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CATALYTIC IRON-MEDIATED ENE CARBOCYCLIZATIONS: FORMAL [4+4]-ENE REACTIONS OF TRIENE ESTERS[1a]

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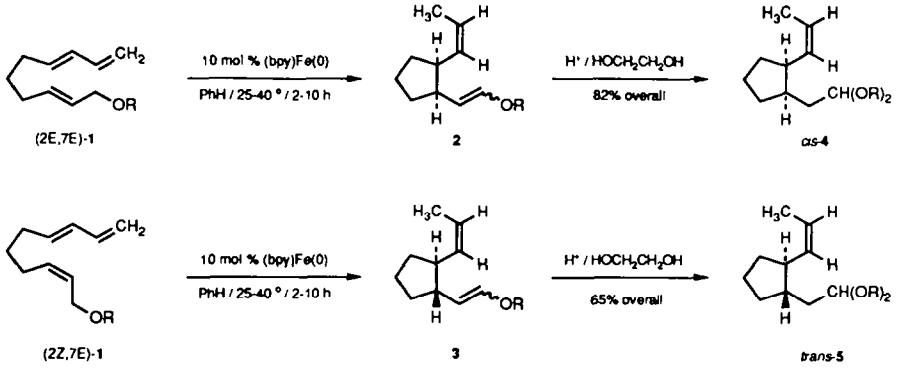
Summary: 2-Substituted-2,7,9-decatrienoates undergo an iron-catalyzed carbocyclization to yield *trans*-disubstituted cyclopentanes in moderate-to-good chemical yields. The cyclization products are formally the result of a [4+4]-ene reaction in which *cis*-propenyl and 2-acroyl functionalities are introduced as appendages to the newly formed cyclopentane ring by the cyclization. Triene ester substrates bearing an alkyl substituent at the 4- or 6-positions cyclize with high 1,2-stereoinduction to yield trisubstituted cyclopentanes in which the relative stereochemistry between three contiguous stereocenters is controlled.

Transition-metal-mediated carbon-carbon bond forming reactions are amongst the most popular new synthetic strategies for the construction of common carbocylic and heterocyclic ring systems.[3] In recent years the synthetic potential of a wide variety of stoichiometric- and/or catalytic-palladium[4], -nickel[5], -zirconium[6], -cobalt[7], and -rhodium[8] mediated carbon-carbon bond construction reactions are under development as interesting cyclization strategies for organic synthesis. In this regard, we[9a-d] and others[9e] have taken an interest in the development of iron-mediated carbocyclization reactions.

In the course of our studies on catalytic iron-mediated carbocyclizations, we have found that triene ethers such as (2E,7E)-**1** and (2Z,7E)-**1** undergo stereoselective ene carbocyclization to give mixture of cyclized products in good-to-excellent chemical yield. The predominant products **2** and **3** are each formed as a 60:40 mixture of stereoisomers, diastereomers which are isomeric about the enol ether double bond. This



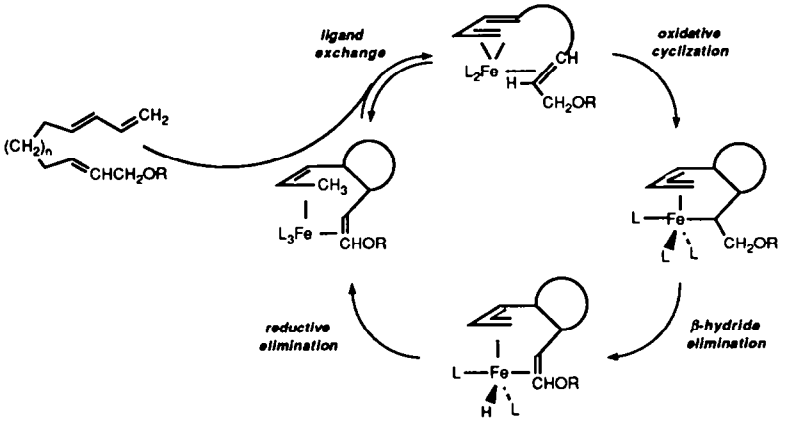
stereochemical ambiguity is removed by the acid catalyzed acetalization or hydrolysis of the crude reaction mixture to yield ethylene acetals **4** and **5** or their corresponding aldehydes in high isomeric purity. It should be noted that in the carbocyclizations of **1**, the alkene geometry determines the cis/trans sense of simple diastereoselection[10], a stereochemical control element that we will return to in the course of our discussion of new triene ester carbocyclizations. Overall, we are finding that the ene carbocyclization of triene ethers is proving to be quite

general with respect to ring size (five- or six-membered rings), ring type (carbocycles or heterocycles), simple diastereoselection in the ring closure, and *trans*-1,2-stereoinduction from non-chelating substituents on the tether chain connecting the diene and olefin moieties.

A key feature in the synthetic utility of the triene ether ene carbocyclization chemistry is that two useful functional groups, the stereodefined di- or trisubstituted alkene and the latent aldehyde, are generated in the course of the cyclization. These functional groups provide a handle for the subsequent chemical elaboration of the cyclized product. It seemed reasonable that other functionalized trienes should undergo ene-type carbocyclizations. The cyclization of appropriate new substrates could generate functionalities in the cyclized product that would complement the triene ether chemistry. With this goal in mind, we now describe our first investigations into the design of new triene substrates for iron catalyzed ene carbocyclization.

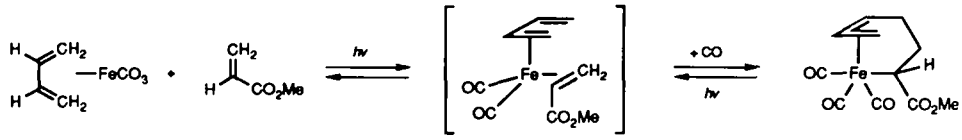
In designing new triene substrates, we must consider the substrate requirements imposed by the catalytic cycle for the cyclization (Scheme I). Three substrate criteria are immediately apparent. 1) The diene and alkene moieties must readily template about the relatively electron rich metal center. 2) The diene and alkene functionalities, as well as the tether unit connecting the diene and the alkene, must accommodate carbon-carbon bond formation via an oxidative cyclization. 3) The metallacyclic intermediate so generated should accommodate facile iron-mediated hydrogen transfer by presenting an exocyclic β-hydrogen for efficient β-hydride elimination.

Scheme I. A Proposed Catalytic Cycle for the Catalytic Iron-Mediated Triene Carbocyclization.



2-Substituted triene ester substrates seemed to be the natural choice for our initial investigations. Grevels and co-workers[11] had demonstrated that an isolable diene-alkene complex, formed stoichiometrically from the photolysis of a tricarbonyliron-diene complex in the presence of methyl acrylate, undergoes reversible oxidative cyclization at or below ambient temperature. Incorporating a substituent in the 2-position of the α,β-unsaturated ester moiety would provide an appropriately placed hydrogen for exocyclic β-hydride elimination as required in the desired ene-reaction. The products arising from the ene carbocyclization of these triene ester substrates would contain an unsaturated ester functionality in the product that should prove to be useful for further synthetic transformation. In addition, good methods for the synthesis of triene esters have been developed in conjunction with investigations into intramolecular Diels-Alder cycloaddition[12] chemistry. This Diels-Alder strategy for the synthesis of bicyclic ring systems has received a great deal of attention in recent years and the successful

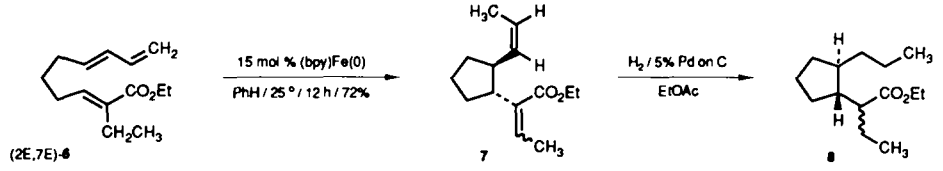
development of the ene carbocyclization of triene esters would provide a complementary new use for these readily accessible substrates.



Results and Discussion

Our investigations into the carbocyclizations of triene esters have focussed on three aspects: a) the influence of the 2-substituent on the facility of the carbocyclization; b) the role of the α,β-unsaturated alkene geometry in directing the sense and degree of simple diastereoselection in the cyclization; and c) the influence of substituents adjacent to the diene and the alkene moieties on directing the stereochemical course of the cyclization.

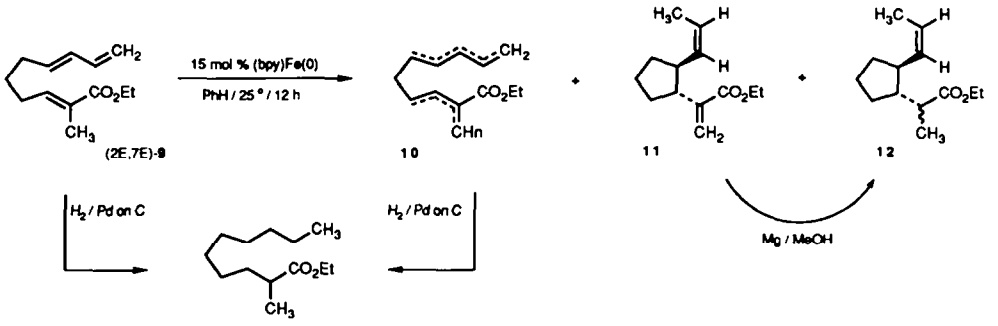
a. The influence of the 2-substituent on the facility of the iron-catalyzed carbocyclization. The five-membered ring precursor containing the 2-ethyl substituent, triene ester **6**, was prepared in three steps from δ-valerolactone by diisobutylaluminum hydride (DIBAL-H) reduction with *in situ* trapping by triethyl 2-phosphonobutyrate[13], PCC oxidation of the hydroxy-ester, and dienylation using the Yamamoto allyldiphenylphosphine oxide procedure[14]. The route, while short, suffers from a stereochemical mixture in the formation of the unsaturated ester (3:1 E:Z) and low yields in the dienylation step (20-30%). The latter problem can be solved by using the alternative allyltriphenylsilane dienylation procedure[15]. The unsaturated ester diastereomers were separated by chromatography on silica and the decatrienoate (2E,7E)-**6** exposed to 10-15 mole percent of the iron ene catalyst[16]. Cyclization proceeds readily (PhH, 25°, 12 h) to produce the formal [4+4]-ene carbocyclization product **7** as a 3:2 mixture of E/Z-diastereoisomers in 72% yield.[16] The isomers are diastereomeric only at the trisubstituted alkene as confirmed by hydrogenation of the individual isomers to the same mixture of cyclopentanes **8**. The trans relative stereochemistry is assigned to the ring substituents (*vide infra*). No other stereo- or regioisomeric ene products were isolated from the reaction.



The simplest five-membered ring precursor, triene ester **9**, was prepared as a 4:1 2E:2Z mixture of olefin isomers via the Horner-Emmons Wittig olefination of (5E) 5,7-octadienal. Cyclization of the (2E,5E)-**9** gave a mixture of products of which the [4+4]-ene product **11** comprised 50-65% of the crude product mixture as determined by capillary gas chromatographic (GC) analysis. The cyclized product **11** could be isolated (*albeit with difficulty in the chromatographic separation*) in only 30-40% yield.

Three major side reactions compromise the yield of ene product obtained from substrate **9**. Reduction of the unsaturated ester to produce ester **12** accounts for up to 10% of the reaction mixture. The structure of the isolated ester **12** was assigned by comparison to an authentic sample obtained via Mg/MeOH reduction[17] of unsaturated ester **11**. The iron-mediated reduction pathway is relatively easy to control, since it only occurs after

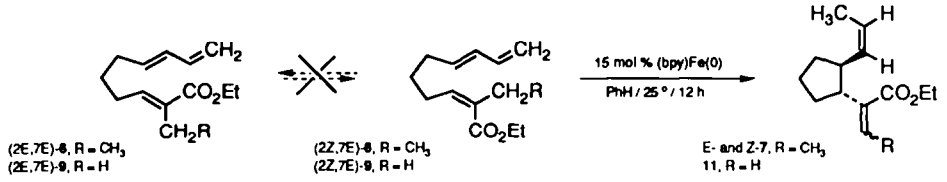
prolonged reaction times. By careful monitoring of the reaction progress, the subsequent product reduction can be minimized. Apparently, decomposition of the starting material and/or product also contributes to the low chemical yield of **11**. The decomposition, which may be occurring during the cyclization reaction or in the product isolation, typically claims 10-30% of the material as judged by the total mass balance at the end of the purification process. The other main deleterious side reaction involves the apparent iron-catalyzed alkene isomerization of the starting triene ester.[18,19] Capillary GC analysis of the crude reaction mixture showed that, in addition to cyclized product **11**, a large number of isomeric compounds were produced by "competitive" alkene isomerization reaction. It proved difficult to obtain even small amounts of any one compound in pure form by chromatography. The isomerization pathway was ultimately implicated by hydrogenation (1 atm H_2 / 5% Pd on C / EtOAc) of a mixture of isomerized products **10** to give only ethyl 2-methyl-decanoate.



