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Fe(III) Mediated Oxidative Radical Cyclisation of Cyclopropanone Acetals

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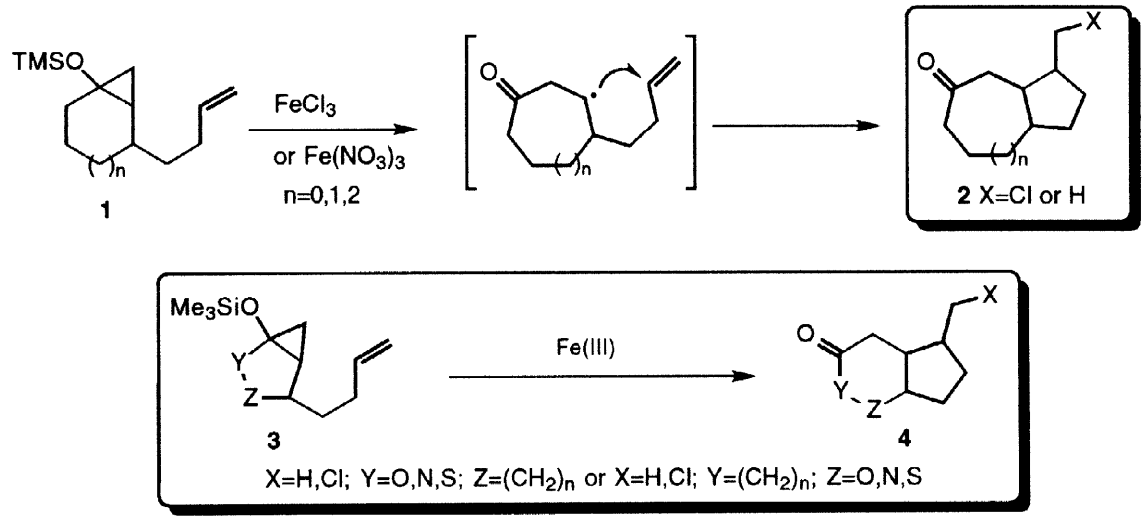
Abstract: A variety of cyclopropanone acetal derivatives were found to undergo facile Fe(III) mediated oxidative radical cyclisation to the corresponding trisubstituted cyclopentane esters in good yield and with diastereoselectivities as high as 23:1.

Introduction

Over the past few years we have been investigating the Fe(III) mediated oxidative cleavage of a variety of cyclopropane derivatives as a potential non-tin method for carbon centred radical generation. More specifically, we have found that cyclopropyl ethers[1] serve as good substrates for the Fe(III) mediated generation and cyclisation of carbon centred radicals *eg* **1→2** (Scheme 1). Following our initial investigations with cyclopropyl ethers it was our aim to extend this reaction to a variety of substrates containing heteroatoms within the carbocyclic ring, thus giving rise to functionalised heterobicyclic products (*ie* **3→4**). In this paper we disclose our full experimental details[2] on the Fe(III) mediated oxidative cyclisation reactions of cyclopropanone acetals for the preparation of highly functionalised cyclopentanes.



Scheme 1

Results and Discussion

The first system we studied was the cyclopropanone acetal **6** which was easily assembled by using our now standard[1] conjugate addition/cyclopropanation sequence. It was found that addition of butenylmagnesium

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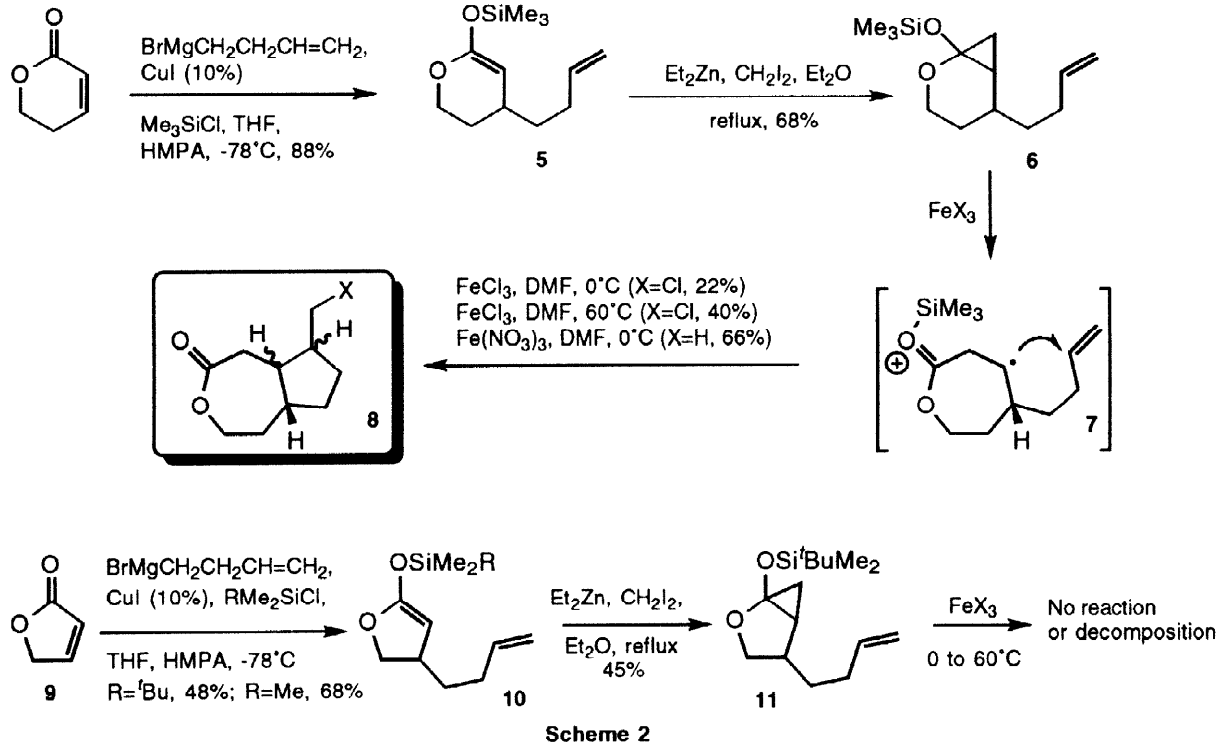
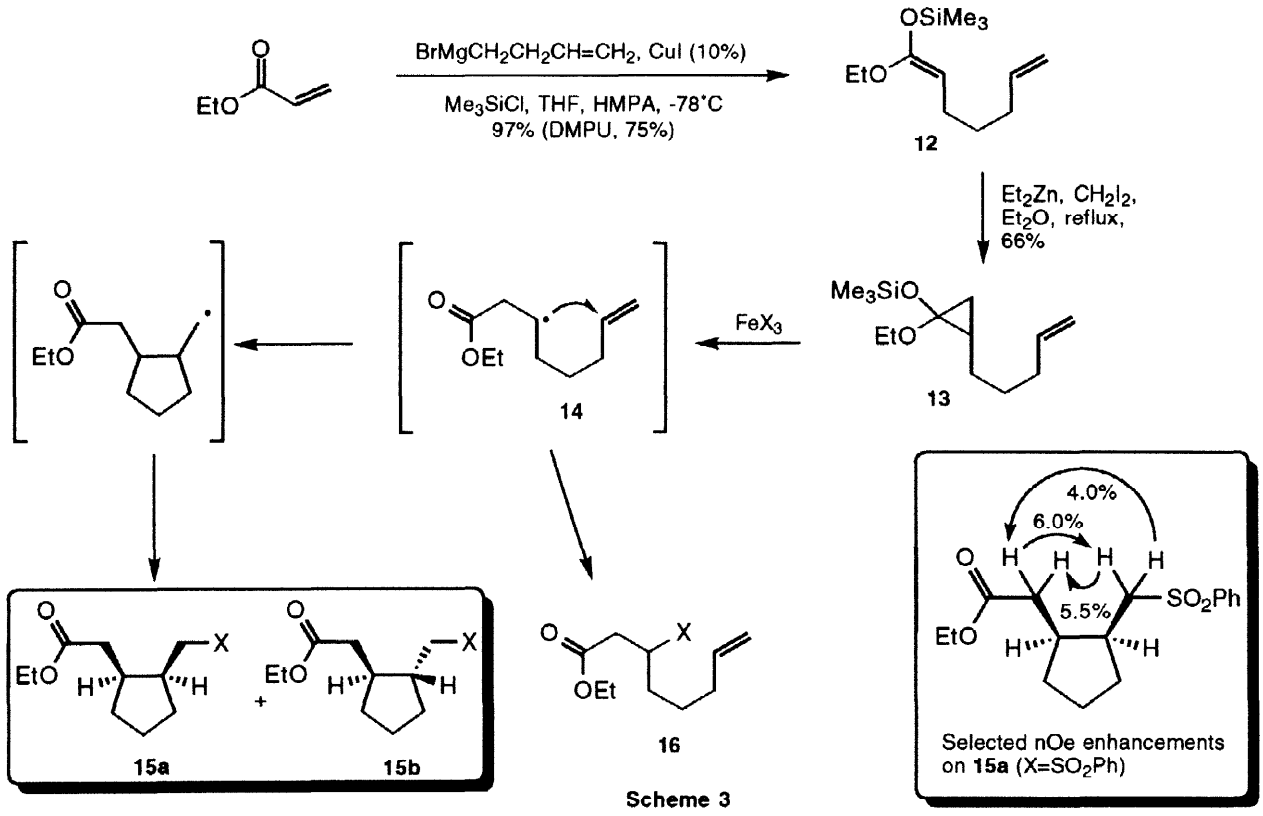
bromide to 5,6-dihydro-2H-pyran-2-one in the presence of TMSCl gave the silylketene acetal **5** in 88% yield following distillation. This product proved to be very labile and was immediately subjected to the Et_2Zn/CH_2I_2 cyclopropanation procedure to give the key cyclopropanone acetal **6** in 68% yield. Treatment of **6** with anhydrous ferric chloride in DMF under our standard conditions[1] gave the ring expansion/cyclisation product **8** (X=Cl) as anticipated, but in poor yield (22%) and as an inseparable mixture of diastereoisomers. Suspecting that the poor yield was due to slow reaction of the cyclopropane with $FeCl_3$ at 0°C, the reaction was repeated at 60°C and a higher yield of 40% was obtained. Treatment of **6** with ferric nitrate in DMF[3] gave a better yield (66%) of the product **8** (X=H) resulting from hydrogen abstraction (Scheme 2). Again an inseparable mixture of diastereoisomers was formed with two major isomers predominating (1:1). Unfortunately it was not possible to assign the relative stereochemistry of these diastereoisomers by NMR. Attempts to implement a similar sequence with 2(5*H*)-furanone **10** were initially thwarted by the instability of the trimethylsilylketene acetal **10** (R=Me_3Si), which proved impossible to cyclopropanate without decomposition. Use of TBDMSCl in the conjugate addition step allowed the isolation of the TBDMS ketene acetal **10** (R=^{t}BuMe$_2$Si), which upon immediate reaction with Et_2Zn/CH_2I_2 gave the TBDMS protected cyclopropanone acetal **11** in moderate overall yield. Attempted oxidative cyclisation with both ferric chloride and nitrate initially gave no reaction and the reaction mixture was slowly warmed to 60°C. This TBDMS protected cyclopropanone acetal showed remarkable thermal stability in the prescence of Fe(III) salts, and it was only at 60°C that decomposition was observed. Unfortunately prolonged heating resulted in complete decomposition to an intractable mixture, with no cyclisation products being observed.



Scheme 2

It is quite clear from the above study that, compared to the analogous cyclopropyltrimethylsilyl ethers (*e.g.* **1**, n=1),[1] the inclusion of a heteroatom dramatically alters the stereochemical outcome of these reactions. This is probably due to conformational differences between the ring expanded lactone radical **7** and the analogous carbocyclic radical in Scheme 1. It is likely that this would have a profound effect on the stereochemical

outcome of the 5-*exo* radical cyclisation. We therefore decided to investigate the Fe(III) oxidations of the simple cyclopropanone acetal **13** with a view to obtaining cyclic products which would be easier to analyse by spectroscopic techniques. To this end the silylketene acetal **12** was prepared in almost quantitative yield by conjugate addition of butenylmagnesium bromide to ethyl acrylate. It is interesting to note that in this case DMPU could be substituted for HMPA, albeit with a decrease in yield. This was contrary to our previous experience with related additions which failed completely with co-solvents other than HMPA. Cyclopropanation of freshly prepared **12** gave access to the cyclopropanone acetal **13**, which proved stable enough to be stored for prolonged periods. With multigram quantities of **13** available we were able to carry out a detailed study of its oxidative cyclisation (Scheme 3) using a variety of Fe(III) species and conditions, the results of which are detailed in Table 1.



Scheme 3

The oxidation of **13** with ferric chloride (Table 1), as previously shown for **6**, was found to be temperature sensitive. For example, in entry 1 a good yield of cyclopropane cleaved material was observed, but the major product was the uncyclised material **16** (X=Cl). This was attributed to the fact that the oxidative cleavage of the cyclopropane ring was slow at 0°C and therefore the concentration of unreacted ferric chloride was able to increase in the reaction mixture. When cleavage to the β-propionyl radical **14** takes place it is then quenched by chlorine abstraction from $FeCl_3$ at a rate faster than 5-*exo* radical cyclisation to the desired product. This was proved by repeating the addition of $FeCl_3$ at 60°C (entry 2), which completely reversed the situation to give cyclised **15** (X=Cl) as the major product. Extending the addition times to 5h at 60°C allowed the almost exclusive formation of **15** (X=Cl), although at the expense of the overall yield (entry 3). We then turned our attention to the use of the complex $[FeCl_2(DMF)_3][FeCl_4]$[4] as a possible substitute for anhydrous ferric chloride. This proved to be very similar in reactivity to ferric chloride itself and also gave the best ratios of

15:16 at elevated temperatures and longer addition times. In fact this complex is superior to ferric chloride due to the smaller reduction in yield at elevated temperatures. Also, from a practical point of view, since this complex is air and moisture stable it is possible to manipulate it without the glove bag protocol required for anhydrous ferric chloride. Entries 10-15 detail the reaction of **13** with anhydrous ferric nitrate in the presence of a number of radical traps. With ferric nitrate alone (entry 10) the cyclised ester **15** (X=H) was obtained as the sole product in 54% yield. As mentioned earlier, we believe that this product arises *via* hydrogen atom abstraction from the solvent by the final cyclised radical. Since there is no uncyclised material formed it is quite likely that this abstraction is a slow process relative to 5-*exo* cyclisation. We reasoned, therefore, that it should be possible to add external radical traps and use this to incorporate, in some cases, further functionality (X) into the final products. Thus, using 1,4-cyclohexadiene as a hydrogen atom source (entry 11) the cyclised ester **15** (X=H) was obtained as before, but in higher yield (76%). Use of diphenyldisulfide as a trap (entry 12) gave a good yield of the sulfide **15** (X=SPh) without any formation of the corresponding uncyclised sulfide **16** (X=SPh). The use of N-chlorosuccinimide (entry 13) gave a 9:1 mixture of **15**:**16** (X=Cl) respectively in good yield (76%). This was a very significant result as the ferric nitrate/NCS combination would appear to be superior, in terms of yield of cyclised product, to all of the results obtained in entries 1-9. A competition experiment between ferric chloride and diphenyldisulfide (entry 15) gave only products resulting from chlorine atom abstraction, thus demonstrating that the rate of chlorine atom abstraction from ferric chloride is rapid compared to the other atom donors used. Finally it should be noted that in all of the examples studied in Table 1, the *cis*-isomer **15(a)** predominates over the *trans*-isomer **15(b)** to the extent of 80-90%. This is clearly demonstrated from the nOe experiments on **15a** (X=SO_2Ph) as shown in Scheme 3.

