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INTRAMOLECULAR [2 + 2] CYCLOADDITIONS OF DIALKYLKETENES WITH ALKENES. REGIOCHEMISTRY OF INTRAMOLECULAR [2 +2] CYCLOADDITIONS OF KETENES WITH ALKENES.

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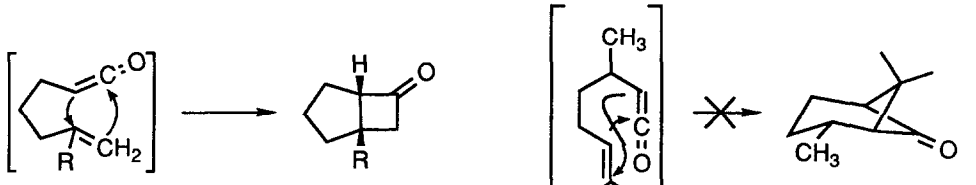
Abstract: Unsaturated dialkylketenes **7a**, **7b** and **7c** undergo intramolecular [2 + 2] cycloadditions to give **8a** (45%), **9b** (23%) and **9c** (45%). Intramolecular cycloadditions of dialkylketenes give higher yields than intramolecular cycloadditions of monoalkylketenes, even though dialkylketenes are less reactive than monoalkylketenes. An intramolecular competition experiment with ketene **17** establishes that *trans*-alkenes are approximately 33 times more reactive than *cis*-alkenes in intramolecular cycloadditions. Ketene **36** furnishes 22% of the expected bicyclo[3.2.0]heptanone **37** and 28% of bicyclo[3.1.1]heptanone **38**.

Introduction

The stereospecific cycloaddition of ketenes to alkenes provides an attractive route to cyclobutanones and is one of the few general methods for carbofunctionalization of alkenes. We and others have recently recognized that the intramolecular version of this reaction provides a general method for the synthesis of polycyclic cyclobutanones.[1,2] Early systematic studies of this reaction suggested that low yields of cycloadducts were obtained from the intramolecular cycloadditions of monoalkylketenes with all but the most nucleophilic alkenes. Greuter and Ernst fount that, while intramolecular cycloaddition of **1a** gives 80% of **2a**, intramolecular cycloaddition of **1b** with a less nucleophilic double bond gives only 3% of **2b**.[3] We found that intramolecular cycloaddition of unsaturated ketene **3** could not be carried out to give **4**.[4] The use of α,β–unsaturated, alkoxy and chloroketenes have been developed to circumvent this reactivity problem with monoalkylketenes.[1]



1a, R = Me
1b, R = H

2a, R = Me
2b, R = H

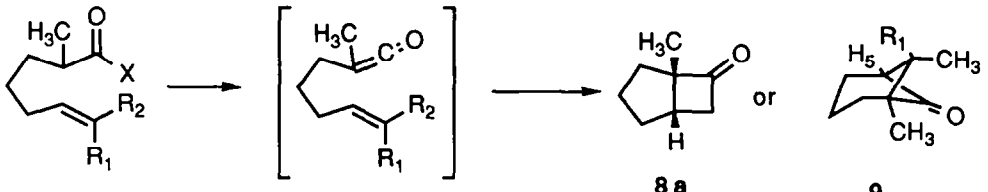
3

4

Dialkylketenes are known to be much less reactive in intermolecular cycloadditions than monoalkylketenes.[5] Intramolecular cycloadditions of dialkylketenes with alkenes have not been systematically explored since yields are poor with monoalkylketenes and would be expected to be worse with less reactive dialkylketenes. There are only a few reports of intramolecular cycloadditions of dialkylketenes and alkenes,[2a,1,6] and in some cases the success of the reaction has been attributed to the rigidity of the tether.[2a] We were interested in examining the intramolecular cycloaddition of unsaturated dialkylketenes in cases where the corresponding monoalkylketene had been examined so that the effect of introducing a second alkyl group onto the ketene could be determined.

Results and Discussion

Intramolecular Cycloadditions of dialkylketenes. Alkylation of the dianion of propionic acid with 5-bromo-1-pentene at 0 °C in THF-HMPA gives acid **5a** in 61% yield.[7] Conversion of acid **5a** to acid chloride **6a** with oxalyl chloride in benzene followed by dropwise addition of **6a** to a solution of Et_3N in benzene at reflux gives 5-methylbicyclo[3.2.0]heptan-6-one (**8a**)[8] in 45% yield. This demonstrates that, contrary to our expectations, introduction of a methyl group onto the ketene increases the yield of the cycloaddition; the corresponding monoalkylketene **1b** gives only 3% of **2b**.[3]



5, X = OH
6, X = Cl

7

8a

9

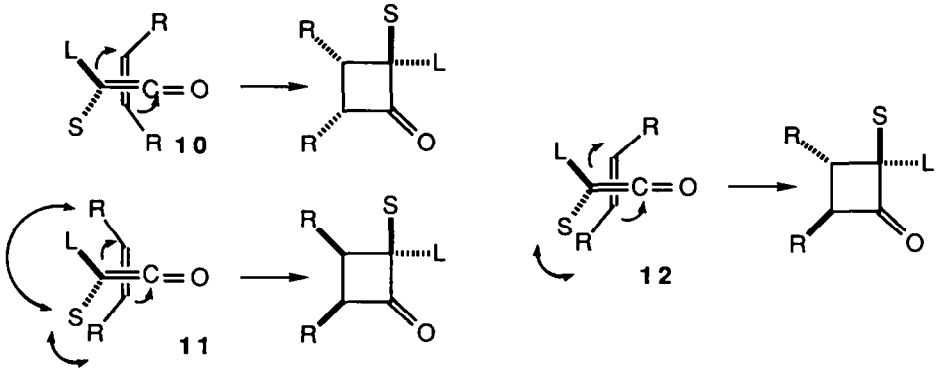
a, $R_1 = R_2 = H$; **b**, $R_1 = H$, $R_2 = CH_3$; **c**, $R_1 = R_2 = CH_3$

Ketenes **7b** and **7c** were prepared to determine the general utility of dialkylketenes in intramolecular cycloadditions. Alkylation of the dianion of propionic acid[7] with 6-iodo-2-methyl-2-hexene and 6-iodo-2-hexene affords acids **5b** (50%) and **5c** (50%). Addition of acid chloride **6b** to Et_3N in toluene at reflux provides 23% of **9b**. Similar treatment of acid chloride **6c** gives 45% of **9c**. The structure of **9c** can be convincingly established based on analysis of the ^1H NMR spectrum. The coupling constant between H_5 and H_7 (R_1) is 0.9 Hz, a value consistent with a calculated[9] dihedral angle of 103° and the coupling constant observed in related compounds.[10a] The corresponding coupling constant should be 4-5 Hz in 5,7-*exo*-dimethylbicyclo[3.2.0]heptan-6-one.[11] The exclusive formation of **9c** is consistent with our observation in related systems that intramolecular cycloadditions of ketenes to *trans*-1,2-disubstituted alkenes proceed in good yield to give mainly or exclusively the bicyclo[3.1.1]heptan-6-one. This regioselectivity is a result of entropically preferred attack of the internal double bond carbon on the ketene carbonyl carbon leading to a six-membered rather than seven-membered ring transition state.