The extent to which this isomerization competes with carbocyclization varies from reaction-to-reaction. We now understand in part why this is the case. Following the course of the cyclization reaction of triene **9** by removing aliquots and analyzing them by capillary GC shows that the isomerization reaction occurs rapidly at short reaction times; within 5-10 minutes after addition of the triene ester to the solution of the iron-catalyst. Subsequently, ene carbocyclization products grow in faster than isomerization products. These observations suggest that some intermediate iron species formed in the course of the reduction by triethylaluminum may be responsible for the isomerization, while some later formed iron species, presumably bpy-Fe(0)$(solvent)_n$, is responsible for the ene carbocyclization.[20]

The rate of the iron-catalyzed isomerization process should be dependent on such variables as the "aging" of the catalyst, the nature of the ligand, the nature of the addend, and the nature of the α,β-unsaturated ester moiety[21]. The latter effect is illustrated by the more successful cyclization of the 2-ethyl substituted triene **6**. Unfortunately, attempts to optimize the reaction conditions for triene **9** by aging the catalyst, thereby allowing sufficient time for complete reduction by triethylaluminum, prior to addition of **9** were largely unsuccessful. In the absence of substrate, the catalyst deactivates over time; likely by disproportionation to catalytically inactive $bpy_2Fe(0)$ and Fe_{metal}.[15] We have also briefly investigated the influence of the other variables. As the ligand for iron in the reactions of **9**, 1,10-phenanthroline gave results comparable to 2,2'-bipyridine. Both were superior to diazodienes[22] or 1,2-bis(diphenylphosphino)ethane, ligands which gave much less active catalysts. Replacement of the furan addend[15] with 2-5 equivalents of norbornadiene or cyclooctatetraene offered no practical advantage. At present, it seems that the reaction conditions will have to be very carefully optimized in the case of isomerization- and/or decomposition-prone unsaturated esters.

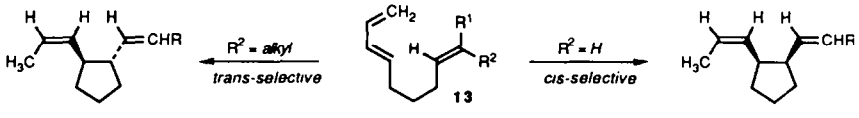
b. The role of the α,β-unsaturated alkene geometry in directing the sense and degree of simple diastereoselection in the cyclization. The carbon-carbon bond formation between two sp^2-hybridized carbon centers of the triene substrate generates vicinal ring substituents in the course of the ene carbocyclization. In the ene carbocyclization of triene ether **1**, the alkene geometry directs the cis/trans-sense of simple diastereoselectivity. The (2E,7E)-**1** gives rise to the *cis-disubstituted* cyclopentane **4**, while the diastereomeric (2Z,7E)-**1** gives rise to the *trans*-substituted cyclopentane **5**. In contrast, (2Z,7E)-**6** and (2Z,7E)-**9** give the same product mixtures as the (2E,7E)-isomers described above. The chemical yields for the cyclizations of the (2Z)-isomers are comparable to those obtained for the (2E)-isomers. In the case of (2Z,7E)-**6** the same 60:40 ratio of E/Z-isomers **7** is produced in the cyclization.



This apparent lack of dependence on the unsaturated ester geometry could in principal arise as the consequence of a facile iron-catalyzed (2E)/(2Z)-alkene isomerization under the cyclization conditions. Following the progress of the cyclization by capillary GC analysis, this does not appear to be the case. Cyclization of the individual (2E)-isomers of **6** and **9** show no evidence for formation of the (2Z)-isomers at a rate competitive with cyclization. Similarly, the (2Z)-isomers of **6** and **9** cyclize without competing isomerization to the (2E)-isomers. Finally, following the cyclization of a mixture of (2E)- and (2Z)-**6** (and similarly with (2E)- and (2Z)-**9**) shows that the isomers are consumed at comparable rates.

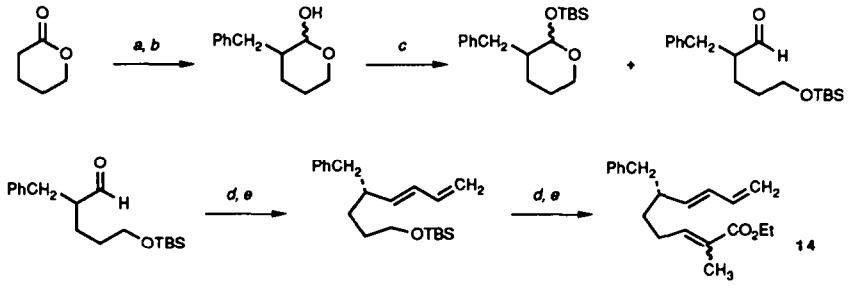
The origin of the stereochemical difference between the five-membered ring carbocyclizations of triene ethers and triene esters presumably lies in the details of the oxidative cyclization of the iron-triene complex (Scheme I). All of the stereochemistry is set by the oxidative cyclization reaction. The simple diastereoselectivity is then determined by either the selective cyclization of one of the two possible diastereomeric triene complexes or alternatively, by selective reaction of one of two rapidly interconverting metallacycles. While the exact reasons for the apparent diastereofacial discrimination in the ene carbocyclizations examined to date is beyond any rational mechanistic discussion, it is instructive to note the empirical correlation that only when the R^1-substituent in the generalized triene structure **13** is hydrogen is a significant amount of the *cis*-product obtained.

Scheme II. The role of alkene geometry in the control of relative stereochemistry in the iron-catalyzed five-membered ring carbocyclizations.



c. The influence of substituents adjacent to the diene and the alkene moieties on directing the stereochemical course of the cyclization. Triene ester substrates containing a stereogenic center in the methylene chain connecting the diene and α,β-unsaturated ester moieties can give rise to

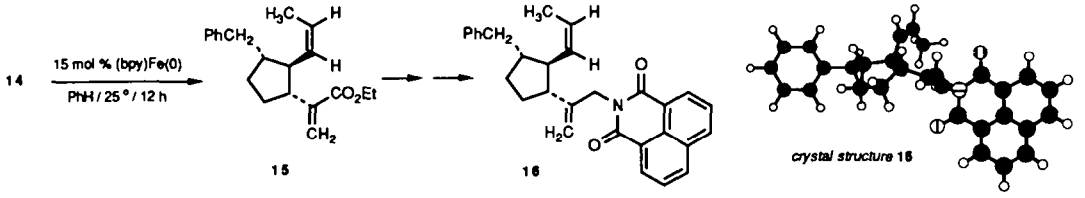
Scheme III. The preparation of benzyl-substituted triene ester **14**.



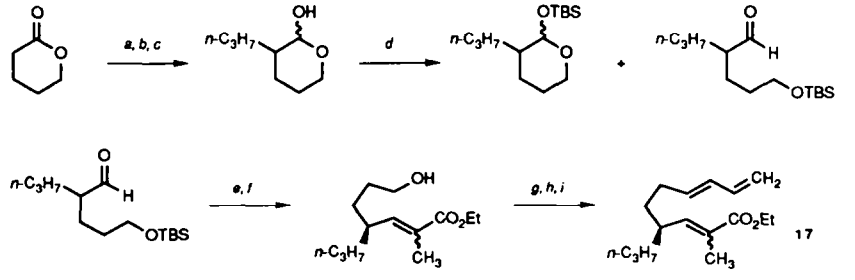
a) 1. 1.1 LDA / THF-HMPA / -78°, 2. $PhCH_2Br$ / -78 -> 25° / 59%; b) 1.0 eq DIBAL-H / THF / -78° / 99%; c) 1.1 TBSCl / imidazole / DMF / 50° / 70%; d) $Li[CH_2CHCHP(O)Ph_2]$ / THF-HMPA / -78 -> 25° / 60%; e) cat Dowex 50W / MeOH / 99%; f) 2.1 DMSO / 1.1 $(COCl)_2$ / 5.5 Et_3N / CH_2Cl_2 / -55 -> 25° / 96%; g) $Li[(EtO)_2P(O)C(CH_3)CO_2Et]$ / THF / 0 -> 25° / 67%.

diastereoisomers upon ene carbocyclization. We have briefly investigated the stereochemical influence of substituents appended adjacent to the diene and α,β-unsaturated ester moieties.

The benzyl-substituted triene ester **14** was prepared starting from δ-valerolactone as outlined in Scheme III. Iron-catalyzed carbocyclization of **14** produces a single isolable ene product in modest chemical yield (30-40%). The trans,trans stereochemical assignment was made after conversion of **15** to imide **16** via DIBAL-H reduction and subsequent Mitsunobu displacement by 1,8-naphthalimide. A crystal structure determination[2] of **16** established the stereochemical relationship between the three contiguous stereogenic centers.

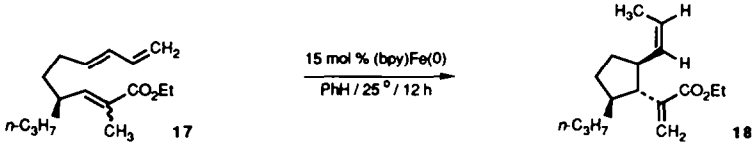


Scheme IV. The preparation of *n*-propyl-substituted triene ester **17**.



a) 1. 1.1 LDA / THF-HMPA / -78°, 2. CH_2CHCH_2Br / -78 -> 25° / 41%; b) 1 atm H_2 / 5% Pd on C / MeOH / 25° / 7 h / 99%; c) 1.0 eq DIBAL-H / THF / -78° / 99%; d) 1.1 TBSCl / imidazole / DMF / 60° / 60%; e) $Li[(EtO)_2P(O)C(CH_3)CO_2Et]$ / THF / 0 -> 25° / 79%; f) cat *p*-TsOH / MeOH / 99%; g) 2.1 DMSO / 1.1 $(COCl)_2$ / 5.5 Et_3N / CH_2Cl_2 / -55 -> 25° / 96%; h) 1. $Li[CH_2CHCHSiPh_3]$ / $(i\text{-}PrO)_4Ti$ / THF / -78° / 1 h, 2. 10% aq HCl / -78° / 90%; i) cat H_2SO_4 / THF / 25° / 72%.

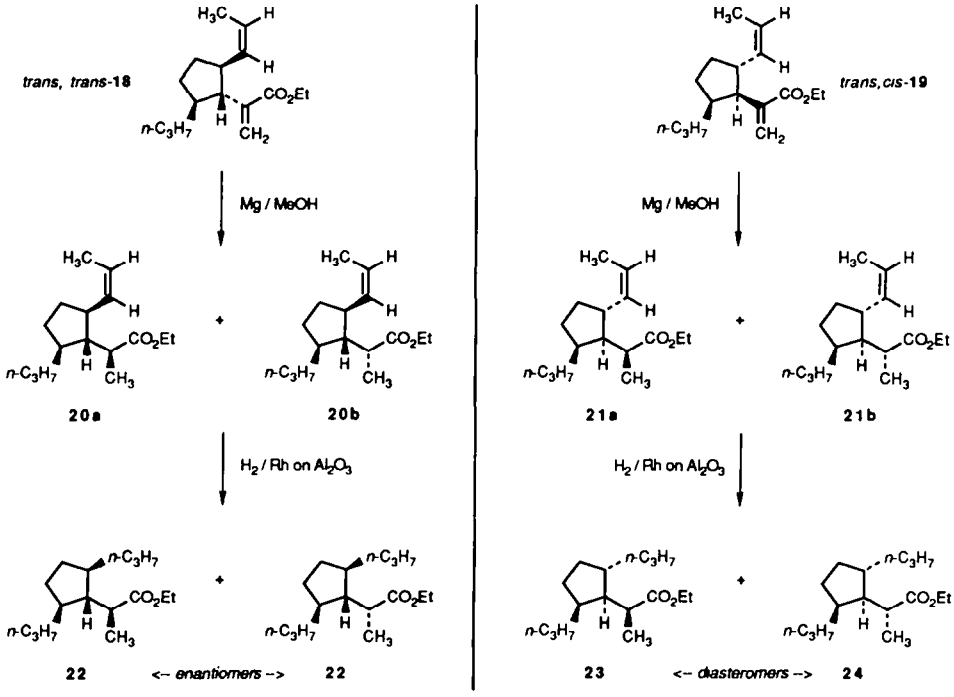
The *n*-propyl-substituted triene ester **17** was prepared as outlined in scheme IV. Iron-catalyzed ene carbocyclization of **17** proceeds as expected. Capillary GC analysis of the crude reaction mixture (the crude recovery was quantitative) shows that the cyclized product comprises 65% of the reaction mixture. However, only a modest yield (30-35%) of **18** could be isolated.