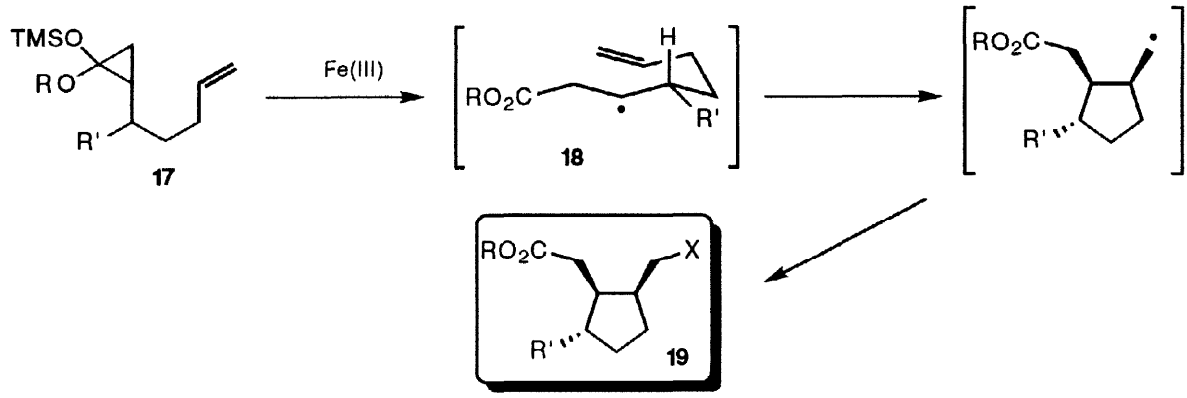
TABLE 1: Oxidative Cyclisation of 13 with $FeCl_3$, $[FeCl_2(DMF)_3][FeCl_4]$ & $Fe(NO_3)_3$

ENTRY	CONDITIONS (Addition time)[a]	% YIELD	15[d]:16	X
1	$FeCl_3$[b], DMF, 0°C, (0.5h)	79	1 : 2.5	Cl
2	$FeCl_3$, DMF, 60°C, (0.5h)	66	3.6 : 1	Cl
3	$FeCl_3$, DMF, 60°C, (5h)	47	19 : 1	Cl
4	$[FeCl_2(DMF)_3][FeCl_4]$[c], DMF, 0°C, (0.5h)	86	1 : 2.5	Cl
5	$[FeCl_2(DMF)_3][FeCl_4]$, DMF, 0°C, (5h)	78	1 : 2.67	Cl
6	$[FeCl_2(DMF)_3][FeCl_4]$, DMF, rt., (5h)	79	1 : 1	Cl
7	$[FeCl_2(DMF)_3][FeCl_4]$, DMF, 40°C, (5h)	53	9.3 : 1	Cl
8	$[FeCl_2(DMF)_3][FeCl_4]$, DMF, 60°C, (0.5h)	89	2 : 1	Cl
9	$[FeCl_2(DMF)_3][FeCl_4]$, DMF, 60°C, (5h)	69	5.4 : 1	Cl
10	$Fe(NO_3)_3$[b], DMF, 0°C, (0.5h)	54	**15** only	H
11	$Fe(NO_3)_3$, 1,4-Cyclohexadiene, DMF, 0°C, (0.5h)	76	**15** only	H
12	$Fe(NO_3)_3$, $(PhS)_2$, DMF, 0°C, (0.5h)	66	**15** only	PhS
13	$Fe(NO_3)_3$, N-Cl-Succinimide, DMF, 0°C, (0.5h)	76	9 : 1	Cl
14	$Fe(NO_3)_3$, N-Br-Succinimide, DMF, 0°C, (0.5h)	Complex mixt.	-	-
15	$FeCl_3$, $(PhS)_2$, DMF, 0°C, (0.5h)	67	1 : 1.67	Cl

[a]Times refer to the dropwise addition of the Fe(III) species in DMF to a solution of **13**. [b]2.2 equivalents. [c]1.1 equivalents. [d]In all cases *cis* **15(a)** was the major isomer (80-90%).

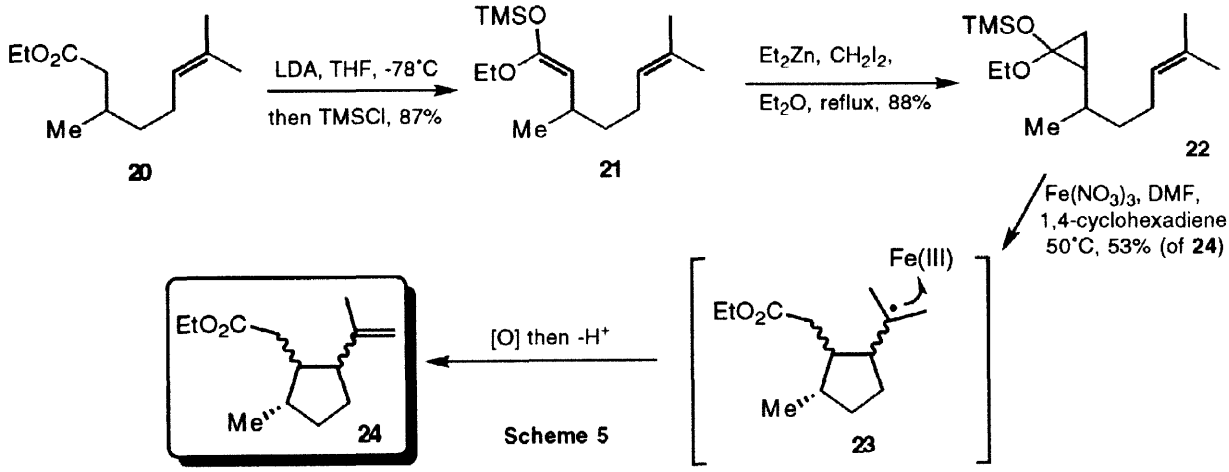
Stereoselectivity

This preferential formation of the *cis*-isomer in related Bu_3SnH initiated cyclisations is well documented and has been rationalised by Beckwith.[5] In the present study we wanted to capitalise on this stereoselectivity and examine the stereochemical influence exerted by a variety of substituents during the oxidative radical cyclisation of substituted cyclopropanone acetals (**17**→**19**, Scheme 4). According to this comprehensive body of work compiled by Beckwith such 5-*exo* radical cyclisations should proceed *via* the chair-like transition state **18**, where the 2-substituent (R') adopts a pseudoequatorial conformation. This then leads to cyclopentane formation and the cyclised product (**19**) will, in principle, be formed with the stereochemistry as shown in Scheme 4.



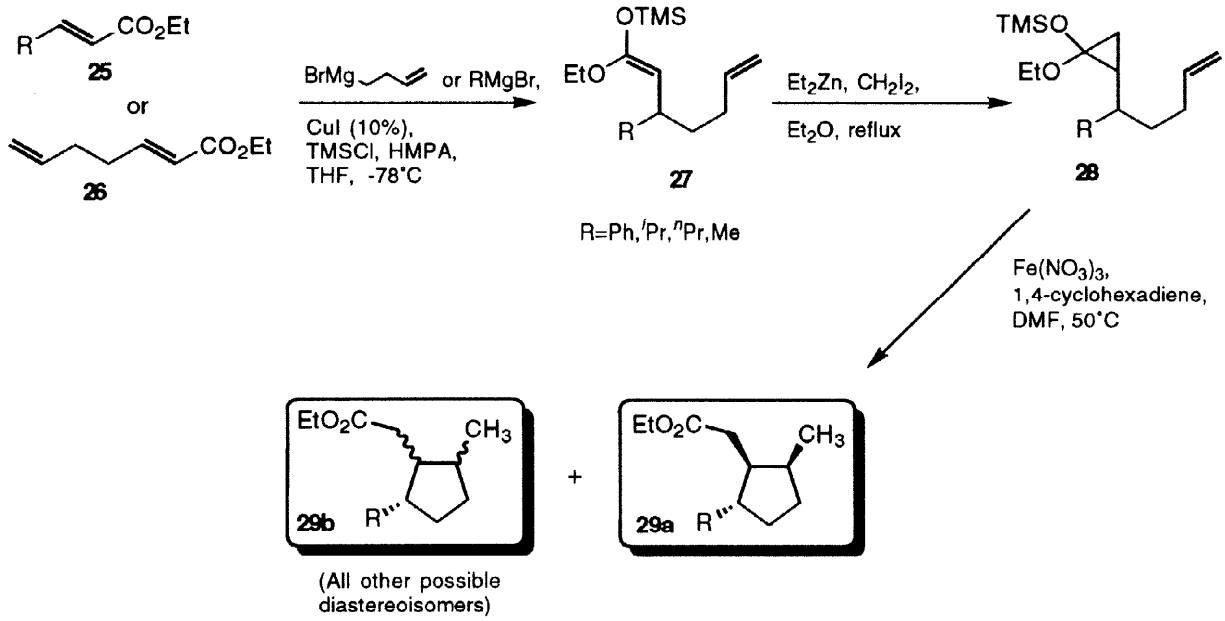
Scheme 4

Initially we elected to study the effect of a methyl group on the cyclisation. Readily available (±)-ethyl citronellate **20** was treated with LDA followed by quenching of the resulting enolate with TMSCl. Following an anhydrous workup the corresponding labile ketene acetal **21** was obtained pure by bulb-to-bulb distillation under reduced pressure. This sensitive ketene acetal proved to be too labile for prolonged storage and was immediately subjected to the Simmons-Smith reaction which gave an excellent yield of the now stable cyclopropanone acetal **22**. Oxidative cyclisation of **22** using ferric nitrate and 1,4-cyclohexadiene as a hydrogen atom donor gave the cyclised product **24** in moderate yield but as a complex mixture of stereoisomers (Scheme 5). The formation of the double bond can be explained by assuming that the resultant cyclised radical **23** undergoes further oxidation by Fe(III) to a cation followed by loss of a proton.[6]



Scheme 5

Although the basic cyclisation sequence was fairly efficient, the initial level of diastereoselection obtained was disappointing. Since alkene formation was confusing the issue it was thought prudent to study a range of simpler cyclopropyl systems (e.g. **28**, Scheme 6) where complications arising from oxidation of the resulting cyclised primary radical would be unlikely. These were readily synthesised by conjugate addition of a number of Grignard reagents to the substituted acrylate esters **25** or **26**,[7] in the presence of TMSCl, to give the corresponding ketene acetals **27** in excellent yield. Cyclopropanation of these reactive ketene acetals under the usual conditions gave the substituted cyclopropanone acetals **28** in good to excellent yield (Scheme 6, Table 2).



Scheme 6

Ferric nitrate oxidation of the cyclopropanone acetals **28** was carried out as before in anhydrous DMF using 1,4-cyclohexadiene as a hydrogen atom donor. In all cases oxidative cyclisation proceeded to give the cyclopentane esters **29a/b** in good yield (Table 2). The lower yield obtained for entry 4 was attributed to the volatility of the cyclised product. In general, the diastereoselection obtained in these oxidative radical cyclisations correlated very well to the Beckwith model in Scheme 4. For example, in entry 1 (R=Ph) the cyclised product **29a** was formed with essentially complete diastereoselection, with only trace amounts of other stereoisomers (**29b**) detectable by NMR spectroscopy. Proof of the relative stereochemistry in **29a** was obtained by nOe experiments on the reduced product **30** (Figure 1). Both the *n*-propyl (entry 3) and *iso*-propyl (entry 2) examples also gave good levels of selection. Although not quite as selective as the phenyl case these two results are consistent with a decrease in the size of the 2-substituent which would influence the preference for adopting a conformation where the substituent is equatorial. Not surprisingly, when R=Me (entry 4) a reduced stereoselectivity was observed. This is consistent with the results obtained with (±)-ethyl citronellate and clearly indicates the weaker stereochemical influence of the smaller methyl group.

TABLE 2: Diastereoselective Oxidative Cyclisation of 27 with $Fe(NO_3)_3$

Entry	R	27	28	29a/b	Ratio[a] 29a:29b
1	Ph	83% (from **25**)	88%	83%	23:1
2	*iso*-C_3H_7	94% (from **26**)	74%	74%	8:1
3	*n*-C_3H_7	92% (from **26**)	86%	69%	6:1
4	Me	94% (from **25**)	92%	69%	2:1

[a]Ratios determined by ^1H NMR

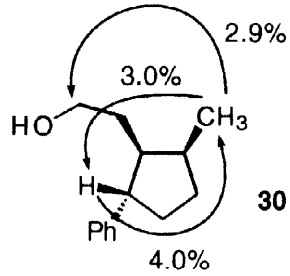
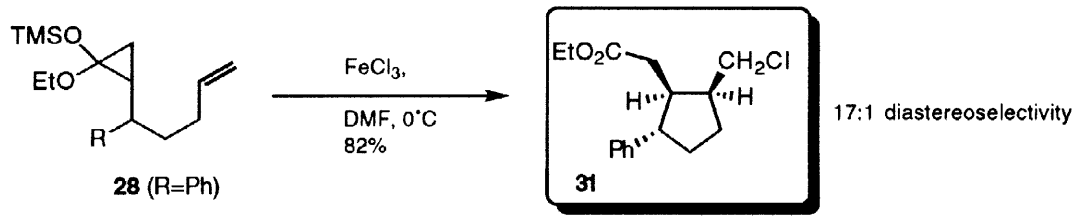


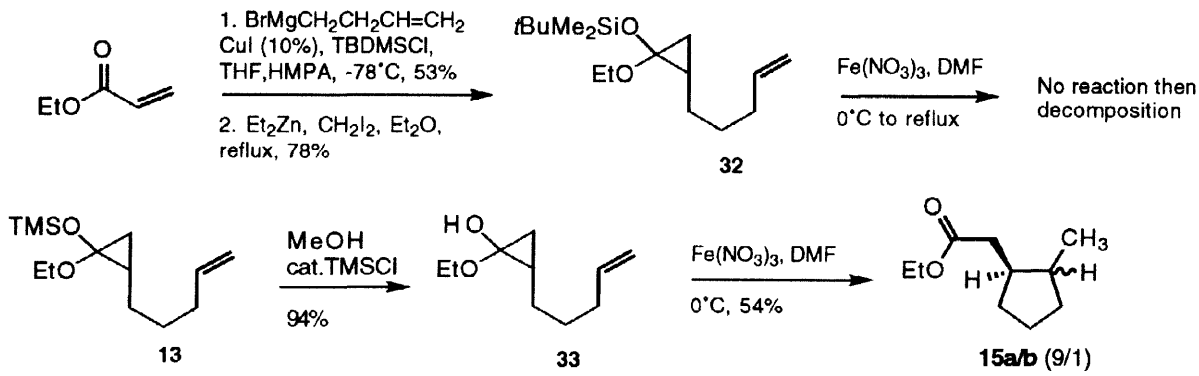
Figure 1: Selected nOe enhancements

Finally, equally good results were obtained in the oxidative cyclisations using ferric chloride as the iron source. For example, treatment of the cyclopropanone acetal **28** (R=Ph) gave the trisubstituted chloromethyl cyclopentane ester **31** with a selectivity of 17:1. The incorporation of a chloromethyl group will be useful for the introduction of further functionality (Scheme 7).



