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PREPARATION OF UNSATURATED α,α-DICHLORO ACID CHLORIDES AND INTRAMOLECULAR [2 + 2] CYCLOADDITIONS OF THE α-CHLOROKETENES REDUCTIVELY GENERATED FROM THEM. EFFECT OF DOUBLE BOND GEOMETRY ON THE CYCLOADDITION

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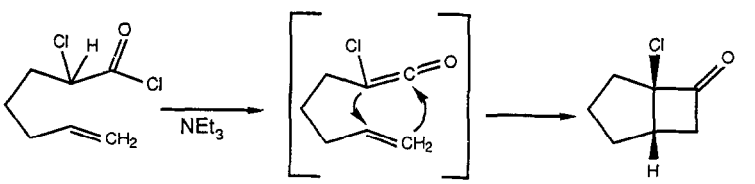
ABSTRACT

Reduction of unsaturated α,α-dichloracid chlorides with zinc dust in THF at reflux generates an unsaturated α-chloroketene which undergoes an intramolecular [2 + 2] cycloaddition in good yield. This reaction can be used with three carbon tethers to prepare 5-chlorobicyclo[3.2.0]heptan-6-ones and 1-chlorobicyclo[3.1.1]heptan-6-ones but fails with larger tethers. Unsaturated ketenes **18** and **28**, with a *trans*-double bond, react stereospecifically to give bicyclo[3.1.1]heptanones **21** and **29** in good yield. Unsaturated ketene **12**, with a *cis*-double bond, reacts with loss of stereochemistry to give a 2:1 mixture of **19** and **21** in poor yield. The greater reactivity of *trans*- than *cis*-double bonds in intramolecular [2 + 2] cycloadditions of ketenes contrasts to intermolecular cycloadditions in which *cis*-double bonds are more reactive. Adducts **41** and **42** containing both a chlorine and exomethylene group can be prepared readily. Reductive dechlorination of adducts can be achieved with either $(n\text{-Bu})_3SnH$ or $CrCl_2$. Ring contraction to give acids **48** and **49** occurs readily on base treatment.

We[1] and others[2] have recently begun to develop the intramolecular [2 + 2] cycloaddition of ketenes to alkenes into a general synthetic method. Although many isolated examples are known,[3] the development of this reaction has been hindered by the limited reactivity of simple alkylketenes which often fail to give any cycloadduct in unconstrained systems, even with an optimal three-atom tether.[2a] Many approaches can be taken to activate the ketene.[1,2] A particularly attractive approach is to introduce a chlorine in the α-position since dichloroketene and chloroalkylketenes have been used with good success in intermolecular cycloadditions.[4] We have recently shown that intramolecular [2 + 2] cycloadditions of unsaturated α-chloroketenes proceed in excellent yield even in those cases where the cycloaddition fails in the absence of the chlorine (see eq. 1).[1f] Unsaturated α-chloroacids were prepared in high yield in a single step by treatment of the acid dianion in THF-HMPA with excess carbon tetrachloride, as a source of electrophilic chlorine, at -78 °C. Treatment of the unsaturated α-chloroacyl chlorides prepared from these acids with Et_3N in benzene at reflux gave the corresponding unsaturated α-chloroketenes, which underwent intramolecular [2 + 2] cycloaddition to provide bicyclo[3.2.0]heptan-6-ones and bicyclo[3.1.1]heptan-6-ones in good yield. The presence of the chlorine in the ketene is crucial, since the corresponding deschloroketenes do not undergo this cycloaddition reaction.



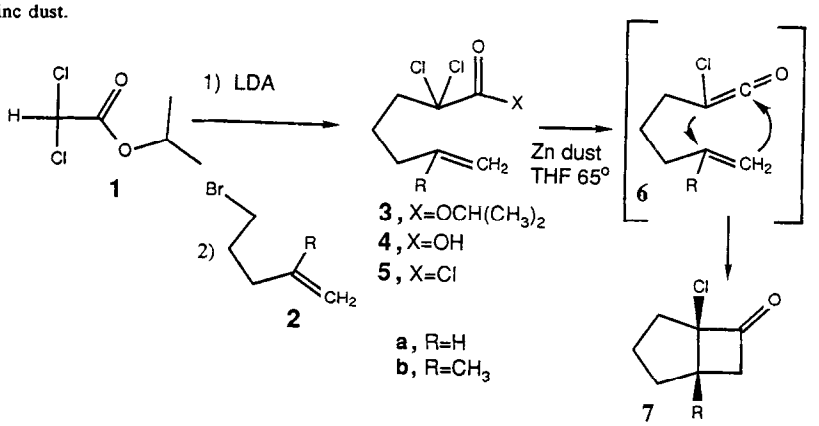
(1)

This procedure is very effective in those cases where the unsaturated acid is readily available. It is less than optimal in those cases in which the unsaturated acid must be constructed from smaller fragments since the chlorine must then be introduced in a separate step after the construction of the carbon skeleton is complete. We therefore turned our attention to the development of procedures for the preparation of unsaturated α-chloroacids by the alkylation of chloroacetic acid derivatives. Preparation of enolates derived from higher α-chloroacids and alkylation of them has been reported.[5] The successful preparation and alkylation of enolates derived from chloroacetic acid has not been reported and all our attempts to modify related literature procedures for this purpose met with failure.

Fortunately, alkylation of isopropyl α,α-dichloroacetate has been reported to proceed in excellent yield.[6] This reaction should be generally useful for the preparation of unsaturated α,α-dichloroacids. Reduction of an unsaturated α,α-dichloroacid chloride with zinc should give the desired chloroketene since zinc reduction of trichloroacetyl chloride is one of two general methods for the preparation of dichloroketene.[4]

RESULTS AND DISCUSSION

Treatment of isopropyl dichloroacetate (1) with lithium diisopropylamide in THF containing one equiv. of HMPA at -78 °C gave the enolate which was treated with 5-bromo-1-pentene (2a) at -20 to -30 °C to give ester 3a in 87% yield.[6a] No reaction occurred at lower temperatures. Hydrolysis of the ester with excess potassium hydroxide in 1:1 methanol-water gave acid 4a in 89% yield. α-Chloroesters are very susceptible to S_N2 displacement, making basic hydrolysis almost impossible.[1f] α,α-Dichloroesters do not undergo S_N2 reactions nearly as readily and can be hydrolyzed without special precautions. Acid 4a was converted to acid chloride 5a by treatment with excess oxalyl chloride in THF at reflux for 2 h. The crude acid chloride was heated at reflux in THF containing a suspension of 2-3 equivalents of zinc dust for 5 h to give cycloadduct 7a[1f] in 58% yield. These results establish that α-chloroketenes such as 6a can be prepared equally well by elimination of hydrogen chloride from the α-chloroacid chloride with Et_3N,[1f] or reductive removal of chlorine from the α,α-dichloroacid chloride with zinc dust.



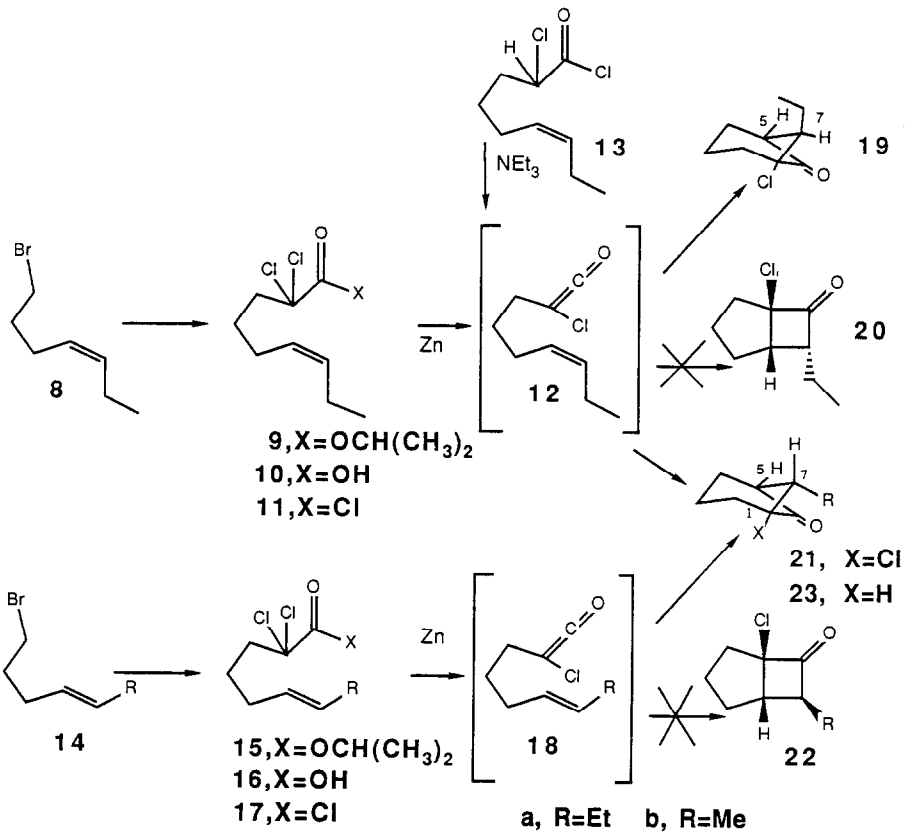
This approach to the synthesis of α-chloroketenes permits us to examine more easily examples in which the unsaturated acid is not available. For instance, alkylation of 1 with 2b gave 3b in 78% yield. Saponification gave acid 4b in 75% yield, which was converted to the acid chloride 5b, which was treated with zinc dust in THF at reflux to give cycloadduct 7b in 64% yield from 4b.