17 **18**

The trans,trans stereochemistry of **18** is assigned based upon the symmetry arguments outlined in Scheme V. For the argument, *trans*-simple diastereoselectivity is assumed. Two possible diastereoisomeric cyclized products are considered, the *trans,trans*-**18** and the *trans,cis*-**19**. Reduction of the unsaturated ester functionality in either **18** or **19** would give rise to a 2-methyl-substituted ester (**20** or **21**, respectively) consisting of a mixture of α- and β-diastereomers. Hydrogenation of this mixture will yield different results depending on whether the starting ene-product is the *trans,trans*-**18** or the *trans,cis*-**19**. In the *trans,trans*-series a single ester **22** would result from hydrogenation of the mixture **20a** and **20b**. In the *trans,cis*-series a mixture of diastereomers **23** and **24** would necessarily result from the hydrogenation of **21a** and **21b**.

Scheme V. The structure assignment of product **18** based upon the stereochemical consequences of reduction of the alkene moieties in the two possible diastereomeric structures, *trans,trans*-**18** and *trans,cis*-**19**.



The cyclized product obtained from the reaction of triene **17** was reduced to a mixture of diastereomeric esters by reaction with magnesium in methanol[17]. The mixture of 2-methyl-substituted esters could be partially resolved on capillary GC analysis and were clearly distinguishable in the 200 MHz ^{1}H and 50 MHz ^{13}C NMR spectra. This mixture of esters was hydrogenated (1 atm H_2 / 5% Rh on alumina / MeOH) to give the saturated ester **20**, which was judged to be a single compound by capillary GC, 360 MHz ^{1}H NMR, and 50 MHz ^{13}C NMR analysis. It should be noted that the choice of the hydrogenation catalyst is crucial to the success of the structure proof. During the study of ring systems related to **5** and **15** in our labs, it has been found that palladium on carbon hydrogenation catalysts frequently effect an apparent epimerization of the ring substituents; presumably via double bond isomerization toward the ring and subsequent hydrogenation. A recent report[23] demonstrates that even a potentially problematic substrate (*i.e* a β,γ-unsaturated ester) does not suffer rhodium-catalyzed double bond isomerization competitive with hydrogenation.

Conclusions

The catalytic iron-mediated ene carbocyclization of triene esters is at present a viable process for only a limited set of triene substrates; in particular 2-substituted triene esters (and perhaps other carboxyl derivatives) that are not prone to iron-promoted isomerization and/or decomposition. In general, high levels of *trans*-simple diastereoselection and *trans*-1,2-stereoinduction are observed in the cyclization reaction. In the latter instance, the relative stereochemistry between three contiguous stereogenic centers can be set with remarkably high selectivity, even in substrates in which the substituent is not particularly sterically demanding (*e.g.* benzyl or *n*-propyl).

The exceptional capability of transition metals to catalyze a wide range of reaction modes, and these often in a highly ligand dependent fashion, greatly complicates the rational design of new substrates. Seemingly minor changes in the substrate can greatly facilitate unwanted reaction modes at the expense of the desired one. The present limitations in the triene ester methodology point out two general features that are relevant to the design of other new catalytic transition-metal-mediated carbocyclizations. In part, the triene ester suffers in that the methodology seeks to generate reactive functionalities in an unmasked form. In contrast, the triene ethers generate the labile aldehyde functionality in a relatively unreactive form. In addition, we have experienced difficulties in this study in the chromatographic separation of cyclization products that are isomeric to starting materials, frequently encountering fortuitous overlap or near overlap of starting material and the isomeric cyclized product. Nonetheless, the present study demonstrates that iron catalyzed carbocyclizations of functionalized triene, other than triene ethers, are indeed feasible. Further studies, particularly studies directed toward the design of new catalysts with higher specificity for carbocyclization over other pathways, are in progress.

Experimental Section

General Procedures. Unless otherwise noted, all reactions are carried out under an atmosphere of nitrogen, and all temperatures are reported in degrees Celsius and are measured externally. THF is distilled under nitrogen from benzophenone ketyl prior to use. Extreme care is taken to ensure that the benzene used in the catalytic iron chemistry is dry and oxygen-free. Benzene is distilled from sodium metal, then redistilled from (purple) sodium benzophenone ketyl. 1-2 mL of diglyme per liter of benzene is added as a ketyl solubilizing agent. Furan and 2-methylfuran are distilled under nitrogen from lithium aluminium hydride prior to use. Hexanes and ethyl acetate (EtOAc) are purified by distillation. Dichloromethane is passed through a column of alumina. Dimethyl sulfoxide (DMSO) and dimethyl formamide (DMF) are dried over 4A sieves, distilled under reduced pressure, then stored over 4A sieves. Hexamethylphosphoramide (HMPA) is dried over calcium hydride (5-10 h, 60°), distilled under reduced pressure, then stored over 4A molecular sieves. Ferric acetylacetonate (Lancaster Synthesis, Windham, NH) is either recrystalized (benzene/hexanes or ethanol) then dried under vacuum (0.01 mm, 25°), or (preferably) sublimed (0.05 mm, 100°). 2,2'-Bipryidine (bpy) is sublimed (0.01 mm, 65°). Triethylaluminum (Aldrich Chemicals) is used as a 1.9 M solution in toluene. After several months of use, stock solutions of triethylaluminum are replaced. Diisobutylaluminum hydride (DIBAL-H) and n-butyllithium are used as a 1.5 M solution

in toluene and a 2.5 M solution in hexanes, respectively. All other reagents received from commercial sources are used without further purification.

^1H and ^{13}C NMR spectra are obtained on a Varian VXR-200, Varian XL-300, or wide bore Nicolet NT 360 spectrometer. IR spectra are obtained on a Perkin-Elmer 298 Infrared or Analect RFX-65 FT-IR spectrophotometer using NaCl plates (neat sample), NaCl solution cells (CCl_4 or $CHCl_3$), or the Attenuated Total Reflectance technique[24] (ATR, neat, ZnSe crystal). Analytical gas chromatographic (GC) measurements are performed on a Varian Vista Series 6000 gas chromatograph equipped with a 30 meter Durabond DB-5 or DB-17 0.25 μm film thickness fused silica capillary column (J & W Scientific, Folsom, CA) and a flame ionization detector. Analytical High Performance Liquid Chromatographic (HPLC) measurements are performed on a Varian Vista Series 54 chromatograph equipped with a EM Merck Hibar, Si 60 (5 μm, 23 x 0.8 cm) silica gel column using HPLC grade (EM Science Omnisolv,) solvents and a Varian Vari-Chrom variable wavelength UV detector set at 250 nm. Preparative HPLC is performed using a Dynamax-60A (8 μm, 25 x 2.14 cm) silica gel column (Rainin, Woburn, CA). GC- and HPLC-detected components are reported as percent area and are uncorrected for relative response. Thin layer chromatographic (TLC) analyses are performed on EM Science Silica Gel 60F-254 (0.25 mm) precoated analytical plates and visualized by applying a solution of 5% phosphomolybdic acid in methanol or by using a hand-held shortwave UV lamp (254 nm). Preparative chromatographic purifications are performed using Davison 60-200 mesh/150 angstrom pore size silica gel (Fisher Scientific) or Amicon 200-425 mesh/60 angstrom pore size flash gel (Amicon Corp, Danvers, MA). Analytical samples are purified by several recrystallizations or by careful chromatography on silica followed by bulb-to-bulb distillation. Combustion analyses are performed by Desert Analytics (Tucson, AZ). High resolution mass spectral (HRMS) determinations are performed by the Midwest Center for Mass Spectrometry (Lincoln, NE) on a Kratos MS-50 mass spectrometer.

Preparation of ethyl 2-methyl-2,7,9-decatrienoate (9). To a stirred, cooled (0°) solution of triethyl 2-phosphonopropionate (3.20 mL, 14.8 mmol) in THF (150 mL) was added n-butyllithium (6.50 mL, 16.3 mmol) followed by a solution of (5E) 5,7-octadienal[25] (1.80 g, 14.8 mmol) in THF (5 mL). After 30 min, the ice bath was removed and the reaction stirred (25°, 1.5 h). The resultant reaction mixture was quenched (1-2 mL satd aq NH_4Cl), concentrated, and the resulting oil diluted with ether (150 mL), then washed with brine (2 x 100 mL), dried ($MgSO_4$), filtered, and concentrated. The residue was chromatographed on silica (60-200 mesh, 95/5 hexanes/EtOAc) to yield 2.40 g (76%) of a mixture of (2E,7E)- and (2Z,7E)-**9**: TLC analysis (90/10 hexanes/EtOAc) R_f 0.49 and 0.42; GC analysis (DB-5, 100-250° @ 5°/min) 6.9 (22.5%, Z-diene) and 8.4 min (77.5%, E-diene); ^1H NMR (300 MHz, $CDCl_3$) δ 6.75 (t, 0.75 H, J = 7.5 Hz, CH=C(R)CH_3, E-isomer), 6.39-6.22 (m, 1 H, CH=CH_2), 6.14-6.02 (m, 1 H, CH=CHCH=CH_2), 5.92 (t, 0.25 H, CH=C(R)CH_3, Z-isomer), 5.71-5.62 (m, 1 H, CH=CHCH=CH_2), 5.10 (d, 1 H, J = 16.9 Hz, CH=C(H)H_{trans}), 4.97 (d, 1 H, J = 9.5 Hz, CH=C(H)H_{cis}), 4.18 (m, 2 H, CH_2CH_3), 2.21-2.08 (m, 4 H), 1.89 (s, 1 H, CH=C(R)CH_3, Z-isomer), 1.82 (s, 2 H, CH=C(R)CH_3, E-isomer), 1.60-1.49 (m, 2 H) and 1.30 ppm (t, 3 H, J = 7.2 Hz, CH_2CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 168.0, 142.2, 141.6, 141.5, 137.1, 136.9, 134.6, 134.2, 131.9, 131.7, 131.4, 131.1, 129.7, 127.9, 117.1, 114.9, 114.7, 60.4, 60.0, 32.2, 32.1, 29.1, 28.9, 28.4, 28.1, 28.0, 27.3, 20.7, 14.3 and 12.4 ppm; IR (CCl_4) 2990(m), 2915(m), 2860(m), 1710(s), 1650(m), 1370(m), 1250(m), 1175(m), 1012(m), 1090(m), 1000(m), 950(m) and 900(m) cm^{-1}; Combustion analysis ($C_{13}H_{20}O_2$: C-74.96%; H-9.68%) found C-75.38%, H-9.87%.