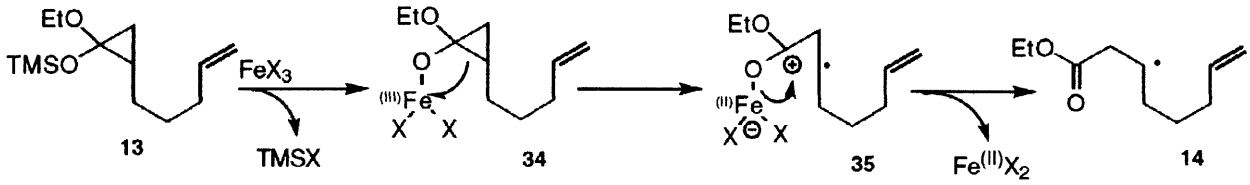
Scheme 7

Mechanism: As stated earlier, we believe that the mechanism of these reactions proceeds *via* oxidation of the cyclopropane by single electron transfer (SET) to the Fe(III) species involved. From the present work it is clear that the use of a TBDMS group rather than a TMS group effectively shuts down the oxidative process (Scheme 2). Further proof of this was obtained on attempted oxidative cyclisation of the TBDMS cyclopropanone acetal **32** which failed to undergo oxidative cyclisation under the usual conditions and decomposed on elevation of the reaction temperature (Scheme 8). If TBDMS cyclopropanone acetals are stable to cleavage under the reaction conditions it would suggest that desilylation is the first step of the mechanism. This was partially substantiated by synthesis of the cyclopropanone hemiacetal **33** which undergoes oxidative cyclisation to **15** without event (Scheme 8). Yields and product ratios similar to those obtained directly from the silylketene acetal **13** were obtained on treatment of the hemiacetal **33** with $FeCl_3$, $[FeCl_2(DMF)_3][FeCl_4]$ or $Fe(NO_3)_3$ in DMF.



Scheme 8

We therefore propose a refinement to our original mechanism which involves initial desilylation of **13** to give the $Fe^{(III)}$ alkoxide **34**. The $Fe^{(III)}$ is then reduced *via* SET to the $Fe^{(II)}$ ate-complex **35**, thus forming the carbon centred radical; loss of $Fe^{(II)}X_2$ would then generate the β-propionyl radical **14** (Scheme 9). Direct cleavage of the $^{(III)}Fe$—O bond in **34** to an alkoxy radical is unlikely as we have previously investigated this and ruled it out in the case of cyclopropyl ethers.[1]

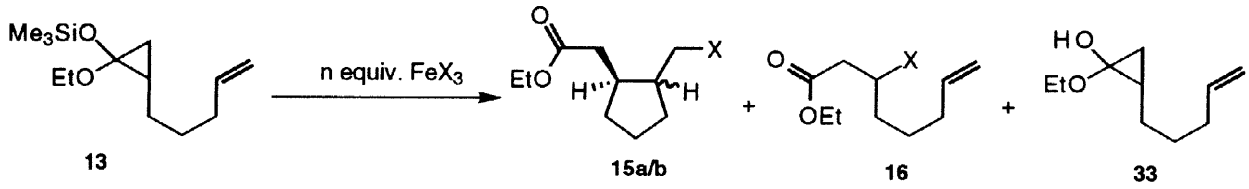


Scheme 9

Good evidence that carbon centred radicals are being formed came from preliminary EPR studies. For example, the cyclopropanone acetal **13** was added to a DMF solution of ferric chloride in an EPR tube. After 5 min the solution was cooled to 70K and data were collected. A very characteristic sinusoidal curve was observed at g=2.005, a value typical of a carbon centred radical. However, hyperfine splitting could not be observed due to the high dielectric constant of DMF which required the spectra to be obtained at low temperature. Further EPR work in other solvents will be necessary to gain more structural information about any carbon centred radicals formed.

Finally, we sought to investigate how many equivalents of the iron species were required for the oxidative cyclisation to occur cleanly. Traditionally, and in accord with literature precedent,[8] we have been using 2.2 equivalents of the respective Fe(III) salts. However, we soon found that treatment of **13** with just 1.1 equivalents of $FeCl_3$ gave rise to the mixture of cyclised and uncyclised product (**15** and **16**) in almost an identical yield to that when the reaction was run with 2.2 equivalents (Table 3, entry 1). Similar results were also obtained when 0.55 equivalents of $[FeCl_2(DMF)_3][FeCl_4]$ (1.1 equivalents in Fe) or 1.1 equivalents of $Fe(NO_3)_3$ were employed (entries 2 and 3). Furthermore, when less than one equivalent of ferric nitrate was employed (entries 4 and 5) there was a corresponding decrease in the yield of the cyclised product. This clearly indicates that one equivalent of the Fe(III) source is required for complete conversion. In these reactions the

cyclopropanone hemi-acetal **33** was a major by-product which, in conjunction with **15**, accounted well for 75% of the mass balance. The formation of **33** can be explained by assuming that the unreacted starting material undergoes hydrolysis on aqueous work-up.



13 15a/b 16 33

TABLE 3: Oxidative Cyclisation of 13 with stoichiometric and sub-stoichiometric equivalents of Fe(III)

ENTRY	CONDITIONS (Addition time)	15/16	33	X
1	1.10 eq. $FeCl_3$, DMF, 40°C, (0.5h)	83% (**15/16**, 1 : 1.2)	0%	Cl
2	0.55 eq. $[FeCl_2(DMF)_3][FeCl_4]$, DMF, 40°C, (0.5h)	66% (**15/16**, 1 : 1.1)	0%	Cl
3	1.10 eq. $Fe(NO_3)_3$, DMF, 0°C, (0.5h)	58% (**15** only)	0%	H
4	0.55 eq. $Fe(NO_3)_3$, DMF, 0°C, (0.5h)	31% (**15** only)	42%	H
5	0.10 eq. $Fe(NO_3)_3$, DMF, 0°C, (0.5h)	11% (**15** only)	64%	H

Acknowledgements

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EXPERIMENTAL

All compounds were prepared as racemic mixtures and any stereochemistry shown is relative. Yields quoted are based on isolated mass and ratios of isomers were determined from integrals of the appropriate peaks in the ^1H NMR spectra. All reactions were carried out in oven or flame dried glassware under an atmosphere of dry, oxygen-free argon. Diethyl ether and THF were dried by distillation from sodium and benzophenone; DMF was dried over barium oxide for 24 h followed by distillation and subsequently stored over 4 Å molecular sieves. The diethyl zinc used was a 1 M solution in hexanes (ex. Aldrich) throughout. All manipulations involving anhydrous iron(III) chloride (ex. Aldrich) were carried out in a glove bag under an atmosphere of dry, oxygen free, nitrogen. Column chromatography was performed using Matrex silica 60 (70-200 μm). Boiling points refer to the oven temperature of a Büchi GKR-50 Kugelröhr during short path bulb-to-bulb distillation. NMR spectroscopy experiments were carried out on Brucker AC250, Jeol EX270, Varian Unity 300, Varian XR400 and Unity 400 MHz FT spectrometers. Chemical shifts are quoted in parts per million (ppm) downfield from tetramethylsilane and are referenced to the residual protio solvent peaks as internal standard. Coupling constants (*J*) are measured in Hz. Infra-red spectra were recorded on a Perkin-Elmer 1720X FT IR spectrophotometer. Microanalysis was performed with a Carlo Erba EA 1108 instrument. Mass spectrometry was carried out on Kratos MS25, HP 5958A, HP G1800A and VG Platform MS instruments.

GENERAL CONJUGATE ADDITION PROCEDURE.

4-(But-3'-enyl)-2-trimethylsilyloxy-5,6-dihydro-(4*H*)-pyran 5: To a stirred suspension of dry magnesium turnings (0.372 g, 15.2 mmol) activated with a single crystal of iodine in THF (24 mL) was added 4-bromo-1-butene (12.2 mmol, 1.24 mL) and the mixture stirred at room temperature for 1 h until the exothermic reaction had subsided and consumption of magnesium had ceased. To the grey/green solution was added HMPA (24.4 mmol, 4.26 mL) and the reaction mixture was cooled to -78°C. Copper iodide (0.193 g, 1.0 mmol) was added. A solution of 5,6-dihydro-2(2*H*)-pyranone (1.0 g, 10.2 mmol) and chlorotrimethylsilane (24.4 mmol, 3.10 mL) in THF (6 mL) was added dropwise over 10 min and the mixture stirred at -78°C for 2 h. It was quenched with triethylamine (10 mL) and then allowed to warm to room temperature. The mixture was poured onto petroleum ether (200 mL) and the solution decanted from the resulting pale grey precipitate. This was washed with further petroleum ether (100 mL). The combined organics were washed with water (4 x 125 mL), dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. The crude product was purified by Kugelröhr distillation to yield the title compound as a clear, colourless liquid (2.04 g, 88%). bp 150-160°C @ 15 mm Hg; ν_{max}/cm^{-1} (thin film) 1744, 1684, 1641; δ^1H (270 MHz; C_6D_6) 5.72, (1H, tdd, *J* 7, *J* 10, *J* 17, C<u>H</u>=CH_2), 5.06-4.88 (2H, m, C<u>H</u>$_2$=CH), 4.03 (1H, d, *J* 3, CH=C), 3.83-3.61 (2H, m, CH_2), 2.09 (1H, m, CH), 1.95 (2H, td, *J* 7, *J* 8, CH_2), 1.49-1.06 (4H, m, CH_2), 0.23 (9H, s, $(CH_3)_3Si$); $\delta^{13}C$ (67.5 MHz; C_6D_6) 155.21 (C), 139.02 (CH), 114.52 (CH_2), 79.25 (CH), 65.59 (CH_2), 37.02 (CH_2), 31.49 (CH_2), 30.81 (CH), 29.09 (CH_2), 0.28 ($(CH_3)_3Si$); *m/z* (EI) 226 {M^+} (8%), 211 (6), 171 (100), 129 (2), 103 (16), 73 (55%); (Found: C, 63.87; H, 9.98. $C_{12}H_{22}O_2Si$ requires C, 63.66; H, 9.80%).

GENERAL CYCLOPROPANATION PROCEDURE.

5-(But-3'-enyl)-1-trimethylsilyloxy-2-oxabicyclo[4.1.0]heptane 6: To a stirred solution of freshly distilled 4-(but-3'-enyl)-2-trimethylsilyloxy-5,6-dihydro-(4*H*)-pyran **5** (1.8 g, 7.95 mmol) in diethyl ether (40 mL) was added diethylzinc (15.9 mmol, 15.9 mL) followed by diiodomethane (15.9 mmol, 1.28 mL). The reaction mixture was heated to reflux for 16 h and then allowed to cool to room temperature. Pyridine (5 mL) was added and the cloudy suspension stirred for 30 min. It was poured into petroleum ether (250 mL) and the cloudy, white liquid decanted from the oily, yellow sludge. This was washed with petroleum ether (150 mL) and the solvent was removed under reduced pressure from the combined organics. The resulting liquid was purified by Kugelröhr distillation to yield the title compound as a clear, colourless liquid (1.3 g, 68%). bp 170-175°C @ 15 mm Hg; ν_{max}/cm^{-1} (thin film) 1641; δ^1H (270 MHz; C_6D_6) 5.69 (1H, tdd, *J* 7, *J* 10, *J* 17, C<u>H</u>=CH_2), 5.01 (2H, m, C<u>H</u>$_2$=CH), 3.65 (1H, ddd, *J* 4, *J* 10, *J* 11, OCH_2), 3.35 (1H, td, *J* 5, *J* 11, OCH_2), 1.98-1.90 (2H, m, CH_2), 1.48-1.18 (4H, m, CH_2), 1.110.83 (3H, m, CH + CH_2), 0.63 (1H, d, *J* 1, CH), 0.30 (9H, s, $(CH_3)_3Si$); $\delta^{13}C$ (67.5 MHz; C_6D_6) 138.71 (CH), 114.70 (CH_2), 84.75 (C), 60.99 (CH_2), 35.50 (CH_2), 31.92 (CH_2), 31.04 (CH), 27.93 (CH_2), 23.93 (CH), 19.80 (CH_2), 1.08 ($(CH_3)_3Si$); *m/z* (EI) 240 {M^+} (7%), 197 (20), 185 (38), 171 (13), 129 (11), 103 (10), 73 (100%); HRMS: *m/z* (CI, NH_4OAc) Found: 241.1628. $C_{13}H_{25}O_2Si$ {[M+H]$^+$} requires 241.1624.

GENERAL IRON(III) CHLORIDE PROCEDURE.

10-Chloromethyl-4-oxabicyclo[5.3.0]decan-3-one 8 (X=Cl): To a stirred solution of 5-(but-3'-enyl)-1-trimethylsilyloxy-2-oxabicyclo[4.1.0] heptane **6** (0.48 g, 2.0 mmol) at 0°C in DMF (40 mL) was

added a solution of anhydrous iron(III) chloride (0.714 g, 4.4 mmol) in DMF (20 mL) over 30 min *via* syringe pump. The lemon yellow solution was stirred at 0°C for 1 h and then allowed to warm to room temperature. It was poured into water (400 mL) and extracted with ethyl acetate (4 x 150 mL). The combined organics were washed with water (200 mL) and brine (200 mL), dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. The crude product was subjected to column chromatography with eluent 20% ethyl acetate in petroleum ether to yield an inseparable mixture of diastereoisomers of the title compound (0.088 g, 22%) as a clear, pale golden oil. The two major diastereoisomers were present in a 1:1 ratio (by ^{13}C NMR spectroscopy) together with traces of other diastereoisomers. ν_{max}/cm^{-1} (thin film) 1734; δ^1H (270 MHz; $CDCl_3$) 4.40-4.10 (2H, m, OCH_2), 3.70-3.35 (2H, m, CH_2Cl), 2.96-1.23 (11H, br m, CH_2 + CH); $\delta^{13}C$ (67.5 MHz; $CDCl_3$) 174.77 (C), 68.93 + 67.92 (OCH_2), 66.81 + 63.56 (CH_2Cl), 47.67 + 46.90 (CH_2), 46.42 + 43.39 (CH), 43.13 + 43.09 (CH), 41.13 + 39.52 (CH), 35.22 + 33.82 (CH_2), 31.48 + 31.00 (CH_2), 27.28 + 26.27 (CH_2); *m/z* (EI) 204 {M^+} (12%, (^{37}Cl)), 202 {M^+} (36, (^{35}Cl)), 167 (100), 153 (6), 138 (13), 125 (38), 109 (40), 93 (41), 81 (84%); HRMS: *m/z* (CI, NH_4OAc) Found: 220.1101. $C_{10}H_{19}ClNO_2$ {$[M+NH_4]^+$} requires 220.1104; (Found: C, 59.31; H, 7.59; Cl, 17.67. $C_{10}H_{15}ClO_2$ requires C, 59.26; H, 7.46; Cl, 17.49%).

Variations to the general procedure: The above reaction was carried out using 2.2 eq. $FeCl_3$ at 60°C and 1.1 eq. $[FeCl_2(DMF)_3][FeCl_4]$ (2.2 eq. in Fe) at 0°C. In both cases the spectral data were consistent with those quoted for the general procedure above.

GENERAL IRON(III) NITRATE PROCEDURE.