The formation of **8a**, **9b**, and **9c** indicates that dialkylketenes undergo intramolecular [2 + 2] cycloadditions with alkenes to give both bridged and fused adducts in good yield. Dialkylketenes give much better yields of cycloadducts than the more reactive monoalkylketenes **1b** and **3**. Apparently, these monoalkylketenes are too reactive. Cycloaddition is fast, but dimerization and oligomerization is even faster so that low yields of cycloadducts are obtained. The methyl substituent on the dialkylketene **7** slows the rate of cycloaddition, but slows the rate of dimerization and oligomerization even more. The very slow rate of dimerization of **7** allows cycloaddition to become the favored process resulting in good yields of adducts **8a**, **9b**, and **9c**.

The cycloaddition of ketenes and alkenes differs from most cycloadditions in which both addends are stable. The yield of a ketene-alkene cycloaddition is not determined by the reactivity of the ketene, but rather by the relative reactivity of the ketene for cycloaddition versus undesired side reactions. Dialkylketenes are less reactive than monoalkylketenes but give higher yields of cycloadducts since the reactivity ratio is more favorable.

Relative Rate of Cycloaddition to *cis*- and *trans*-Alkenes. We have recently shown that intramolecular [2 + 2] cycloadditions of ketenes with *trans*-alkenes are much more facile than those with *cis*-alkenes.[10a] This result contrasts with intermolecular cycloadditions of ketenes in which *cis*-alkenes are more rapid than those of *trans*-alkenes.[5] This observation while surprising, can be easily understood by examining the transition state for a concerted $[_{\pi}2_s + _{\pi}2_a]$ cycloaddition.[12] *Intermolecular* cycloaddition of a ketene with a *cis*-alkene can occur through unhindered transition state **10** or through very hindered transition state **11**, where S and L are the small and large substituents on the ketene. The stereochemistry of the cycloadducts confirms that cycloaddition proceeds through **10**. *Intermolecular* cycloaddition of a ketene with a *trans*-alkene must occur through the moderately hindered transition state **12**. This cycloaddition is slower due to steric hindrance.



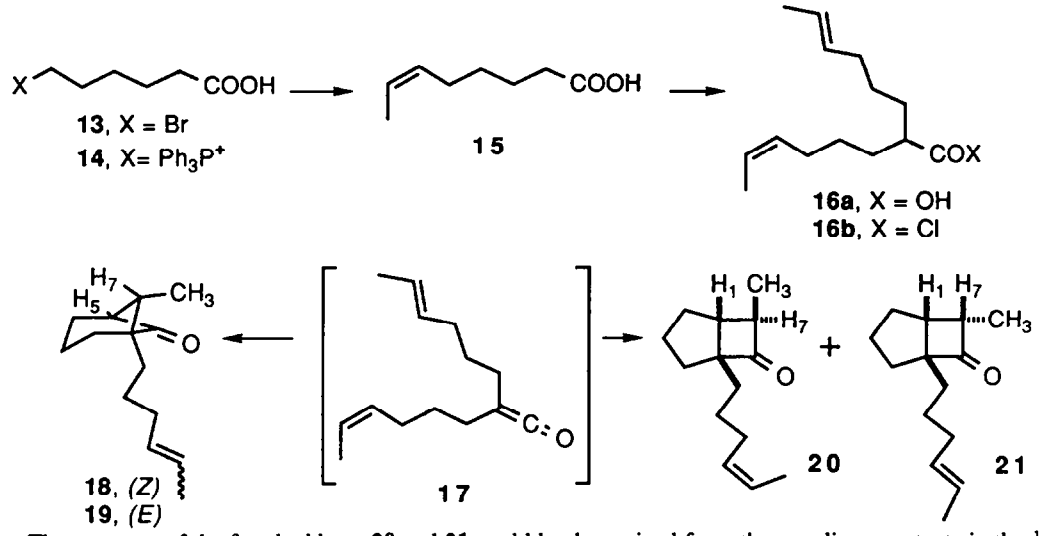
In contrast, a similar analysis suggests that the opposite should be the case in *intramolecular* cycloadditions. Intramolecular cycloaddition of a ketene with a *trans*-alkene will still occur through the moderately hindered transition state **12**. Intermolecular cycloaddition of a ketene with a *cis*-alkene must occur through the very hindered transition state **11** since the unhindered transition state **10** is not accessible with a three-atom tether.

Having established that dialkylketenes undergo intramolecular cycloadditions with alkenes in good yield, we were in a position to carry out a competition experiment between *cis*- and *trans*-alkenes, something that cannot usually be done in intramolecular cycloadditions. Analysis of the ratio of cycloadducts from dialkenylketene **17** will establish the relative reactivities of *cis*- and *trans*-alkenes in an intramolecular cycloaddition.

Bromo acid **13** is converted to the phosphonium salt **14**.[13] Treatment of **14** with sodium hydride in DMSO provides the ylide that is treated with acetaldehyde to give acid **15** as a 12:1 Z-E mixture.[13] Alkylation of the dianion of **15**[7] with *(E)*-6-iodo-2-hexene furnishes 38% of acid **16a**. Acid **16a** is converted to acid chloride **16b**, that is added to a solution of Et_3N in toluene at reflux to give 34% of a 5:1 mixture of **18** and **19** and 6% of a 5:1 mixture of **20** and **21**.

The structure of the major isomer **18** follows from an analysis of the coupling constants in the ^1H NMR spectrum. The alkenyl protons are coupled to each other with J equal to 10.8 Hz, indicating that the double bond is cis. The coupling constant $J_{5,7}$ is 0 Hz, establishing that **18** is an *anti*-7-methylbicyclo[3.1.1]heptan-6-one as discussed above for **9c**. The minor isomer **19** could not be separated from **18** making structure assignment difficult. The ^1H NMR spectra of these isomers are very similar suggesting that they differ only in the stereochemistry of the side chain double bond. The carbon spectra are also very similar. The alkene carbons

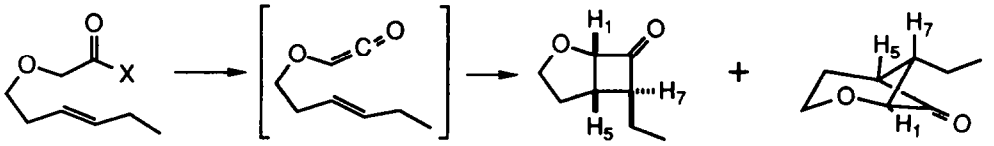
of **19** are shifted downfield from those of **18** by 0.8 ppm suggesting that the side chain double bond of **19** is trans.



The structure of the fused adducts **20** and **21** could be determined from the coupling constants in the ^1H NMR spectrum. In **20**, H_7 absorbs at δ 2.56 and is coupled to H_1 with J = 4.7 Hz. In **21**, H_7 absorbs at δ 3.32 and is coupled to H_1 with J = 10.0 Hz. These values are very close to model compounds lacking the alkenyl side chain.[11] The alkenyl protons in the major isomer **20** are coupled to each other with J = 10.8 Hz indicating that the double bond is cis.

Bridged cycloadduct **18** (28%) and fused cycloadduct **20** (5%) are both the result of stereospecific addition of the ketene to the *trans*-alkene. Fused cycloadduct **21**(1%) results from addition to the *cis*-alkene. Bridged cycloadduct **19** (6%) could be formed from cycloaddition of the E,E isomer of ketene **17** which constituted a 10% impurity. It also could have formed by a non-stereospecific addition to the *cis*-alkene as we have observed with a related chloroketene.[10a] These results suggest that a *trans*-alkene is approximately 33 times more reactive than a *cis*-alkene in an intramolecular cycloaddition with a dialkylketene.