Iron-catalyzed carbocyclization of triene ester 9. To a cooled (0-5°), stirred solution of ferric acetylacetonate (125 mg, 0.35 mmol), 2,2'-bipyridine (55 mg, 0.35 mmol) and furan (0.5 mL) in dry oxygen-free benzene (10 mL) was added triethylaluminum (0.57 mL, 1.1 mmol) dropwise. The resulting dark blue solution was removed from the ice bath, stirred (1-2 min), then a solution of triene **9** (300 mg, 1.39 mmol) in benzene (2 mL) was added dropwise. The resulting solution was stirred (4-5 h), then filtered through a plug of silica (hexanes/EtOAc), concentrated, and the residue chromatographed on silica (99/1 hexanes/EtOAc) to yield 100 mg (33%) of **11** and 30 mg (10%) of **12**. Characterization of **11**: TLC analysis (90/10 hexanes/EtOAc) R_f = 0.38; GC analysis (DB-5, 100-250° @ 5°/min) 6.0 min; ^1H NMR (300 MHz, $CDCl_3$) δ 6.09 (s, 1 H, R(R')C=CH_2), 5.49 (s, 1 H, R(R')C=CH_2), 5.42 (m, 1 H, CH=C(H)CH_3), 5.21 (dd, 1 H, J = 10.5, 10.5 Hz, CH=C(H)CH_3), 4.20 (q, 2 H, J = 7.2 Hz, CH_2CH_3), 2.82 (m, 1 H, CHCH=C(H)CH_3), 2.60 (m, 1 H, CHC(R)=CH_2), 1.92-2.09 (m, 1 H, CH_2CHC(R)=CH_2), 1.84-1.91 (m, 1 H, CH_2CH(R)CH=C(H)CH_3), 1.66-1.76 (m, 2 H), 1.58 (dd, 3 H, J = 1.5, 6.6 Hz, CH=C(H)CH_3), 1.52 (m, 1 H, CH_2CHC(R)=CH_2), 1.35 (m, 1 H, CH_2CH(R)CH=C(H)CH_3) and 1.30 ppm (t, 3 H, J = 7.2 Hz, CH_2CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 167.3 (C=O), 143.0, 134.0, 123.7, 122.8, 60.4, 48.8, 42.9, 33.1, 32.5, 23.6, 14.3 and 13.2 ppm; IR (CCl_4) 2960(s), 2875(m), 1718(s), 1445(m), 1368(m), 1320(m), 1301(m), 1265(m), 1230(m), 1165(s), 1135(s), 1025(m) and 940(m) cm^{-1}.

Compound **11** was converted to its 1-naphthyl carbamate via the sequence: a) DIBAL-H, 0°, THF b) CH_2Cl_2, pyridine, 1-naphthyl isocyanate, reflux, 10 h. Combustion analysis of the carbamate derivative ($C_{22}H_{25}NO_2$: C-78.77%; H-7.51%) found C-78.98%, H-7.43%.

Spectroscopic characterization of **12**: ^1H NMR (300 MHz, $CDCl_3$) δ 5.35 (m, 1 H, CH=$CHCH_3$), 5.22 (dd, 1 H, J = 11.0, 11.0 Hz, CH=$CHCH_3$), 4.08 (q, 2 H, J = 7.0 Hz, OCH_2CH_3), 2.57 (m, 1 H), 2.41 (m, 1 H), 1.72-1.80 (m), 1.60 (d, 3 H, J = 9.0 Hz, CH=$CHCH_3$), 1.35-1.51 (m), 1.22 (t, 3 H, J = 7.0 Hz, OCH_2CH_3), 1.11 (d, 3 H, J = 8.0 Hz, $CH(CH_3)CO_2Et$) and 0.82-0.95 (m) ppm.

Preparation of α-benzyl-δ-valerolactone (32821-74-2). To a cooled (-78°) stirred solution of HMPA (19.1 mL, 11.0 mmol) and diisopropylamine (7.7 mL, 55 mmol) in THF (300 mL) was added n-butyllithium (23.0 mL, 58.0 mmol). After 5 min, a solution of δ-valerolactone (4.60 mL, 50.0 mmol) in THF (10 mL) was added. After an additional, 10 min benzyl bromide (5.90 mL, 50.0 mmol) was added. The reaction mixture slowly warmed to ambient temperature over 5 h, then quenched by the addition of satd aq NH_4Cl (1-2 mL) and concentrated. The residue was diluted with ether (200 mL) and washed with brine (3 x 100 mL). The organic layer was further diluted with hexanes (100 mL), again washed with brine (3 x 100 mL), then dried ($MgSO_4$), filtered, and concentrated. The residue was chromatographed on silica (60-200 mesh, 90/10 hexanes/EtOAc) to yield 5.60 g (59%) of

α-benzyl-δ-valerolactone as a clear liquid that crystallized in the freezer: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.35-7.15 (m, 5 H, ArH), 4.37-4.20 (m, 2 H, CO_2CH_2), 3.37 (dd, 1 H, J = 8.9, 13.6 Hz, CHCH(H)Ph), 2.70 (dd, 1 H, CHCH(H)Ph) overlapping with 2.8-2.6 (m, 1 H, CH_2CHCH_2Ph), 1.95-1.7 (m, 3 H) and 1.6-1.4 ppm (m, 1 H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 174.0, 138.7, 129.0, 128.3, 126.3, 68.4, 41.3, 37.0, 23.9 and 21.7 ppm; IR (CCL_4) 1741 cm^{-1} (s, C=O).

Preparation of (5E) 1-(*tert*-butyldimethylsilyloxy)-4-(phenylmethyl)pentanal. To a cooled (-78°) stirred solution of α-benzyl-δ-valerolactone (11.10 g, 58.3 mmol) in dry THF (300 mL) was added DIBAL-H (38.9 mL, 58.3 mmol) via syringe pump (0.81 mL/min). After the addition was complete, the reaction mixture was stirred (1 h, -78°), then quenched by the careful addition of excess $Na_2SO_4(H_2O)_{10}$ (ca 10 g), celite (ca 7 g) and ether (ca 150 mL). The resulting slurry was stirred (10 h), dried (anhyd Na_2SO_4, ca. 2 g), filtered through celite, and concentrated to yield 11.20 g (99%) of lactol, a mixture of epimers that was used without further purification: ^{1}H NMR (200 MHz, $CDCl_3$) δ
7.19 (m, 5 H, ArH), 4.96 (dd, 0.5 H, J = 2.5, 2.5 Hz, C(H)CH_{eq}(OH)OR), 4.51 (br d, 0.5 H, J = 6.3 Hz, C(H)CH_{ax}(OH)OR), 4.49 (br s, 0.5 H, OH), 3.97 (d, 0.5 H, J = 11.5 Hz) overlapping with 3.95 (br s, 0.5 H, OH), 3.63-3.2 (overlapping m, 1.5 H), 3.07 (dd, 0.5 H, J = 4.0, 13.5 Hz, $CHCH_2Ph$), 2.71 (dd, 0.5 H, J = 7.2, 13.5 Hz, $CHCH_2Ph$), 2.57-2.3 (overlapping m, 1 H), 2.1-1.85 (br m, 0.5 H), 1.8-1.4 (m, 4 H) and 1.3-1.1 ppm (m, 0.5 H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 139.5, 139.1, 128.6, 128.4, 127.5, 125.2, 125.2, 98.2, 92.7, 64.5, 59.1, 42.6, 41.1, 37.3, 36.6, 25.8, 24.6, 23.9 and 22.7 ppm.

To a stirred, heated (50°) solution of crude lactol (8.04 g, 41.8 mmol) and imidazole (4.27 g, 62.7 mmol) in DMF (250 mL) was added a solution of *tert*-butyldimethylsilyl chloride (TBDMSCl, 7.25 g, 48.1 mmol) in DMF (30 mL) via syringe pump (0.32 mL/min). The reaction was stirred (40 min), then cooled, and taken up in ether (300 mL). The combined organics were washed with satd aq $NaHCO_3$ (100 mL), brine (2 x 100 mL), then dried ($MgSO_4$), filtered, concentrated, and chromatographed on silica (60-200 mesh, 95:5 hexanes:EtOAc) to yield 7.78 g (70%) of 1-(*tert*-butyldimethylsilyloxy)-4-benzylpentanal as a colorless oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.65 (d, 1H, J = 2.4 Hz, CHO), 7.10-7.35 (m, 5H, ArH), 3.56 (t, 2H, J = 6.0 Hz, CH_2OSi), 2.96 (dd, 1H, J = 6.5, 13.1 Hz, C(H)HAr), 2.70 (dd, 1H, C(H)HAr) overlapping with 2.55-2.65 (m, 1H, CHCHO), 1.45-1.75 (m, 4H, CH_2CH_2), 0.86 (s, 9H, $C(CH_3)_3$) and 0.02 ppm (s, 6H, $Si(CH_3)_2$); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 213.4 (C=O), 128.9 (Ar), 128.8 (Ar), 128.4 (Ar), 126.3 (Ar), 62.6 (CH_2O), 53.1 (CHCHO), 35.1 (CH_2), 30.0 (CH_2), 25.8 ($C(CH_3)_3$), 24.9 (CH_2Ar), 18.2 ($C(CH_3)_3$), and -5.4 ($Si(CH_3)_2$); FT-IR (neat, NaCl) 2952 (s), 2926 (s), 2855 (s), 1727 (C=O, s), 1255 (s) and 1102 cm^{-1} (s). 2.34 g (22%) of 2-(*tert*-butyldimethylsilyloxy)tetrahydro-3-(phenylmethyl)-2H-pyran was also recovered.

Preparation of (5E) 1-(*tert*-butyldimethylsilyloxy)-4-(phenylmethyl)-5,7-octadiene. To a stirred, cooled (-78°) solution of allyldiphenylphosphine oxide[14] (7.93 g, 31.7 mmol) and HMPA (11.0 mL, 11.3 g, 63 mmol) in THF (500 mL) was added dropwise a solution of n-butyllithium (12.50 mL, 31.2 mmol). The resulting red solution was stirred (5 min), then a solution of 1-(*tert*-butyldimethylsilyloxy)-4-(phenylmethyl)-pentanal (7.68 g, 28.8 mmol) in THF (20 mL) was added dropwise over 35 minutes. The resulting solution was slowly warmed to room temperature (12 h) with formation of a orange precipitate. After quenching with water (ca 5 mL), the reaction was concentrated and the residue diluted with 400 mL of hexane:EtOAc (70:30). The combined organics were washed with water (100 mL), brine (2 x 100 mL), then dried ($MgSO_4$), filtered, concentrated, and chromatographed on silica (260-400 mesh, 95:5 hexanes:EtOAc) to yield 5.71 g (60%) of (5E) 1-(*tert*-butyldimethylsilyloxy)-4-(phenylmethyl)-5,7-octadiene as a colorless oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.23 (m, 5 H, ArH), 6.27 (ddd, 1 H, J = 10.1, 10.3, 17.0 Hz, CH_2=CHCH=CHR), 5.91 (dd, 1 H, J = 10.3, 15.4 Hz, CH_2=CHCH=CHR), 5.50 (dd, 1 H, J = 8.6, 15.4 Hz, CH_2=CHCH=CHR), 5.03 (ddd, 1 H, J = 0.4, 1.3, 17.0 Hz, CH_{cis}(H)=CHCH=CHR), 4.92 (ddd, 1 H, J = 0.5, 1.3, 10.3 Hz, CH_{trans}(H)=CHCH=CHR), 3.54 (t, 2 H, J = 6.3 Hz, CH_2CH_2OSi), 2.63 (d, 2 H, J = 7.0 Hz, $CHCH_2Ph$), 2.85-2.35 (m, 1 H, $CHCH_2Ph$), 1.6-1.1 (m, 4 H, CH_2CH_2), 0.85 (s, 9 H, $Si(CH_3)_2C(CH_3)_3$) and 0.01 ppm (s, 6 H, $Si(CH_3)_3C(CH_3)_3$); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 140.4, 138.7, 137.2, 131.1, 129.3, 128.1, 125.8, 115.0, 63.2, 44.2, 42.1, 30.5, 30.4, 26.0, 18.3, and -5.3 ppm; IR (neat, ATR) 3026(m), 2949(s), 2921(s), 2895(s), 2883(s), 2854(s), 1603(m), 1494(m), 1471(s), 1462(s), 1453(s), 1387(m), 1360(m), 1254(s), 1097(s), 1056(m), 1031(m), 1003(s), 980(m), 949(s) and 938(s) cm^{-1}; Combustion analysis ($C_{21}H_{34}O$: C-76.30%; H-10.37%) found C-76.46%, H-10.58%.