10-Methyl-4-oxabicyclo[5.3.0]decan-3-one 8 (X=H): A solution of iron(III) nitrate nonahydrate (1.778 g, 4.4 mmol) in DMF (20 mL) was stirred over 4 Å molecular sieves for 12 h. It was added dropwise over 30 min *via* syringe pump to a stirred solution of 5-(but-3'-enyl)-1-trimethylsilyloxy-2-oxabicyclo[4.1.0] heptane **6** (0.48 g, 2.0 mmol) in DMF (40 mL) at 0°C. The orange/red solution was stirred at 0°C for a further 1 h and then allowed to warm to room temperature. It was poured onto water (400 mL) and extracted with ethyl acetate (4 x 150 mL). The combined organics were washed with water (200 mL) and brine (200 mL), dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. The resultant pale yellow liquid was purified by column chromatography with eluent 20% ethyl acetate in petroleum ether to give an inseparable mixture of diastereoisomers of the title compound (0.205 g, 66%) as a clear, pale golden liquid. The two major diastereoisomers were present in a 1:1 ratio (by ^1H NMR spectroscopy) together with traces of other diastereoisomers. ν_{max}/cm^{-1} (thin film) 1734; δ^1H (270 MHz; $CDCl_3$) 4.38-4.12 (2H, m, OCH_2), 2.89-1.18 (11H, br m, CH_2 + CH), 1.04 (1.25H, d, *J* 6, CH_3 (major, diastereoisomer 1)) 0.97 (0.25H, d, *J* 7, CH_3 (minor, diastereoisomer 3)), 0.96 (0.25H, d, *J* 7, CH_3 (minor, diastereoisomer 4)), 0.83 (1.25H, d, *J* 7, CH_3 (major, diastereoisomer 2)); $\delta^{13}C$ (67.5 MHz; $CDCl_3$) Major diastereoisomers: 175.72 + 174.34 (C), 69.08 + 67.05 (OCH_2), 44.87 + 44.75 (CH), 43.78 + 41.06 (CH), 36.03 + 35.94 (CH), 35.89 + 34.20 (CH_2), 33.77 + 31.92 (CH_2), 31.00 + 30.75 (CH_2), 29.44 + 29.26 (CH_2), 19.36 + 16.68 (CH_3); *m/z* (EI) 168 {M^+} (52%), 166 (17), 140 (21), 138 (23), 124 (19), 108 (86), 95 (94), 94 (76), 81 (100%); HRMS: *m/z* (CI, NH_4OAc) Found: 186.1450. $C_{10}H_{20}NO_2$ {$[M+NH_4]^+$} requires 186.1494; (Found: C, 71.16; H, 9.47. $C_{10}H_{16}O_2$ requires C, 71.39; H, 9.59%).

4-(But-3'-enyl)-2-trimethylsilyloxy-4,5-dihydrofuran 10 (R=TMS): Following the general conjugate addition procedure described above, using magnesium turnings (0.434 g, 17.8 mmol), THF (24 mL), 4-bromo-1-butene (14.3 mmol, 1.44 mL), HMPA (28.5 mmol, 4.97 mL), CuI (0.226 g, 1.2 mmol), 2(5*H*)-furanone **9** (1.0 g, 11.9 mmol) and chlorotrimethylsilane (28.5 mmol, 3.62 mL), to yield the title compound as a clear, colourless liquid (1.708 g, 68%). bp 170-175°C @ 15 mm Hg; ν_{max}/cm^{-1} (thin film) 1781, 1684, 1642; δ^1H (270 MHz; C_6D_6) 5.67 (1H, tdd, *J* 7, *J* 10, *J* 17, C<u>H</u>=CH_2), 4.99-4.91 (2H, m, C<u>H</u>$_2$=CH), 4.13 (1H, t, *J* 9, OCH_2), 3.87 (1H, d, *J* 2, CH=C), 3.71 (1H, dd, *J* 6, *J* 9, OCH_2), 2.80-2.68 (1H, m, CH), 1.95-1.81 (2H, m, CH_2), 1.37-1.24 (2H, m, CH_2), 0.17 (9H, s $(CH_3)_3Si$); $\delta^{13}C$ (67.5 MHz; C_6D_6) 159.30 (C) 138.76 (CH), 114.58 (CH_2), 73.54 (OCH_2), 73.43 (CH), 41.03 (CH), 36.11 (CH_2), 31.54 (CH_2), -0.14 ($(CH_3)_3Si$); *m/z* (EI) 213 {[M+H]$^+$} (14%), 169 (100), 129 (23), 81 (41), 79 (22), 75 (92), 73 (65%); (Found: C, 61.92; H, 9.34. $C_{11}H_{20}O_2Si$ requires C, 62.21; H, 9.49%).

4-(But-3'-enyl)-2-(*tert.*-butyldimethylsilyloxy)-4,5-dihydrofuran 10 (R=TBDMS): Following the general conjugate addition procedure described above, using magnesium turnings (4.34 g, 17.8 mmol), THF (24 mL), 4-bromo-1-butene (14.3 mmol, 1.44 mL), HMPA (28.5 mmol, 4.97 mL), CuI (0.226 g, 1.2 mmol), 2(5*H*)-furanone **9** (1.0 g, 11.9 mmol) and chloro-*tert.*-butyldimethylsilane (2.148 g, 14.3 mmol), to yield the title compound as a clear, colourless liquid (1.45 g, 48%). bp 125-130°C @ 0.1 mbar; ν_{max}/cm^{-1} (thin film) 1781, 1683, 1641; δ^1H (270 MHz; C_6D_6) 5.67 (1H, tdd, *J* 7, *J* 10, *J* 17, C<u>H</u>=CH_2), 5.00-4.90 (2H, m, C<u>H</u>$_2$=CH), 4.23 (1H, dd, *J* 9, *J* 9, OCH_2), 3.88 (1H, d, *J* 2, CH=C), 3.70 (1H, dd, *J* 6, *J* 9, OCH_2), 2.77-2.70 (1H, m, CH), 1.90-1.80 (2H, m, CH_2), 1.47-1.20 (2H, m, CH_2), 0.96 (9H, s, $(CH_3)_3CSi$), 0.20 (6H, s, $(CH_3)_2Si$); $\delta^{13}C$ (67.5 MHz; C_6D_6) 159.46 (C), 138.76 (CH), 114.58 (CH_2), 73.77 (CH), 73.50 (CH_2), 41.03 (CH), 36.09 (CH_2), 31.58 (CH_2), 25.67 ($(\underline{C}H_3)_3CSi$), 18.28 ($(CH_3)_3\underline{C}Si$), -4.59 ($(CH_3)_2Si$); *m/z* (EI) 254 {[M+H]$^+$} (2%), 169 (36), 131 (7), 81 (11), 75 (100%); It was not possible to obtain an accurate elemental analysis due to the lability of this compound.

4-(But-3'-enyl)-1-(*tert.*-butyldimethylsilyloxy)-2-oxabicyclo[3.1.0]hexane 11: To a stirred solution of freshly distilled 4-(but-3'-enyl)-2-(*tert.*-butyldimethylsilyloxy)-4,5-dihydrofuran **10** (R=TBDMS) (0.996 g, 3.9 mmol) in diethyl ether (16 mL) was added diethylzinc (11.7 mmol, 11.7 mL) followed by diiodomethane (11.7 mmol, 0.94 mL). The reaction mixture was heated to reflux for 2 h. After this time TLC showed some product formation together with some decomposition beginning to occur. It was allowed to cool to room temperature and worked up following the general cyclopropanation procedure to yield the title compound as a clear, colourless liquid (0.467 g, 45%). bp 130-135°C @ 0.3 mbar; ν_{max}/cm^{-1} (thin film) 1641; δ^1H (270 MHz; C_6D_6) 5.71-5.56 (1H, m, C<u>H</u>=CH_2), 4.97-4.89 (2H, m, C<u>H</u>$_2$=CH), 3.61 (1H, dd, *J* 3, *J* 9, OCH_2), 3.34 (1H, dd, *J* 7, *J* 9, OCH_2), 1.83 (2H, apparent q, *J* 7 CH_2), 1.68 (1H, apparent dq, *J* 3, *J* 7, CH), 1.44-1.27 (2H, m, CH_2), 1.21 (1H, dd, *J* 5, *J* 9, *exo*-CH_2), 1.02 (4.5H, s, $(CH_3)_3CSi$), 1.01 (4.5H, s, $(CH_3)_3CSi$), 0.99-0.87 (2H, m, CH-5 + *endo*-CH_2), 0.28 (3H, s, $(CH_3)_2Si$), 0.26 (3H, s, $(CH_3)_2Si$); $\delta^{13}C$ (67.5 MHz; C_6D_6) 138.46 (CH), 114.78 (CH_2), 94.65 (C), 71.92 (OCH_2), 41.87 (CH), 33.79 (CH_2), 32.23 (CH_2), 25.94 ($(\underline{C}H_3)_3CSi$), 25.56 (CH), 18.01 (CH_2), 13.20 ($(CH_3)_3\underline{C}Si$), -3.55 ($(CH_3)_2Si$), -3.73 ($(CH_3)_2Si$); *m/z* (EI) 268 {M$^+$} (13%), 211 (100), 169 (16), 129 (28), 73 (25%); HRMS: *m/z* (CI, NH_4OAc) Found: 286.2202. $C_{15}H_{32}NO_2Si$ {[M+NH_4]$^+$} requires 286.2202; (Found: C, 66.87; H, 10.60. $C_{15}H_{28}O_2Si$ requires C, 67.11; H, 10.51%).

1-Ethoxy-1-trimethylsilyloxy-1,6-heptadiene 12: Following the general conjugate addition procedure described above, using magnesium turnings (1.582 g, 65 mmol), THF (120 mL), 4-bromo-1-butene (60 mmol, 6.1 mL), HMPA (120 mmol, 20.9 mL), CuI (0.95 g, 5.0 mmol), ethyl acrylate (5.0 g, 50 mmol) and chlorotrimethylsilane (120 mmol, 15.25 mL) to yield the title compound as a clear, colourless liquid (11.062 g, 97%). bp 155-160°C @ 15 mm Hg; ν_{max}/cm^{-1} (thin film) 1740, 1680, 1641; δ^1H (270 MHz; C_6D_6) (Two geometrical isomers were present in a 2:1 ratio, assigned to E (major) and Z (minor) at the ketene acetal.) 5.87 (1H, tdd, *J* 7, *J* 10, *J* 17, C<u>H</u>=CH$_2$), 5.11-4.95 (2H, m, C<u>H$_2$</u>=CH), 3.87 (0.33H, q, *J* 7, CH=C (minor)), 3.76 (0.66H, q, *J* 7, CH=C (major)), 3.45 (0.66H, q, *J* 7, OC<u>H$_2$</u>CH$_3$ (minor)), 3.40 (1.33H, q, *J* 7, OC<u>H$_2$</u>CH$_3$ (major)), 2.27-2.05 (4H, m, CH$_2$), 1.54 (2H, m, *J* 7, CH$_2$), 1.08 (1H, t, *J* 7, OCH$_2$C<u>H$_3$</u> (minor)), 0.99 (2H, t, *J* 7, OCH$_2$C<u>H$_3$</u> (major)), 0.23 (6H, s, (CH$_3$)$_3$Si (major)), 0.15 (3H, s, (CH$_3$)$_3$Si (minor)); $\delta^{13}C$ (67.5 MHz; C_6D_6) Major isomer: 156.19 (C), 139.39 (<u>C</u>H=CH$_2$), 114.38 (<u>C</u>H$_2$=CH), 76.20 (<u>C</u>H=C), 62.77 (O<u>C</u>H$_2$CH$_3$), 33.79 (CH$_2$), 30.81 (CH$_2$), 24.73 (CH$_2$), 14.42 (OCH$_2$<u>C</u>H$_3$), 0.55 ((CH$_3$)$_3$Si); Minor isomer: 153.52 (C), 139.30 (<u>C</u>H=CH$_2$), 114.38 (<u>C</u>H$_2$=CH), 85.92 (<u>C</u>H=C), 62.77 (O<u>C</u>H$_2$CH$_3$), 33.79 (CH$_2$), 30.59 (CH$_2$), 24.64 (CH$_2$), 15.05 (OCH$_2$<u>C</u>H$_3$), -0.26 ((CH$_3$)$_3$Si); *m/z* (EI) 229 {[M+H]$^+$} (4%), 185 (28), 156 (15), 147 (24), 117 (19), 111 (53), 110 (100), 101 (18), 88 (90%); (Found: C, 63.38; H, 10.51. $C_{12}H_{24}O_2Si$ requires C, 63.10; H, 10.59%).

1-Ethoxy-2-(pent-4'-enyl)-1-(trimethylsilyloxy)cyclopropane 13: Following the general cyclopropanation procedure described above, using 1-ethoxy-1-trimethylsilyloxy-1,6-heptadiene **12** (11.0 g, 48 mmol), diethyl ether (192 mL), diethylzinc (96 mmol, 96 mL) and diiodomethane (96 mmol, 7.72 mL) to yield the title compound as a clear, colourless liquid (7.805 g, 66%). bp 160-170°C @ 15 mm Hg; ν_{max}/cm^{-1} (thin film) 1641, 1450; δ^1H (270 MHz; C_6D_6) (Two diastereoisomers were present in a 2:1 ratio.) 5.87-5.70 (1H, m, C<u>H</u>=CH$_2$), 5.08-4.96 (2H, m, C<u>H$_2$</u>=CH), 3.78-3.66 (1H, m, OC<u>H$_2$</u>CH$_3$), 3.56-3.38 (1H, m, OC<u>H$_2$</u>CH$_3$), 2.07-1.97, (2H, m, CH$_2$), 1.66-1.23 (4H, br m, CH$_2$), 1.12-1.06 (3H, m, OCH$_2$C<u>H$_3$</u>), 1.04-0.80 (2H, br m, *exo*-CH$_2$ + CH), 0.38 (1H, m, *J* 11, *J* 6, *endo*-CH$_2$), 0.23 (6H, s, (CH$_3$)$_3$Si (major)), 0.22 (3H, s, (CH$_3$)$_3$Si (minor)); $\delta^{13}C$ (67.5 MHz; C_6D_6) Major diastereoisomer: 139.12 (<u>C</u>H=CH$_2$), 114.54 (<u>C</u>H$_2$=CH), 89.26 (C), 61.44 (O<u>C</u>H$_2$CH$_3$), 33.99 (CH$_2$), 29.06 (CH$_2$), 28.54 (CH$_2$), 23.98 (CH), 18.62 (CH$_2$), 15.41 (OCH$_2$<u>C</u>H$_3$), 0.83 ((CH$_3$)$_3$Si); Minor diastereoisomer: 139.03 (<u>C</u>H=CH$_2$), 114.54 (<u>C</u>H$_2$=CH), 89.06 (C), 62.04 (O<u>C</u>H$_2$CH$_3$), 34.04 (CH$_2$), 28.94 (CH$_2$), 28.38 (CH$_2$), 26.98 (CH), 20.35 (CH$_2$), 15.45 (OCH$_2$<u>C</u>H$_3$), 0.90 ((CH$_3$)$_3$Si); *m/z* (EI) 242 {M$^+$} (9%), 199 (27), 187 (12), 173 (26), 129 (16), 124 (22), 119 (17), 117 (26), 103 (18), 81 (25), 75 (29), 73 (100%); HRMS: *m/z* (CI, NH_4OAc) Found: 243.1774. $C_{13}H_{27}SiO_2$ {[M+H]$^+$} requires 243.1780; (Found: C, 64.32; H, 10.93. $C_{13}H_{26}SiO_2$ requires C, 64.41; H, 10.81%).