Cycloaddition of Alkoxyketenes with *trans*-Alkenes. We have previously shown that alkoxyketenes do not undergo cycloaddition with *cis*-alkenes.[14] Alkoxyketeniminium salts do react with *cis*-alkenes giving mixtures of cycloadducts whose exact ratio depend on the reaction conditions. Alkoxyketeniminium salts undergo Friedel-Crafts acylations with *trans*-alkenes instead of [2 + 2] cycloadditions.[10a] Since we have established that *trans*-alkenes are more reactive than *cis*-alkenes in intramolecular cycloadditions, it was of interest to examine the cycloaddition of an alkoxyketene with a *trans*-alkene. *trans*-3-Hexen-1-ol is converted to acid **22a** as previously described.[14] Acid **22a** is converted to acid chloride **22b** with oxalyl chloride. Acid chloride **22b** is added to Et_3 N in toluene at reflux to give 10% of **24**[14] and 30% of **25**. The structure of **25** follows from $J_{1,7}$ and $J_{5,7}$ which are both 0 Hz, a value consistent only with *anti*-7-ethyl-2-oxabicyclo[3.1.1]heptan-6-one. The long range coupling constant $J_{1,5}$ is 7 Hz as is typically observed in bicyclo[3.1.1]heptanones.[14]

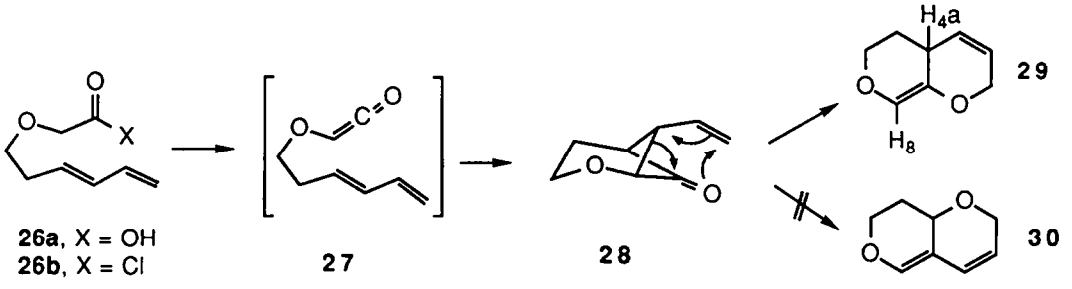


22a, X = OH
22b, X = Cl

23 **24** **25**

The formation of **25** and **24** from intramolecular cycloaddition to a *trans*-alkene and the failure of the alkoxyketene to add to the *cis*-alkene, indicates that alkoxyketenes react more rapidly with *trans*-alkenes than with *cis*-alkenes, as we have previously observed with chloroketenes,[10a] vinylketenes[10a] and dialkylketenes. With all classes of ketenes the bicyclo[3.1.1]heptanone is the major product; in some cases it is the exclusive product.

Cycloaddition of Alkoxyketenes with Dienes. Dienes are more nucleophilic than alkenes and therefore react more rapidly in intermolecular cycloadditions with ketenes. With two recent exceptions,[2b,i] the intramolecular cycloadditions of ketenes with dienes have not been investigated. Due to the ease of synthesis, dienyloxyketenes provide an attractive vehicle for studying the suitability of dienes in intramolecular [2 + 2] cycloadditions. *trans*-3,5-Hexadien-1-ol[15] is converted to 69% of acid **26a** as previously described.[14] Treatment of acid **26a** with oxalyl chloride provides acid chloride **26b** which is added to Et_3N in toluene at reflux to give 40% of **29**. Presumably, ketene **27** undergoes the expected cycloaddition to give cycloadduct **28**. Formation of a bicyclo[3.1.1]heptanone, rather than a bicyclo[3.2.0]heptanone, from **27** should be even more highly favored than with **23** due to the electronic effects of the terminal double bond.[1,4,14] 3-Vinylcyclobutanone **28** is not stable at 110 °C and undergoes a retro-Claisen rearrangement[16] driven by relief of cyclobutane ring strain[16a] to give **29**. MMX calculations suggest that **29** is 8.2 kcal/mol more stable than **28**.[9] We attempted to prepare **28** at lower temperatures at which it might be stable. Unfortunately, neither **28** nor **29** were formed on addition of **26b** to a solution of Et_3N in benzene at 25, 50 or 80 °C. Pyran **29** could also be formed directly from **27** by a Diels-Alder reaction of the diene with the carbonyl group of the ketene.



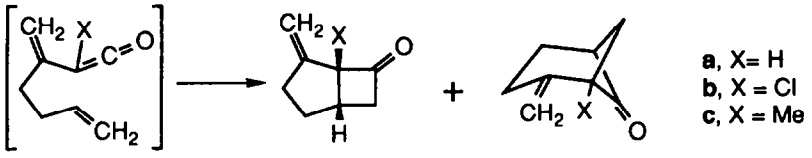
26a, X = OH
26b, X = Cl

27 **28** **29** **30**

The structure of **29** follows from analysis of the ^1H and ^{13}C NMR Spectra. H_8 absorbs at δ 6.48 and is coupled to H_{4a} with J = 1.9 Hz. The other olefinic protons absorb as a broad singlet at δ 5.73. In the ^{13}C NMR spectrum there are absorptions at δ 68.6 and 65.5, in the region expected for sp^3 carbons attached to oxygens,

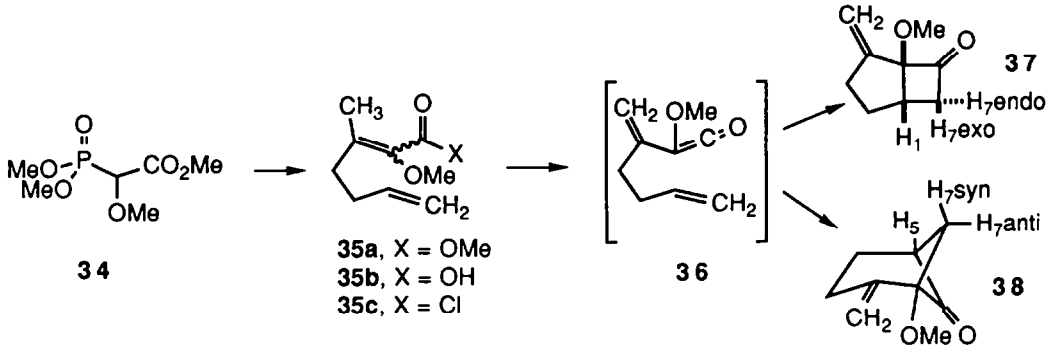
and upfield at δ 30.9 and 29.8. The other possible retro-Claisen product **30** would be expected to have three absorptions downfield between δ 60 and 70 and only one upfield near δ 30.

Cycloaddition of α-Methoxy-α,β-unsaturated Ketenes with Alkenes. We have previously examined the cyclizations of ketenes **31a-c**. Ketenes **31a** and **31b** give only the expected fused adducts **32a** (58%)[17] and **32b** (35%).[10a] To our surprise, we found that ketene **31c** affords both **32c** (29%) and **33c** (7%).[18] This is one of the very few cases in which the electronic effects of the substituent on the alkene do not control the regiochemistry of the cycloaddition.[19] We therefore decided to examine the effect of other α-substituents on the stereochemistry of the cycloaddition.