Preparation of (5E) 4-(phenylmethyl)-5,7-octadien-1-ol. To a stirred solution of 1-(*tert*-butyldimethylsilyloxy)-4-(phenylmethyl)-5,7-octadiene (8.47 g, 25.6 mmol) in MeOH (75 mL) was added 0.75 g of Dowex 50W-8X resin (50-100 mesh). The reaction mixture was stirred (12 h), then filtered, concentrated, and the resulting oil chromatographed on silica (60-200 mesh, 70:30 hexanes:EtOAc) to yield 5.49 g (99%) of (5E) 4-(phenylmethyl)-5,7-octadien-1-ol as a clear oil: GC analysis (DB-5, 100-250 @ 5°/min) 13.1 (5%, Z-diene) and 13.5 min (95%, E-diene); IR (neat) 3385 (br s, OH), 3085 (m), 3025 (m), 2917 (m), 2848 (m), 1649 (m), 1603 (m), 1495 (s), 1452 (s), 1088 (s), 1002 (s) and 899 (s) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.31-7.11 (m, 5 H, ArH), 6.29 (ddd, 1 H, J = 10.2, 10.2, 16.8 Hz, CH=CH_2), 5.93 (dd, 1 H, J = 10.3, 15.2 Hz, CH=CHCH=CH_2), 5.50 (dd, 1H, J = 8.7, 15.2 Hz, CH=CHCH=CH_2), 5.04 (d, 1H, J = 16.9 Hz, CH=CH_{trans}(H)), 4.95 (d, 1H, J = 10.0 Hz, CH=CH_{cis}(H)), 3.56 (t, 2H, J = 6.3 Hz, CH_2OH), 2.65 (d, 2 H, J = 6.9 Hz, CH_2Ph), 2.32 (br s, 1H) and 1.65-1.24 ppm (m, 5H); ^{13}C NMR (50.3 MHz, $CDCl_3$), δ 140.2, 138.3, 137.0, 131.3, 129.2, 128.1, 125.8, 115.2, 62.9, 44.2, 42.0, 30.5 and 30.3 ppm; Combustion analysis ($C_{15}H_{20}O$: C-83.28%; H-9.36%) found C-82.93%, H-9.36%.

Preparation of ethyl (7E) 2-methyl-6-(phenylmethyl)-7,9-decatrienoate (14): To a cooled (-55°, internally measured) solution of oxalyl chloride (1.0 mL, 11 mmol) in CH_2Cl_2 (150 mL) was added DMSO (1.6 mL, 23 mmol) dropwise. After 2 min, (5E) 4-(phenylmethyl)-5,7-octadien-1-ol (2.30 g, 10.4 mmol) in 10 mL CH_2Cl_2 was added. The clear reaction mixture

stirred for 15 min (-55°) at which point triethylamine (7.2 mL, 52 mmol) was added. After 5 min (-55°), the cold bath was removed. Upon warming to ambient temperature, the reaction mixture was washed with water (150 mL) and the aqueous layer was back extracted with CH_2Cl_2 (100 mL). The combined organic extracts were washed with brine (3 x 150 mL), then dried ($MgSO_4$), filtered, and concentrated. The residue (oil and solid) was filtered through a plug of silica (ca 10 g, 70/30 hexanes/EtOAc) and concentrated to yield 2.10 g (96%) of aldehyde as a pale yellow liquid, which was used without further purification: TLC analysis (70/30 hexanes/EtOAc) R_f 0.56 (trace) and 0.44 (major).

To a cooled (0°) solution of triethyl 2-phosphonopropionate (2.1 mL, 9.9 mmol) in THF (100 mL) was added n-butyllithium (4.4 mL, 11 mmol). To the resulting solution was added a solution of crude aldehyde (2.10 g, 9.9 mmol) in THF (5 mL). After stirring 30 min (0°), the cold bath was removed, the reaction stirred an additional 1.5 h (25°), then quenched with satd aq NH_4Cl (1-2 mL) and concentrated. The resulting oil was diluted with ether (150 mL), washed with brine (3 x 80 mL), then dried ($MgSO_4$), filtered, concentrated, and the residue chromatographed on silica (260-400 mesh, 95/5 hexanes/EtOAc) to yield 2.00 g (67%) of triene ester **14** as a 3:1 mixture of (2E,7E)- and (2Z,7E)-isomers: TLC analysis (70/30 hexanes/EtOAc) R_f 0.66 (major 2E-isomer) and 0.58 (minor 2Z-isomer); HPLC analysis (SiO_2, 99/1 hexanes/EtOAc @ 1.5 mL/min) 6.0 (25%, 2Z-isomer) and 9.0 min (75%, 2E-isomer); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.30-7.18 (m, 5 H, **ArH**), 6.68 (dt, 0.85 H, J = 1.3, 7.9 Hz, CH=CRR', 2E-isomer), 6.40-6.19 (m, 1 H, $CH{=}CH_2$), 6.04-5.79 (m, 1.15 H, $CH{=}CHCH{=}CH_2$, CH=CRR', 2Z-isomer), 5.49 (dd, 1 H, J = 8.8, 15.3 Hz, $CHCH_2Ph$), 5.03 (dd, 1 H, J = 1.7, 16.9 Hz, $CH{=}CH_{trans}(H)$), 4.96 (dd, 1 H, J = 1.7, 10.1 Hz, $CH{=}CH_{cis}(H)$), 4.17 (q, 2 H, J = 7.1 Hz, CH_2CH_3), 2.65 (d, 1 H, J = 6.6 Hz, CH_2Ph), 2.42-2.05 (m, 3 H), 1.86 (s, 0.45 H, $CH{=}CCH_3$, 2Z-isomer), 1.78 (s, 2.6 H, $CH{=}CCH_3$, 2E-isomer), 1.65-1.31 (m, 2 H) and 1.28 ppm (t, 3 H, J = 7.1 Hz, CH_2CH_3); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 168.1 (C=O), 142.2 (2Z), 141.8, 139.9, 138.1 (2Z), 137.7, 137.0 (2Z), 136.9, 131.7, 131.3 (2Z), 129.2, 128.1, 128.0, 127.8 (2Z), 125.9, 125.8 (2Z), 115.4 ($CH{=}CH_2$), 115.1 (2Z, $CH{=}CH_2$), 60.3 (CH_2CH_3), 60.0 (2Z, CH_2CH_3), 44.2 ($CHCH_2Ph$), 44.1 (2Z, $CHCH_2Ph$), 41.9 (2Z, CH_2Ph), 41.8 (CH_2Ph), 33.9 (2Z), 32.9, 27.4 (2Z), 26.5, 20.6, 14.2 and 12.3 ppm; IR (neat, ATR) 2977(m), 2922(m), 1705(s), 1649(m), 1603(m), 1495(m), 1453(m), 1388(m), 1366(m), 1307(m), 1264(s), 1200(m), 1173(m), 1123(m), 1095(m), 1081(m), 1030(m), 1003(s), 899(m), 744(s) and 698(s) cm^{-1}; HRMS (EI, 100°, $C_{20}H_{26}O_2$ = 298.1934) found 298.1931 *m/z*.

Iron-catalyzed carbocyclization of triene ester 14. To a cooled (0-5°), stirred solution of ferric acetylacetonate (48.9 mg, 0.14 mmol), 2,2'-bipyridine (21.6 mg, 0.14 mmol) and furan (0.5 mL) in dry oxygen-free benzene (10 mL) was added triethylaluminum (0.23 mL, 0.44 mmol) dropwise. The resulting dark blue solution was removed from the ice bath, stirred (1-2 min), then a solution of triene **14** (290 mg, 0.97 mmol) in benzene (2 mL) was added dropwise. The resulting solution was stirred (7 h), then filtered through a plug of silica (hexanes/EtOAc), concentrated, and the residue chromatographed on silica (260-400 mesh, 99/1 hexanes/EtOAc) to yield **15** as a clear liquid: HPLC analysis (SiO_2, 99/1 hexanes/EtOAc @ 1.5 mL/min) 4.3 min; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.17-7.29 (m, 5 H, **ArH**), 6.08 (s, 1 H, $R(R')C{=}CH_2$), 5.52-5.61 (m, 1 H, $CH{=}CHCH_3$), 5.48 (s, 1 H, $R(R')C{=}CH_2$), 5.19 (t, 1 H, J = 9 Hz, $CH{=}CHCH_3$), 4.18 (q, 2 H, J = 7.2 Hz, CH_2CH_3), 2.91 (dd, 1 H, J = 3.4, 13.1 Hz, $CHCH{=}CHCH_3$), 2.52-2.73 (m, 2 H), 2.31 (dd, 1 H, J = 10.3, 13.2 Hz), 1.65-2.01 (m, 3 H), 1.61 (dd, 3 H, J = 1.7, 6.7 Hz, $CH{=}CHCH_3$), 1.40-1.55 (m, 2 H) and 1.2 ppm (t, 3 H, J = 7.1 Hz, CH_2CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 167.3 (C=O), 143.2, 141.7, 133.0, 128.9, 128.8, 128.1, 125.6, 125.4, 125.0, 123.0 ($R(R')C{=}CH_2$), 60.4 (CH_2CH_3), 49.0, 48.7, 48.6, 40.3 (CH_2Ph), 30.6, 30.1, 14.2, and 13.4 ppm; FT-IR (ATR) 2934(m), 2913(m), 1713(s), 1495(m), 1452(m), 1367(m), 1322(m), 1296(m), 1267(m), 1238(m), 1184(m), 1148(s), 1112(m), 1029(m), 938(m), 752(m), 721(s) and 699(s) cm^{-1}.

Preparation of naphthalimide 16. To a cooled (0°) solution of unsaturated ester **15** (180 mg, 0.60 mmol) in THF (30 mL) was added DIBAL-H (0.88 mL, 1.3 mmol). After slowly warming to ambient temperature (2 h), the reaction mixture was quenched by the addition of methanol (ca. 1 mL), then concentrated, diluted with ether and washed with satd aq potassium sodium tartrate (50 mL) and brine (2 x 60 mL). The organic layer was dried ($MgSO_4$), filtered, concentrated, and the residue chromatographed on silica (260-400 mesh, 90/10 hexanes/EtOAc) to yield 120 g (80%) of the allylic alcohol as a clear oil: GC analysis (DB-5, 200-250° @ 5°/min) 18.9 (87%) and 19.4 min (13%); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.32-7.11 (m, 5 H, **ArH**), 5.63-5.52 (m, 1 H, $CH{=}CHCH_3$), 5.22 (dq, 1 H, J = 1.7, 10.9 Hz, $CH{=}CHCH_3$), 5.02 (d, 1 H, J = 1.4 Hz, $C{=}CH_2$), 4.91 (d, 1 H, J = 1.4 Hz, $C{=}CH_2$), 4.06 (s, 2 H, CH_2OH), 2.89 (dd, 1 H, J = 3.7, 13.2 Hz, CH_2Ph), 2.55-2.22 (m, 3 H), 1.92-1.66 (m, 4 H), 1.63 (dd, 3 H, J = 1.7, 6.8 Hz, CH_3) and 1.59-1.34 ppm (m, 2 H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 151.5 ($C{=}CH_2$), 141.7 (ipso-Ar), 133.6, 128.8, 128.7, 128.0, 125.6, 125.2, 108.2 ($C{=}CH_2$), 65.4 (CH_2OH), 49.7, 49.6, 48.8, 40.3 (CH_2Ph), 30.5, 30.1 and 13.5 ppm (CH_3); IR (neat, ATR) 3325(br, OH), 3025(m), 3004(m), 2912(m), 2866(m), 2504(m), 1495(m), 1452(m), 1406(m), 1374(m), 1076(m), 1030(m), 895(m), 751(m), 718(s) and 698(s) cm^{-1}.

To a cooled (0°), stirred suspension of the allylic alcohol (120 mg, 0.47 mmol), triphenylphosphine (250 mg, 0.94 mmol), and 1,8-naphthalimide (190 mg, 0.94 mmol) in THF (ca. 3 mL) was added diethylazodicarboxylate (0.15 mL, 0.94 mmol). The resulting suspension was warmed slowly to ambient temperature, stirred (2 h), then diluted with EtOAc, filtered through a plug of silica (hexanes/EtOAc), concentrated, and the residue chromatographed on silica (260-400 mesh, 70/30 hexanes/EtOAc) to yield 160 mg (79%) of naphthalimide **16** as a white solid: mp 103-106°; HPLC analysis (silica, 90/10 hexanes/EtOAc) 7.9 min (100%); ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.60 (dd, 2 H, J = 1.0, 7.2 Hz, ArH), 8.21 (dd, 2 H, J = 1.0, 8.2 Hz, ArH), 7.75 (t, 2 H, J = 7.4 Hz, ArH), 7.26-7.14 (m, 5 H, C_6H_5), 5.61-5.48 (m, 1 H, $CH{=}CHCH_3$), 5.27 (br dd, 1 H, $CH{=}CHCH_3$), 4.85 (br s, 1 H, $C{=}CH_2$), 4.76 (d, 2 H, J = 1.7 Hz, NCH_2), 4.61 (br s, 1 H, $C{=}CH_2$), 2.92 (dd, 1 H, J = 3.3, 13.1 Hz, CH_2Ph), 2.62-2.25 (m, 3 H), 2.03-1.78 (m, 4 H), 1.73 (dd, 3 H, J = 1.5, 6.7 Hz, CH_3), 1.51-1.32 ppm (m, 1 H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 145.9 (C=O), 141.9 (C=O), 133.9, 133.5, 131.6, 131.3, 128.8, 128.7, 128.2, 128.1, 126.9, 125.5, 125.4, 125.3, 122.6, 106.8 ($C{=}CH_2$), 51.1, 49.3, 49.1, 43.4, 40.3 (CH_2Ph), 30.4, 30.1 and 13.5 ppm (CH_3); IR (neat, ATR) 2944(m), 2921(m), 1703(s), 1659(s), 1628(m), 1586(m), 1452(m), 1437(m), 1407(m), 1380(m), 1341(m), 1235(s), 1180(m), 1150(m), 1028(m), 965(m), 846(m), 779(s), 754(m) and 700(m) cm^{-1}.