(2-Chloromethyl)cyclopentane-1-acetic acid ethyl ester 15a/b (X=Cl): Following the general iron(III) chloride procedure, in which a solution of iron(III) chloride (0.714 g, 4.4 mmol) in DMF (20 mL) is added to a solution of 1-ethoxy-2-(pent-4'-enyl)-1-(trimethylsilyloxy)cyclopropane **13** (0.485 g, 2.0 mmol), in DMF (40 mL). The crude product was subjected to column chromatography with eluent 2% diethyl ether in petroleum ether to yield a clear, colourless liqiud (0.324 g, 79%) which proved to be an inseparable mixture of the title compound and 3-chloro-7-octenoic acid ethyl ester (**16**, X=Cl) in a ratio of 1:2.5. (^1H NMR spectroscopy indicated that the diastereoisomers **15a** and **15b** were in a ratio of 8:1.) ν_{max}/cm^{-1} (thin film)

1734, 1641; δ^1H (400 MHz; $CDCl_3$) **15a/b** (X=Cl): 4.14 (2H, m, $OC\underline{H}_2CH_3$), 3.59 (0.17H, dd, *J* 7, *J* 11, CH_2Cl (minor)), 3.51 (0.83H, dd, *J* 7, *J* 11, CH_2Cl (major)), 3.44 (0.17H, dd, *J* 8, *J* 11, CH_2Cl (minor)), 3.39 (0.83H, dd, *J* 8, *J* 11, CH_2Cl (major)), 2.48 (1H, m, CH), 2.45 (1H, m, CH_2-C), 2.35 (1H, m, CH), 2.17 (1H, m, CH_2-C), 1.86 (1H, m, CH_2), 1.83 (1H, m, CH_2), 1.71-1.60 (2H, m, CH_2), 1.50 (1H, m, CH_2), 1.38 (1H, m, CH_2), 1.26 (3H, t, *J* 7, $OCH_2C\underline{H}_3$); **16** (X=Cl): 5.77 (1H, tdd, *J* 7, *J* 10, *J* 17, $C\underline{H}$=CH_2), 5.08-4.94 (2H, m, $C\underline{H}_2$=CH), 4.29 (1H, m, CH-Cl), 4.17 (2H, q, *J* 11, $OC\underline{H}_2CH_3$), 2.75 (1H, d, *J* 2, CH_2-C), 2.72 (1H, d, *J* 1, CH_2-C), 2.08 (2H, m, CH_2), 1.76 (2H, m, CH_2), 1.64 (1H, m, CH_2), 1.53 (1H, m, CH_2), 1.26 (3H, t, *J* 7, $OCH_2C\underline{H}_3$); δ^{13}C (100 MHz; $CDCl_3$) **15a/b** (X=Cl): 173.06 (C), 60.40 ($O\underline{C}H_2CH_3$), 45.82 (CH_2Cl), 44.55 (CH), 38.38 (CH), 34.54 (CH_2-C), 30.95 (CH_2), 28.97 (CH_2), 22.50 (CH_2), 14.16 ($OCH_2\underline{C}H_3$); **16** (X=Cl): 170.17 (C), 138.02 ($\underline{C}H$=CH_2), 115.08 ($\underline{C}H_2$=CH), 60.86 ($O\underline{C}H_2CH_3$), 57.81 (CH-Cl), 43.70 ($\underline{C}H_2$-C), 37.32 (CH_2), 32.94 (CH_2), 25.47 (CH_2), 14.23 ($OCH_2\underline{C}H_3$); **15a/b +16** *m/z* (EI) 206 {M^+} (3%, (^{37}Cl)), 204 {M^+} (9, (^{35}Cl)), 169 (42), 168 (47), 161 (15), 159 (41), 158 (11), 123 (27), 122 (17), 101 (18), 95 (100), 94 (97), 88 (62), 81 (50), 80 (45%); (Found: C, 58.98; H, 8.40; Cl, 17.45. $C_{10}H_{17}ClO_2$ requires C, 58.68; H, 8.37; Cl, 17.32%).

Variations to the general procedure: The above reaction was carried out using 2.2 eq. $FeCl_3$ and 1.1 eq. $[FeCl_2(DMF)_3][FeCl_4]$ (2.2 eq. in Fe), at various temperatures up to 60°C, with 0.5 h or 5 h addition times of the iron(III) solution (Table 1). In all cases the spectral data were consistent with those quoted for the general procedure above.

2-Methylcyclopentane-1-acetic acid ethyl ester 15a/b (X=H): Following the general iron(III) nitrate procedure described above, in which a solution of iron(III) nitrate nonahydrate (1.778 g, 4.4 mmol) in DMF (20 mL) is added to a solution of 1-ethoxy-2-(pent-4'-enyl)-1-(trimethylsilyloxy)cyclopropane **13** (0.485 g, 2.0 mmol) in DMF (40 mL). The resulting pale yellow liquid was purified by column chromatography with eluent 2% diethyl ether in petroleum ether to yield the title compound (0.184 g, 54%) as a clear, colourless liquid. Two diastereoisomerswere present in a 9:1 ratio by ^{1}H NMR spectroscopy. ν_{max}/cm^{-1} (thin film) 1734; δ^1H (270 MHz; $CDCl_3$) 4.13 (2H, q, *J* 7, $OC\underline{H}_2CH_3$), 2.60-2.03 (4H, m, CH_2 + CH), 1.85-1.10 (6H, br m, ring-CH_2) 1.26 (3H, t, *J* 7, $OCH_2C\underline{H}_3$), 0.97 (0.36H, d, *J* 6, CH_3 (minor)), 0.82 (2.64H, d, *J* 6, CH_3 (major)); δ^{13}C (67.5 MHz; $CDCl_3$) Major diastereoisomer: 173.89 (C), 60.09 ($O\underline{C}H_2CH_3$), 39.62 (CH), 36.03 (CH), 35.65 (CH_2), 33.10 (CH_2), 30.01 (CH_2), 22.52 (CH_2), 15.13 ($OCH_2\underline{C}H_3$), 14.25 (CH_3); Minor diastereoisomer: 173.89 (C), 60.09 ($O\underline{C}H_2CH_3$), 44.02 (CH), 40.46 (CH), 39.30 (CH_2), 34.39 (CH_2), 32.32 (CH_2), 23.17 (CH_2), 17.91 ($OCH_2\underline{C}H_3$), 17.04 (CH_3); *m/z* (EI) 170 {M^+} (31%), 142 (8), 127 (23), 125 (39), 89 (38), 88 (100%); (Found: C, 70.20; H, 10.63. $C_{10}H_{18}O_2$ requires C, 70.55; H, 10.66%).

Reactions of 13 in the presence of external radical traps: The reaction was repeated as above using ferric nitrate in the presence of a number of external radical traps.

2-Methylcyclopentane-1-acetic acid ethyl ester 15a/b (X=H): As for **15a/b** (X=H) above, with a solution of iron(III) nitrate nonahydrate (1.778 g, 4.4 mmol) in DMF (20 mL) added to a solution of 1-ethoxy-2-(pent-4'-enyl)-1-(trimethylsilyloxy)cyclopropane **13** (0.485 g, 2.0 mmol) and 1,4-cyclohexadiene

(6.0 mmol, 0.41 mL) in DMF (40 mL) to afford the title compound (0.267 g, 76%) as a clear, colourless liquid. The spectral data were consistent with those previously described.

(2-Phenylsulfanylmethyl)cyclopentane-1-acetic acid ethyl ester 15a/b (X=SPh): As for **15a/b** (X=H) above, with a solution of iron(III) nitrate nonahydrate (1.778 g, 4.4 mmol) in DMF (20 mL) added to a solution of 1-ethoxy-2-(pent-4'-enyl)-1-(trimethylsilyloxy)cyclopropane **13** (0.485 g, 2.0 mmol) and diphenyldisulfide (0.655 g, 3.0 mmol) in DMF (40 mL) to yield the title compound (0.369 g, 66%) as a clear, colourless liquid. Two diastereoisomers were present in a 9:1 ratio by ^{1}H NMR spectroscopy. ν_{max}/cm^{-1} (thin film) 1734, 1585, 1481, 1440; δ^1H (270 MHz; $CDCl_3$) 7.34-7.13 (5H, br m, Ph), 4.13 (2H, q, *J* 7, $OC\underline{H}_2CH_3$), 3.12 (0.1H, dd, *J* 6, *J* 12, $C\underline{H}_2SPh$ (minor)), 2.98 (0.9H, dd, *J* 6, *J* 12, $C\underline{H}_2SPh$ (major)), 2,80 (0.1H, dd, *J* 9, *J* 12, $C\underline{H}_2SPh$ (minor)), 2.72 (0.9H, dd, *J* 9, *J* 12, CH_2SPh (major)), 2.54-2.41 (2H, m, CH + CH_2-C), 2.28-2.13 (2H, m, CH + CH_2-C), 1.98-1.07 (6H, br m, ring-CH_2), 1.25 (3H, t, *J* 7, $OCH_2C\underline{H}_3$); δ^{13}C (67.5 MHz; $CDCl_3$) Major diastereoisomer: 173.26 (C), 136.39 (C-Ph), 128.93 (Ph x 2), 128.82 (Ph x 2), 125.75 (Ph), 60.31 ($O\underline{C}H_2CH_3$), 41.37 (CH), 38.89 (CH), 34.84 ($\underline{C}H_2SPh$), 34.77 ($\underline{C}H_2$-C), 30.66 (CH_2), 30.17 (CH_2), 22.59 (CH_2), 14.22 ($OCH_2\underline{C}H_3$); Minor diastereoisomer: 173.26 (C), 136.39 (C-Ph), 128.93 (Ph x 2), 128.82 (Ph x 2), 125.75 (Ph), 60.31 ($O\underline{C}H_2CH_3$), 44.68 (CH), 41.91 (CH), 39.65 ($\underline{C}H_2SPh$), 38.74 ($\underline{C}H_2$-C), 32.47 (CH_2), 32.01 (CH_2), 23.65 (CH_2), 14.22 ($OCH_2\underline{C}H_3$); *m/z* (EI) 278 {M^+} (100%), 233 (30), 169 (70), 123 (39), 110 (44), 109 (20), 95 (67), 81 (56%); (Found: C, 68.87; H, 7.98; S, 11.12. $C_{16}H_{22}O_2S$ requires C, 69.03; H, 7.97; S, 11.51%).

(2-Chloromethyl)cyclopentane-1-acetic acid ethyl ester 15a/b (X=Cl): As for **15a/b** (X=H) above, with a solution of iron(III) nitrate nonahydrate (1.778 g, 4.4 mmol) in DMF (20 mL) added to a solution of 1-ethoxy-2-(pent-4'-enyl)-1-(trimethylsilyloxy)cyclopropane **13** (0.485 g, 2.0 mmol) and *N*-chlorosuccinimide (0.32 g, 2.4 mmol) in DMF (40 mL) to yield a clear, colourless liqiud (0.31 g, 76%). This proved to be a mixture of the title compound and 3-chloro-7-octenoic acid ethyl ester **16** (X=Cl) in the ratio 9:1. The spectral data were consistent with those previously described.

Attempted preparation of (2-phenylsulfanylmethyl)cyclopentane-1-acetic acid ethyl ester 15a/b (X=SPh): Following the iron(III) chloride procedure for **15a/b** (X=Cl) above, with a solution of iron(III) chloride (0.714 g, 4.4 mmol) in DMF (20 mL) added to a solution of 1-ethoxy-2-(pent-4'-enyl)-1-(trimethylsilyloxy)cyclopropane **13** (0.485 g, 2.0 mmol) and diphenyldisulfide (0.655 g, 3.0 mmol) in DMF (40 mL) to yield a clear, colourless liqiud (0.276 g, 67%). This proved to be a mixture of (2-chloromethyl)cyclopentane-1-acetic acid ethyl ester **15** (X=Cl) and 3-chloro-7-octenoic acid ethyl ester **16** (X=Cl) in the ratio 1:1.67. The spectral characterisations were consistent with those previously described.

(2-Phenylsulfonylmethyl)cyclopentane-1-acetic acid ethyl ester 15a/b (X=SO_2Ph): To a stirred solution of (2-phenylsulfanylmethyl)cyclopentane-1-acetic acid ethyl ester **15a/b** (X=SPh) (0.1 g, 0.36 mmol) in methanol (5 mL) at room temperature was added dropwise over 5 min a solution of Oxone® (0.68 g, 1.1 mmol) in water (5 mL). The immediate mildly exothermic reaction produced a white precipitate. The reaction mixture was stirred at room temperature for 3 h. It was poured onto water (100 mL) and extracted with chloroform (2 x 75 mL). The combined organics were dried over $MgSO_4$, filtered and the solvent

removed under reduced pressure to yield the title compound (0.11 g, 99%) as a viscous, colourless oil. Two diastereoisomers were present in a 9:1 ratio by ^{1}H NMR spectroscopy. ν_{max}/cm^{-1} (thin film) 1735, 1626, 1526, 1308, 1143; δ^1H (270 MHz; $CDCl_3$) 7.93 (2H, m, Ph), 7.70-7.55 (3H, m, Ph), 4.09 (2H, q, *J* 7, $OC\underline{H}_2CH_3$), 3.26 (0.1H, dd, *J* 4, *J* 14, $C\underline{H}_2SO_2Ph$ (minor)) 3.20 (0.9H, dd, *J* 4, *J* 14, $C\underline{H}_2SO_2Ph$ (major)), 3.02 (0.1H, dd, *J* 9, *J* 14, $C\underline{H}_2SO_2Ph$ (minor)), 2.96 (0.9H, dd, *J* 9, *J* 14, $C\underline{H}_2SO_2Ph$ (major)), 2.51-2.39 (2H, br m, CH), 2.25 (1H, dd, *J* 6, *J* 15, CH_2-C), 2.08 (1H, dd, *J* 9, *J* 15, CH_2-C), 1.93-1.32 (6H, br m, ring-CH_2), 1.23 (3H, t, *J* 7, $OCH_2C\underline{H}_3$); δ^{13}C (270 MHz; $CDCl_3$) Major diastereoisomer: 172.60 (C), 142.15 (C-Ph), 133.64 (Ph x 2), 129.29 (Ph), 127.91 (Ph x 2), 60.47 ($\underline{C}H_2SO_2Ph$), 57.14 ($O\underline{C}H_2CH_3$), 39.16 (CH), 36.78 (CH), 34.84 ($\underline{C}H_2$-C), 30.42 (CH_2), 29.83 (CH_2), 21.98 (CH_2), 14.18 ($OCH_2\underline{C}H_3$); Minor diastereoisomer: 172.60 (C), 142.15 (C-Ph), 133.64 (Ph x 2), 129.29 (Ph), 127.91 (Ph x 2), 61.29 ($\underline{C}H_2SO_2Ph$), 57.14 ($O\underline{C}H_2CH_3$), 42.48 (CH), 39.53 (CH), 38.86 (CH_2), 34.04 (CH_2), 32.88 (CH_2), 23.63 (CH_2), 14.18 ($OCH_2\underline{C}H_3$); *m/z* (EI) 310 {M^+} (4%), 265 (21), 169 (100), 143 (11), 123 (49), 95 (82), 81 (59%); HRMS; *m/z* (CI, NH_4OAc) Found: 328.1579. $C_{16}H_{26}NO_4S$ {$[M+NH_4]^+$} requires 328.1583; (Found: C, 61.59; H, 7.16; S, 10.02. $C_{16}H_{22}O_4S$ requires C, 61.91; H, 7.14; S, 10.33%). Preparative HPLC on a portion of this material, using a Gilson Prep. 239 apparatus with CN-SB3-13753 column and eluent 1% ethanol in heptane, yielded two isomers; **15a** (X=SO_2Ph) (9 mg) and **15b** (X=SO_2Ph) (1 mg). Coupling constants were as previously quoted for the mixture of diastereoisomers. **15a** (X=SO_2Ph): δ^1H (400 MHz; $CDCl_3$) 7.93 (2H, m, Ph), 7.64 (1H, m, Ph), 7.56 (2H, m, Ph), 4.09 (2H, q, $OC\underline{H}_2CH_3$), 3.20 (1H, dd, $C\underline{H}_2SO_2Ph$-α), 2.96 (1H, dd, $C\underline{H}_2SO_2Ph$-β), 2.51-2.39 (2H, br m, CH), 2.25 (1H, dd, $C\underline{H}_2$-C-α), 2.08 (1H, dd, $C\underline{H}_2$-C-β), 1.93-1.32 (6H, ring-CH_2), 1.23 (3H, t, $OCH_2C\underline{H}_3$); nOe (400MHz; $CDCl_3$) $C\underline{H}_2SO_2Ph$-α to $C\underline{H}_2$-C-β (5.5%), $C\underline{H}_2SO_2Ph$-β to $C\underline{H}_2$-C-β (4.0%), $C\underline{H}_2$-C-α to $C\underline{H}_2SO_2Ph$-α (6.0%) (confirms *cis* stereochemistry). **15b** (X=SO_2Ph): δ^1H (400 MHz; $CDCl_3$) 7.93 (2H, m, Ph), 7.64 (1H, m, Ph), 7.56 (2H, m, Ph), 4.09 (2H, q, $OC\underline{H}_2CH_3$), 3.25 (1H, dd, $C\underline{H}_2SO_2Ph$-α), 3.01 (1H, dd, $C\underline{H}_2SO_2Ph$-β), 2.40 (1H, dd, $C\underline{H}_2$-C-α), 2.19 (1H, dd, $C\underline{H}_2$-C-β), 1.93-1.32 (8H, CH + ring-CH_2), 1.23 (3H, t, $OCH_2C\underline{H}_3$); nOe (400MHz; $CDCl_3$) showed no peak enhancement from irradiation at either $C\underline{H}_2SO_2Ph$-α or $C\underline{H}_2SO_2Ph$-β (confirms *trans* stereochemistry).