We have previously found that *cis*-chloroketene 12, prepared by elimination of hydrogen chloride from 13, gave a 40% yield of a ~2:1 mixture of cycloadducts to which we tentatively assigned structures 20 and 19, respectively.[1f] The assignment was based partially on the ^1H and ^{13}C NMR spectra of the cycloadducts and partially on presumed mechanistic analogy with our previous studies of cycloadditions of related alkoxyketeniminium salts which gave a similar mixture of regioisomeric adducts.[1e] To determine the effect of the stereochemistry of the double bond on the regioselectivity of the cycloaddition we prepared *trans*-ketene 18a.

Alkylation of 1 with bromide 14a gave ester 15a which was hydrolyzed to give 16a in 40% yield from 14a. Conversion to acid chloride 17a and reduction of 17a to ketene 18a with zinc dust in DME[7] at reflux gave a single adduct in 57% yield. To our surprise, the ^1H and ^{13}C NMR spectra clearly demonstrated that this adduct was identical to the minor adduct obtained from 12. The differing behavior of 12 and 18a was remarkable and unanticipated. Initially, we felt that the different methods of ketene generation might be responsible for the discrepancy in reactivity. We therefore prepared ester 9 in 84% yield by alkylation of 1 with 8. Saponification gave acid 10 in 84% yield which was converted to acid chloride 11 and reduced to give *cis*-ketene 12. Cycloaddition of *cis*-ketene 12, prepared reductively, gave a 30% yield of a 2:1 mixture of the same adducts obtained from 12 prepared by elimination of hydrogen chloride from 13.

These results established that there are fundamental differences in reactivity between ketenes 12 and 18a which are not artifacts of the methods of ketene generation. Before examining the factors responsible for these differences, the structures of the adducts must be unambiguously assigned. *trans*-Ketene 18a underwent a stereospecific reaction to give a single adduct which must be either 21a or 22a. *cis*-Ketene 12 gave the same adduct as a minor product and 19 or 20 as the major product. Once we have determined the structures of the adducts we will be able to address the fundamental mechanistic question. Why does the *trans*-ketene 18a give a

single adduct in good yield while the *cis*-ketene **12** undergoes a non-stereospecific cycloaddition in much lower yield?

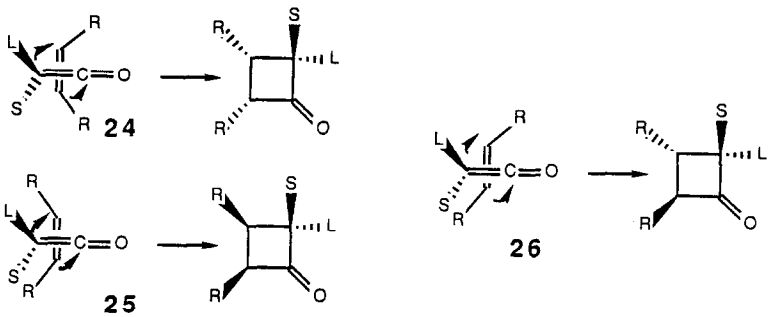


Since the ethyl group complicated the analysis of the NMR spectra of the cycloadducts, *trans*-ketene **18b**, containing a methyl group on the double bond, was prepared. Alkylation of **1** with **14b** gave **15b** in 86% yield which was saponified to give **16b** in 81% yield. Conversion to the acid chloride **17b** and reduction of **17b** with zinc dust gave **21b** in 66% yield. The structure was unambiguously established by analysis of the ^{1}H NMR spectrum and further chemical transformations. Decoupling of the methyl group at δ 1.08 indicated that H-7 absorbs at δ 2.28 and is coupled to H-5 with J = 1.5 Hz as expected for a dihedral angle of 100°. The proton adjacent to the ethyl group in **19** is coupled to the adjacent methine with J = 7 Hz as expected for a dihedral angle of 30° (*vide infra*). The proton adjacent to the carbonyl group should absorb much further downfield in **20** and **22** and should be coupled to the adjacent methine with J ~ 9 and 4 Hz, respectively.[8] The structure assignment was confirmed by reductive dechlorination of **21b** with 5 equivalents of $(n\text{-Bu})_3$SnH in THF at reflux for 48 h to give **23** in 80% yield. The structure of **23** was unambiguously established by analysis of the ^{1}H and ^{13}C NMR spectra. The ^{13}C NMR spectra showed only six peaks since the molecule has a plane of symmetry. Methine proton H-7 absorbs at δ 1.95 (tq, J = 1, 7 Hz). The coupling constant of 1 Hz between H-7 and the adjacent methine hydrogens is expected since the dihedral angle is 100°. The ^{1}H NMR spectra of **23** is quite different from the previously reported spectra[8] of *endo*- and *exo*-7-methylbicyclo[3.2.0]heptan-6-one in which H-7 absorbs at δ 3.31 (ddq, J = 10.3, 3.4, 7.3) and δ 2.57 (ddq, J = 4.4, 3.1, 7.1), respectively. These results conclusively establish that the cycloadduct obtained from **18** is **21**.

The major adduct from **12** is the bicyclo[3.1.1]heptan-6-one **19**. Methine proton H-7 absorbs at δ 2.24 (ddd, J = 7, 7, 7 Hz). The coupling constant of 7 Hz between H-7 and H-5 is consistent with the expected dihedral angle of 30°. The methine proton H-7 of **20** should absorb near δ 3.0 with a coupling constant of 3-5 Hz between H-1 and H-7.[8] *cis*-Ketene **12**, like *trans*-ketene **18**, underwent cycloaddition to give only bicyclo[3.1.1]heptan-6-ones but as a mixture of stereoisomers in much lower yield. With unsymmetrically substituted double bonds, leading bond formation occurs between the carbonyl carbon of the ketene and the less substituted end of the

double bond. With 1,2-disubstituted double bonds, in which there are no strong electronic preferences, leading bond formation occurs exclusively between the carbonyl carbon and the internal end of the double bond to give a bicyclo[3.1.1]heptanone. Why does the *trans*-ketene **18** give a single adduct in good yield while the *cis*-ketene **12** undergoes a non-stereospecific cycloaddition in much lower yield?

cis-Alkenes are much more reactive than *trans*-alkenes in intermolecular cycloadditions with ketenes.[9] Cycloadditions with *cis*-alkenes are always stereospecific, while loss of stereochemistry has occasionally been observed with *trans*-alkenes.[9] These results have been used as evidence for a concerted reaction proceeding through a $[\pi^2_s + \pi^2_a]$ transition state. Intermolecular cycloaddition of a ketene with a *cis*-alkene can occur through unhindered transition state **24** or very hindered transition state **25**, where S and L are the small and large substituents on the ketene. The stereochemistry of the cycloadducts confirms that cycloaddition proceeds through **24**. Intermolecular cycloaddition of a ketene with a *trans*-alkene must occur through the moderately hindered transition state **26**. This cycloaddition is slower due to steric hindrance. Loss of stereocontrol will occur when steric hindrance is sufficient to allow stepwise reaction to occur at a competitive rate.[9]