A crystal suitable for x-ray analysis was obtained by diffusion controlled recrystallization from benzene/pentane. Compound **16** crystal data: $C_{30}H_{29}NO_2$; M = 435.56; monoclinic; a = 5.195 (3), b = 19.833 (3), c = 22.934 (2) angstrom, β = 92.84 (2)°; V = 2360 (1) A^3; space group $P2_1/c$ (#14); Z = 4; D_c = 1.23 g/cm^3; MoKα radiation, λ = 0.7069 angstrom; μ(MoKα) = 0.71 cm^{-1}; F(000) = 928.[2]

Preparation of tetrahydro-3-propyl-2H-pyran-2-one[26] (22791-77-1). To a cooled (-78°) solution of HMPA (86.9 mL, 0.50 mol) and diisopropylamine (19.3 mL, 0.14 mol) in THF (500 mL) was added n-butyllithium (54.9 mL, 0.14 mol). After 10 min a solution of δ-valerolactone (11.6 mL, 0.13 mol) in THF (25 mL) was added. After an additional 10 min, allyl bromide (11.9 mL, 0.14 mol) was added, and the reaction mixture was slowly warmed to room temperature. After 5 h (25°), the reaction was quenched by the addition of satd aq NH_4Cl (1-2 mL), then concentrated. The residue was diluted with ether (450 mL), washed with water (2 x 200 mL) and brine (2 x 200 mL), then dried ($MgSO_4$), filtered, and concentrated. The resulting orange liquid was bulb-to-bulb distilled (0.1 mm, 130°), then chromatographed on silica (260-400 mesh, 85/15 hexanes/EtOAc) to yield 7.30 g (41%) of the tetrahydro-3-(2-propenyl)-2H-pyran-2-one (50994-84-8) as a colorless liquid: TLC analysis (90/10 hexanes/EtOAc) R_f 0.34; GC analysis (DB-5, 50-250° @ 10°/min) 7.4 min (100%); ^1H NMR (200 MHz, $CDCl_3$) δ 5.90-5.70 (m, 1 H, $CH{=}CH_2$), 5.10 (dd, 2 H, J = 10.1, 17.0 Hz, $CH{=}CH_2$), 4.30 (m, 2 H, CH_2O), 2.68-2.50 (m, 2 H), 2.38-2.25 (m, 1 H), 2.14-2.01 (m, 1 H), 1.98-1.85 (m, 1 H) and 1.68-1.51 ppm (m, 1 H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 173.6 (C=O), 134.9 ($C{=}CH_2$), 117.1 ($C{=}CH_2$), 68.2 (CH_2O), 39.0 (CHC=O), 35.2, 23.9 and 21.7 ppm; IR (neat, ATR) 1723(s), 1641(m), 1440(m), 1399(m), 1388(m), 1255(m), 1219(m), 1151(s), 1083(s), 1000(m), 984(m), 971(m), 962(m), 913(s), 662(m), 656(m) and 653(m) cm^{-1}; HRMS (EI, 25°, $C_8H_{12}O_2$ = 140.0838) found 140.0837 *m/z*.

To a stirred (25°) solution of tetrahydro-3-(2-propenyl)-2H-pyran-2-one (6.60 g, 47.1 mmol) in methanol (50 mL) was added 5% palladium-on-carbon (0.13 g). The resultant slurry was stirred under an atmosphere of hydrogen (1 atm, 7 h). The resulting reaction mixture was filtered through a plug of celite then concentrated to yield 6.70 g (99%) of tetrahydro-3-propyl-2H-pyran-2-one (RN 22791-77-1), that was used without further purification: GC analysis (DB-5, 100-250° @ 10°/min) 3.5 min (100%).

Preparation of 1-(*tert*-butyldimethylsiloxy)-4-formyl-heptane. To a cooled (-78°) solution of tetrahydro-3-propyl-2H-pyran-2-one (7.00 g, 49.2 mmol) in dry THF (225 mL) was added DIBAL-H (32.8 mL, 49.2 mmol) via syringe pump (0.81 mL/min). After the addition was complete, the reaction mixture was stirred (1 h, -78°), then quenched by the addition of $Na_2SO_4(H_2O)_{10}$ (ca 10 g), celite (ca. 7 g) and ether (ca. 150 mL). The resulting slurry was stirred (10 h, 25°), dried (anhyd Na_2SO_4, ca. 2 g), filtered through celite, and concentrated to yield 7.10 g (99%) of lactol, which was used without further purification.

To a heated (60°) solution of lactol (7.10 g, 49.2 mmol) and imidazole (5.00 g, 73.8 mmol) in DMF (150 mL) was added a solution of TBDMSCl (8.20 g, 54.1 mmol) in DMF (20 mL) via syringe pump (0.78 mL/min). After 45 min, the reaction mixture was cooled (25°), diluted with ether (400 mL), then washed with water (1 x 100 mL), satd aq $NaHCO_3$ (1 x 200 mL) and brine (1 x 200 mL). The organic layer was dried ($MgSO_4$), filtered, concentrated, and the residue chromatographed on silica (260-400 mesh, 95/5 hexanes/EtOAc) to yield 7.60 g (60%) of 1-(*tert*-butyldimethylsiloxy)-4-formyl-heptane, as a light yellow oil: TLC analysis (70/30 hexanes/EtOAc) R_f 0.62; GC analysis (DB-5, 100-250° @ 10°/min) 6.3 min (100%); ^1H NMR (200 MHz, $CDCl_3$) δ 9.52 (s, 1 H, RCHO), 3.57 (s, 2 H, CH_2O), 2.20 (br s, 1 H, CHRCHO), 1.61-1.22 (m, 8 H), 0.86 (br s, 12 H, CH_2CH_3 overlapping with $C(CH_3)_3$) and 0.0 ppm (s, 6 H, $Si(CH_3)_2$); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 213.2 (C=O), 62.6 (CH_2O), 51.3, 31.0, 30.0, 25.8, 25.1, 20.1, 18.2 and 13.9 ppm; IR (neat, ATR) 2955(m), 2927(m), 2856(m), 1727(s), 1707(m), 1471(m), 1463(m), 1254(s), 1095(s), 938(m), 834(s), 813(m) and 773(s) cm^{-1}.

Preparation of ethyl 2-methyl-4-propyl-7-(*tert*-butyldimethylsiloxy)-hept-2-enoate (25). To a cooled (0°) solution of triethyl 2-phosphonopropionate (6.30 mL, 29.4 mmol) in THF (200 mL) was added n-butyllithium (12.9 mL, 32.3 mmol). To the resulting solution was added a solution of 1-(*tert*-butyldimethylsiloxy)-4-formyl-heptane (7.60 g, 29.4 mmol) in THF (5 mL). After stirring (0°) for 30 minutes, the ice bath was removed. After an additional 45 min (25°), the reaction mixture was quenched with satd aq NH_4Cl (1-2 mL) and concentrated. The resulting oil was diluted with ether (250 mL), washed with water (1 x 150 mL) and brine (3 x 80 mL), then dried ($MgSO_4$), filtered, concentrated, and the residue chromatographed on silica (260-400 mesh, 95/5 hexanes/EtOAc) to yield 8.00 g (79%) of the ethyl heptenoate as a 70:30 mixture of E- and Z-isomers: TLC analysis (95/5 hexanes/EtOAc) R_f 0.47 (major E-isomer) and 0.42 (minor Z-isomer); GC analysis (DB-5, 100-250 @ 10°/min) 9.8 (70%, E-isomer) and 10.7 min (30%, Z-isomer); (Note: The spectral data reported below was obtained for a portion of the sample that was enriched to 90% E-isomer.) ^1H NMR (200 MHz, $CDCl_3$) δ 6.42 (d, 0.1 H, CHR=C, Z-isomer), 5.52 (dd, 0.9 H, J = 1.4, 10.5 Hz, CHR=C, E-isomer), 4.15 (q, 2 H, J = 7.2 Hz, OCH_2CH_3), 3.52 (t, 2 H, J = 6.4 Hz, CH_2OSi), 3.02 (br s, 1 H, $SiOCH_2(CH_2)_2CHR$), 1.86 (d, 0.9 H, J = 1.5 Hz, C=C(R)CH_3, E-isomer), 1.84 (d, 0.1 H, J = 1.5 Hz, C=C(R)CH_3, Z-isomer), 1.47-1.12 (m, 10 H), 0.85 (br s, 12 H, $CH_2CH_2CH_3$ overlapping with $SiC(CH_3)_3$) and 0.0 ppm (s, 6 H, $Si(CH_3)_2$); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 168.4 (C=O), 147.0 (R(H)C=C), 127.2 (R(H)C=C), 63.3, 63.1 (Z), 59.9, 38.4 (Z), 38.1, 37.9, 37.5 (Z), 31.6, 31.4 (Z), 30.6, 26.0, 20.9, 20.5 (Z), 20.4, 18.3 (Z), 14.3 and 14.2 ppm; FT-IR (ATR) 2954(m), 2928(m), 2856(m), 1716(s), 1251(m), 1210(m), 1188(m), 1154(m), 1095(s), 834(s), 813(m) and 773(s) cm^{-1}; Combustion analysis ($C_{19}H_{38}O_3Si$: C-66.61%; H-11.18%) found C-66.89%, H-11.41%.

Preparation of ethyl 2-methyl-4-propyl-7-hydroxy-hept-2-enoate (26). To a stirred (25°) solution of **25** (4.00 g, 11.6 mmol) in methanol (30 mL) was added a catalytic amount of *p*-TsOH (5-10 mg). After 2 h, the reaction mixture was concentrated, the residue diluted with ether (200 mL) and washed with satd aq $NaHCO_3$ (1 x 100 mL) and brine (2 x 100 mL), then dried ($MgSO_4$), filtered and concentrated to yield 2.60 g (99%) of alcohol, which was used without further purification: TLC analysis (70:30 hexanes:EtOAc) R_f 0.3; GC analysis (DB-5, 100-250 @ 10°/min) 6.7 (70%, E-isomer) and 7.7 min (30%, Z-isomer).

To a cooled (-55°, internally measured) solution of oxalyl chloride (1.10 mL, 12.8 mmol) in CH_2Cl_2 (160 mL) was added dimethyl sulfoxide (1.80 mL, 25.5 mmol) dropwise. After 2 min, the crude alcohol (2.60 g, 11.6 mmol) in CH_2Cl_2 (10 mL) was added. The clear reaction mixture was stirred for 15 min (-55°) at which point triethylamine (8.1 mL, 58 mmol) was added. The resulting milky white reaction mixture was stirred for 5 min (-55°) then the cold bath was removed. Upon warming to ambient temperature, the reaction mixture was washed with water (100 mL) and the aqueous layer back extracted with CH_2Cl_2 (50 mL). The combined organic extracts were washed with brine (2 x 150 mL), then dried ($MgSO_4$), filtered, and concentrated. The residue (oil and solid) was filtered through a plug of silica (ca 10 g, 70/30 hexanes/EtOAc) and concentrated to yield 2.50 g (96%) of aldehyde **26** as a pale yellow liquid, which was used without further purification: TLC analysis (90:10 hexanes:EtOAc) R_f 0.26 and 0.19; GC analysis (DB-5, 100-250 @ 10°/min) 5.9 (70%, E-isomer) and 6.8 min (30%, Z-isomer).

