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A NEW TWO-CARBON OLEFIN HOMOLOGATION PROCEDURE THAT LEADS TO α-CHLOROENONES. AN EFFICIENT SYNTHESIS OF d,l-MUSCONE

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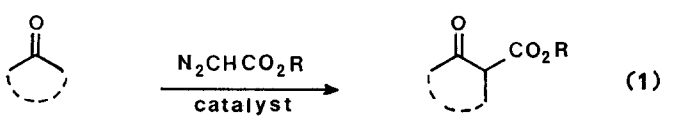
Summary: Dichloroketene-olefin cycloadducts, α,α-dichlorocyclobutanones, are easily converted to α-chloroenones through a 3-step (2-pot) sequence of reactions. The overall result is the insertion of a functionalized 2-carbon unit between the original olefinic carbons. The efficiency of the method is demonstrated by a high-yield synthesis of d,l-muscone.

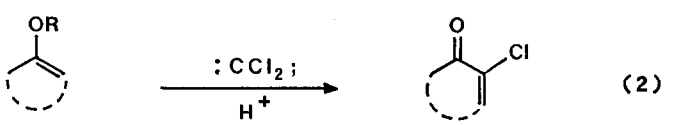
Introduction

The multitude of ring and chain homologation methods developed to date reflects the importance of this type of transformation in synthesis.[1]

Quite frequently, because of methodological constraints or, simply, a lack of substrate availability, one or more carbon atoms must be inserted into a lower ring or chain homologue. Procedures that can efficiently accomplish this with concomitant introduction of useful, ultimately removable, functionality are particularly valuable in that they provide additional synthetic flexibility. The well-known ketone→β-keto ester[1,2] and enol ether→α-chloroenone[1a,3] methods, which are generalized in eqs 1 and 2, exemplify one-carbon homologations of this type:

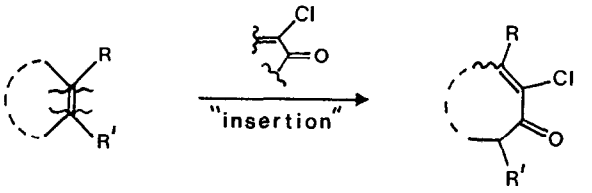


(1)



(2)

Although a number of two-carbon homologation procedures exist,[4] few have this often desirable feature. In this paper we describe a new two-carbon olefin homologation method that affords α-chloroenones, intermediates of proven versatility (eq 3).[5] The efficiency of the method is

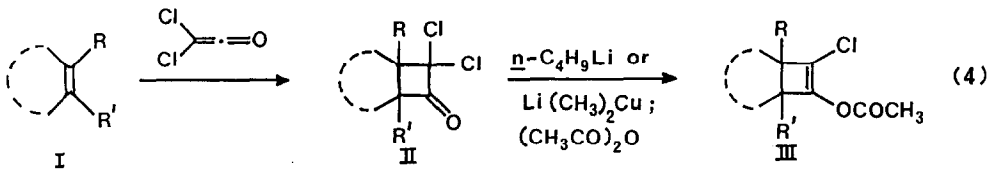


(3)

demonstrated by a high-yield synthesis of d,l-muscone.

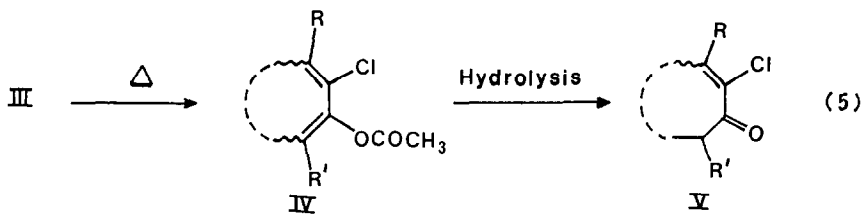
Discussion

In the context of another program,[6] it was found that 2-chloro-1-cyclobutenyl acetates could be readily prepared from the corresponding dichloroketene-olefin cycloadducts, as shown in eq 4. We anticipated that these cyclobutenes III would undergo a facile thermally induced rearrangement[7] to



(4)