31 **32** **33**

Reaction of **34**[20,21] with sodium hydride and 5-hexen-2-one in THF affords 80% of **35a** as a mixture of isomers. The formation of a mixture of isomers is of no consequence since both will be converted to **36** by kinetic deprotonation of the more acid methyl proton.[17] Hydrolysis with KOH affords acid **35b** which is converted to acid chloride **35c** with oxalyl chloride. Addition of Et_3N to a solution of acid chloride **35c** in toluene at reflux furnishes 22% of **37** and 28% of **38**.[22]



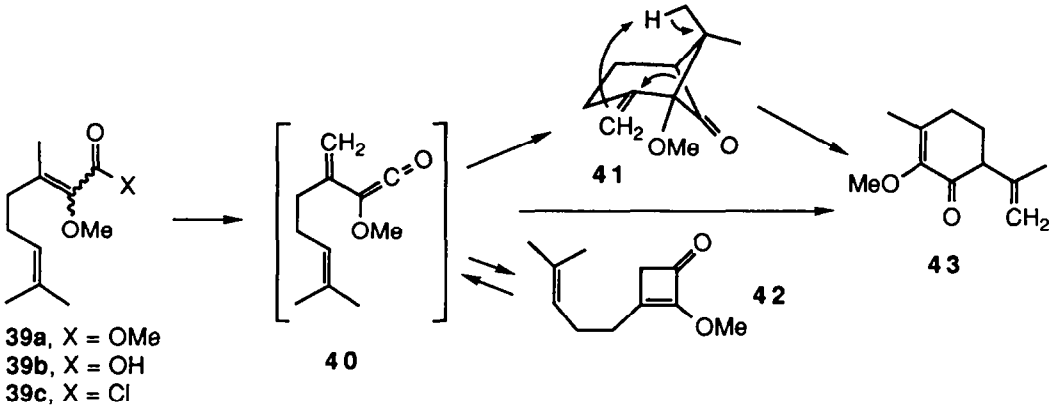
34 **35a**, X = OMe; **35b**, X = OH; **35c**, X = Cl **36**

The structures of **37** and **38** follow from analysis of the coupling constants of the cyclobutane protons. In the bicyclo[3.2.0]heptanone **37**, $J_{1,7exo}$ = 9.7 Hz, $J_{1,7endo}$ = 6.2 Hz, and $J_{7endo,7exo}$ = 18.0 Hz. These values are typical for this ring system.[11] In the bicyclo[3.1.1]heptanone **38**, $J_{1,7anti}$ = 7.4 Hz, $J_{1,7syn}$ = 1.5 Hz, and $J_{7anti,7syn}$ = 9.2 Hz. These values are typical for this ring system.[14,18]

Bicyclo[3.1.1]heptanone **38** is the major product in the cycloaddition of ketene **36**. Addition of the least substituted, most nucleophilic carbon to the ketene carbonyl will give bicyclo[3.2.0]heptanone **37**. However, the initial bond formation for this reaction gives an entropically disfavored seven-membered ring transition state. The electronically disfavored initial bond formation in the cycloaddition that leads to bicyclo[3.1.1]heptanone **38** gives an entropically favored six-membered ring transition state. The preference for initial bond formation

giving a six-membered ring transition state is significant since bicyclo[3.1.1]heptanones are the exclusive or major products when the electronic effects are removed with a *trans*-1,2-substituted alkene. However, with most terminal alkenes the electronic effects favoring the formation of a bicyclo[3.2.0]heptanone are stronger than the entropic effects favoring formation of a bicyclo[3.1.1]heptanone. Ketene **36** is an exception. Apparently, the substituent effects in ketenes **36** and **31c** are such that the entropic effects favoring the formation of the bicyclo[3.1.1]heptanone are comparable to the electronic effects favoring the formation of the bicyclo[3.2.0]heptanone.

Reaction of **34** with sodium hydride and 6-methyl-5-hepten-2-one in THF affords ester **39a** as a mixture of isomers.[21,22] Hydrolysis with KOH affords acid **39b** (51% from **34**) that is converted to acid chloride **39c** with oxalyl chloride in THF at reflux. Addition of Et_3N to a solution of **39c** in toluene at reflux, followed by reflux for 4 h, provides 17% of bicyclo[3.1.1]heptanone **41**, 20% of cyclobutenone **42** and 10% of cyclohexenone **43**.



39a, X = OMe
39b, X = OH
39c, X = Cl

Bicyclo[3.1.1]heptanone **41** is the expected product of this reaction. We have previously reported the formation of the cyclobutenones by electrocyclic ring closure of α,β-unsaturated ketenes that contain a substituent on the ketene and α-carbon, and are β-unsubstituted.[23,24] Ketene **40**, with this substitution pattern, should give cyclobutenone **42**. At 130 °C the ring closure is reversible, so that these cyclobutenones can be converted to the expected [2 + 2] cycloadducts.[23] However, heating cyclobutenone **42** in toluene at 140 °C gives only cyclohexenone **43**. We believe that cyclobutenone **42** undergoes the expected ring opening to give ketene **40** which cyclizes as expected to give bicyclo[3.1.1]heptanone **41**. However, at 140 °C, bicycloheptanone **41** is not stable, and undergoes a retro-ene reaction to give cyclohexenone **43**. Heating bicycloheptanone **41** at 140 °C in toluene gives cyclohexenone **43**, establishing that **41** is a competent intermediate in the conversion of **42** to **43**. Cyclohexenone **43** could also be formed directly by Friedel-Crafts acylation.

We have established that dialkylketenes should be generally useful in intramolecular [2 + 2] cycloadditions, that *trans*-alkenes are approximately 33 times more reactive than *cis*-alkenes in these cycloadditions and that in some cases entropic effects can overcome electronic effects leading to the formation of bicyclo[3.1.1]heptanones from terminal alkenes.

Experimental Section

6-Iodo-2-methyl-2-hexene (8a) was prepared by an orthoester Claisen rearrangement of 2-methyl-3-buten-2-ol with triethyl orthoacetate,[25a] and reduction of the ester with lithium aluminum hydride.[25b] The alcohol was converted to the mesylate with mesyl chloride in CH_2Cl_2 which was reacted with sodium iodide in acetone. *(E)*-6-Iodo-2-hexene (**8b**) was prepared in the same manner from the commercially available alcohol.

2-Methyl-6-heptenoic acid (5a) was prepared by the procedure of Pfeffer and Silbert.[7] To a stirred solution of diisopropylamine (1.23 g, 12.6 mmol) in 8.1 mL of THF at 0 °C was added n-butyllithium (4.9 mL of a 2.6 M solution in hexane, 12.6 mmol) dropwise via syringe. The resulting solution was stirred at 0 °C for 30 min. To this solution was added propionic acid (0.407 g, 5.49 mmol) in 2 mL of THF at 0 °C resulting in immediate formation of a white precipitate. HMPA (1.96 g, 11.0 mmol) was then added at 0 °C. Most of the precipitate dissolved and the solution became yellow in color. After stirring this solution for 1 h at 25 °C, the solution was cooled to 0 °C and 5-bromo-1-pentene (0.818 g, 5.49 mmol) was added rapidly. The resulting colorless solution was stirred at 25 °C for 2 h. The reaction was quenched by acidification to pH 2 with 10% hydrochloric acid. The solution was then extracted three times with ether. The combined organic layers were washed with brine and dried. Evaporation of solvent gave 0.719 g of crude **5a**. Purification of a 0.691 g portion by flash chromatography on silica gel (85:15:0.2 hexane:EtOAc:AcOH) gave 0.456 g (61%) of pure **5a**:[26] ^{1}H NMR 5.80 (ddt, 1, J = 17.1, 10.2, 6.7), 5.01 (ddt, 1, J = 17.1, 3, 1.2), 4.96 (ddt, 1, J = 10.2, 3, 1.2), 2.47 (br tq, 1, J = 7, 7.6), 2.07 (br dt, 2, J = 7, 7), 1.68 (m, 1), 1.37-1.53 (m, 3), 1.19 (d, 3, J = 7.6).