Preparation of ethyl 2-methyl-4-propyl-2,7,9-decatrienoate (17). To a cooled (0°), solution of allyltriphenylsilane (3.70 g, 12.2 mmol) in dry THF (50 mL) was added dropwise a solution of n-butyllithium (5.10 mL, 12.8 mmol). The resulting solution was stirred (1 h, 0°), then cooled (-78°) and titanium tetraisopropoxide (3.60 mL, 12.2 mmol) was added. The resulting solution was stirred (0.5 h, -78°), then a solution of aldehyde **26** (2.50 g, 11.1 mmol) in dry THF (5 mL) was added dropwise. The resulting yellow solution was stirred (1 h, -78°), then quenched by the addition of 10% aq HCl (1-2 mL) and warmed to ambient temperature. The heterogeneous reaction mixture was taken up in ether (200 mL) and washed with satd aq $NaHCO_3$ (1 x 100 mL) and brine (2 x 100 mL). The organic phase was dried ($MgSO_4$), filtered, concentrated, and the residue chromatographed on silica (260-400 mesh, 90/10 hexanes/EtOAc) to yield 5.20 g (90%) of a mixture of β-hydroxysilanes as a thick oil: TLC analysis (70/30 hexanes/EtOAc) R_f 0.19 and 0.26; HPLC analysis (SiO_2, 95/5 hexanes/EtOAc @ 1.5 mL/min) 9.3 (35%) and 9.6 min (65%); ^1H NMR (200 MHz, $CDCl_3$) δ 7.62-7.28 (m, 15 H, ArH), 5.97 (ddd, 1 H, J = 10.6, 10.6, 15.8 Hz, $CH{=}CH_2$), 5.48 (d, 1 H, J = 10.4 Hz, $CH{=}C(R)R'$), 5.05 (d, 1 H, J = 12.1 Hz, $CH{=}CH_{cis}(H)$), 4.98 (d, 1 H, J = 17.5 Hz, $CH{=}CH_{trans}(H)$), 4.10 (q, 2 H, J = 7.2 Hz, OCH_2CH_3), 3.92 (br s, 1 H), 2.98 (br s, 1 H), 2.64 (m, 1 H), 1.84 (s, 3 H, $CH{=}CCH_3$), 1.48-1.12 (m, 10 H) and 0.82 ppm (m, 2 H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 147.0, 136.4, 134.9, 134.7, 134.3, 134.2, 129.4, 127.7, 117.4, 117.3, 71.5, 71.2, 60.0, 59.9, 40.2, 40.0, 38.2, 38.1, 37.6, 34.5, 34.4, 31.8, 31.7, 20.8, 20.4, 14.3 and 14.1 ppm; IR (neat, ATR) 3517(br), 3068(m), 2976(m), 2952(m), 2926(m), 1700(m), 1427(s), 1210(m), 1179(m), 1106(m), 1043(m), 1028(m), 997(m), 901(m), 738(s), 698(s), 679(s), 587(s), 581(m) and 577(m) cm^{-1}; HRMS analysis (EI, 25°, $C_{34}H_{42}O_3Si$ = 526.2905) found 526.2892 *m/z*.

To a stirred solution (25°) of β-hydroxysilanes (5.00 g, 9.49 mmol) in THF (50 mL) was added concentrated sulfuric acid (8 drops). The resulting solution was heated to reflux (65°). After 10 h, the reaction mixture was cooled (25°), neutralized with $NaHCO_3$ (ca. 0.2 g) and concentrated. The resulting thick oil was diluted with ether (200 mL), washed with satd aq $NaHCO_3$ (1 x 100 mL) and brine (1 x 100 mL), then dried ($MgSO_4$), filtered, and concentrated. The residue was taken up in hexanes (ca. 20 mL) and cooled (0°, 12 h). The crystallized triphenylsilanol was then filtered off and the filtrate concentrated to yield crude triene ester **17** as a yellow liquid: GC analysis (DB-5, 100-250 @ 10°/min) 7.0 (20%, 2E,7Z-triene), 7.1 (51%, 2E,7E-triene), 8.0 (10%, 2Z,7Z-triene) and 8.1 min (19%, 2Z,7E-triene). The crude triene was chromatographed on silica (260-400 mesh, 98/2 hexanes/EtOAc) to yield 1.90 g (65% over two steps) of isomeric triene esters as a pale yellow liquid. Analytical data for a chromatography fraction consisting of 14% (2E,7Z)-triene, 30% (2E,7E)-triene, 18% (2Z,7Z)-triene and 38% (2Z,7E)-triene: TLC analysis (95/5 hexanes/EtOAc) R_f 0.67 and 0.58; ^1H NMR (200 MHz, $CDCl_3$) δ 6.69-4.89 (m, 6 H, vinyl H's), 4.18 (m, 2 H, OCH_2CH_3), 2.16-1.99 (m, 2 H), 1.91 (s, 1 H, $CH{=}CCH_3$), 1.83 (s, 2 H, $CH{=}CCH_3$), 1.57-1.20 (m, 10 H) and 0.87 ppm (t, 3 H, $(CH2)_2CH_3$); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 146.6, 146.5, 137.3, 137.1, 135.3, 135.3, 134.7, 132.7, 132.3, 132.2, 132.1, 131.3, 130.9, 129.5, 129.1, 127.7, 116.9, 116.6, 14.8, 114.5, 60.4, 60.0, 38.1, 38.0, 37.8, 37.7, 37.4, 35.5, 35.0, 34.6, 30.3, 25.6, 25.5, 20.9, 20.4, 20.3, 14.3, 14.2, 14.1 and 12.9 ppm; IR (neat, ATR) 2954(m), 2928(m), 1709(s), 1649(m), 1465(m), 1450(m), 1370(m), 1253(m), 1213(m), 1190(m), 1172(m), 1165(m), 1117(m), 1093(m), 1034(m), 1003(m), 899(m) and 751(m) cm^{-1}; HRMS analysis (EI, 75°, $C_{16}H_{26}O_2$ = 250.1934) found 250.1928 *m/z*.

Iron-catalyzed carbocyclization of triene ester 17. To a cooled (0-5°), stirred solution of ferric acetylacetonate (127 mg, 0.36 mmol), 2,2'-bipyridine (56.2 mg, 0.36 mmol) and furan (1.0 mL) in dry oxygen-free benzene (20 mL) was added triethylaluminum (0.58 mL, 1.10 mmol) dropwise. The resulting dark blue solution was removed from the ice bath, stirred (1-2 min), then a solution of triene **17** (600 mg, 2.40 mmol) in benzene (5 mL) was added dropwise. The resulting solution was stirred (7 h), then filtered through a plug of silica (hexanes/EtOAc) and concentrated. The residue was chromatographed on silica (260-400 mesh, 99/1 hexanes/EtOAc), followed by preparative HPLC (Rainin Dynamax, 60A SiO_2, 99/1 hexanes/EtOAc @ 5 mL/min) to yield **18** as a clear liquid: TLC analysis (95/5 hexanes/EtOAc) R_f = 0.67; HPLC analysis (SiO_2, 100% hexanes @ 1.5 mL/min) 5.1 min; GC analysis (DB-5, 150-151° @ 0.1°/min) 4.5 min; ^1H NMR (200 MHz, $CDCl_3$) δ 6.12 (d, 1 H, J = 1.5 Hz, $C{=}CH_2$), 5.55 (d, 1 H, J = 1.5 Hz, $C{=}CH_2$), 5.32 (m, 1 H, $CH{=}CHCH_3$), 5.21 (dd, 1 H, J = 10, 10 Hz, $CH{=}CHCH_3$), 4.20 (q, 2 H, J = 7.1 Hz), 2.95 (m, 1 H), 1.82-2.22 (m, 4 H), 1.51 (dd, 3 H, J = 1.5, 6.5 Hz, $CH{=}CHCH_3$), 1.12-1.38 (m, 9 H) and 0.85 ppm (t, 3 H, J = 6.7 Hz, $(CH_2)_2CH_3$); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 167.4 ($C{=}O$), 142.6 ($C{=}CH_2$), 134.5, 124.4 ($C{=}CH_2$), 123.5, 60.3 (OCH_2CH_3), 56.5, 44.8, 44.4, 37.3, 31.5, 30.6, 21.3, 14.3, 14.2 and 13.0 ppm; FT-IR (ATR) 2954(m), 2932(m), 2870(m), 1716(s), 1465(m), 1456(m), 1323(m), 1264(m), 1236(m), 1177(m), 1134(m), 1028(m) and 725(m) cm^{-1}; HRMS analysis (EI, 50°, $C_{16}H_{26}O_2$ = 250.1934) found 250.1934 *m/z*.

Reduction of 18. To a stirred solution of α,β-unsaturated ester **18** (75 mg, 0.30 mmol) in freshly distilled methanol (5 mL) was added magnesium turnings (40 mg, 1.65 mmol). (The reaction initiated after stirring ca 15 min and a cloudy white slurry gradually forms.) After 3 h, the reaction was complete as judged by TLC analysis and was quenched by the careful addition of 6 N HCl (ca 1 mL). The resulting clear solution was diluted with ether (50 mL), washed with satd aq $NaHCO_3$ (1 x 40 mL) and brine (1 x 40

mL), then dried ($MgSO_4$), filtered and concentrated to yield 70 mg (93%) of **20a** and **20b** as a pale yellow oil, which was used without further purification: GC analysis (DB-5, 125-126 @ 0.1°/min) showed two partially resolved peaks at 4.8 min; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.45-5.15 (m, 2 H, CH=CH), 4.08 (overlapping q, 2 H, OCH_2CH_3, two isomers), 2.69-2.42 (m, 2 H, $CHCO_2Et$ overlapping with CH=C(H)CH(R)R'), 1.78-1.53 (m, 6 H), 1.38-1.14 (m, 9 H), 1.11 (overlapping d, 3 H, J = 4.5, 4.8 Hz, $CH=C(H)CH_3$, two isomers) and 0.92-0.83 ppm (m, 4 H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 176.2 (C=O), 175.9 (C=O), 135.8, 135.7, 123.1 (OCH_2), 122.6 (OCH_2), 59.9 ($CHCO_2Et$), 59.8 ($CHCO_2Et$), 55.0, 54.9, 42.4, 41.7, 41.2, 41.0, 40.9, 40.5, 38.4, 38.3, 32.2, 31.9, 30.8, 30.6, 29.7, 21.4, 14.4 (CH_3), 14.3 (CH_3), 14.2 (CH_3), 14.1 (CH_3), 13.5 (CH_3), 13.4 (CH_3) and 13.0 (CH_3) ppm; IR (neat, ATR) 2954(m), 2952(m), 2936(m), 2928(m), 2919(m), 1731(s), 1461(m), 1454(m), 1254(m), 1182(m), 1173(s), 1160(s), 1153(m), 1144(m) and 1053(m) cm^{-1}.

Hydrogenation of 20a and 20b. To a stirred slurry of 5% rhodium on alumina (5 mg) in dry methanol (1.5 mL) under hydrogen (1 atm) was added a solution of **20a** and **20b** (4.0 mg, 0.016 mmol) in methanol (ca 50 uL). After 40 min, the reaction was filtered through a plug of celite/silica to yield 3.5 mg (88%) of ester **22**: GC analysis (DB-5, 125-126° @ 0.1°/min) 3.9 min (100%); ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.11 (q, 2 H, J = 7.3 Hz, OCH_2CH_3), 2.44 (m, 1 H, $CHCO_2Et$), 1.69-1.60 (m, 4 H), 1.31-1.06 (m, 17 H) and 0.90-0.82 ppm (m, 6 H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 176.5 (C=O), 60.0 ($CHCO_2Et$), 54.3 (OCH_2CH_3), 43.1, 42.5, 41.7, 38.8, 38.5, 30.9, 30.7, 21.4, 14.3, 14.2 and 13.9 ppm; IR (neat, ATR) 2954(s), 2927(s), 2871(m), 1734(s), 1464(m), 1378(m), 1253(m), 1174(m), 1162(m) and 1096(m) cm^{-1}; HRMS analysis (EI, 25°, $C_{16}H_{30}O_2$ = 254.2337) found 254.2243 *m/z*.

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References and Notes.