1-Ethoxy-2-(1',5'-dimethylhex-4'-enyl)-1-(trimethylsilyloxy)cyclopropane 22: To a stirred solution of diisopropylamine (10.2 mmol, 1.3 mL) in THF (20 mL) at -78°C was added ^{n}butyllithium (2.5 M in hexanes) (10.2 mmol, 4.1 mL). The solution was allowed to warm to room temperature for 15 min and was then re-cooled to -78°C. A solution of (±)-ethyl citronellate **20** (2.0 g, 10.2 mmol) in THF (5 mL) was added dropwise and the mixture stirred at -78°C for 30 min before dropwise addition of chlorotrimethylsilane (10.2 mmol, 1.3 mL). After a further 1 h at -78°C the mixture was allowed to warm to room temperature. It was stirred for 2 h and and then poured onto cold (-78°C) petroleum ether (500 mL). The resulting suspension was filtered through Celite® and the solvent removed under reduced pressure. The residual yellow oil was purified by Kugelröhr distillation (125°C @ 10 mm Hg) to yield **1-ethoxy-3,7-dimethyl-1-trimethyl silyloxy-1,6-octadiene 21** as a clear, colourless oil (2.39 g, 87%). Due to the lability of **21** no spectroscopic data was obtained. This compound was immediately subjected to the general cyclopropanation conditions using **21** (2.48 g, 9.2 mmol), diethyl ether (20 mL), diiodomethane (20 mmol, 20mL) and diiodomethane (20 mmol, 1.61 mL). The resultant crude product, obtained as a yellow oil, was purified by column chroatography with eluent 10% ethyl acetate in petroleum ether to yield the title compound as a clear,

colourless oil (2.32 g, 82%). Rigorous assignment of spectroscopic data was impossible due to the complex mixture of diastereoisomers obtained. ν_{max}/cm^{-1} (thin film) 1653; δ^1H (270 MHz; C_6D_6) 5.23-5.10 (1H, m), 3.79-3.73 (1H, m), 3.46-3.39 (1H, m), 2.04-1.98 (2H, m), 1.68-1.56 (6H, m), 1.48-1.15 (5H, m), 1.13-0.68 (6H, m), 0.53-0.38 (1H, m), 0.14 (9H, m); $\delta^{13}C$ (68.5 MHz; C_6D_6) 131.61 + 131.45 + 131.24 + 131.12 (C), 124.82 + 124.73 + 124.36 + 124.27 (CH), 89.91 + 89.62 + 89.45 + 89.14 (C), 62.40 + 62.28 + 61.75 + 61.67 (CH_2), 38.26 + 38.13 + 37.84 + 37.67 (CH), 38.28 + 38.15 + 38.08 + 37.96 (CH_2), 34.56 + 34.48 + 34.43 + 34.38 (CH_2), 29.94 + 29.83 + 29.72 (CH), 26.24 + 26.12 + 25.92 + 25.83 + 25.67 (CH_2), 20.67 + 20.35 + 20.13 (CH_3), 16.45 + 16.36 + 16.23 + 15.98 + 15.78 + 15.45 (CH_3), 1.13 + 1.08 + 0.87 (CH_3); *m/z* (EI) 284 {M^+} (11%), 173 (76), 151 (5), 129 (17), 109 (16), 73 (100%).

5-Methyl-2-(prop-2'-enyl)cyclopentane-1-acetic acid ethyl ester 24: A solution of iron(III) nitrate nonahydrate (1.43 g, 3.52 mmol) in DMF (10 mL) was stirred at room temperature over 4Å molecular sieves for 18 hours. A solution of **22** (0.5 g, 1.76 mmol) and 1,4-cyclohexadiene (3.52 mmol, 0.34 mL) in DMF (10 mL) was added dropwise at room temperature over 2 h. The solution was then stirred for a further 1 h before water (200 mL) was added. The resulting suspension was extracted with diethyl ether (3 x 200 mL). The combined organics were washed with water (2 x 150 mL), dried ($MgSO_4$), filtered and solvent removed under reduced pressure to give a colourless oil. This was purified by column chromatography with eluent 5% ethyl acetate in petroleum ether to yield a clear, colourless oil (0.196 g, 53%). Rigorous assignment of spectroscopic data was impossible due to the complex mixture of diastereoisomers obtained. ν_{max}/cm^{-1} (thin film) 1734, 1647; δ^1H (270 MHz; C_6D_6) 4.75-4.62 (2H, m), 4.13-4.05 (2H, m), 2.29-1.80 (5H, m), 1.70-1.48 (4H, m), 1.24-1.18 (3H, m), 0.98-0.95 (3H, m), 0.89-0.81 (3H, m); $\delta^{13}C$ (68.5 MHz; C_6D_6) 173.69 + 172.90 (C), 124.19 + 123.52 (C), 111.12 + 110.84 + 109.72 + 108.73 (CH_2), 59.95 + 59.87 (CH_2), 46.74 + 46.33 + 46.06 (CH), 44.82 + 44.67 + 44.51 (CH), 38.83 + 38.69 + 38.30 (CH), 37.65 + 37.04 + 36.66 (CH_2), 32.98 + 32.68 + 32.51 (CH_2), 31.27 + 31.04 + 30.81 (CH_2), 21.78 + 21.21 + 20.72 + 20.21 + 20.11 (CH_3), 14.14 + 14.05 + 13.79 (CH_3); *m/z* (EI) 210 {M^+} (26%), 167 (100), 136 (20), 123 (38), 107 (54), 93 (60), 81 (46), 69 (35%); (Found: C, 74.14; H, 10.60. $C_{13}H_{22}O_2$ requires C, 74.30; H, 10.50%).

1-Ethoxy-2-(1'-phenylpent-4'-enyl)-1-(trimethylsilyloxy)cyclopropane 28 (R=Ph): Following the general conjugate addition procedure described above, using magnesium turnings (0.36 g, 16.5 mmol), THF (30 mL), 4-bromo-1-butene (13.2 mmol, 1.34 mL), HMPA (26.4 mmol, 4.78 mL), CuI (0.26 g, 1.37 mmol), ethyl cinnamate **25** (R=Ph) (11.0 mmol, 1.91 mL) and chlorotrimethylsilane (26.4 mmol, 3.35 mL) to give a colourless oil. This was purified by Kugelröhr distillation (125°C @ 1 mm Hg) to yield **1-ethoxy-3-phenyl-1-trimethylsilyloxy-1,6-heptadiene 27** (R=Ph) as a clear, colourless oil (2.79 g, 83%). This product was carried straight through to the preparation of **28** (R=Ph). Following the general cyclopropanation procedure, using **27** (R=Ph) (2.83 g, 9.2 mmol), diethyl ether (20 mL), diethylzinc (18.3 mmol, 18.3 mL) and diiodomethane (18.3 mmol, 1.48 mL) to give a yellow oil. This was purified by column chromatography with eluent 10% ethyl acetate in petroleum ether to yield the title compound as a clear, colourless oil (2.6 g, 88%). Rigorous assignment of spectroscopic data was impossible due to the complex mixture of diastereoisomers obtained. ν_{max}/cm^{-1} (thin film) 1640, 1603; δ^1H (270 MHz; C_6D_6) 7.26-7.13 (5H, m, Ph), 5.87-5.68 (1H, m), 5.08-4.92 (2H, m), 3.56-3.27 (1H, m), 2.56-2.38 (1H, m), 2.12-1.79

(3H, m), 1.32-0.79 (6H, m), 0.62-0.41 (2H, m), 0.36 (9H, m); $\delta^{13}C$ (68.5 MHz; C_6D_6) 145.38 + 145.07 + 145.03 (Ph), 138.91 + 138.84 (CH), 128.23 + 128.14 + 128.06 + 127.98 + 127.84 + 127.79 + 125.94 + 125.67 (Ph), 114.27 + 114.21 (CH_2), 89.40 + 89.08 + 88.51 + 88.09 (C), 61.85 + 61.25 (CH_2), 44.41 + 44.33 + 44.18 (CH), 35.63 + 34.26 (CH_2), 31.48 + 31.36 (CH_2), 30.19 + 29.40 (CH), 18.23 + 18.15 (CH_2), 15.06 + 14.98 + 14.83 (CH_3), 0.47 (CH_3); *m/z* (EI) 318 {M^+} (31%), 249 (4), 199 (12), 173 (100), 117 (60), 91 (13), 73 (53%) (Found: C, 71.71; H, 9.20. $C_{19}H_{30}O_2Si$ requires C, 71.70; H, 9.43%).

5*S-Methyl-2*S**-phenylcyclopentane-1*S**-acetic acid ethyl ester 29** (R=Ph): Following the general iron(III) nitrate procedure described above, with addition of a DMF solution of iron(III) nitrate nonahydrate (1.268 g, 3.14 mmol) in DMF (15 mL) to a solution of 1-ethoxy-2-(1'-phenylpent-4'-enyl)-1-(trimethylsilyloxy)cyclopropane **28** (R=Ph) (0.5 g, 1.57 mmol) and 1,4-cyclohexadiene (3.44 mmol, 0.32 mL) in DMF (30 mL) at room temperature. The resulting pale yellow liquid was purified by column chromatography with eluent 5% ethyl acetate in petroleum ether to give the title compound as a clear, colourless oil (0.32 g, 83%). ν_{max}/cm^{-1}(film) 1736 (C=O), 1602 (Ph). δH (270 MHz; C_6D_6) 0.90 (3H, d , J = 6 Hz, CH_3), 1.14 (3H, t, J = 7 Hz, $OCH_2\underline{CH_3}$), 1.31-1.48 (1H, m), 1.61-1.82 (2H, m) 2.01-2.49 (5H, m), 2.72 (1H, m, CH), 3.91 (2H, q, J = 7 Hz, $O\underline{CH_2}CH_3$), 7.14-7.27 (5H, m, Ph). δC (68.5 MHz; C_6D_6) 14.11 (CH_3), 16.03 (CH_3), 33.12 (CH_2), 33.48 (CH_2), 34.47 (CH_2), 35.25 (CH), 47.63 (CH), 49.52 (CH), 60.07 (CH_2), 126.13 (Ph), 127.64 (Ph), 128.37 (Ph), 173.33 (C=O). *m/z* (EI) 246 {M^+} (28%), 201 (12), 158 (100), 143 (63), 117 (12), 104 (10), 91 (12%). Found: C 78.27%, H 8.76%. $C_{16}H_{22}O_2$ requires: C 78.05%, H 8.94%.

5*S-Methyl-2*S**-phenylcyclopentane-1*S**-acetic acid:** A stirred solution of 5*S**-methyl-2*S**-phenylcyclopentane-1*S**-acetic acid ethyl ester **29** (R=Ph) (0.51 g, 2.07 mmol) in 2M NaOH (30 mL) and ethanol (10 mL) was heated to reflux for 2 h. The solution was cooled to room temperature before water (100 mL) was added. The solution was acidified with conc. HCl and extracted with ethyl acetate (3 x 100 mL). The combined organic extracts were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure to give a yellow oil. The crude material was purified by column chromatography with eluent 30% ethyl acetate in petroleum ether to afford the title compound as a clear, colourless oil (0.37 g, 82%). ν_{max}/cm^{-1} (thin film) 3027, 1700, 1602; δ^1H (270 MHz; $CDCl_3$) 7.31-7.13 (5H, m, Ph), 2.69 (1H, q, *J* 2, CH), 2.49-2.03 (6H, m), 1.79-1.63 (1H, m), 1.48-1.37 (1H, m), 0.93 (3H, d, *J* 2, CH_3); $\delta^{13}C$ (68.5 MHz; C_6D_6) 168.65 (C), 128.38 (Ph), 127.58 (Ph), 126.04 (Ph), 49.59 (CH), 47.82 (CH), 35.45 (CH), 34.08 (CH_2), 33.35 (CH_2), 32.98 (CH_2), 15.86 (CH_3); *m/z* (EI) 218 {M^+} (26%), 158 (100), 143 (76), 129 (7), 117 (23), 104 (27), 91 (23%); (Found: C, 76.89; H, 8.27. $C_{14}H_{18}O_2$ requires C, 77.06; H, 8.26%).

2*S-(2'-Hydroxymethyl)-3*S**-methyl-1*S**-phenylcyclopentane 30:** A solution of 5*S**-methyl-2*S**-phenylcyclopentane-1*S**-acetic acid (0.28 g, 1.28 mmol) and lithium aluminium hydride (0.21 g, 5.5 mmol) in THF (10 mL) was stirred at room temperature for 8 h before ethyl acetate (5 mL) was added dropwise. Water (100 mL) was added and the solution stirred at room temperature for 1 h. The mixture was extracted with ethyl acetate (3 x 100 mL) and the combined organics dried over $MgSO_4$, filtered and the solvent evaporated under reduced pressure to give a colourless oil. This was purified by column

chromatography with eluent 30% ethyl acetate in petroleum ether to afford the title compound (0.138 g, 53%) as a clear, colourless oil. ν_{max}/cm^{-1} (thin film) 3333, 1602; δ^1H (270 MHz; $CDCl_3$) 7.30-7.12 (5H, m, Ph), 3.51-3.35 (2H, m, $C\underline{H}_2OH$), 2.70 (1H, m, CH), 2.30-1.92 (4H, m), 1.70-1.34 (4H, m), 0.90 (3H, d, *J* 7, CH_3); $\delta^{13}C$ (68.5 MHz; $CDCl_3$) 128.39 (Ph), 127.55 (Ph), 125.91 (Ph), 61.90 (CH_2), 49.60 (CH), 48.07 (CH), 35.67 (CH), 33.36 (CH_2), 33.24 (CH_2), 32.45 (CH_2), 15.47 (CH_3); *m/z* (EI) 204 {M^+} (54%), 186 (18), 158 (83), 143 (42), 117 (28), 104 (100), 91 (28%); (Found: C, 81.89; H, 9.91. $C_{14}H_{20}O$ requires C, 82.35; H, 9.80%).

5*R-(Chloromethyl)-2*S**-phenylcyclopentane-1*S**-acetic acid ethyl ester 31**: Following the general iron(III) chloride procedure described above, with addition of a solution of iron(III) chloride (1.61 g, 9.6 mmol) in DMF (15 mL) to a solution of (1-ethoxy-2-(1'-phenylpent-4'-enyl)-1-(trimethylsilyloxy) cyclopropane (**28**, (R=Ph)) (1.5 g, 4.72 mmol) in DMF (30 mL), over an addition time of 4 h and a reaction temperature of 50°C. The resultant colourless oil was purified by column chromatography with eluent 10% ethyl acetate in petroleum ether to yield the title compound (1.11g, 82%) as a clear, colourless oil. ν_{max}/cm^{-1} (thin film) 1734, 1602; δ^1H (270 MHz; $CDCl_3$) 7.22-7.06 (5H, m, Ph), 3.88 (2H, q, *J* 7, $OC\underline{H}_2CH_3$), 3.55 (1H, dd, *J* 5, *J* 11, CH_2Cl), 3.37 (1H, dd, *J* 8, *J* 11, CH_2Cl), 2.29-2.12 (2H, m), 2.10-2.00 (4H, m), 1.71-1.65 (3H, m), 1.06 (3H, t, *J* 7, $OCH_2C\underline{H}_3$); $\delta^{13}C$ (68.5 MHz; C_6D_6) 144.30 (C), 128.73 (Ph), 127.89 (Ph), 126.64 (Ph), 60.13 ($O\underline{C}H_2CH_3$), 50.57 (CH), 46.91 (CH), 46.73 (CH_2), 43.02 (CH), 33.80 (CH_2), 33.50 (CH_2), 29.19 (CH_2), 14.08 ($OCH_2\underline{C}H_3$); *m/z* (EI) 280 {M^+} (12%), 235 (7), 192 (35), 143 (100), 117 (21), 91 (34), 77 (4%).

