture of crude **68** (1.50 g, 3.88 mmol) and *tert*-butyl alcohol (0.39 g, 5.3 mmol) in 60 mL of THF was added to a −78 °C solution of lithium (0.54 g, 78 mmol) in 200 mL of $EtNH_2$. The mixture was warmed to −50 °C and was allowed to stir for 1 h between −50 and −40 °C. After the mixture was cooled to −78 °C, the reaction was quenched by the slow addition of saturated aqueous NH_4Cl. The colorless solution was warmed to 0 °C, and the mixture concentrated via aspirator. Once concentrated, saturated aqueous $NaHCO_3$ was added, and the mixture extracted with 3 × 200 mL of pentane. The organic fractions were combined and dried ($MgSO_4$). The resulting oil was dissolved in 50 mL of acetone/water (20:1), and *p*-toluenesulfonic acid monohydrate (50 mg) was added. After this mixture was heated at reflux for 20 h, the solution was cooled and quenched with saturated aqueous $NaHCO_3$, and the acetone was removed in vacuo. The aqueous solution was extracted with 3 × 50 mL of pentane, and the combined organics were dried ($MgSO_4$). After concentration of this solution, the mixture was dissolved in 10 mL of CH_2Cl_2, and 219 mg of pyridinium dichromate (0.58 mmol) was added. After being stirred for 3 h, the reaction mixture was diluted with ether and then filtered. Flash chromatography with petroleum ether/ether (9:1) was employed to give 537 mg of **69** (68%).

(1*S,2*S**,6*S**,8*S**)-8,11,11-Trimethyltricyclo[6.3.0.0^{2,6}]undecan-3-one (73).** To a 0 °C solution of **69** (372 mg, 1.94 mmol) in 25 mL of ether was added boron trifluoride etherate (667 mg, 4.84 mmol) via syringe. After being stirred for 30 min at 0 °C, the reaction mixture was cooled to −28 °C (*o*-xylene/CO_2), and $N_2CHCO_2CH_2CH_3$ (4.84 mmol) was added. The reaction was stirred for 5 h at −28 °C and then quenched with saturated aqueous $NaHCO_3$. After being stirred for 1 h, the mixture was extracted with 3 × 50 mL of ether. The combined organics were concentrated to an oil and dissolved in 35 mL of DMSO. To this solution were added NaCl (124 mg, 2.13 mmol) and H_2O (105 mg, 5.82 mmol). The mixture was heated to 150 °C and maintained at that temperature for 5 h. After cooling to room temperature, 40 mL of water was added, and the mixture was extracted with 3 × 50 mL of ether. The combined organics were dried ($MgSO_4$) and then concentrated to an oil. VPC analysis revealed a 5.0:1.0 mixture of two products. Separation of the products was achieved through flash chromatography. Elution on silica gel with petroleum ether/ether (9:1) produced 293 mg of **73** (73%) with R_f = 0.29 and 52 mg of **74** (13%) with R_f = 0.21.

73: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.75–2.85 (m, 1 H), 2.25–2.35 (m, 3 H), 1.96–2.08 (m, 1 H), 1.94–1.98 (m, 1 H), 1.75–1.87 (m, 2 H), 1.54–1.59 (m, 2 H), 1.38–1.54 (m, 2 H), 0.99–1.17 (m, 1 H), 1.11 (s, 3 H), 1.07 (s, 3 H), 0.94 (s, 3 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 222.2, 64.0, 57.1, 52.8, 47.5, 42.2, 42.0, 41.5, 40.0, 34.8, 30.8, 30.2, 26.0, 23.9; IR (neat) 2950, 2860, 1740, 1460, 1170 cm^{-1}.

Anal. Calcd for $C_{14}H_{22}O$: C, 81.50; H, 10.75. Found: C, 81.42; H, 10.66.

74: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.60–2.72 (m, 1 H), 2.46–2.59 (m, 1 H), 2.23–2.42 (m, 2 H), 2.19 (dd, *J* = 3.3, 18.8 Hz, 1 H), 1.99 (dd, *J* = 7.6, 18.8 Hz, 1 H), 1.99 (dd, *J* = 7.6, 13.6 Hz, 1 H), 1.36–1.58 (m, 6 H), 1.22 (s, 3 H), 0.99 (s, 3 H), 0.96 (s, 3 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 220.0, 67.7, 53.2, 48.2, 45.1, 44.3, 44.1, 42.6, 42.0, 41.3, 41.2, 32.7, 30.8, 25.7; IR (neat) 2950, 2870, 1740, 1460, 1410, 1150 cm^{-1}.

Anal. Calcd for $C_{14}H_{22}O$: C, 81.50; H, 10.75. Found: C, 81.24; H, 10.66.