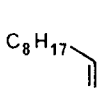
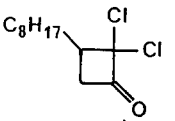
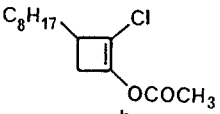
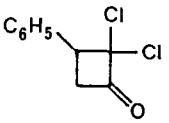
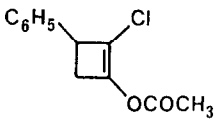
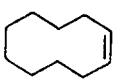
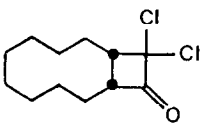
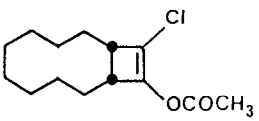
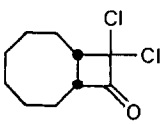
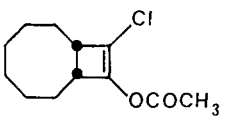
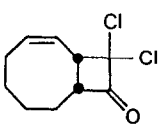
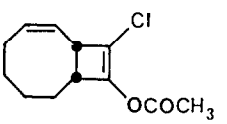
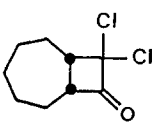
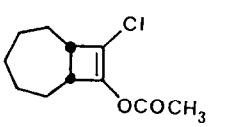
yield the dienes IV, which on hydrolysis could be expected to furnish the synthetically useful chloroenones V (eq 5). This proved to be correct.



(5)

The α,α-dichlorocyclobutanones were easily obtained from a variety of olefins by using trichloroacetyl chloride, phosphorus oxychloride, and zinc-copper couple in ether, the Hassner modification[8] of the Ghosez-Brady procedure.[9] As can be seen from the results given in Table I, the yields were generally excellent. While the α-chloroenolates could be generated from these cycloadducts with either n-butyllithium or lithium dimethylcuprate, use of the latter reagent was found to give reproducibly higher yields (∿ quantitative) of the enol acetates (III, eq 4), formed *on* addition of acetic anhydride.[10]

Table I. Conversion of Olefins to Chlorocyclobutenyl Acetates.

Olefin	Dichlorocyclobutanone (yield)	Chlorocyclobutenyl Acetate[a]
 1a	 2a[b] (88%)	 3a[b]
 1b	 2b[c] (86%)	 3b
 1c	 2c (93%)	 3c
 1d	 2d[d] (91%)	 3d
 1	 2e (74%)	 3e
 1f	 2f[e] (83%)	 3f

[a] Essentially quantitative yields. Acetates were used without purification.
[b] References 10,21. [c] References 8, 9b, 21. [d] Reference 22. [e] Reference 21.

As anticipated, the facility of the conrotatory ring opening of these cyclobutenes varied considerably (Table II).[7] The monocyclic compounds **3a** and **3b**, the bicyclododecene **3c**, and the bicyclodecadiene **3e** could be transformed with relative ease, whereas the bicyclodecene **3d** required more vigorous conditions. In analogy with literature precedent,[4b,7] the yet smaller bicyclononene **3f** underwent no apparent reaction at 216 °C for 3 days; at higher temperatures decomposition was observed. These results reflect the relative difficulty of incorporating in the products the trans double bond that is generated on conrotatory ring opening of the cyclobutenes. The accelerating effect of an additional double bond (**3e**) has been previously noted.[7]

The major stereoisomers of the rearranged products **4a–e** show in their ^{1}H NMR spectra methyl ($-OCOCH_3$) resonances that are up-field relative to those of the corresponding minor isomers; the major stereoisomers have tentatively been assigned the E($OCOCH_3$)-Z(Cl) configurations on the basis of the stereochemistry of certain of the hydrolysis products (see below).

Hydrolysis of the enol acetates under basic conditions led to intractable material, a consequence undoubtedly of the base sensitivity of the resultant α-chloroenones. Fortunately, however, hydrolysis under acidic conditions proved effective. The best results were obtained by using a catalytic amount of sulfuric acid in ethanol,[11] but trifluoroacetic acid in methylene chloride (with or without mercuric chloride)[12] could also be employed. By adding ethanol containing a catalytic amount of sulfuric acid directly to the thermolysis solution and then warming the resulting solution at 50 °C for 24 h, the α-chloroenones **5a–e** could be secured in overall yields based on the starting olefins that ranged from 36 to 66%.