1-Ethoxy-2-(1'-isopropylpent-4'-enyl)-1-(trimethylsilyloxy)cyclopropane 28 (R=^{i}Pr): Following the general conjugate addition procedure described above but using magnesium turnings (0.23 g, 9.75 mmol), THF (20 mL), 2-bromopropane (7.8 mmol, 0.71 mL), HMPA (15.6 mmol, 2.8 mL), CuI (0.13 g, 0.65 mmol), ethyl-2,6-heptadienoate **26** (1.0 g, 6.5 mmol) and chlorotrimethylsilane (15.6 mmol, 1.98 mL) to yield **1-ethoxy-3-isopropyl-1-trimethylsilyloxy-1,6-heptadiene 27** (R=^{i}Pr) as a clear, colourless oil (1.65 g, 94%) following distillation (120°C @ 10 mm Hg). Cyclopropanation was carried out following the general cyclopropanation procedure, using **27** (R=^{i}Pr) (1.65 g, 6.1 mmol), diethyl ether (20 mL), diethylzinc (13 mmol, 13 mL) and diiodomethane (13 mmol, 1.07 mL). The crude product was purified column chroatography with eluent 5% ethyl acetate in petroleum ether to yield the title compound as a clear, colourless oil (1.29 g, 74%). Rigorous assignment of spectroscopic data was impossible due to the complex mixture of diastereoisomers obtained. ν_{max}/cm^{-1} (thin film) 1641; δ^1H (270 MHz; $CDCl_3$) 5.86-5.73 (1H, m), 5.00-4.92 (2H, m), 3.75-3.72 (1H, m), 3.42-3.41 (1H, m), 2.15-1.73 (3H, m), 1.44-1.23 (4H, m), 1.14 (3H, m), 0.88 (6H, m), 0.48-0.46 (2H, m), 0.14 (9H, s); $\delta^{13}C$ (67.8 MHz; $CDCl_3$) 139.91 + 139.67 (CH), 113.95 + 113.69 (CH_2), 88.23 + 87.96 (C), 61.06 + 60.09 ($O\underline{C}H_2CH_3$), 42.95 + 42.49 (CH), 32.11 + 31.29 (CH_2), 30.89 + 29.62 (CH_2), 30.35 + 30.17 (CH), 26.45 + 26.25 (CH), 20.02 + 19.94 (CH_3), 18.67 + 18.35 (CH_3), 15.33 + 15.27 (CH_3), 1.01 + 0.72 (CH_3); *m/z* (EI) 284 {M^+} (4%), 241 (14), 173 (7), 151 (3), 119 (22), 95 (36), 73 (100%).

2-Isopropyl-5-methylcyclopentane-1-acetic acid ethyl ester 29a/b (R=^{i}Pr): Following the general iron(III) nitrate procedure described above, with addition of a solution of iron(III) nitrate nonahydrate

(1.615 g, 4.0 mmol) in DMF (20 mL) to a solution of 1-ethoxy-2-(1'-isopropylpent-4'-enyl)-1-(trimethylsilyloxy)cyclopropane **28** (R=^{i}Pr) (0.5 g, 1.8 mmol) and 1,4-cyclohexadiene (3.6 mmol, 0.35 mL) in DMF (40 mL) at 40°C. The resulting pale yellow liquid was purified by column chromatography with eluent 5% ethyl acetate in petroleum ether to give the title compound (0.28 g, 74%) as a clear, colourless oil. Two diastereoisomers **29a** and **29b** were present in an 8:1 ratio respectively by ^{1}H NMR spectroscopy. ν_{max}/cm^{-1} (thin film) 1735; δ^{1}H (300 MHz; $CDCl_3$) 4.14 (1.78H, q, *J* 7, $OC\underline{H}_2CH_3$ (major)), 4.14 (0.22H, q, *J* 7, $OC\underline{H}_2CH_3$ (minor)), 2.33-2.21 (2H, m), 2.17-2.09 (1H, m), 1.72-1.48 (4H, m), 1.28 (2.67H, t, *J* 7, $OCH_2C\underline{H}_3$ (major)), 1.28 (0.33H, t, *J* 7, $OCH_2C\underline{H}_3$ (minor)), 1.24-1.21 (1H, m), 0.92 (0.33H, d, *J* 7 CH_3 (minor)), 0.91 (2.67H, d, *J* 7, CH_3 (major)), 0.88 (0.33H, d, *J* 6, CH_3 (minor)), 0.87 (2.67H, d, *J* 7, CH_3 (major)), 0.84 (0.33H, d, *J* 6, CH_3 (minor)), 0.84 (2.67H, d, *J* 7, CH_3 (major)); δ^{13}C (75.5 MHz; C_6D_6) Major diastereoisomer: 173.98 (C), 60.01 ($O\underline{C}H_2CH_3$), 49.65 (CH), 39.79 (CH), 34.34 (CH), 33.85 (CH_2), 30.82 (CH_2), 30.19 (CH), 23.70 (CH_2), 18.83 ($OCH_2\underline{C}H_3$), 15.91 (CH_3), 13.10 (CH_3), 12.10 (CH_3); Minor diastereoisomer: 174.21 (C), 59.93 ($O\underline{C}H_2CH_3$), 51.89 (CH), 40.97 (CH), 34.34 (CH), 33.85 (CH_2), 30.67 (CH_2), 30.05 (CH), 23.83 (CH_2), 19.46 ($OCH_2\underline{C}H_3$), 15.91 (CH_3), 13.10 (CH_3), 12.10 (CH_3); *m/z* (EI) 212 {M^{+}} (8%), 211 (53), 165 (15), 137 (27), 124 (28), 123 (100), 101 (20), 95 (42), 81 (92), 69 (68%); (Found: C, 73.48; H, 11.36. $C_{13}H_{24}O_2$ requires C, 73.58; H, 11.32%).

1-Ethoxy-2-(1'-propylpent-4'-enyl)-1-(trimethylsilyl)oxycyclopropane 28 (R=^{n}Pr): Following the general conjugate addition procedure but using magnesium turnings (0.23 g, 9.75 mmol), THF (20 mL) 1-bromopropane (7.8 mmol, 0.71 mL), HMPA (15.6 mmol, 2.8 mL), CuI (0.13 g, 0.65 mmol), ethyl-2,6-heptadienoate **26** (1.0 g, 6.5 mmol) and chlorotrimethylsilane (15.6 mmol, 1.98 mL) to yield **1-ethoxy-3-propyl-1-trimethylsilyloxy-1,6-heptadiene 27** (R=^{n}Pr) as a clear, colourless oil (1.62 g, 92%) following distillation (120°C @ 10 mm Hg). Cyclopropanation was carried out following the general cyclopropanation procedure using **27** (R=^{n}Pr) (1.62 g, 5.7 mmol), diethyl ether (20 mL), diethylzinc (12 mmol, 12 mL) and diiodomethane (12 mmol, 1mL). The crude product was purified by column chromatography with eluent 5% ethyl acetate in petroleum ether to yield the title compound as a clear, colourless oil (1.4 g, 86%). Rigorous assignment of spectroscopic data was impossible due to the complex mixture of diastereoisomers obtained. ν_{max}/cm^{-1} (thin film) 1642; δ^{1}H (270 MHz; C_6D_6) 5.92-5.83 (1H, m), 5.15-4.99 (2H, m), 3.85-3.77 (1H, m), 3.42-3.35 (1H, m), 2.21-2.07 (2H, m), 1.65-1.29 (6H, m), 1.17 (3H, m), 1.11-1.05 (1H, m), 0.94-0.82 (6H, m), 0.49-0.39 (2H, m), 0.21 (9H, s); δ^{13}C (67.8 MHz; $CDCl_3$) 139.21 + 139.15 (CH), 113.65 + 113.59 (CH_2), 88.93 + 88.50 (C), 61.45 + 60.60 (CH_2), 36.51 + 36.42 (CH), 36.23 + 35.70 + 35.32 (CH_2), 33.48 + 32.72 (CH_2), 30.71 + 30.55 (CH_2), 28.29 + 28.18 (CH), 20.05 + 19.42 (CH_2), 14.73 + 14.61 (CH_3), 14.10 + 13.91 (CH_3) 0.32 + 0.29 (CH_3); *m/z* (EI) 284 {M^{+}} (2%), 229 (8), 173 (40), 143 (23), 117 (41), 73 (100%).

2-Propyl-5-methylcyclopentane-1-acetic acid ethyl ester 29a/b (R=^{n}Pr): Following the general iron(III) nitrate procedure described above, with addition of a solution of iron(III) nitrate nonahydrate (1.615 g, 4.0 mmol) in DMF (40 mL) to a solution of 1-ethoxy-2-(1'-propylpent-4'-enyl)-1-(trimethylsilyl oxy)cyclopropane **28** (R=^{i}Pr) (0.5 g, 1.8 mmol) and 1,4-cyclohexadiene (3.6 mmol, 0.35 mL) in DMF (20 mL) at 40°C. The resulting pale yellow liquid was purified by column chromatography with eluent 5% ethyl acetate in petroleum ether to give the title compound (0.26 g, 69%) as a clear, colourless oil. Two

diastereoisomers **29a** and **29b** were shown to be present in a 6:1 ratio respectively by ^{1}H NMR spectroscopy. ν_{max}/cm^{-1} (thin film) 1736; δ^1H (270 MHz; $CDCl_3$) 4.13 (1.71H, q, *J* 7, $OC\underline{H}_2CH_3$ (major)), 4.12 (0.29H, q, *J* 7, $OC\underline{H}_2CH_3$ (minor)), 2.33-2.21 (2H, m), 2.31-2.14 (2H, m), 1.93-1.72 (2H, m), 1.61-1.43 (2H, m), 1.41-1.30 (3H, m), 1.26 (2.57H, t, *J* 7, $OCH_2C\underline{H}_3$ (major)), 1.25 (0.43H, t, *J* 7, $OCH_2C\underline{H}_3$ (minor)), 1.22-1.12 (3H, m), 0.96 (0.43H, d, *J* 7, CH_3 (minor)), 0.90-0.88 (3H, m), 0.83 (2.57H, d, *J* 7, CH_3 (major)); δ^{13}C (67.8MHz; C_6D_6) 174.04 (C (major)), 60.16 ($O\underline{C}H_2CH_3$ (minor)), 59.95 ($O\underline{C}H_2CH_3$ (major)), 45.12 (CH (major)), 42.73 (CH (major)), 37.54 (CH_2 (major)), 35.63 (CH (minor)), 35.58 (CH (major)), 34.96 (CH_2 (major)), 31.79 (CH_2 (major)), 31.68 (CH_2 (minor)), 29.92 (CH_2 (major)), 21.19 (CH_2 (major)), 15.37 (CH_3 (major)), 14.14 (CH_3 (major)), 14.02 (CH_3 (major)), 13.95 (CH_3 (minor)); *m/z* (EI) 212 {M$^+$} (6%), 167 (14), 155 (7), 143 (6), 125 (52), 88 (100), 81 (89), 69 (57%); (Found: C, 73.46; H, 11.34. $C_{13}H_{24}O_2$ requires C, 73.58; H, 11.32%).

1-Ethoxy-2-(1'-methylpent-4'-enyl)-1-(trimethylsilyloxy)cyclopropane 28 (R=Me): Following the general conjugate addition procedure above, using magnesium turnings (0.92 g, 39 mmol), THF (30 mL), 4-bromo-1-butene (31.2 mmol, 3.16 mL), HMPA (62.4 mmol, 11.2 mL), CuI (0.52 g, 2.6 mmol), ethyl crotonate **25** (R=Me) (26 mmol, 3.2 mL) and chlorotrimethylsilane (62.4 mmol, 7.92 mL) to afford **1-ethoxy-3-methyl-1-trimethylsilyloxy-1,6-heptadiene 27** (R=Me) as a clear, colourless oil (5.98 g, 94%) following distillation (120°C @ 15 mm Hg). Cyclopropanation was carried out following the general cyclopropanation procedure, using **27** (R=Me) (5.98 g, 24.5 mmol), diethyl ether (20 mL), diethylzinc (49 mmol, 49 mL) and diiodomethane (49 mmol, 3.92 mL). The crude product was purified by column chromatography with eluent 5% ethyl acetate in petroleum ether to yield the title compound as a clear, colourless oil (5.82 g, 92%). ν_{max}/cm^{-1}(thin film) 1642; δ^1H (300 MHz; $CDCl_3$) 5.73-5.58 (1H, m), 4.93-4.72 (2H, m), 3.67-3.51 (1H, m), 3.36-3.22 (1H, m), 2.08-1.79 (2H, m), 1.63-1.28 (4H, m), 1.15-0.98 (3H, m), 0.96-0.64 (5H, m), 0.38-0.21 (2H, m), 0.09 (9H, m); δ^{13}C (75.5 MHz; $CDCl_3$) 139.68 + 139.58 (CH), 114.09 + 113.96 (CH_2), 89.05 + 88.33 (C), 61.31 + 61.21 (CH_2), 36.23 + 35.96 (CH_2), 31.44 + 31.24 (CH_2), 30.97 + 29.97 (CH), 20.19 + 19.76 (CH_2), 18.71 + 18.39 (CH), 15.22 (CH_3), 0.85 + 0.66 + 0.63 (CH_3); *m/z* (EI) 256 {M$^+$} (2%), 211 (19), 173 (17), 75 (27), 73 (100%).