5-Methylbicyclo[3.2.0]heptan-6-one (8a). A solution of acid **5a** (0.150 g, 1.05 mmol) in 5.6 mL of benzene was treated with oxalyl chloride (0.660 g, 5.25 mmol) to give the acid chloride **6a** which was dissolved in 5 mL of benzene and added dropwise to a solution of Et_3N (0.425 g, 4.20 mmol) in benzene (16 mL) at reflux. The reaction was heated for an additional 4 h after the addition was completed. Workup gave 0.200 g of crude **8a**. Purification of a 0.181 g portion by evaporative distillation (25 °C, 0.10 torr) gave 53.7 mg (45%) of pure **8a**:[8] ^{1}H NMR 3.19 (dd, 1, H_{7exo}, J = 19.4, 10.3), 2.47 (dd, 1, H_{7endo}, J = 19.4, 4.8), 2.46 (m, 1), 2.03 (dd, 1, J = 13.0, 6.1), 1.48-1.93 (m, 4), 1.35 (m, 1), 1.25 (s, 3); ^{13}C NMR 217.9 (C=O), 71.1 (C, C_5), 48.8 (CH_2), 37.2 (CH_2), 36.1 (CH, C_1), 32.8 (CH_2), 25.3 (CH_2), 18.4 (CH_3).

2,7-dimethyl-6-octenoic acid (5b) was prepared from propionic acid (0.500 g, 6.75 mmol) and 6-iodo-2-methyl-2-hexane (**22b**) as described above. Purification by flash chromatography on silica gel (90:10:0.2 hexane:EtOAc:AcOH) gave 0.588 g (51%) of pure **5b**[27] ^{1}H NMR 5.10 (qqt, 1, J = 1.4, 1.4, 7.2), 2.46 (tq, 1, J = 7.0, 7.0), 1.99 (br dt, 2, J = 7.2, 7.2), 1.68 (d, 3, J = 1.0), 1.60 (s, 3), 1.31-1.51 (m, 4), 1.18 (d, 3, J = 7.0); ^{13}C NMR 183.9, 132.2, 124.6, 39.8, 33.6, 28.3, 27.8, 26.1, 18.1, 17.2; IR (neat) 2950, 2910, 1695, 1455, 1405, 1369, 1380, 1227, 930 cm^{-1}.

1,7,7-Trimethylbicyclo[3.1.1]heptan-6-one (9b). Acid **5b** (0.148 g, 0.867 mmol) was converted to the acid chloride as described above. The acid chloride was added dropwise to a mixture of Et_3N (0.351 g, 3.47 mmol) in toluene at reflux. The solution was heated at reflux for 5 h and was worked up to give 0.161 g of crude product. Purification of a 0.133 g portion by flash chromatography on silica gel gave 19.8 mg (23%) of pure **9b**: ^{1}H NMR 2.50 (dd, 1, H_5, J = 5.3, 1.8), 2.05-2.31 (m, 3), 1.75-1.89 (m, 1), 1.46-1.66 (m, 2), 1.13 (s, 3), 1.01 (s, 3), 0.87 (s, 3); ^{13}C NMR 217.7 (C=O), 63.7 (C), 63.5 (CH), 36.3 (CH_2), 32.5 (C), 27.9 (CH_2), 25.2 (CH_3), 17.1 (CH_2), 15.3 (CH_3), 13.8 (CH_3); IR (neat) 2953, 1774, 1450, 1368, 1257, 1093, 1013, 798 cm^{-1}.

***(E)*-2-methyl-6-octenoic acid (5c)** was prepared from propionic acid (0.234 g, 3.14 mmol) and *(E)*-6-iodo-2-hexene (0.664 g, 3.16 mmol) as described above. Purification by flash chromatography on silica gel (90:10:0.2 hexane:EtOAc:AcOH) gave 0.248 g (50%) of pure **5c**:[28] ^{1}H NMR 5.44 (dq, 1, J = 15.1, 4.7), 5.38 (dt, 1, J = 15.1, 4.4), 2.46 (br tq, 1, J = 7, 7.0), 1.99 (br dt, 2, J = 6, 4.4), 1.58-1.75 (m, 1), 1.64 (d, 3, J = 4.7), 1.32-1.51 (m, 3), 1.18 (d, 3, J = 7.0); ^{13}C NMR 183.3, 130.8, 125.2, 139.3, 33.0, 32.4, 27.0, 17.9, 16.8; IR (neat) 2940, 1713, 1465, 1415, 1477, 1290, 1237, 959 cm^{-1}.

***anti*-1,7-Dimethylbicyclo[3.1.1]bicycloheptan-6-one (9c).** A solution of acid **5c** (0.178 g, 1.14 mmol) in benzene was treated with oxalyl chloride (0.724 g, 5.70 mmol) to give the acid chloride as previously described. The acid chloride was dissolved in benzene and added dropwise to a mixture of Et_3N (0.46 g, 4.56 mmol) in benzene at reflux. The solution was heated for 12 h and was worked up to give 0.217 g of crude **9c**. Purification of a 0.179 g sample by flash chromatography on silica gel (97:3 ether:pentane) gave 58.2 mg (45%) of pure **9c**: ^{1}H NMR 2.63 (ddd, 1, H_5, J = 4.1, 8.0, 0.9), 2.12-2.35 (m, 3), 2.06 (ddd, 1, J = 13.0, 8.0, 4.2), 1.95 (dq, 1, H_7, J = 0.9, 6.9), 1.70-1.81 (m, 1), 1.59 (ddddd, 1, J = 14.4, 8, 8, 8, 8), 0.97 (d, 3, J = 6.9), 0.95 (s, 3); ^{13}C NMR 215.4 (C=O), 64.1 (C), 62.3 (CH, C_5), 41.6 (CH_2), 35.7 (CH, C_7), 33.0 (CH_2), 18.4

(CH_2), 14.6 (CH_3), 14.0 (CH_3); IR (neat) 2929, 2842, 1765, 1457, 1387, 1280, 1082, 1039, 995, 900, 866 cm^{-1}. Anal. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 77.87, 10.45.

(Z)-6-Octenoic Acid 15. Bromoacid **13** was converted to phosphonium salt **14** as previously described.[13] Conversion of phosphonium salt **14** to the ylide with dimsyl sodium in DMSO as previously described,[13] followed by addition of acetaldehyde gave acid **15**[29] as an 11:1 mixture of (*Z*) and (*E*) isomers: ^1H NMR 5.45 (dqt, 1, *J* = 10.8, 6.6, 1.5), 5.36 (dqt, 1, *J* = 10.8, 1.7, 7.0), 2.36 (t, 2, *J* = 7.3), 2.07 (br dt, 2, *J* = 7, 7), 1.60 (dd, 3, J = 6.5, 1.5), 1.58-1.73 (m, 2), 1.34-1.48 (m, 2); ^{13}C NMR 180.1, 130.0, 124.3, 33.9, 28.9, 26.4, 24.3, 12.7.