The α-chloroenones **5a**, **5b**, and **5e** were formed as stereochemically homogeneous compounds. The α-chloroenones **5c** and **5d**, however, were produced as 60:40 and 80:20 mixtures, respectively. The Z configuration has been assigned to the products **5a**[5d] and **5b**[13] on the basis of NMR correlations[14] and literature analogy.[5a,e] The major isomer of **5c** and the minor isomer of **5d** have also been assigned the Z stereochemistry on the basis of the down-field ^{1}H NMR chemical shifts of the ß-hydrogens (**5c** major: 6.91; **5d** minor: 7.11 versus **5c** minor: 5.87; **5d** major: 5.84)* and the identical λmax value (241 nm) for **5a**, **5c** major, and **5d** minor.+ The product **5e** showed $J_{4,5}$ = 11.3 Hz, which establishes the Z configuration for the γ,δ-double bond; controlled hydrogenation (H_2/Pd-C, $CH_3CO_2C_2H_5$) of **5e** generated the major isomer of **5d**, and therefore the configuration of the α,ß-double bond must be E. The correctness of the above assignments has in large measure been confirmed by the conversion of the major and minor isomers of **5c** and the major isomer of **5d** to the

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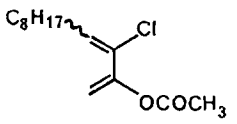
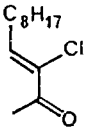
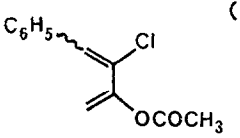
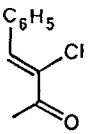
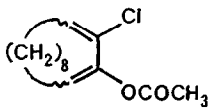
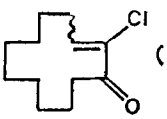
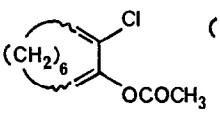
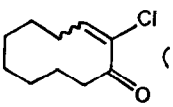
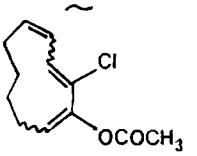
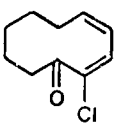
* Stork and Macdonald have reported a value of 6.83 ppm for the ß-H of (Z)-2-chloro-2-cyclopentadecen-1-one.[5a] The Z and E stereoisomers of an acyclic α-chloroenone were found to have values of 6.85 and 6.03 ppm, respectively.[5e]

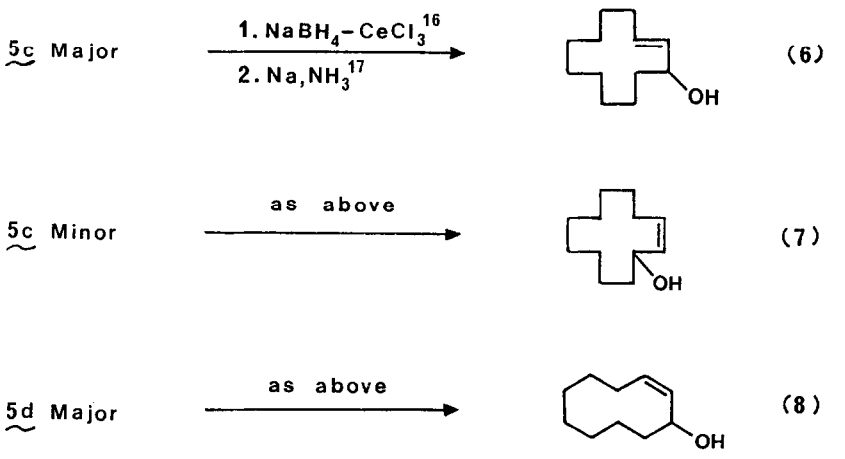
\+ In that the separated isomers of **4c** are converted with virtually no isomerization to the respective isomers of **5c**, the major isomer of **4c** and probably of the others is E($OCOCH_3$)-Z(Cl).

Table II. Conversion of Chlorocyclobutenyl Acetates to Chloroenones

Chlorocyclobutenyl Acetate	Diene (solvent, temp., time, isomer ratio[a])	α-Chloroenones (isomer ratio, Z:E[a])	Overall Yield from Olefin
3a	 4a	(toluene, reflux, 24 h, 90:10)  5a[b]	(100:0) 66 %
3b	 4b	(ClCH$_2$CH$_2$Cl, reflux, 24 h, 90:10 [or toluene, 90°C[c], 24 h, 85:15])  5b[d]	(100:0) 50 %
3c	 4c	(toluene, 105°C[c], 20 h, 60:40)  5c	(60:40) 62 %
3d	 4d	(diglyme, 145°C[c], 24 h [or xylene, reflux, 20 h] 60:40)  5d	(20:80) 54 %
3e	 4e	(toluene, reflux, 24 h, 70:30)  5e	(0:100) 36 %
3f	no reaction (triglyme, 216°C[c], 3 days)		