2,5-Dimethylcyclopentane-1-acetic acid ethyl ester 29a/b (R=Me): Following the general iron(III) nitrate procedure described above, with addition of a solution of iron(III) nitrate nonahydrate (1.697 g, 4.2 mmol) in DMF (20 mL) to a solution of 1-ethoxy-2-(1'-methylpent-4'-enyl)-1-(trimethylsilyloxy)-cyclopropane **28** (R=Me) (0.5 g, 1.9 mmol) and 1,4-cyclohexadiene (4.0 mmol, 0.38 mL) in DMF (40 mL) at 50°C. The resulting pale yellow liquid was purified by column chromatography with eluent 5% ethyl acetate in petroleum ether to give the title compound (0.24 g, 69%) as a clear, colourless oil. ν_{max}/cm^{-1} (thin film) 1738; δ^1H (300 MHz; $CDCl_3$) 4.15 (1.3H, q, *J* 7, $OC\underline{H}_2CH_3$ (major)), 4.14 (0.67H, q, *J* 7, $OC\underline{H}_2CH_3$ (minor)), 2.36-2.15 (2H, m), 1.91-1.76 (2H, m), 1.69-1.62 (1H, m), 1.46-1.31 (2H, m), 1.28 (2H, t, *J* 7, $OCH_2C\underline{H}_3$ (major)), 1.27 (1H, t, *J* 7, $OCH_2C\underline{H}_3$ (minor)), 1.21-1.05 (2H, m), 0.99 (1H, d, *J* 7, CH_3 (minor)), 0.98 (2H, d, *J* 7, CH_3 (major)) 0.89 (1H, d, *J* 7, CH_3 (minor)), 0.84 (2H, d, *J* 7, CH_3 (major)); δ^{13}C (75.5 MHz; $CDCl_3$) 174.00 (C), 60.21 (CH_2), 59.94 (CH_2), 46.74 (CH), 37.38 (CH), 36.31 (CH), 35.31 (CH), 34.61 (CH_2), 32.43 (CH_2), 32.23 (CH_2), 31.95 (CH_2), 31.83 (CH_2), 31.72 (CH_2), 31.41 (CH_2), 19.56 (CH_3), 19.05 (CH_3), 15.69 (CH_3), 14.00 (CH_3), 13.97 (CH_3); *m/z* (EI) 184 {M$^+$} (8%), 183

(47), 137 (19), 109 (67), 95 (100), 81 (25%); (Found: C, 71.59; H, 10.89. $C_{11}H_{20}O_2$ requires C, 71.74; H, 10.67%)

1-Ethoxy-1-(*tert.*-butyldimethylsilyloxy)-1,6-heptadiene: Following the general conjugate addition procedure described above, using magnesium turnings (0.63 g, 26 mmol), THF (48 mL), 4-bromo-1-butene (24 mmol, 2.44 mL), HMPA (48 mmol, 8.36 mL), CuI (0.38 g, 2.0 mL), ethyl acrylate (2.0 g, 20 mmol) and chlorotrimethylsilane (7.24 g, 48 mmol), to yield the title compound as a clear, colourless liquid (2.84 g, 53%). NMR spectroscopy indicated a mixture of two geometrical isomers, present in a 2:1 ratio. These were assigned to E (major) and Z (minor) stereochemistry at the ketene acetal. bp 170-75°C @ 1 mbar; ν_{max}/cm^{-1} (thin film) 1740, 1679, 1642; δ^1H (270 MHz; C_6D_6) 5.82 (1H, tdd, *J* 7, *J* 10, *J* 17, C<u>H</u>=CH$_2$), 5.10-4.91 (2H, m, C<u>H$_2$</u>=CH), 3.98-3.74 (2.33H, m, CH=C + OC<u>H$_2$</u>CH$_3$), 3.41 (0.22H, q, *J* 7, OC<u>H$_2$</u>CH$_3$ (minor)), 3.39 (0.44H, q, *J* 7, OC<u>H$_2$</u>CH$_3$ (major)), 2.22-2.04 (4H, m, CH$_2$), 1.49 (2H, m, *J* 7, CH$_2$), 1.08 (1H, t, *J* 7, OCH$_2$C<u>H$_3$</u> (minor)), 0.99 (2H, t, *J* 7, OCH$_2$C<u>H$_3$</u> (major)), 0.94 (6H, s, (CH$_3$)$_3$CSi (major)), 0.92 (3H, s, (CH$_3$)$_3$CSi (minor)) 0.14 (4H, s, (CH$_3$)$_2$Si (major)), 0.02 (2H, s, (CH$_3$)$_2$Si (minor)); $\delta^{13}C$ (67.5 MHz; C_6D_6) Major isomer: 153.64 (C), 139.30 (<u>C</u>H=CH$_2$), 114.42 (<u>C</u>H$_2$=CH), 86.26 (<u>C</u>H=C), 62.92 (O<u>C</u>H$_2$CH$_3$), 33.82 (CH$_2$), 30.60 (CH$_2$), 25.79 ((<u>C</u>H$_3$)$_3$CSi), 24.70 (CH$_2$), 18.32 ((CH$_3$)$_3$<u>C</u>Si), 15.01 (OCH$_2$<u>C</u>H$_3$), -4.88 ((CH$_3$)$_2$Si); Minor isomer: 153.64 (C), 139.37 (<u>C</u>H=CH$_2$), 114.74 (<u>C</u>H$_2$=CH), 75.98 (<u>C</u>H=C), 62.75 (O<u>C</u>H$_2$CH$_3$), 33.90 (CH$_2$), 30.82 (CH$_2$), 25.97 ((<u>C</u>H$_3$)$_3$CSi), 24.80 (CH$_2$), 18.32 ((CH$_3$)$_3$<u>C</u>Si), 14.42 (OCH$_2$<u>C</u>H$_3$), -3.93 ((CH$_3$)$_2$Si); *m/z* (EI) 270 {M$^+$} (10%), 215 (58), 185 (23), 171 (13), 129 (14), 115 (13), 110 (15), 103 (44), 88 (15), 75 (57), 73 (100%); HRMS: *m/z* (CI, NH$_4$OAc) Found: 271.2093. $C_{15}H_{31}O_2Si$ requires {[M+H]$^+$} 271.2093.

1-Ethoxy-2-(pent-4'-enyl)-1-(*tert.*-butyldimethylsilyloxy)cyclopropane 32: Following the general cyclopropanation procedure described above, but using 1-ethoxy-1-(*tertiary*-butyldimethylsilyloxy)-1,6-heptadiene (2.47 g, 9.2 mmol), diethyl ether (37 mL), diethylzinc (18.4 mmol, 18.4 mL) and diiodomethane (18.4 mmol, 1.49 mL). The crude material was purified by column chromatography with eluent 1% diethyl ether in petroleum ether to yield the title compound as a clear, colourless liquid (2.04 g, 78%). NMR spectroscopy indicated a mixture of two diastereoisomers in a 2:1 ratio. ν_{max}/cm^{-1} (thin film) 1642, 1473, 1450; δ^1H (270 MHz; C_6D_6) 5.90-5.71 (1H, m, C<u>H</u>=CH$_2$), 5.09-4.95 (2H, m, C<u>H$_2$</u>=CH), 3.82-3.70 (1H, m, OC<u>H$_2$</u>CH$_3$), 3.56-3.31 (1H, m, OC<u>H$_2$</u>CH$_3$), 2.10-1.97, (2H, m, CH$_2$), 1.65-1.20 (4H, br m, CH$_2$), 1.12-1.06 (4H, m, OCH$_2$C<u>H$_3$</u> + *exo*-CH$_2$), 1.00-0.81 (1H, m, CH), 0.98 (3H, s, (CH$_3$)$_3$CSi (minor)), 0.97 (6H, s, (CH$_3$)$_3$CSi (major)), 0.41 (1H, m, *endo*-CH$_2$), 0.25 (2H, s, (CH$_3$)$_2$Si (minor)), 0.19 (4H, s, (CH$_3$)$_2$Si (major)); $\delta^{13}C$ (67.5 MHz; C_6D_6) Minor diastereoisomer: 139.03 (<u>C</u>H=CH$_2$), 114.58 (<u>C</u>H$_2$=CH), 89.04 (C), 62.02 (O<u>C</u>H$_2$CH$_3$), 34.04 (CH$_2$), 28.88 (CH$_2$), 28.38 (CH$_2$), 27.10 (CH), 25.90 ((<u>C</u>H$_3$)$_3$CSi), 18.75 (CH$_2$), 17.92 ((CH$_3$)$_3$<u>C</u>Si), 15.39 (OCH$_2$<u>C</u>H$_3$), -3.50 ((CH$_3$)$_2$Si); Major diastereoisomer: 139.14 (<u>C</u>H=CH$_2$), 114.58 (<u>C</u>H$_2$=CH), 89.04 (C), 61.42 (O<u>C</u>H$_2$CH$_3$), 34.11 (CH$_2$), 29.22 (CH$_2$), 28.77 (CH$_2$), 25.94 ((<u>C</u>H$_3$)$_3$CSi), 23.73 (CH), 20.94 (CH$_2$), 18.08 ((CH$_3$)$_3$<u>C</u>Si), 15.39 (OCH$_2$<u>C</u>H$_3$), -4.27 ((CH$_3$)$_2$Si); *m/z* (EI) 284 {M$^+$} (3%), 241 (8), 215 (8), 185 (5), 147 (18), 103 (48), 80 (16), 75 (39), 73 (100%); HRMS: *m/z* (CI, NH$_4$OAc) Found: 302.2517. $C_{16}H_{36}NSiO_2$ {[M+NH$_4$]$^+$} requires 302.2515; (Found: C, 67.51; H, 11.19. $C_{16}H_{32}SiO_2$ requires C, 67.54; H, 11.33%).

1-Ethoxy-2-(pent-4'-enyl)-cyclopropanol 33: A solution of 1-ethoxy-2-(pent-4'-enyl)-1-(trimethylsilyloxy)cyclopropane **13** (4.85 g, 20 mmol) in methanol (30 mL) was stirred at room temperature for 2 h. After this time no reaction had occurred so a single drop of chlorotrimethylsilane was added. After stirring for a further 30 min at room temperature no starting material remained. The methanol was removed under reduced pressure and the resulting pale golden liquid subjected to column chromatography with eluent 5% diethyl ether in petroleum ether. Pure fractions were obtained and evaporated to dryness under reduced pressure to yield the title compound as a clear, colourless liquid (3.21 g, 94%) as a mixture of two diasteriomers in a 2:1 ratio. ν_{max}/cm^{-1} (thin film) 3392, 3078, 1737, 1717, 1642; δ^1H (270 MHz; $CDCl_3$) 5.79 (1H, tdd, *J* 7, *J* 10, *J* 17, C<u>H</u>=CH$_2$), 5.03-4.89 (2H, m, C<u>H$_2$</u>=CH), 3.70 (0.66H, q, *J* 7, OC<u>H$_2$</u>CH$_3$ (minor)), 3.69 (1.33H, q, *J* 7, OC<u>H$_2$</u>CH$_3$ (major)), 3.32 (0.33H, br s, OH (minor)), 3.10 (0.66H, br s, OH (major)), 2.11-2.10 (2H, m, CH$_2$), 1.59-1.34 (4H, br m, CH$_2$), 1.27-1.09 (1H, br m, *exo*-CH$_2$), 1.19 (1H, t, *J* 7, OCH$_2$C<u>H$_3$</u> (minor)), 1.17 (2H, t, *J* 7, OCH$_2$C<u>H$_3$</u> (major)), 1.06-0.94 (1H, m, CH), 0.49-0.42 (1H, m, *endo*-CH$_2$); $\delta^{13}C$ (67.5 MHz; $CDCl_3$) Minor diastereoisomer: 138.89 (<u>C</u>H=CH$_2$), 114.32 (<u>C</u>H$_2$=CH), 88.02 (C), 62.30 (O<u>C</u>H$_2$CH$_3$), 33.48 (CH$_2$), 28.50 (CH$_2$), 27.46 (CH$_2$), 26.88 (CH), 19.25 (CH$_2$), 15.42 (OCH$_2$<u>C</u>H$_3$); Major diastereoisomer: 138.89 (<u>C</u>H=CH$_2$), 114.41 (<u>C</u>H$_2$=CH), 88.02 (C), 61.62 (O<u>C</u>H$_2$CH$_3$), 33.48 (CH$_2$), 28.79 (CH$_2$), 27.50 (CH$_2$), 25.48 (CH), 19.25 (CH$_2$), 15.42 (OCH$_2$<u>C</u>H$_3$); *m/z* (EI) 170 {M$^+$} (14%), 130 (58), 117 (48), 97 (56), 88 (94), 81 (66), 67 (68), 54 (75), 41 (100%); (Found: C, 70.68; H, 10.78. $C_{10}H_{18}O_2$ requires C, 70.55; H, 10.66).

(2-Chloromethyl)cyclopentane-1-acetic acid ethyl ester 15a/b (X=Cl): Following the general iron(III) chloride procedure described above, in which a solution of iron(III) chloride (0.714 g, 4.4 mmol) in DMF (20 mL) is added to a solution of 1-ethoxy-2-(pent-4'-enyl)-cyclopropanol **33** (0.341 g, 2.0 mmol) in DMF (40 mL). The crude product was subjected to column chromatography with eluent 2% diethyl ether in petroleum ether to yield a clear, colourless liqiud (0.25 g, 62%) which proved to be a mixture of the title compound and its isomer, 3-chloro-7-octenoic acid ethyl ester **16** in the ratio 1:1.9. The spectral data were consistent with those described previously.

The reaction was also carried out using $[FeCl_2(DMF)_3][FeCl_4]$ (1.20 g, 2.2 mmol) instead of iron(III) chloride to yield a clear, colourless liquid (0.34 g, 84%) which proved to be a mixture of the title compound and **16** in the ratio 1:1.4. The spectral data were consistent with those described previously.

2-Methylcyclopentane-1-acetic acid ethyl ester 15a/b (X=H): Following the general iron(III) nitrate procedure described above, in which a solution of iron(III) nitrate nonahydrate (1.78 g, 4.4 mmol) in DMF (20 mL) is added to a solution of 1-ethoxy-2-(pent-4'-enyl)-cyclopropanol **33** (0.34 g, 2.0 mmol) in DMF (40 mL). The resulting pale yellow liquid was purified by column chromatography with eluent 2% diethyl ether in petroleum ether to yield the title compound (0.18 g, 54%) as a clear, colourless liquid. The spectral data were consistent with those described previously .

Reaction of 13 With Fewer Equivalents of Fe(III)

(2-Chloromethyl)cyclopentane-1-acetic acid ethyl ester 15a/b (X=Cl): As for the general iron(III)chloride procedure previously described for (2-chloromethyl)cyclopentane-1-acetic acid ethyl ester **15a/b** (X=Cl) but using only 1.1 eq iron(III) chloride (0.36 g, 2.2 mmol). The reaction mixture had to be

heated to 40°C for 1 h before conversion of starting material took place. The usual work-up was carried out to yield a clear, colourless liquid (0.34 g, 83%) which proved to be a mixture of the title compound and 3-chloro-7-octenoic acid ethyl ester **16** in a ratio of 1:1.2. The spectral data were consistent with those previously described.

The reaction was also carried out using only 0.55 eq $[FeCl_2(DMF)_3][FeCl_4]$ (0.60 g, 1.1 mmol). The reaction mixture had to be heated to 40°C before conversion of starting material took place. The usual work up was carried out to yield a clear, colourless liquid (0.27 g 66%) which proved to be a mixture of the title compound and 3-chloro-7-octenoic acid ethyl ester **16** in a ratio of 1:1.1. The spectral data were consistent with those previously described.

2-Methylcyclopentane-1-acetic acid ethyl ester 15a/b (X=H): As for the general iron(III) nitrate procedure previously described for 2-methylcyclopentane-1-acetic acid ethyl ester **15a/b**, (X=H) but using only 1.1 eq iron(III) nitrate nonahydrate (0.89 g, 2.2 mmol) to yield the title compound (0.20 g, 58%) as a clear, colourless liquid. The spectral data were consistent with those previously described.

The above reaction was repeated using only 0.55 eq iron(III) nitrate nonahydrate (0.44 g, 1.1 mmol) to yield the title compound (0.10 g, 31%) as a clear, colourless liquid. A second, more polar, product was obtained as a clear, colourless liquid (0.14 g, 42%) and was identified as 1-ethoxy-2-(pent-4'-enyl)-cyclopropanol **33**. The spectral data were consistent with those previously described.

The above reaction was repeated using only 0.1 eq iron(III) nitrate nonahydrate (0.081 g, 0.2 mmol) to yield the title compound (0.038 g, 11%) as a clear, colourless liquid. A second, more polar, product was obtained as a clear, colourless liquid (0.22 g, 64%) and was identified as 1-ethoxy-2-(pent-4'-enyl)-cyclopropanol **33**. The spectral data were consistent with those previously described.

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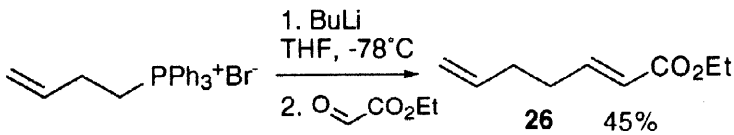
7. In our hands the ester **26** was best prepared by the following Wittig sequence:



26 45%

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