(E)-2-((Z)-4-Hexen-1-yl)oct-6-enoic Acid (16a). (Z)-6-Octenoic acid **15** (0.327 g, 2.30 mmol) was converted to the dienolate as previously described.[7] Addition of (E)-6-iodo-2-hexene (0.483 g, 2.30 mmol) and reaction as described above gave 0.498 g of crude **16a**. Purification of a 0.408 g portion by flash chromatography on silica gel (90:10:0.2 hexane:EtOAc:AcOH) gave 0.159 g (38%) of pure **16a**: ^1H NMR 5.51-5.37 (m, 4), 2.31-2.38 (m, 1), 2.05 (dt, 2, *J* = 7.3, 7.3), 1.98 (br dt, 2, *J* = 7, 7), 1.64 (d, 3, *J* = 4.6), 1.60 (dd, 3, *J* = 6.5, 1.4), 1.48 (br tt, 2, *J* = 5, 5), 1.31-1.42 (m, 6); ^{13}C NMR 182.4, 130.8, 130.0, 125.2, 124.2, 45.3, 32.4, 31.7, 31.6, 27.2 (2 carbons), 26.6, 17.9, 12.8; IR (neat) 3013, 2918, 2853, 1707, 1457, 1284, 1232, 963 cm^{-1}. Anal. Calcd for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78. found: C, 74.98; H, 10.86.

***exo*-5-((Z)-4-Hexen-1-yl)-7-methylbicyclo[3.2.0]heptan-6-one (20), *endo*-5-((E)-4-hexen-1-yl)-7-methylbicyclo[3.2.0]heptan-6-one (21), *anti*-1-((Z)-4-hexen-1-yl)-7-methylbicyclo[3.1.1]heptan-6-one (18) and *anti*-1-((E)-4-hexen-1-yl)-7-methylbicyclo-[3.1.1]heptan-6-one (19).** A solution of acid **16a** (0.126 g, 0.562 mmol) in benzene was treated with oxalyl chloride (0.357 g, 2.81 mmol) as previously described, to give the acid chloride which was then added dropwise to a mixture of Et_3N (0.230 g, 2.25 mmol) in toluene at reflux. After addition, the solution was heated for an additional 4 h and was then worked up as usual to give 0.172 g of a crude mixture of adducts. Purification of a 0.144 g portion of the crude material by flash chromatography on silica gel (95:5 hexane:EtOAc) gave 6.0 mg (6%) of an inseparable 5:1 mixture (by GC analysis) of **20** and **21** followed closely by 32.3 mg (34%) of an inseparable 4.7:1 mixture (by GC analysis) of **18** and **19**.

The data for the **20** and **21** were obtained from the mixture: IR ($CDCl_3$) 2915, 2843, 1758 cm^{-1}.

The data for **20**: ^1H NMR 5.47 (dqt, 1, *J* = 10.8, 6.1, 1.5), 5.35 (dqt, 1, *J* = 10.8, 0.8, 7.1), 2.56 (dq, 1, H_7, *J* = 4.7, 7.6), 2.14 (br dd, 1, *J* = 5, 5), 2.02 (br tt, 2, *J* = 8, 8), 1.24-1.98 (m, 10), 1.59 (dd, 3, *J* = 6.1, 0.8), 1.17 (d, 3, *J* = 7.6); ^{13}C NMR 217.3 (C=O), 130.2 (HC=), 124.2 (HC=), 73.0 (C, C_5), 55.7 (CH), 43.3 (CH), 34.9 (CH_2), 33.7 (CH_2), 32.7 (CH_2), 27.2 (CH_2), 25.8 (CH_2), 25.3 (CH_2), 13.7 (CH_3), 12.8 (CH_3).

The data for **21**: ^1H NMR 5.29-5.55 (m, 2), 3.32 (dq, 1, H_7, *J* = 10.0, 7.5), 1.2-2.18 (m, 18), 0.97 (d, 3, *J* = 7.5).

The data for **18** and **19** were determined from the mixture: IR (neat) 3016, 2931, 2864, 1772, 1450, 1382, 1266, 1066 cm^{-1}. Anal. Calcd for $C_{14}H_{22}O$: C, 74.95; H, 10.78. Found: C, 74.98; H, 10.86.

The data for **18**: ^1H NMR 5.46 (dqt, 1, *J* = 10.8, 6.4, 1.5), 5.35 (dqt, 1, *J* = 10.8, 1.4, 7.1), 2.58 (dd, 1, H_5, *J* = 3.6, 3.2), 2.18-2.32 (m, 3), 2.06 (ddd, 1, *J* = 11.4, 7.6, 3.4), 2.02 (br dt, 2, *J* = 7, 7), 1.95 (q, 1, H_7, *J* = 6.8), 1.50-1.84 (m, 1), 1.60 (dd, 3, J = 6.4, 1.4), 1.36-1.57 (m, 2), 1.42 (dt, 2, *J* = 1.8, 6.3), 1.14-1.25 (m, 1), 0.99 (d, 3, *J* = 6.8); ^{13}C NMR 215.3 (C=O), 130.1 (HC=), 124.2 (HC=), 67.4 (C), 62.1 (CH), 38.6 (CH_2), 35.8 (CH), 33.2 (CH2), 28.1 (CH_2), 27.3 (CH_2), 23.5 (CH_2), 18.8 (CH_2), 14.6 (CH_3), 12.8 (CH_3).

The data for **19**: ^1H NMR 5.53-5.30 (m, 2), 1.10-2.62 (m, 14), 1.64 (d, 3, *J* = 5.7), 0.98 (d, 3, *J* = 6.8); ^{13}C NMR 130.9 (HC=), 125.2 (HC=), 33.1 (CH_2), 28.0 (CH_2), 17.9 (CH_3). Nine carbons were not observed.

***trans*-3-Hexenyl-1-oxyacetic Acid (22a).** *trans*-3-Hexen-1-ol (1.0 mL, 0.82 g, 8.14 mmol) was added to a suspension of NaH (0.41 g of 60% suspension in mineral oil, 10.36 mmol) in 6 mL of THF at 25 °C under N_2. The mixture was stirred at 25 °C for 0.5 h and bromoacetic acid (1.14 g, 8.2 mmol) dissolved in 5 mL of THF was added. The mixture was heated at reflux for 5 h, cooled and then stirred at 25 °C for 12 h. Normal workup[14] gave 0.60 g (46%) of *trans*-3-hexenyl-1-oxyacetic acid (**22a**): ^1H NMR 5.65-5.35 (m, 2), 4.15 (s, 2) 3.58 (t, 2, *J* = 6.9), 2.33 (dt, 2, *J* = 7.5, 6.8), 2.02 (m, 2), 0.97 (t, 3, *J* = 7.5); ^{13}C NMR 175.5, 134.9, 124.3, 71.8, 67.6, 32.6, 25.5, 13.6; IR 1730 cm^{-1}. Anal. Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.40; H, 9.21.

6-Ethyl-2-oxabicyclo[3.1.1]heptan-6-one (25) and 6-Ethyl-2-oxabicyclo[3.2.0]-heptan-7-one (24). Oxalyl chloride (0.30 mL, 0.44 g, 3.52 mmol) was added to a solution of acid **22a** (0.19 g, 1.17 mmol) in 6 mL of dry THF under N_2 at 25 °C. The mixture was heated at reflux for 2 h, cooled and the solvent

was removed in vacuo. The residue was treated with two additional portions of dry THF, each time removing solvent and excess oxalyl chloride in vacuo.