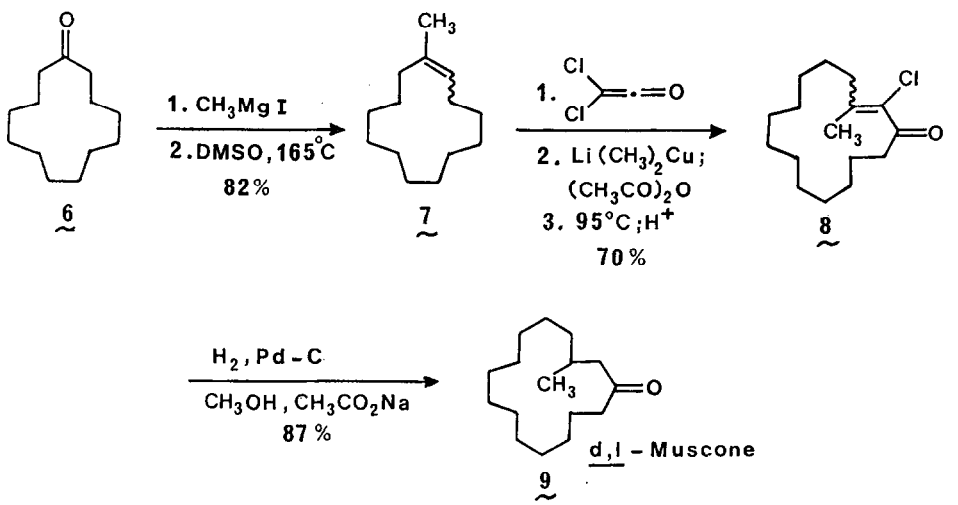
[a] By ^{1}H NMR. [b] Reference 5d. [c] Bath temperature. [d] Reference 13

corresponding known allylic alcohols of established[15] stereochemistry (eqs 6-8):



An efficient synthesis of d,l-muscone (3-methylcyclopentadecanone),[18] the odorous principle of musk, has been developed through the use of this new homologation sequence and is shown in Scheme I.

Scheme I



1-Methylcyclotridecene, obtained in 82% yield by treatment of cyclotridecanone with methylmagnesium iodide[19] followed by hot DMSO,[20] was smoothly converted to the α-chloroenone **8** by the above procedure (70% yield). The facile cyclobutene ring opening (95 °C, ≤ 20 h) is noteworthy. Catalytic hydrogenation[5b] of **8** then served to deliver d,l-muscone (**9**) in 87% yield. The overall yield of muscone from **6** is 50%.

In that α-chloroenones are valuable intermediates in synthesis, this new 2-carbon homologation method should prove to be particularly useful.

Experimental Section

Solvents were generally distilled prior to use: tetrahydrofuran and ether from sodium-benzophenone, toluene, xylene, and dimethyl sulfoxide from calcium hydride, and dichloroethane from calcium chloride. Phosphorus oxychloride was distilled from potassium carbonate and trichloroacetyl chloride was distilled from calcium chloride.

Thin-layer chromatography was performed on Merck $60F_{254}$ (0.25 mm) sheets, which were visualized with molybdophosphoric acid in ethanol. Merck 70-230 silica gel 60 was employed for column chromatography. A Perkin-Elmer Model 298 or 397 spectrophotometer was used to record IR spectra (as neat liquid films, unless noted otherwise). The UV spectra were recorded on a Beckman DB-GT spectrophotometer. A Bruker WP 80 SY or AM 300 spectrometer was employed for the ^1H NMR spectra ($CDCl_3$ solution). Mass spectra were obtained on an AEI MS-30 mass spectrometer (70 eV, direct insert probe) or on a VG Micromass 70 70F instrument. Melting points were obtained with a Buchi-Tottoli apparatus and are not corrected. Microanalyses were performed by the Central Service of the CNRS. The olefins **1e-f** were purchased from either Aldrich or Fluka.