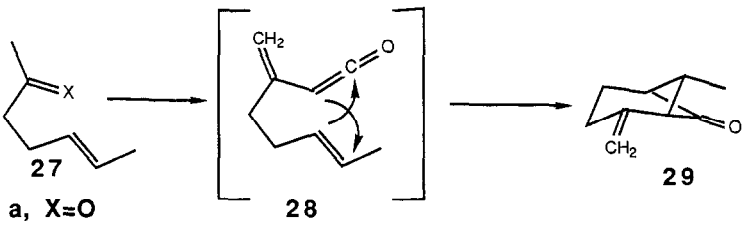


In contrast, similar analysis suggests that *trans*-alkenes should be more reactive than *cis*-alkenes in intramolecular cycloadditions. Intramolecular cycloaddition of a ketene with a *trans*-alkene will still occur through the moderately hindered transition state **26**. However, intramolecular cycloaddition of a ketene with a *cis*-alkene must occur through the very hindered transition state **25** since the unhindered transition state **24** is not accessible with a three-atom tether. Therefore the cycloaddition of **12** proceeds, at least in part, by a stepwise mechanism to give a mixture of **19** and **21** in poorer yield than the concerted cycloaddition of **18** which gives only **21**.

This analysis of the effect of double bond stereochemistry should be valid for other classes of intramolecular ketene cycloadditions. Type II Intramolecular cycloadditions of α,β-unsaturated ketenes[1g,h] show a similar reactivity pattern.[10] A Carroll rearrangement[11] of 3-buten-2-yl acetoacetate gave *trans*-5-hepten-2-one (**27a**) in 80% yield. Horner-Emmons Wittig reaction of **27a** with triethyl phosphonoacetate gave **27b** in 51% yield which was hydrolyzed to give **27c** in quantitative yield. Reaction of **27c** with excess oxalyl chloride gave acid chloride **27d**.[1g,h] Treatment of acid chloride **27d** with Et_3N in benzene at reflux for 2 h gave ketene **28** which underwent a stereo- and regiospecific cycloaddition to give adduct **29** in 56% yield from **27c**. No cyclobutanone is obtained from the isomeric ketene with the *cis*-double bond. Therefore, *trans*-double bonds are also much more reactive toward α,β-unsaturated ketenes in intramolecular [2 + 2] cycloadditions.

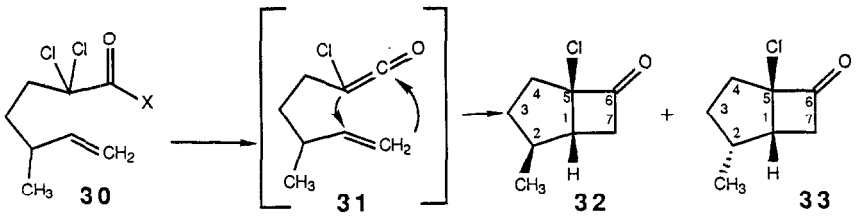
The stereochemistry of **29** was assigned by analysis of the ^1H NMR spectrum. H-1 absorbs at δ 3.31 as a doublet, J = 7.2 Hz and H-5 absorbs at δ 2.81 as a multiplet. These data correspond closely to related systems[1g] and establish that the product is a bicyclo[3.1.1]heptan-6-one since the protons next to the carbonyl group absorb further downfield in 4-methylenebicyclo[3.2.0]heptan-6-ones.[1g,h] The stereochemistry at C-7 is established by the absorption of H-7 at δ 2.13 as a broad quartet, J = 6.8 Hz. The small coupling constants between H-7 and vicinal bridgehead hydrogens is expected since the dihedral angle is 100°. Coupling constants of ~7 Hz are expected in the *syn*-isomer in which the dihedral angle is 30°.

Other examples of the effect of stereochemistry on the intramolecular cycloadditions of ketenes with 1,2-disubstituted alkenes are not available since this class of alkenes is the least reactive in these cycloadditions. 1,2-Disubstituted alkenes do not react with alkoxyketenes. *cis*-1,2-Disubstituted alkenes do undergo an intramolecular cycloaddition with alkoxyketeniminium salts.[1e] *trans*-1,2-Disubstituted alkenes undergo an ene reaction instead.[1e] Since the cycloadditions of alkoxyketeniminium salts are stepwise rather than concerted the change in reactivity pattern is not relevant to our analysis of ketene cycloadditions.[12]



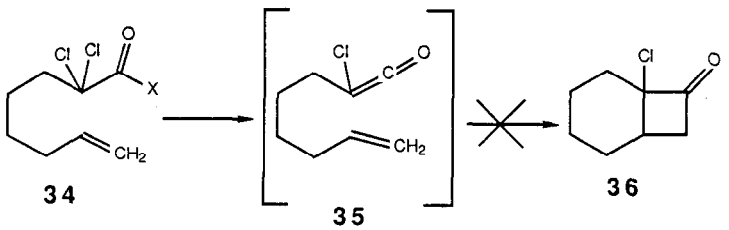
a, X=O
b, X=$CHCO_2Et$
c, X=$CHCO_2H$
d, X=CHCOCl

Chloroketene **31** was prepared to determine the ability of substituents on the tether to control the stereochemistry of the cycloaddition. Alkylation of **1** with 3-methyl-5-bromo-1-pentene gave **30a** in 78% yield. Saponification gave acid **30b** in 75% yield. Reaction of **30b** with oxalyl chloride gave acid chloride **30c** which was reduced with zinc dust in THF at reflux to give ketene **31** which underwent cycloaddition to give a 1.6:1 mixture of **32** and **33** in 65% yield. The stereochemistry of the cycloadducts was convincingly established by examination of the ^{13}C NMR spectra, as previously reported in related systems.[13,1h,j] The γ-gauche butane interaction of the methyl group with carbon-7 in the *endo*-isomer **33** results in upfield shifts of the methyl carbon (5.5 ppm), carbon-2 (3.5 ppm), carbon-1 (3.0 ppm) and carbon-7 (6.2 ppm) as compared to the *exo*-isomer **32**.



a, X=$OCH(CH_3)_2$ b, X=OH c, X=Cl

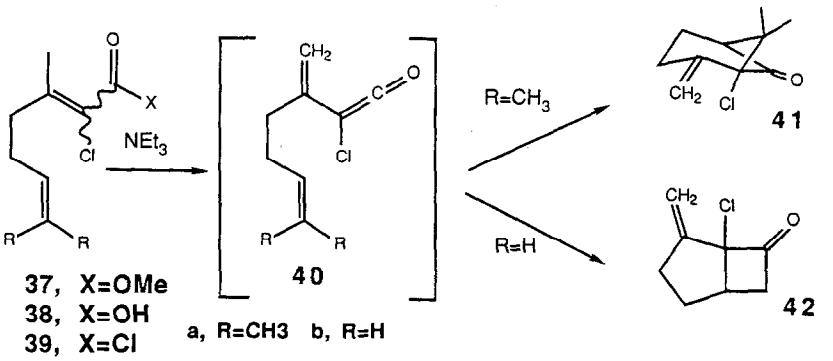
Ketene **35** was prepared to examine the suitability of chloroketene cycloadditions for the preparation of bicyclo[4.2.0]octan-7-ones. Bicyclo[4.2.0]octanones have been prepared in some intramolecular ketene cycloadditions,[1a,2a,g] although these reactions are much less general than the formation of bicyclo[3.2.0]heptanones.[1,2] Alkylation of **1** with 6-bromo-1-hexene gave **34a** which was hydrolyzed and converted to the acid chloride **34c**. Reduction of **34c** with zinc dust gave the ketene **35** which did not undergo cycloaddition to give **36**. Presumably the cycloaddition of **35** with a four atom tether is much slower than cycloadditions with a three atom tether so that dimerization or polymerization of **35** is faster than cycloaddition.