[1] a) A preliminary account of this work was presented: Takacs, J.M.; Newsome, P.W.; Kuehn, C. 196th National Meeting of the American Chemical Society, Los Angeles, CA, September 1988, ORGN Abs No. 200. b) This work was performed in part at the University of Utah and is taken in part from the dissertation of Peter W. Newsome: Newsome, P.W. Ph.D. Thesis, University of Utah, 1989. c) University of Utah, Salt Lake City, UT 84112.

[2] Questions regarding the crystal structure determination of compound **16** should be directed to Dr. Fusao Takusagawa, Department of Chemistry, University of Kansas.

[3] a) Pearson, A.J. "Metallo-organic Chemistry", John Wiley & Sons, New York, 1985, ISBN 0-471-90440-6; b) Davies, S.G. "Organotransition Metal Chemistry: Applications to Organic Synthesis", Pergamon Press, New York, 1982, ISBN 0-08-030714-0.

[4] For some recent leading references on catalytic palladium-mediated carbocyclizations, see: a) Takacs, J.M.; Zhu, J. *Tetrahedron Lett.* **1990**, *31*, 1117-20; b) Takacs, J.M.; Zhu, J. *J. Org. Chem.* **1989**, *54*, 5193-5; c) Zhang, Y.; Negishi, E. *J. Am. Chem. Soc.* **1989**, *111*, 3454-6; d) Trost, B. M.; Lee, D.C. *J. Org. Chem.* **1989**, *54*, 2271-4; e) Trost, B.M.; *Angew. Chem. Int. Ed., Engl.* **1989**, *28*, 213-5; f) Oppolozer, W. *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 38-52; g) Negishi, E.; Iyer, S.; Rousset, C.J. *Tetrahedron Lett.* **1989**, *30*, 291-4; h) Trost, B.M., Luengo, J.I. *J. Am. Chem. Soc.* **1988**, *110*, 8239-41; i) Larock, R.C.; Song, H.; Baker, B.E.; Gong, W.H. *Tetrahedron Lett.* **1988**, *29*, 2919-22; j) Abelman, M.M.; Overman, L.E. *J. Am. Chem. Soc.* **1988**, *110*, 2328-9; k) Trost, B.M.; Lee, D.C. *J. Am. Chem. Soc.* **1988**, *110*, 7255-8; l) Trost, B.M.; Matsuda, K. *J. Am. Chem. Soc.* **1988**, *110*, 5233-5; m) Trost, B.M.; Tanoury, G.J. *J. Am. Chem. Soc.* **1988**, *110*, 1636-8; n) Stille, J.K.; Tanaka, M. *J. Am. Chem. Soc.* **1987**, *109*, 3785-6; n) Trost, B.M. *Accts. Chem. Res.* **1990** *23*, 34-42.

[5] For some recent leading references on catalytic nickel-mediated carbocyclizations, see: a) Wender, P.A.; Jenkins, T.E. *J. Am. Chem. Soc.* **1989**, *111*, 6432-4; b) Wender, P.A., Ihle, N.C., Correia, C.R.D. *J. Am. Chem. Soc.* **1988**, *110*, 5904-6; d) Trost, B.M.; Tour, J.M. *J. Am. Chem. Soc.* **1988**, *110*, 5231-33; e) Trost,

B.M.; Tour, J.M. *J. Am. Chem. Soc.* **1987**, *109*, 5268-70; f) Tsuda, T.; Kiyoi, T.; Miyane, T.; Saegusa, T. *J. Am. Chem. Soc.* **1988**, *110*, 8570-2; g) Tamao, K.; Kobayashi, K.; Ito, Y. *J. Am. Chem. Soc.* **1988**, *110*, 1286-8; h) Hernandez, E.; Hoberg, H. *J. Organomet. Chem.* **1987**, *328*, 403-12; i) Behr, A.; Freundenberg, U.; Keim, W. *J. Molec. Cat.* **1986**, *35*, 9-17; j) Chiusoli, G.P. *J. Organomet. Chem.* **1986**, *300*, 57.

[6] For some recent leading references on zirconium-mediated carbocyclizations, see: a) Negishi, E.; Holmes, S.J.; Tour, J.M.; Miller, J.A.; Cederbaum, F.E.; Swanson, D.R.; Takahashi, T. *J. Am. Chem. Soc.* **1989**, *111*, 3336-46; b) Nugent, W. A.; Taber, D. F. *J. Am. Chem. Soc.* **1989**, *111*, 6435-7; c) Negishi, E.; Takahashi, T. *Synthesis* **1988**, 1-19; d) Buchwald, S.L.; Nielsen, R.B. *Chem. Rev.* **1988**, *88*, 1047-58; d) Yasuda, H.; Okamoto, T.; Matsuoko, Y.; Nakamura, A.; Kai, Y.; Kanehisa, N.; Kasai, N. *Organometallics* **1989** *8*, 1139-52.

[7] For some recent leading references on cobalt-mediated carbocyclizations, see: a) Almansa, C.; Moyano, A.; Serratosa, F. *Tetrahedron* **1988**, *44*, 2657-62; b) Schore, N.E.; Rowley, E.G. *J. Am. Chem. Soc.* **1988**, *110*, 5224-5; c) Smit, W. A.; Gybin, A. S.; Shashkov, A. S.; Strychkov, Y. T.; Kyz'mina, L. G.; Mikaelian, G. S.; Caple, R.; Swanson, E. D. *Tetrahedron Lett.* **1986**, *27*, 1241-4; d) Billington, D.C.; Willison, D. *Tetrahedron Lett.* **1984**, *25*, 4041-4; e) Exon, C.; Magnus, P. *J. Am. Chem. Soc.* **1983**, *105*, 2477; f) Lautens, M.; Crudden, C.M. *Tetrahedron Lett.* **1989**, *30*, 4803-6; g) Harvey, D.F.; Johnson, B.M.; Ung, C.S.; Vollhardt, K.P.C. *Synlett* **1989**, 15-5.

[8] For some recent leading references on rhodium-mediated carbocyclizations, see: a) Taura, Y.; Tanaka, M.; Funakoshi, K.; Sakai, K. *Tetrahedron Lett.* **1989**, *30*, 6349-52; b) Funakoshi, K.; Togo, N.; Taura, Y; Sakai, K. *Chem. Pharm. Bull.* **1989** *37*, 1776-9; c) James, B.R.; Young, C.G. *J. Organomet. Chem.* **1985** *285*, 321-32.

[9] a) Takacs, J.M.; Anderson, L.G.; Creswell, M.W.; Takacs, B.E. *Tetrahedron Lett.* **1987**, *28*, 5627-30; b) Takacs, J.M.; Anderson, L.G. *J. Am. Chem. Soc.* **1987**, *109*, 2200-02; c) Takacs, J.M.; Anderson, L.G.; Bindu Madhavan, G.V.; Creswell, M.W.; Seely, F.L.; Devroy, W.F. *Organometallics* **1986**, *5*, 2395-8; d) Takacs, B.E.; Takacs, J.M. *Tetrahedron Lett.* **1990**, *31*, 0000; e) Pearson, A.J.; Zettler, M.W. *J. Am. Chem. Soc.* **1989**, *111*, 3908-18.

[10] Heathcock, C.H. in "Asymmetric Synthesis", J.D. Morrison, Ed., Academic Press, New York, 1983, Vol. 3.

[11] a) Akiyama, T.; Grevels, F.-W.; Reuvers, J.G.A.; Ritterskamp, P. *Organometallics* **1983**, *2*, 157-60; b) Tolstikov, G.A.; Dzhemilev, U.M.; Khusnutdinov, R.I. *J. Org. Chem., USSR (Engl. Transl.)* **1979**, *15*, 694.

[12] Craig, D. *Chem. Soc. Rev.* **1987**, *16*, 187-238.

[13] a) Takacs, J.M.; Helle, M.A.; Seely, F.L. *Tetrahedron Lett.* **1986**, *27*, 1257-60; b) triethyl 2-phosphonobutyrate: registry number 17145-91-4.

[14] Ukai, J.; Ikeda, Y.; Ikeda, N.; Yamamoto, H. *Tetrahedron Lett.* **1983**, *24*, 4029-32.

[15] Ikeda, Y.; Yamamoto, H. *Bull. Chem. Soc. Jap.* **1986**, *59*, 657-8.

[16] Unless otherwise noted the following procedure is used to prepare the active iron catalyst. 10-15 mol % of $Fe(acac)_3$ is reduced in situ by 3.1 equivalents of triethylaluminum (benzene, O-5°). Prior to the reduction, 1.1 equivalents of a bidentate ligand (2,2'-bipyridine unless otherwise noted) and 10 equivalents of solubilizing addend (furan or 2-methylfuran unless otherwise noted) are added to the solution of the $Fe(acac)_3$ in benzene. A solution of the triene ester substrate in benzene is added to the iron catalyst approximately 5 min after the addition of triethylaluminum. The resulting mixture is then warmed to ambient temperature. For the chemistry of related catalyst preparations, see: a) Dieck, H. tom; Diercks, R. *Angew Chem., Int. Ed. Engl.* **1983**, *22*, 778-779; b) Su, A. C. L. *Adv. Organomet. Chem.* **1979**, *17*, 269-318; c) Genet, J. P.; Ficini, J. *Tetrahedron Lett.* **1979**, *20*, 1499-1502; d) Carbonaro, A.; Greco, A.; Dall'Asta, G. *J. Organomet. Chem.* **1969**, *20*, 177-182; e) Carbonaro, A.; Greco, A.; Dall'Asta, G. *J. Org. Chem.* **1968**, *33*, 3948-50; f) Hata, G.; Aoki, D. *J. Org. Chem.* **1967**, *32*, 3754-8.

In many cases, the nature of the chelating ligand dramatically influence the course of the reaction. The addend plays a less dominant role in the chemistry and is employed principally to slow down the

disproportionation of the active catalyst to yield the catalytically inactive $bpy_2Fe(0)$ and precipitated Fe_{metal}. The apparent disproportionation occurs at an appreciable rate in the absence of triene substrate. The $Fe(acac)_3$ is reduced in the absence of triene ester to avoid the known reaction of enones with triethylaluminum. See: Evans, D.A.; Chapman, K.T.; Bisaha, J. *J. Am. Chem. Soc.* **1988**, *110*, 1238-56.

[17] a) Hudlicky, T.; Sinai-Zingde, G.; Natchus, M. G. *Tetrahedron Lett.* **1987**, *28*, 5287-5290; b) Brettle, R.; Shibib, S. M. *J. Chem. Perkin Trans. I* **1981**, 2912-2919.

[18] At this point we can not rule out partial alkene and/or diene reduction as possible side reactions as well.

[19] a) Hubert, A.J.; Georis, A.; Warin, R.; Teyssie, P.J. *J. Chem. Soc., Perkin Trans. 2* **1972**, 366-70; b) Jolly, P.W.; Stone, F.G.A.; Machenzie, K. *J. Chem. Soc.* **1965**, 6416-20.

[20] We recognize that, based upon the results obtained from monitoring the course of the reaction by GC, it can be reasonably argued that the active catalytic species for ene carbocyclization is itself generated in the course of the isomerization reaction. We cannot rule out this possibility. However, we feel that this is unlikely since large amounts of isomerization are not a prerequisite for successful ene carbocyclization of the related triene ethers.

[21] In the iron-catalyzed ene carbocyclization reactions of triene ethers **1**, the $Fe(acac)_3$ can be reduced in the presence of the triene ether substrate (see reference 15) and only small amounts (1-10%) of isomerization products are observed. The triene ether isomerization products arise principally by isomerization of the diene moiety. These observations, and the more "normal" ene reactivity of triene ester **6** as compared to the unusually facile isomerization in the case of the triene **9**, suggest that the predominant mode of isomerization in the triene ester involves the α,β-unsaturated ester moiety rather than the diene moiety.

[22] Dieck, H. tom; Dietrich, J *Chem. Ber.* **1984**, *117*, 694-701.

[23] Ibuka, T.; Tanaka, M.; Nishi, S.; Yamamoto, Y. *J. Am. Chem. Soc.* **1989**, *111*, 4864-72.

[24] Attenuated Total Reflectance: Wilks, Jr., P.A. *Amer. Lab.* **1972**, *4*, 42.

[25] a) Registry Number 74930-36-2; b) Roush, W.R.; Gillis, H.R.; Ko, A.I. *J. Am. Chem. Soc.* **1982**, *104*, 2269-83.

[26] Herrmann, J.L.; Schlessinger, R.H. *J. Chem. Soc., Chem. Commun.* **1973**, 711-2.