Δ$^{9(12)}$-Capnellene (75). A precooled solution of ketone **74** (179 mg, 0.87 mmol) in 3 mL of ether was added to a solution of **3** (342 mg, 1.20 mmol) in 3 mL of ether at −40 °C. To this mixture was added pyridine (123 mg, 1.56 mmol) via syringe. The reaction was maintained at −40 °C for 30 min and then allowed to warm to ambient temperature over the period of 1 h. The reaction was then quenched by the addition of 50 mL of pentane and exposure to oxygen. After being stirred for 3 h, the mixture was filtered through a silica gel pad and washed through with pentane. The solution was concentrated under aspirator (30 mmHg) at 0 °C. The resulting oil was taken up in 20 mL of pentane and filtered through a pad of silica gel, washed through with pentane, and concentrated under reduced pressure and temperature to produce 165 mg of **75** (93%) as a colorless liquid: R_f (TLC, pentane) = 0.71; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.89 (s, 1 H), 4.78 (s, 1 H), 2.62–2.68 (m, 1 H), 2.42–2.60 (m, 2 H), 2.30–2.40 (m, 1 H), 1.64–1.77 (m, 3 H), 1.42–1.56 (m, 5 H), 1.21 (dd, *J* = 9.5, 13.2 Hz, 1 H), 1.15 (s, 3 H), 1.05 (s, 3 H), 0.98 (s, 3 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 158.2, 104.5, 68.8, 53.1, 52.0, 47.7, 45.8, 42.1, 41.5, 40.4, 31.7, 31.4, 30.7, 28.9, 25.9; IR (neat) 3070, 2940, 2860, 1650, 1460, 1385, 1370, 1365, 875 cm^{-1}; exact mass calcd for $C_{15}H_{24}$ 204.1878, found 204.1880.

Anal. Calcd for $C_{15}H_{24}$: C, 88.16; H, 11.84. Found: C, 88.12; H, 11.72.

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Registry No. **1**, 83876-46-4; **3**, 67719-69-1; 11, 90076-32-7; **12a**, 39589-98-5; **12b**, 7288-32-6; **12c**, 123640-00-6; **12** anhydride, 129-64-6; **13a**, 123640-09-5; **13b**, 123640-14-2; **13c**, 123640-15-3; (±)-**16a**, 123639-70-3; (±)-**16b**, 123640-01-7; (±)-**16c**, 123640-05-1; (±)-**18a**, 123673-92-7; (±)-**19a**, 123639-71-4; (±)-**19b**, 123640-02-8; (±)-**20a**, 123639-72-5; (±)-**20b**, 123640-03-9; (±)-**21**, 123639-73-6; (±)-**22**, 123639-74-7; (±)-**23**, 67999-50-2; (±)-**24**, 117835-14-0; (±)-**25**, 123639-75-8; **26**, 123640-10-8; **27**, 123640-11-9; (±)-**29**, 123639-76-9; (±)-**30**, 123639-77-0; (±)-**32**, 123639-78-1; (±)-**33**, 123748-85-6; (±)-**34a**, 123639-79-2; (±)-**34b**, 123640-04-0; **35**, 123640-16-4; **36**, 123640-17-5; (±)-**37**, 123639-80-5; **38**, 99798-41-1; **39**, 123640-12-0; **40a**, 123640-13-1; **41a**, 123748-93-6; (±)-**42a**, 123639-81-6; (±)-**43a**, 123748-86-7; (±)-**44a**, 123639-82-7; (±)-**45a**, 123748-87-8; (±)-**46a**, 123639-83-8; (±)-**50**, 123639-84-9; (±)-**51**, 123639-85-0; (±)-**52**, 123748-88-9; (±)-**53**, 123639-86-1; (±)-**53** regioisomer, 123640-06-2; (±)-**53** acid, 123639-99-6; (±)-**53** acid, regioisomer, 123639-98-5; (±)-**53** acid chloride, 123640-07-3; (±)-**50** acid chloride, regioisomer, 123640-08-4; (±)-**57**, 123639-87-2; (±)-**58**, 123748-89-0; (±)-**59**, 123639-88-3; (±)-**60**, 123639-89-4; (±)-**61**, 123748-90-3; (±)-**62**, 123639-90-7; (±)-**64**, 100206-60-8; (±)-**65**, 123639-91-8; (±)-**66**, 100206-61-9; (±)-**67**, 123639-92-9; (±)-**68**, 123639-93-0; (±)-**69**, 100206-62-0; **70**, 123639-95-2; (±)-**71** isomer 1, 123639-95-2; (±)-**71** isomer 2, 123748-91-4; (±)-**72** isomer 1, 123639-96-3; (±)-**72** isomer 2, 123748-92-5; (±)-**73**, 81331-89-7; (±)-**74**, 123639-97-4; (±)-**75**, 81370-78-7; CH_2=$CHCO_2H$, 79-10-7; 1-methylcyclopentadiene, 96-39-9; α,α-dimethyl-γ-butyrolactone, 3709-08-8; cyclopentadiene, 542-92-7; maleic anhydride, 108-31-6.