a, X=$OCH(CH_3)_2$ b, X=OH c, X=Cl

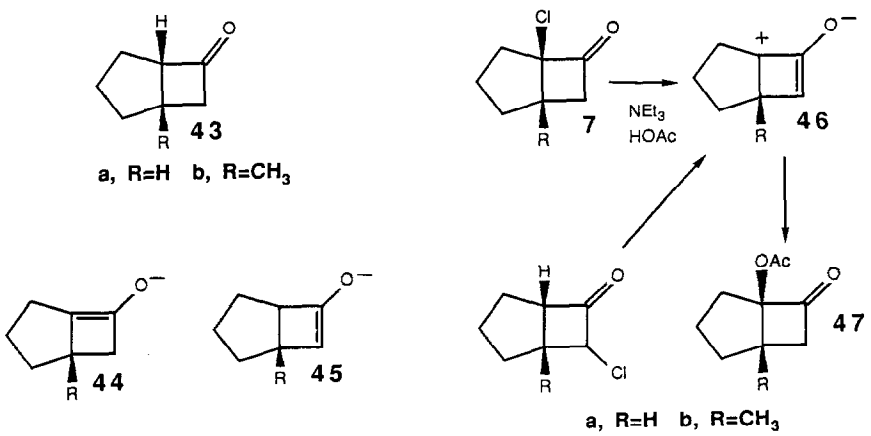
Preparation and Intramolecular Cycloaddition of α-Chloro-α,β-unsaturated Ketenes. Since both the α-chloro group[1f] and the α,β-unsaturated double bond[1g-j] facilitate the cycloaddition we chose to combine them in a single ketene in order to produce a more highly functionalized adduct. α-Chloro-α,β-unsaturated ketenes have been prepared by Dreiding and co-workers by treatment of γ-substituted α-chloroacryloyl chlorides with base and used with good success in intermolecular cycloadditions.[14] Acrylate ester **37a** was prepared as a mixture of stereoisomers by treatment of 6-methyl-5-hepten-2-one with methyl trichloroacetate, zinc dust and Et_2AlCl by the procedure of Oshima, Nozaki and co-workers.[15] The production of a mixture of stereoisomers was of no conse-

quence since we have shown that deprotonation of the acid chloride occurs on the methyl group regardless of the stereochemistry of the double bond.[1h] Hydrolysis of **37a** gave **38a** which was converted to the acid chloride **39a** by reaction with excess oxalyl chloride in toluene at 50 °C. Reaction of **39a** with Et_3N in toluene at reflux gave a 42% yield of cycloadduct **41**. In a similar manner, 5-hexen-2-one was converted to **39b**. Reaction with Et_3N in benzene at reflux gave a 35% yield of cycloadduct **42**. These results establish that the regiochemistry of these intramolecular [2 + 2] cycloadditions, like all others which we have examined,[1] is controlled by the electronic effects of substituents on the double bond. The presence of both the chlorine and the double bond on the ketene leads to a more highly functionalized adduct. The yield of the cycloadduct however, is comparable to that obtained from monoactivated ketenes.



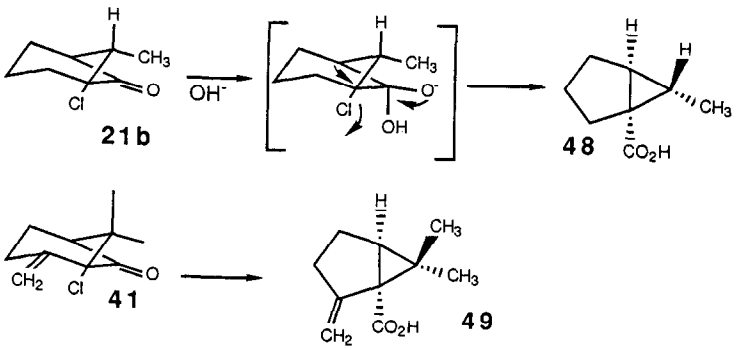
Reactions of Chlorobicycloheptanones. Bicycloheptanones are versatile synthetic intermediates.[4,16] The chemistry of 7-chloro- and 7,7-dichlorobicyclo[3.2.0]heptan-6-ones, prepared by the addition of chloroketenes to cyclopentadiene, has been extensively explored. Since neither 5-chlorobicyclo[3.2.0]heptan-6-ones nor 1-chlorobicyclo[3.1.1]heptan-6-ones are known, we decided to explore the reactivity and synthetic utility of these cycloadducts. Reductive removal of chlorine from 7-chlorobicyclo[3.2.0]heptan-6-ones can be accomplished easily with a wide variety of reducing agents[4,16] including zinc in acetic acid, zinc/copper couple[17] and chromous chloride.[18] Reductive removal of chlorine from 5-chlorobicyclo[3.2.0]heptan-6-ones proved to be much more difficult. Reduction of **7a** with zinc dust in acetic acid was not practical. No reaction occurred at 25 °C; reaction at reflux gave a mixture of the reduction product **43a** and the substitution product **47a**. Reduction to **43a** could be achieved with difficulty using zinc/copper couple in THF at reflux for 4 d. Reduction of **7b** did not occur at all under any of these conditions. The ease of reduction of α-chloroketones should correspond to the stability of the enolate which is formed. Molecular mechanics calculations[19] suggest that enolate **44**, which will be formed from the reduction of **7**, is less stable than enolate **45**, which will be formed by reduction of 7-chlorobicyclo[3.2.0]heptan-6-one, by 11 kcal/mol.

Fortunately, reductive removal of chlorine could be accomplished readily with chromous chloride in acetone.[18] Reduction of **7a** with chromous chloride in acetone for 1.5 h at 25 °C gave a 80% yield of **43a**.[20] Reduction of **7b** was slower, but could be accomplished in 24 h to give **43b**[21] in 78% yield.



Although reduction of **7** is more difficult than reduction of 7-chlorobicyclo[3.2.0]heptan-6-ones, nucleophilic substitution can be accomplished easily. Treatment of **7a** with triethylammonium acetate[18b] in acetone at reflux for 5 d gave an 83% yield of **47a**. Similarly **7b** was converted to **47b** in 96% yield. Substitution occurs by enolization and loss of chloride to give **46** or an equivalent intermediate which reacts with the nucleophile at C-5. Cine substitution of 7-chlorobicyclo[3.2.0]heptan-6-ones also proceeds through **46** to give **47**. Intermediate **46** reacts with nucleophiles at C-5 rather than C-7 since enolate **44** that is produced is much more stable than enolate **45** that would be produced by attack at C-7.

Reduction of 1-chlorobicyclo[3.1.1]heptan-6-ones is much more difficult because the enolate is inaccessible. Reduction of **21** to give **23** was accomplished with difficulty with excess $(n\text{-Bu})_3SnH$ and AIBN in THF at reflux. Treatment of **21** with base resulted in facile ring contraction[4,16] to give **48** as a single isomer in 92% yield. Similarly, reaction of **41** with aqueous lithium hydroxide gave **49**[23] in 72% yield.



Conclusion. The results presented above establish that α-chloroketenes prepared by reduction of α,α-dichloroacid chlorides undergo facile intramolecular [2 + 2] cycloaddition reactions to give synthetically useful adducts. The stereospecific synthesis of bicyclo[3.1.1]heptanones from *trans*-1,2-disubsituted alkenes, which has not been previously observed in intramolecular cycloadditions should be generally useful. The greater reactivity of *trans*- than *cis*-double bonds in intramolecular [2 + 2] cycloaddtions of ketenes contrasts to intermolecular cycloadditions in which *cis*-double bonds are more reactive.

EXPERIMENTAL SECTION

Materials and Methods. NMR spectra were recorded on Varian EM-390 and XL-300 spectrometers in $CDCl_3$ unless otherwise indicated. Chemical shifts are reported in δ and coupling constants are reported in Hz. IR spectra were obtained on a Perkin-Elmer 683 spectrometer. Combustion analyses were performed by Galbraith Laboratories. All air-sensitive reactions were run under nitrogen in flame-dried glassware with magnetic stirring. Reagents were added via oven-dried syringes through septa. All solvents for air or moisture sensitive reactions were dried by standard procedures.

Preparation of Starting Materials. Isopropyl dichloroacetate (**1**) was prepared from dichloroacetic acid and isopropanol by the literature procedure.[6] Bromides **2b**,[24] **8**,[25a] **14a**,[25] **14b**,[26] and **30**[24] were prepared from the corresponding alcohol via conversion to the mesylate with mesyl chloride and Et_3N in methylene chloride[27] followed by treatment of the mesylate with lithium bromide in acetone. All alcohols were commercially available except for (*E*)-4-heptenol[25c] which was prepared by an orthoester Claisen rearrangement[28] of 1-penten-3-ol with triethyl orthoacetate and reduction of the resulting ester with LAH. Chloroacrylate **37a** was prepared by the literature procedure.[15] (*E*)-5-Hepten-2-one (**27a**)[29] was prepared in 80% yield by Wilson and Price's modification of the Carroll rearrangement.[11] Horner-Emmons Wittig reaction of triethyl phosphonoacetate with **27a** gave **27b**[30] as a 4:1 *E*-*Z* mixture in 51% yield. Hydrolysis with sodium hydroxide in 1:1 EtOH-H_2O gave a quantitative yield of **27c**[30].