The crude acid chloride **22b** was taken up in 10 mL of dry toluene and added over 0.5 h to a solution of NEt_3 (0.42 mL, 0.30 g, 3.01 mmol) in 25 mL of dry toluene at reflux under N_2. The mixture was heated at reflux for an additional 6 h, cooled, and stirred at 25 °C for 12 h. The mixture was washed with H_2O and saturated NaCl solution, then dried ($MgSO_4$) and the solvent was removed in vacuo to give 0.24 g of crude product. Flash chromatography on silica gel (92:8 hexane: EtOAc) gave 53.9 mg (33%) of **25** followed by 20 mg (12%) of **24**.

The data for **25**: ^{1}H NMR 4.39 (d, 1, J = 6.9), 4.05 (ddd, 1, J = 2.0, 6.9, 11.5), 3.84 (ddd, 1, J = 5.8, 11.5, 10.7), 3.01 (br dd, 1, J = 6.9, 5.8), 2.54 (dddd, 1, J = 1.8, 6.9, 10.7, 12.5), 2.35 (dddd, 1, J = 2.0, 5.8, 12.5, 5.8), 1.91 (dd, 1, J = 8.1, 8.1), 1.38-1.21 (m, 2), 0.94 (t, 3, J = 7.3); ^{13}C NMR 211.2, 93.4, 62.9, 61.8, 43.4, 35.4, 22.1, 11.8; IR 1780 cm^{-1}.

The data for **24** are identical to those previously reported.[14]

3,5-Hexadienyl-1-oxyacetic Acid (26a). 3,5-Hexadien-1-ol[15] (0.91 g, 9.30 mmol) was added to a suspension of a NaH (0.91 g, 9.30 mmol) in 5 mL of THF at 25 °C under N_2. The mixture was stirred at 25 °C for 20 min and bromoacetic acid (1.59 g, 11.45 mmol) in 5 mL of THF was added. The solution was heated at reflux for 6 h and stirred at 25 °C for 12 h. Normal workup gave 0.89 g (62 %) of acid **26a**: ^{1}H NMR 6.32 (ddd, 1, J = 17.0, 10.3, 10.0), 6.11 (ddd, 1, J = 15.2, 10.3, 0.7), 5.67 (dt, 1, J = 15.2, 7.0), 5.10 (dd, 1, J = 17.0, 1.4), 4.98 (dd, 1, J = 10.0, 1.4), 4.12 (s, 2), 3.59 (t, 2, J = 6.7), 2.40 (dt, 2, J = 7.0, 6.7); ^{13}C NMR 175.4, 136.7, 133.1, 130.2, 115.8, 71.1, 67.6, 32.5; IR 1740 cm^{-1}.

2,4a,5,6-Tetrahydropyrano[3,4-*b*]pyran (29). Oxalyl chloride (0.34 mL, 0.51 g, 3.99 mmol) was added to a mixture of **26a** (0.24 g, 1.51 mmol) and NaH (0.14 g of a 60% suspension in mineral oil, 3.39 mmol) in 6 mL of dry THF at 25 °C under N_2. The mixture was heated at reflux for 1.5 h, cooled, and the solvent was removed in vacuo. The residue was treated with two additional portions of THF, each time removing solvent and excess oxalyl chloride in vacuo. The crude acid chloride **26b** was taken up in 10 mL of dry toluene and added over 1.5 h to a solution of Et_3N (0.54 mL, 3.85 mmol) in 25 mL of dry toluene at reflux. The mixture was heated at reflux for 3 h, then stirred at 25 °C for 12 h. Workup as usual gave 0.22 g of crude product. Evaporative distillation gave 83 mg (40%) of **29** still containing traces of impurities: ^{1}H NMR 6.49 (d, 1, J = 1.95), 5.73 (s, 3), 4.36 (dd, 1, J = 16, 3, 0.5), 4.19 (ddd, 1, J = 16, 3, 0.5), 4.11 (ddd, 1, 10.7, 3.5, 2.5), 3.78 (dddd, 1, 12.5, 10.7, 1.9, 0.5), 3.1 (m, 1), 2.02 (dddd, 1, J, 13.6, 6.2, 2.5, 1.9), 1.60 (dddd, 1, J = 13.6, 3.7, 1.9, 0.5); ^{13}C NMR 132.0, 128.53, 126.4, 125.3, 68.6, 65.5, 30.9, 29.8.

Methyl 2-Methoxy-3-methyl-2,6-heptadienoate (35a). Trimethyl methoxyphosphonoacetate (**34**)[20,21] (1.89 g, 8.87 mmol) in 10 mL of THF was added to NaH (0.37 g of 60% suspension in mineral oil, 9.26 mmol) in 5 mL of THF over 1 h at 25 °C under N_2. The mixture was stirred for 0.5 h, and allyl acetone (1.10 mL, 0.92 g, 9.48 mmol) was added over 0.5 h. The mixture was heated at reflux for 3 h, and stirred at 25 °C for an additional 12 h. Normal workup gave 1.29 g (79%) of crude **35a** which was used directly without further purification: ^{1}H NMR 5.82 (ddt, 1, J = 17.1, 10.2, 6.3), 5.02 (d, 1, J = 17.1), 4.98 (d, 1, J = 10.2), 3.78 (s, 3), 3.50 (s, 3), 2.63 (t, 0.5 x 2, J =7.6), 2.39 (t, 0.5 x 2, J = 8.2), 2.24-2.19 (m, 2), 2.10 (s, 0.5 x 3), 1.91 (s, 0.5 x 3); IR (neat) 1720 cm^{-1}.

2-Methoxy-3-methyl-2,6-heptadienoic acid (35b). Ester **35a** (1.29 g, 7.00 mmol) was added to a solution of KOH (1.04 g, 18.54 mmol) in 30 mL of 1:1 MeOH:H_2O. The mixture was heated at reflux for 2 h, cooled, and extracted four times with Et_2O. The aqueous layer was acidified to pH 2 with dilute HCL and extracted four times with Et_2O. The combined organic layers were washed with H_2O and saturated NaCl solution, then dried ($MgSO_4$), and the solvent was removed in vacuo to give 0.82 g of **35b** as a 1:1 mixture of *E* and *Z* isomers (64.5% yield over 2 steps): ^{1}H NMR 5.82 (ddt, 1, J = 17.1, 10.2, 6.3), 5.02 (d, 1, J = 17.1), 4.98 (d, 1, J = 10.2), 3.50 (s, 3), 2.63 (t, 0.5 x 2, J = 7.6), 2.39 (t, 0.5 x 2, J = 8.2), 2.24-2.19 (m, 2), 2.10 (s, 0.5 x 3), 1.91 (s, 0.5 x 3); ^{13}C NMR (169.4, 169.0), (143.8, 143.0), (142.3, 141.3), (137.7, 137.5), (115.1, 114.2), (59.9, 59.6), (33.1, 32.5), (32.4, 31.5), (18.2, 18.0); IR (neat) 1720 cm^{-1}.