Isopropyl 2,2-Dichloro-6-heptenoate (3a). *n*-BuLi (7.0 mL of 2.5 M solution in hexane, 17.5 mmol) was added to diisopropylamine (3.3 mL, 2.38 g, 23.55 mmol) in 10 mL of dry THF at 0 °C under N_2. HMPA (3.5 mL, 3.61 g, 20.11 mmol) was then added, and the solution was stirred at 0 °C for 0.5 hr. The temperature was lowered to -78 °C and isopropyl dichloroacetate (**1**) (2.5 mL, 3.0 g, 17.62 mmol) was added over 45 min, and the solution was stirred for an additional 0.5 h at -78 °C. 5-Bromo-1-pentene (**2a**) (2.7 mL, 3.40 g, 22.78 mmol) was then added and the temperature was raised to -20 °C over 2 h, and stirred at -20 °C for an additional 0.5 h.

The mixture was poured into a mixture of 20 g of ice and 2 mL of conc. H_2SO_4, the layers were separated, and the aqueous layer was extracted with pentane (3 x 20 mL). The combined organic extracts were washed with H_2O, brine (2 x 20 mL), dried ($MgSO_4$) and the solvent was removed in vacuo to give 4.89 g of crude product. Flash chromatography on silica gel (92:8 hexane-EtOAc) gave 4.12 g (97.6%) of **3a**: ^{1}H NMR 5.79 (ddt, 1, J = 17, 10, 6.8), 5.10 (qq, 1, J = 6.8, 6.8), 5.05 (br d, 1, J = 17), 5.01 (br d, 1, J = 10), 2.41 (m, 2), 2.13 (dt, 2, J = 6.8, 6.8), 1.69 (m, 2), 1.35 (d, 6, J = 6.8); ^{13}C NMR 165.3, 137.4, 115.5, 85.0, 71.8, 44.4, 32.7, 24.3, 21.3; IR (neat) 1760 cm^{-1}.

2,2-Dichloro-6-heptenoic acid (4a). Ester **3a** (4.02 g, 16.82 mmol) was added to a solution of KOH (4.41 g, 16.82 mmol) in 50 mL of 1:1 H_2O:MeOH solution. The mixture was heated at reflux for 2 hr, cooled, and extracted twice with Et_2O. The aqueous layer was acidified to pH 1 with conc. HCl, and was then extracted four times with Et_2O. The combined organic extracts were washed with H_2O (4 x 20 mL), brine, dried ($MgSO_4$), and the solvent was removed in vacuo to give 2.83 g (88.5%) of **4a**: ^{1}H NMR 5.79 (ddt, 1, J = 17.0, 10.0, 6.8), 5.17 (br d, 1, J = 17.0), 5.02 (br d, 1, J = 10.0), 2.25 (m, 2), 2.16 (dt, 2, J = 6.9, 6.9), 1.76 (m, 2); ^{13}C NMR 170.0, 137.3, 115.6, 84.3, 44.3, 32.7, 24.2; IR (neat) 1730 cm^{-1}.

5-Chlorobicyclo[3.2.0]heptan-6-one (7a). Oxalyl chloride (0.20 mL, 300 mg, 2.29 mmol) was added to acid **4a** (0.13 g, 0.66 mmol) in 5 mL of THF under N_2, and the mixture was heated at reflux for 2 hr. After cooling, the solvent and excess oxalyl chloride were removed in vacuo and the residue was treated with additional THF (2 x 3 mL) and the solvent and residual oxalyl chloride were removed in vacuo to give acid chloride **5a** which was used immediately.

Crude **5a** was taken up in 10 mL of dry THF and was added over a 2 hr period to a mixture of zinc dust (100 mg, 1.44 mmol) in 20 mL of THF at reflux. The mixture was heated at reflux for 5 hr and then stirred at 25 °C for 12 hr. The mixture was filtered through celite, the celite was washed with Et_2O. The filtrate was concentrated to half its original volume and an equal amount of pentane was added to precipitate zinc salts. The mixture was filtered and the filtrate was concentrated in vacuo to give 170 mg of crude **7a**. Flash chromatography (10:1 hexane-Et_2O) gave 51.7 mg (58%) of pure **7a**: ^{1}H NMR 3.39 (dd, 1, J = 18.5, 10.0), 2.93 (ddd, 1, J = 5.3, 10.0, 11.0), 2.60 (dd, 1, J = 18.5, 5.3), 2.39 (dd, 1, J = 6.4, 12.5), 1.70-2.18 (m, 5); ^{13}C NMR 204.8, 82.2, 48.3, 41.0, 38.6, 31.9, 24.6; IR (neat) 1780 cm^{-1}. The spectral data are identical to those previously described.[1f]

Isopropyl 2,2-Dichloro-6-methyl-6-heptenoate (3b). Isopropyl dichloroacetate (1) (1.0 mL, 1.21 g, 7.05 mmol) was added to LDA and HMPA as described above and **2b** (1.44 g, 8.85 mmol) was added. Normal workup gave 1.80 g of crude **3b**. Flash chromatography on silica gel (93:7 hexane-EtOAc) gave 1.45 g (81.2%) of **3b**: ^{1}H NMR 5.22 (qq, 1, J = 6.2, 6.2), 4.75 (br s, 1), 4.71 (br s, 1), 2.39 (m, 2), 2.09 (t, 2, J = 6.9), 1.72 (s, 3), 1.68-1.80 (m, 2), 1.35 (d, 6, J = 6.2); ^{13}C NMR 165.4, 144.4, 110.8, 85.0, 71.8, 44.4, 36.7, 22.9, 22.1, 21.3; IR (neat) 1758 cm^{-1}; Anal. Calcd for $C_{11}H_{18}Cl_2O_2$: C, 52.19; H, 7.18. Found: C, 52.00; H, 7.40.

2,2-Dichloro-6-methyl-6-heptenoic Acid (4b). Hydrolysis of ester **3b** (1.25 g, 4.94 mmol) as described above gave 830 mg (89.3%) of **4b**: ^{1}H NMR 4.77 (br s, 1), 4.73 (br s, 1), 2.40 (m, 2), 2.12 (t, 2, J = 7.6), 1.69-1.83 (m, 2), 1.73 (s, 3); ^{13}C NMR 170.7, 144.3, 111.1, 84.2, 44.2, 36.7, 22.7, 22.1; IR (neat) 1742 cm^{-1}.

1-Methyl-5-chlorobicyclo[3.2.0]heptan-6-one (7b). Acid **4b** (260 mg, 1.22 mmol) was converted to the acid chloride which was added to zinc dust (200 mg, 3.04 mmol) in THF at reflux to give 190 mg of crude **7b**. Flash chromatography on silica gel (95:5 hexane-EtOAc) gave 120 mg (64.0%) of **7b**: ^{1}H NMR 2.87 (d, 1, J = 18.6), 2.80 (d, 1, J = 18.6), 2.42 (dd, 1, J = 13.2, 6.6), 1.85-2.05 (m, 3), 1.60-1.85 (m, 2), 1.36 (s, 3); ^{13}C NMR 205.6, 84.5, 54.6, 43.5, 39.5, 39.4, 23.3, 21.8; IR (neat) 1790 cm^{-1}. Anal. Calcd for $C_8H_{11}ClO$: C, 60.57; H, 6.99. Found: C, 60.72; H, 7.08.

Isopropyl 2,2-Dichloro-*cis*-6-nonenoate (9). Isopropyl dichloroacetate (0.75 mL, 900 mg, 5.29 mmol) was added to LDA and HMPA as described above and **8** (1.33 g, 7.53 mmol) was added. Normal workup gave 1.44 g of crude **9**. Flash chromatography on silica gel (96:4 hexane-EtOAc) gave 1.21 g (83.5%) of **9**: ^{1}H NMR 5.15-5.55 (m, 2), 5.10 (qq, 1, J = 6.2, 6.2), 2.35-2.45 (m, 2), 1.98-2.15 (m, 4), 1.55-1.70 (m, 2), 1.32 (d, 6, J = 6.2), 0.95 (t, 3, J = 6.4); ^{13}C NMR 165.4, 132.8, 127.6, 85.0, 71.8, 44.4, 26.2, 25.2, 21.3, 20.5, 14.2; IR (neat) 1758 cm^{-1}.

2,2-Dichloro-*cis*-6-nonenoic Acid (10). Hydrolysis of ester **9** (1.18 g, 4.40 mmol) as described above gave 830 mg (83.5%) of **10**: ^{1}H NMR 5.15-5.55 (m, 2), 2.38-2.44 (m, 2), 1.96-2.18 (m, 4), 1.62-1.74 (m, 2), 1.24 (t, 3, J = 6.6); ^{13}C NMR 170.6, 133.0, 127.4, 84.2, 44.4, 26.1, 25.1, 20.6, 14.2; IR (neat) 1740 cm^{-1}. Anal. Calcd for $C_9H_{14}Cl_2O_2$: C, 47.25; H, 6.43. Found: C, 48.02; H, 6.27.

***syn*- and *anti*-1-Chloro-7-ethylbicyclo[3.1.1]heptan-6-one (19 and 21a).** Acid **10** (0.19 g, 0.84 mmol) was converted to the acid chloride which was added to zinc dust (0.15 g, 2.23 mmol) in THF at reflux as described above to give 0.13 g of crude cycloadduct. Flash chromatography on silica gel (96:4 hexane-EtOAc) gave 15 mg

(10%) of **21a** followed by 29 mg (19%) of **19**. The spectral data for **21a** are described below. The spectral data for **19** are identical to those provided for the compound incorrectly assigned structure **18** in reference 1f.

Isopropyl 2,2-Dichloro-*trans*-6-nonenoate (15a). Isopropyl dichloroacetate (1.0 mL, 1.21 g, 7.05 mmol) was added to LDA and HMPA in THF as described above and **14a** (1.57 g, 9.00 mmol) was added. Normal workup gave 1.88 g of crude **15a**. Flash chromatography on silica gel (10:1 hexane-Et_2O) gave 1.38 g (73.5%) of **15a**: ^1H NMR 5.45 (m, 2), 5.15 (qq, 1, J = 6.2, 6.2), 2.39 (m, 2), 2.05 (m, 4), 1.64 (m, 2), 1.32 (d, 6, J = 6.2), 0.97 (t, 3, J = 7.5); IR (neat) 1740 cm^{-1}.

2,2-Dichloro-*trans*-6-nonenoic Acid (16a). Hydrolysis of ester **15a** (1.06 g, 3.95 mmol) as described above gave 0.48 g (40% from **14a**) of **16a**: ^1H NMR 5.45 (m, 2), 2.42 (m, 2), 2.05 (m, 4), 1.82 (m, 2), 0.98 (t, 3, J = 7.5); ^{13}C NMR 171.2, 133.5, 127.5, 84.2, 44.4, 31.6, 25.5, 24.9, 13.8; IR (neat) 1742 cm^{-1}.

***anti*-1-Chloro-7-ethylbicyclo[3.1.1]heptan-6-one (21a).** Acid **16a** (0.22 g, 1.00 mmol) was converted to the acid chloride which was added to zinc dust (0.161 g, 2.46 mmol) in DME at reflux as described above to give 0.28 g of crude **21a**. Flash chromatography on silica gel (10:1 Hexane-Et_2O) gave 0.10 g (57%) of **21a**: ^1H NMR 2.92 (dd, 1, J = 3.4, 3.4), 2.65 (ddd, 1, J = 13.0, 8.0, 8.0), 2.53 (ddd, 1, J = 13.0, 8.0, 4.5), 2.25-2.31 (m, 1), 2.16-2.24 (m, 1), 2.08 (br dd, 1, J = 10.5, 4.5), 1.85-1.94 (m, 1), 1.65-1.84 (m, 2), 0.96-1.16 (m, 1), 0.98 (t, 3, J = 7.2); ^{13}C NMR 204.5, 77.6, 57.6, 46.1, 43.2, 31.8, 22.8, 19.4, 11.6; IR (neat) 1792 cm^{-1}. Anal. Calcd for $C_9H_{13}ClO$: C, 62.61; H, 7.59. Found: C, 62.22; H, 7.53.

Isopropyl 2,2-Dichloro-*trans*-6-octenoate (15b). Isopropyl dichloroacetate (1.21 g, 7.05 mmol) was added to LDA and HMPA as described above and **14b** (1.38 g, 8.48 mmol) was added. Normal workup gave 1.78 g of crude **15b**. Flash chromatography on silica gel (19:1, hexane-Et_2O) gave 1.44 g (80.8%) of **15b**: ^1H NMR 5.2-5.5 (m, 2), 5.10 (qq, 1, J = 5.7, 5.7), 2.38 (m, 2), 2.05-2.09 (m, 2), 1.56-1.72 (m, 2), 1.65 (d, 3, J = 6.0), 1.33 (d, 6, J = 5.7); ^{13}C NMR 165.4, 130.0, 126.0, 85.1, 71.8, 44.5, 31.7, 25.0, 21.3, 17.9; IR (neat) 1762 cm^{-1}.

2,2-Dichloro-*trans*-6-octenoic Acid (16b). Hydrolysis of ester **15b** (1.20 g, 4.74 mmol) as described above gave 1.00 g (85.5%) of **15b**: ^1H NMR 5.44 (m, 2), 2.38 (m, 2), 2.02-2.12 (m, 2), 1.62-1.72 (m, 2), 1.65 (d, 3, J = 6.0); ^{13}C NMR 170.4, 129.8, 126.2, 84.4, 44.4, 31.6, 24.9, 17.6; IR (neat) 1735 cm^{-1}.

***anti*-1-Chloro-7-methylbicyclo[3.1.1]heptan-6-one (21b).** Acid **15b** (290 mg, 1.36 mmol) was converted to the acid chloride which was added to zinc dust (220 mg, 3.14 mmol) in DME at reflux to give 200 mg of crude **21b**. Flash chromatography on silica gel (97:3 hexane-EtOAc) gave 143 mg (66.3%) of **21b**: ^1H NMR 2.81 (ddd, 1, J = 1.5, 3.6, 3.6), 2.62 (ddd, 1, J = 14.0, 9.7, 8.3), 2.52 (ddd, 1, J = 14.0, 8.7, 4.7), 2.28 (dq, 1, J = 1.5, 7.3), 2.19-2.25 (m, 2), 1.82-1.95 (m, 1), 1.60-1.82 (m, 1), 1.08 (d, 3, J = 7.3); ^{13}C NMR 204.2, 78.5, 60.5, 42.8, 39.1, 31.5, 19.4, 15.6; IR (neat) 1792 cm^{-1}. Anal. Calcd for $C_8H_{11}ClO$: C, 60.58; H, 6.99; Cl, 22.34. Found: C, 60.97; H, 7.16; Cl, 21.96.

***anti*-7-Methylbicyclo[3.1.1]heptan-6-one (23).** $(n\text{-}Bu)_3SnH$ (160 mg, 0.56 mmol) was added to a solution of **21b** (17.5 mg, 0.11 mmol) and AIBN (8.1 mg, 0.084 mmol) in 2 mL of dry THF under N_2. The mixture was heated at reflux for 48 h, cooled, and the solvent was removed in vacuo. The residue was purified by flash chromatography on silica gel (19:1 pentane-Et_2O) to give 11 mg (80%) of **23** containing traces of tin compounds: ^1H NMR 2.67 (br s, 2), 2.26-2.32 (m, 4), 1.95 (qt, 1, J = 6.7, 1.0), 1.59-1.64 (m, 2), 1.10 (d, 3, J = 6.7); ^{13}C NMR 63.0, 33.8, 33.1, 17.9, 17.5, the carbonyl carbon was not observed; IR (neat) 1780 cm^{-1}.