1-Methoxy-2-methylenebicyclo[3.1.1]heptan-6-one (38) and 5-Methoxy-4-methylenebicyclo[3.2.0]heptan-6-one (37). Oxalyl chloride (0.34 mL, 0.51 g, 3.99 mmol) was added to a solution of acid **35b** (0.30 g, 1.68 mmol) in 6 mL of THF under N_2 at 25 °C. The mixture was heated at reflux for 1.5 h, cooled, and the solvent was removed in vacuo. The residue was treated with two additional portions of THF, each time removing solvent and excess oxalyl chloride in vacuo. Toluene (20 mL) was added to the crude acid chloride and the solution was heated at reflux. Et_3N (0.60 mL, 0.43 g, 4.30 mL) in 5 mL of THF

was added, and the mixture was heated at reflux for an additional 4 h, then stirred at 25 °C for 12 h. The solution was washed with H_20 and saturated NaCl solution, then dried ($MgSO_4$), and the solvent was removed in vacuo to give 0.26 g of crude product. Flash chromatography on silica gel (96:4 hexane:EtOAc) gave 71 mg (28%) of **38** followed by 56 mg (21%) of **37**.

The data for **38**: ^{1}H NMR 5.20 (dd, 1, J = 2.0, 2.0), 4.92 (dd, 1, J = 2.0, 2.0), 3.47 (s, 3), 3.01 (dddd, 1, J = 7.4, 3.6, 3.6, 1.4), 2.64 (ddddd, 1, J = 16.2, 8.1, 8.1, 2.0, 2.0), 2.40 (ddddd, 1, J = 16.2, 6.4, 6.4, 1.2, 1.2), 2.28 (dd, 1, J = 9.2, 7.4), 2.10 (ddd, 2, J = 8.1, 6.4, 3.6), 1.99 (dd, 1, J = 9.2, 1.5); ^{13}C NMR 204.5, 148.0, 108.0, 77.5, 53.3, 49.3, 27.9, 26.4, 25.7; IR (neat) 1780 cm^{-1}.

The data for **37**: ^{1}H NMR 5.32 (dd, 1, J = 2.2, 2.2), 5.29 (dd, 1, J = 2.2, 2.2), 3.32 (s, 3), 3.09 (ddd, 1, J = 9.9, 6.3, 6.0), 2.94 (dd, 2, J = 18.0, 9.7), 2.66-2.54 (m, 2), 2.51 (dd, 1, J = 18.0, 6.2), 2.02 (dddd, 1, J = 13.0, 11.0, 8.9, 6.0), 1.89 (dddd, 1, J = 13.0, 6.3, 3.0, 0); ^{13}C NMR 204.6, 146.9, 112.6, 104.3, 53.4, 44.9, 35.2, 30.0, 29.7; IR (neat) 1785 cm^{-1}.

Methyl 2-Methoxy-3,7-dimethyl-2,6-octadienoate (39a) was prepared from **34** (1.93 g, 9.12 mmol) and 6-Methyl-5-heptene-2-one (1.28 g, 10.16 mmol) as described above for **35a** to give 1.63 g (84%) of **39a** as a mixture of isomers which was used directly without further purification: ^{1}H NMR 5.10 (br t, 1), 3.8 (s, 3), 3.6 (s, 3), 2.51 (t, 0.5 x 2, J = 8.4), 2.32 (t, 0.5 x 2, J = 8.4), 2.17 (m, 2), 2.10 (s, 0.5 x 3), 1.92 (s, 0.5 x 3), 1.70 (0.5 x 3), 1.69 (s, 0.5 x 3), 1.63 (s, 0.5 x 3), 1.62 (s, 0.5 x 3); IR (neat) 1725 cm^{-1}.

2-Methoxy-3,6-dimethyl-2,7-octadienoic Acid (39b). Hydrolysis of ester **39a** (1.63 g, 7.70 mmol) as described above for **35b** gave 0.92 g of **39b** as a 1:1 mixture of isomers (50.8% over 2 steps): ^{1}H NMR 5.15 (br t, 1), 3.60 (s, 3), 2.55 (t, 0.5 x 2, J = 8.4), 2.21 (t, 0.5 x 2, J = 8.4), 2.15 (m, 2), 2.12 (s, 0.5 x 3), 1.92 (s, 0.5 x 3), 1.70 (s, 0.5 x 3), 1.69 (s, 0.5 x 3), 1.63 (s, 0.5 x 3), 1.62 (s, 0.5 x 3); ^{13}C NMR (169.3, 168.8), (144.2, 143.8), (141.1, 140.9), (132.5, 132.5), (123.5, 1234.3), (60.0, 59.6), (33.9, 33.4), (26.9, 26.1), 25.63, (18.4, 18.1), (17.6, 17.5); IR (neat) 1690 cm^{-1}.

7,7-Dimethyl-1-methoxy-2-methylenebicyclo[3.1.1]heptan-6-one (41), 2-Methoxy-3-(4-methyl-3-pentenyl)-2-cyclobutenone (42) and 2-Methoxy-3-methyl-6-(1-methylethenyl)-2-cyclohexen-1-one (43). Acid **39b** (0.19 g, 0.94 mmol) was converted to acid chloride **39c** as described above. Toluene (20 mL) was added to crude **39c** and the solution was heated at reflux. Et_3N (0.34 mL, 0.25 g, 2.44 mmol) in 5 mL of toluene was added, and the mixture was heated at reflux for an additional 5 h. The mixture was then cooled, washed with H_20 and saturated NaCl solution, then dried ($MgSO_4$), and the solvent was removed in vacuo to give 0.161 g of crude product. Flash chromatography on silica gel (96:4 Hexane: EtOAc) gave 29.2 mg (17%) of **41**, followed by 34.7 mg (22%) of **42**, and 15.9 mg (10%) of **43**.

The data for **41**: ^{1}H NMR 4.99 (dd, 1, J = 1.2, 1.2), 4.96 (dd, 1, J = 1.2, 1.2), 3.63 (s, 3), 2.51-2.45 (m, 1), 2.42-2.30 (m, 1), 1.96-2.08 (m, 2), 1.13 (s, 3), 1.03 (s, 3); ^{13}C NMR 204.2, 146.1, 107.7, 74.0, 59.5, 55.1, 36.7, 28.1, 24.4, 22.7, 16.9; IR (neat) 1790 cm^{-1}.

The data for **42**: ^{1}H NMR 5.15 (br t, 1, J = 7.2), 3.90 (s, 3), 2.72 (s, 2), 2.51 (t, 2, J = 7.5), 2.25 (dt, 1, J = 7.2, 7.5), 1.69 (s, 3), 1.62 (s, 3); ^{13}C NMR 185.9, 148.9, 133.1, 123.3, 122.9, 74.0, 57.5, 42.8, 28.4, 25.7, 24.8; IR (neat) 1760 cm^{-1}.

The data for **43**: ^{1}H NMR 4.95 (dd, 1, J = 1.2, 1.2), 4.76 (dd, 1, J = 1.2, 1.2), 3.64 (s, 3), 3.03 (dd, 1, J = 10.5, 4.8), 2.42-2.37 (m, 2), 2.12-1.91 (m, 2), 1.91 (s, 3), 1.75 (s, 3); ^{13}C NMR 145.0, 143.1, 113.6, 59.7, 55.1, 30.0, 27.1, 20.6, 17.5, carbonyl carbon and two quaternary carbons not observed; IR (neat) 1680 cm^{-1}.

Cyclobutenone **42** (36.4 mg, 0.20 mmol) in 4 ml of dry toluene in a sealed tube was heated at 130-135 °C for 3 d. The solution was cooled, and the solvent was removed in vacuo to give 24.5 mg (67.3%) of cyclohexenone **43.** Bicyclo[3.1.1]heptanone **41** (21.4 mg, 0.12 mmol) in 3 mL of dry toluene in a sealed tube was heated at 130-140 °C for 3 d. The mixture was cooled and the solvent was removed to give 14.2 mg (64%) of cyclohexenone **43**.

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