***anti*-7-Methyl-2-Methylenebicyclo[3.1.1]heptan-6-one (29).** Acid **27c** (110 mg, 0.70 mmol) in 3 mL of dry benzene was added dropwise at 0 °C to a suspension of hexane-washed NaH (102 mg of 60% dispersion in mineral oil, 2.55 mmol) in 1 mL of dry benzene. The solution was stirred at 25 °C for 30 min and cooled to 0 °C. Oxalyl chloride (0.15 mL, 1.75 mmol) was added dropwise. The reaction mixture was stirred at 25 °C for 2 h and heated at reflux for 30 min. The solution was cooled to 25 °C and excess oxalyl chloride and the solvent were removed in vacuo to give a quantitative yield of crude **27d**.

Crude **27d** in 30 mL of dry benzene was added to a solution of dry Et_3N (0.29 mL, 2.08 mmol) in 12 mL of benzene at reflux and heating was continued for 2 h. The reaction was worked up by the addition of 10 mL of water and the aqueous layer was extracted with hexane (4 x 25 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was removed in vacuo to give 119 mg of crude **29**. Flash chromatography on silica gel (97:3 pentane-EtOAc) gave 55 mg (56%) of pure **29**: ^1H NMR 4.73 (br s, 2), 3.31 (d, 1, J = 7.2), 2.81 (dddd, 1, J = 7.2, 3.6, 3.6, 0.8), 2.53 (ddddd, 1, J = 1.8, 1.8, 5.8, 8.8, 16.3), 2.15-2.38 (m, 3), 2.13 (br q, 1, J = 6.8), 1.16 (d, 3, J = 6.8); ^{13}C NMR 208.2, 149.9, 108.6, 73.3, 62.1, 31.7, 29.0, 25.4, 17.3; IR ($CDCl_3$) 3090, 2965, 2885, 1775, 1645, 1260 cm^{-1}

Isopropyl 2,2-Dichloro-5-methyl-6-heptenoate (30a). Isopropyl dichloroacetate (1.0 mL, 1.21 g, 7.05 mmol) was added to LDA and HMPA as described above and 5-bromo-3-methyl-1-pentene (1.48 g, 9.06 mmol) was added.

Normal workup gave 1.83 g of crude **30a**. Flash chromatography on silica gel (93:7 hexane-EtOAc) gave 1.40 g (78%) of **30a**: ^{1}H NMR 5.65 (ddd, 1, J = 16.8, 10.2, 7.5), 5.09 (qq, 1, J = 6.6), 4.99 (br d, 1, J = 16.8), 4.96 (br d, 1, J =10.2), 2.29-2.48 (m, 2), 2.10-2.20 (m, 1), 1.50-1.63 (m, 2), 1.32 (d, 6, J = 5.3), 1.03 (d, 2, J = 6.9); ^{13}C NMR 165.0, 143.3, 113.7, 85.2, 71.8, 43.0, 37.3, 31.7, 21.3, 20.2; IR (neat) 1740 cm^{-1}.

2,2-Dichloro-5-methyl-6-heptenoic Acid (30b). Hydrolysis of ester **30a** (1.29 g, 5.11 mmol) as described above gave 800 mg (75%) of **30b**: ^{1}H NMR 5.65 (ddd, 1, J = 16.8, 10.2, 7.5), 4.99 (br d, 1, J = 16.8), 4.96 (br d, 1, J = 10.2), 2.32-2.52 (m, 2), 2.15-2.25 (m, 1), 1.50-1.72 (m, 2), 1.03 (d, 3, J = 6.9); ^{13}C NMR 169.6, 143.2, 113.8, 85.2, 42.9, 37.4, 31.5, 20.2; IR (neat) 1742 cm^{-1}. Anal. Calcd for $C_8H_{12}Cl_2O_2$: C, 45.12; H, 5.97; Cl 33.40. Found: C, 45.52; H, 5.73; Cl 33.59.

endo **and** *exo*-**5-Chloro-2-methylbicyclo[3.2.0]heptan-6-one (32 and 33)** Acid **31b** (300 mg, 1.40 mmol) was converted to the acid chloride **30c** which was added to zinc dust (220 mg, 3.4 mmol) in THF to give 140 mg of crude **32** and **33**. Flash chromatography on silica gel (96:4 hexane-EtOAc) gave 55.1 mg (24.7%) of **33** followed by 88.9 mg (39.9%) of **32**.

The data for **33**: ^{1}H NMR 3.03-3.35 (m, 1), 2.74-2.86 (m, 2), 2.43-2.51 (m, 1), 2.36 (dd, 1, J = 12.9, 6.5), 1.88-2.07 (m, 2), 1.34-1.46 (m, 1), 1.02 (d, 3, J = 6.6); ^{13}C NMR 204.5, 82.4 (C-5), 45.5 (C-1), 42.4 (C-7), 37.9 (C-4), 36.6 (C-2), 31.8 (C-3), 14.8 (CH_3); IR (neat) 1792 cm^{-1}.

The data for **32**: ^{1}H NMR 3.33 (dd, 1, J = 20.1, 11.1), 2.56-2.62 (m, 2), 2.43-2.51 (m, 1), 2.22 (dd, 1, J = 12.6, 7.2), 1.87-2.07 (m, 2), 1.73 (ddq, 1, J = 13.2, 6.9, 1.5), 1.40 (d, 3, J = 6.9); ^{13}C NMR 204.0, 82.4 (C-5), 48.6 (C-7), 48.5 (C-1), 40.1 (C-2), 36.2 (C-4), 36.1 (C-3), 20.3 (CH_3); IR (neat) 1795 cm^{-1}.

2-Chloro-3,7-dimethyl-2,6-octadienoic Acid (38a). Ester **37a**[15] (1.73 g, 8.0 mmol) was added to KOH (2.03 g, 36 mmol) in 50 mL of 1:1 MeOH:H_2O. The mixture was heated at reflux for 2 h and worked up as usual to give 1.20 g (74%) of **38a**: ^{1}H NMR 10.8 (br s, 1), 5.10 (t, 1, J = 7.5), 2.65 (t, 2, J = 7.8), 2.20 (m, 2), 2.23 (s, 0.33 x 3, *E*-isomer), 2.07 (s, 0.67 x 3, *Z*-isomer), 1.69 (s, 0.33 x 3, *E*-isomer), 1.67 (s, 0.67 x 3, *Z*-isomer), 1.62 (s, 0.33 x 3, *E*-isomer), 1.60 (s, 0.67 x 3, *Z*-isomer); IR (neat) 1730 cm^{-1}.

7,7-Dimethyl-1-chloro-2-methylenebicyclo[3.1.1]heptan-6-one (41). Oxalyl chloride (0.35 mL, 520 mg, 4.10 mmol) was added to acid **38a** (350 mg, 1.73 mmol) in 6 mL of THF. The solution was heated at reflux for 2 h, cooled and the solvent was removed in vacuo to give crude **39a**. Crude acid chloride **39a** was taken up in 10 mL of toluene which was added to a refluxing solution of Et_3N (0.54 mL, 320 mg, 3.09 mmol) in 35 mL of toluene. Normal workup gave 280 mg of crude product which was purified by flash chromatography on silica gel (96:4 hexane-EtOAc) to give 130 mg (42%) of **41**: ^{1}H NMR 5.30 (d, 1, J = 2.6), 5.02 (d, 1, J = 2.6), 2.84 (dd, 1, J = 3.9, 2.0), 2.40-2.60 (m, 2), 2.08-2.22 (m, 2), 1.18 (s, 3), 1.08 (s, 3); ^{13}C NMR 202.5, 146.4, 110.9, 85.4, 61.4, 38.8, 27.7, 25.3, 23.8, 16.2; IR (neat) 1795 cm^{-1}.

Methyl 2-Chloro-3-Methyl-2,6-Heptadienoate (37b). Methyl trichloroacetate (2.62 g, 15.20 mmol) and 5-hexene-2-one (1.27 g, 12.94 mmol) in 10 mL of dry THF were added over a 2.5 h period to a mixture of zinc dust (2.67 g, 40.86 mmol) and Et_2AlCl (8.5 mL of 1 M solution in hexane, 8.5 mmol) in 40 mL of THF at 0 °C under N_2. The mixture was stirred at 0 °C for an additional 2 hr. 2N HCl was added, and the solution was extracted with Et_2O (4 x 20 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$), and the solvent was removed in vacuo to give 2.70 g of crude **37b**. Flash chromatography on silica gel (95:5 hexane-EtOAc) gave 1.43 g (58.7%) of **37b** as a 1:2 mixture of (*E*) and (*Z*) isomers: ^{1}H NMR 5.80 (m, 1), 5.00 (d, 1, J = 18.0), 4.95 (d, 1, J = 10.5), 3.80 (s, 3), 2.65 (t, 2, J = 7.5), 2.10-2.45 (m, 2), 2.15 (s, 0.33 x 3, *E*-isomer), 2.05 (0.67 x 3, *Z*-isomer); IR (neat) 1725 cm^{-1}.

2-Chloro-3-Methyl-2,6-heptadienoic Acid (38b). Ester **37b** (1.43 g, 7.6 mmol) was added to KOH (5.43 g, 97 mmol) in 50 mL of 1:1 mL of MeOH:H_2O. The mixture was heated at reflux for 2 h then worked up as usual to give 1.22 g (90.6%) of **38b** as a 1:2 mixture of (*E*) and (*Z*) isomers: ^{1}H NMR 11.5 (br s, 1), 5.80 (m, 1), 5.00 (d, 1, J = 18.0), 4.95 (d, 1, J = 10.5), 2.65 (t, 2, J = 7.5), 2.10-2.45 (m, 2), 2.15 (s, 0.33 x 3, *E*-isomer), 2.05 (s, 0.67 x 3, *Z*-isomer); IR (neat) 1740 cm^{-1}.

4-Methylene-5-chlorobicyclo[3.2.0]heptan-6-one (42). Oxalyl chloride (0.80 mL, 1.16 g, 9.17 mmol) was added to acid **38b** (530 mg, 3.00 mmol) in 5 mL of THF under N_2. The solution was heated at reflux for 2 h, cooled, and the solvent was removed in vacuo. The residue was treated with additional THF and the residual oxalyl chloride and solvent were removed in vacuo.

Crude acid chloride **39b** was taken up in 10 mL of toluene and was added to a refluxing solution of Et_3N (1.0 mL, 730 mg, 7.20 mmol) in 40 mL of toluene over 1 h. The mixture was heated at reflux for 2 h, then stirred at room temperature for 14 h. The mixture was added to H_2O, the layers were separated and the organic layer was washed with brine, dried ($MgSO_4$) and the solvent was removed in vacuo to give 540 mg of crude **42**.

Flash chromatography on silica gel (19:1 hexane-EtOAc) gave 160 mg (35%) of **42**: ^{1}H NMR 5.43 (d, 1, J = 2.2, 2.2), 5.33 (d, 1, J = 2.2, 2.2), 3.37 (dd, 1, J = 18.2, 9.6), 3.07 (ddd, 1, J = 9.6, 6.6, 6.4), 2.83 (dd, 1, J = 18.2, 6.4), 2.65-2.75 (m, 2), 2.19 (dddd, 1, J = 13.1, 10.2, 9.3, 6.6), 1.90 (ddd, 1, J = 13.1, 9.2, 2.9); ^{13}C NMR 199.3, 147.2, 114.1, 82.5, 48.0, 42.6, 30.9, 29.4; IR (neat) 1790 cm^{-1}.

Bicyclo[3.2.0]heptan-6-one (43a). $CrCl_2$ (1.35 M in H_2O, 1.25 mL, 1.68 mmol) was added to **7a** (50.1 mg, 0.35 mmol) in 2 mL of degassed acetone under N_2. The mixture was stirred for 1.5 hr at 25 °C. Et_2O was added, and the layers were separated. The Et_2O layer was washed with H_2O, brine, and the combined aqueous layer was re-extracted with Et_2O. The combined Et_2O layers were dried ($MgSO_4$), and the solvent was removed in vacuo to give 30.4 mg (80%) of pure **43a**: ^{1}H NMR 3.55 (m, 1), 3.21 (ddd, 1, J = 18.3, 9.3, 4.4), 2.9 (m, 1), 2.50 (ddd, 1, J = 18.3, 4.3, 3.4), 1.5-2.1 (m, 6); ^{13}C NMR 64.8, 51.5, 32.7, 29.8, 28.9, 24.7; IR (neat) 1778 cm^{-1}. The spectral data are identical to those previously described.[20]

1-Methylbicyclo[3.2.0]heptan-6-one (43b). $CrCl_2$ (2.0, 1.35 M soln, 2.7 mmol) was added to **7b** (52.4 mg, 0.33 mmol) in 5 mL of acetone under N_2. The mixture was stirred at room temperature for 24 hr and worked up described above to give 31.7 mg (78.0%) of **7b**: ^{1}H NMR 3.02 (m, 1), 2.83 (dd, 1, J = 17.8, 4.5), 2.70 (dd, 1, J = 8.3, 3.3), 1.50-2.10 (m, 6), 1.45 (s, 3); IR (neat) 1775 cm^{-1}. The spectral data are identical to those previously described.[21]

5-Acetoxybicyclo[3.2.0]heptan-6-one (47a). Et_3N (0.06 mL, 43 mg, 0.43 mmol) and acetic acid (0.03 mL, 32 mg, 0.52 mmol) were added to **7a** (34.7 mg, 0.24 mmol) in 2 mL of acetone, and the solution was heated at reflux for 5 days. The mixture was filtered, and pentane was added. The solution was then washed with H_2O, brine, dried ($MgSO_4$), and the solvent was removed in vacuo to give 33.6 mg (83.3%) of **47a**: ^{1}H NMR 3.46 (dd, 1, J = 18.3, 10.2), 3.10 (m, 1), 2.31 (dd, 1, J = 18.3, 5.1), 2.08 (s, 3), 1.60-1.22 (m, 6); IR (neat) 1794, 1746 cm^{-1}. The spectral data are identical to those previously described.[18b]

5-Acetoxy-1-methylbicyclo[3.2.0]heptan-6-one (47b). Et_3N (0.06 mL, 46 mg, 0.43 mmol) and acetic acid (0.03 mL, 30 mg, 0.52 mmol) was added to **7b** (26.4 mg, 0.17 mmol) in 2 mL of acetone. The solution was heated at reflux for 5 days, then worked up as described above to give 30.1 mg (96%) of **47b**: ^{1}H NMR 3.20 (d, 1, J = 18.3), 2.56 (d, 1, J = 18.3), 2.10 (s, 3), 1.50-2.20 (m, 6), 1.30 (s, 3); IR (neat) 1792, 1758 cm^{-1}.

***anti*-6-Methylbicyclo[3.1.0]hexane-1-carboxylic acid (48).** Cyclobutanone **42** (43.8 mg, 0.28 mmol) was added to LiOH (34.7 mg, 1.45 mmol) in 2 mL of H_2O. The mixture was stirred at room temperature for 2 hr. The solution was acidified to pH 1 with 10% HCL and extracted with Et_2O. The combined Et_2O layers were washed with brine, dried ($MgSO_4$), and the solvent was removed to give 39.8 mg (92%) of **48**: mp 74-76 °C; ^{1}H NMR 2.04 (ddd, 1, J = 12.9, 11.1, 8.4), 1.91 (br dd, 1, J = 12.9, 8.4), 1.60-1.81 (m, 4), 1.25 (apparent s, 3), 1.20-1.35 (m, 2); ^{1}H NMR (C_6D_6) 1.26 (d, 3, J = 6.3); ^{13}C NMR 181.3, 36.5, 36.0, 28.5, 27.1, 24.8, 21.6, 12.1; IR (neat) 1690 cm^{-1}

6,6-Dimethyl-2-methylenebicyclo[3.1.0]hexane-1-carboxylic acid (49).[23] Ketone **41** (20.6 mg, 0.11 mmol) was added to LiOH (23.3 mg, 0.97 mmol) in 2 mL of H_2O. The mixture was stirred at room temperature for 2 h and worked up as described above for the preparation of **48**. The crude product was recrystallized from pentane to give 13.6 mg (72%) of **49**: mp 90-92 °C; ^{1}H NMR 5.47 (br s, 1), 5.10 (br s, 1), 2.79-2.62 (m, 1), 2.20-2.35 (m, 1), 2.11 (dd, 1, J = 6.9, 0.5), 2.09-1.97 (m, 1), 1.55-1.65 (dddd, 1, J = 13.9, 8.5, 4.2, 0.5), 1.27 (s, 3), 1.04 (s, 3); ^{13}C NMR 179.0, 147.2, 109.0, 40.9, 36.0, 33.5, 31.6, 22.8, 22.0, 17.3; IR (CCl_4) 1695 cm^{-1}.

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