α,α-Dichlorocyclobutanones 2a-f. General procedure.[8] To a stirred mixture of the olefin **1** and 2 equiv of zinc-copper couple in dry ether (2 mL/mmol **1**) under nitrogen was added over 1 h a solution of 1.5 equiv of trichloroacetyl chloride and 1.5 equiv of phosphorus oxychloride in dry ether (1 mL/mmol **1**). (An excess of the olefin **1e** was used.) After the reaction was stirred for 14 h, the ether solution was separated from the excess couple and added to hexane, and the resulting mixture was partially concentrated under reduced pressure in order to precipitate the zinc chloride. The supernatant was decanted and washed successively with cold water, cold aqueous sodium bicarbonate solution, water, and brine, and then dried over anhydrous sodium sulfate. Evaporation of the solvent under reduced pressure afforded the crude product, which was purified by distillation or recrystallization. **2,2-Dichloro-3-octylcyclobutanone (2a)**:[10,21] 88% yield; IR 1805 cm^{-1}; ^1H NMR δ 0.89 (t, J = 5.7 Hz, 3H), 1.28 (br s, 14H), 2.65-3.45 (m, 3H). **2,2-Dichloro-3-phenylcyclobutanone (2b)**:[8,9b,21] 86% yield; mp 65-66 °C (hexane); IR ($CHCl_3$) 3060, 3040, 1810 cm^{-1}; ^1H NMR δ 3.30-3.90 (m, 2H), 4.12-4.37 (m, 1H), 7.4 (m, 5H). **12,12-Dichlorobicyclo[8.2.0]dodecan-11-one (2c)**: 93% yield; IR 1800 cm^{-1}; ^1H NMR δ 1.10-2.10 (m, 16H), 2.80-3.20 (m, 1H), 3.58-3.88 (m, 1H); mass spectrum, m/e 250, 248. **10,10-Dichlorobicyclo[6.2.0]decan-9-one (2d)**:[22] 91% yield; IR 1800 cm^{-1}; ^1H NMR δ 1.00-2.30 (m, 12H), 2.94 (pseudo t, J = 10.5 Hz, 1H), 3.46-3.76 (m, 1H). **10,10-Dichlorobicyclo[6.2.0]dec-2-en-9-one (2e)**: 74% yield; IR 3020, 1803 cm^{-1}; ^1H NMR δ 1.00-2.50 (m, 8H), 3.85-4.10 (m, 2H), 5.55-6.15 (m, 2H); mass spectrum, m/e 220, 218. **9,9-Dichlorobicyclo[5.2.0]nonan-8-one (2f)**:[21] 83% yield; IR 1804 cm^{-1}; ^1H NMR δ 1.00-2.40 (m, 10H), 2.90-3.35 (m, 1H), 3.75-4.15 (m, 1H).

Chlorocyclobutenyl Acetates 3a-f. General Procedure.[10] To a stirred solution at -50 °C of lithium dimethylcuprate [2 equiv, prepared from 2 equiv of copper (I) iodide in tetrahydrofuran (4 mL/mmol) at -20 °C by adding 4 equiv of methyllithium in ether and then warming the mixture to 0°C] was added dropwise the α,α-dichlorocyclobutanone **2** in tetrahydrofuran (2 mL/mmol). After being stirred at -50 to -40 °C for 20 min, the mixture was treated with acetic anhydride (1 mL/mmol **2**) and then allowed to warm to room temperature. The mixture was stirred at room temperature for 3 h after which it was poured into a stirred mixture of ether, hexane, and aqueous ammonium chloride-ammonium hydroxide. The chlorocyclobutenyl acetate, isolated in the normal manner in essentially quantitative yield, was used in the next reaction without purification. **2-Chloro-3-octyl-1-cyclobuten-1-yl Acetate (3a)**:[10] IR 1780, 1685 cm^{-1}; ^1H NMR δ 0.88 (t, J = 5.4 Hz, 3H), 1.29 (br s, 14H), 2.16 (s, 3H), 2.20-3.10 (m, 3H). **2-Chloro-3-phenyl-1-cyclobuten-1-yl Acetate (3b)**: IR 1775, 1685 cm^{-1}; ^1H NMR δ 2.19 (s, 3H), 2.70 (dd, J = 2, 12 Hz, 1H), 3.40 (dd, J = 4.5, 12 Hz, 1H), 3.80 (dd, J = 2, 4.5 Hz, 1H), 7.30 (br s, 5H). **12-Chlorobicyclo[8.2.0]dodec-11-en-11-yl Acetate (3c)**: IR 1775, 1695 cm^{-1}; ^1H NMR δ 1.10-2.00 (m, 16H), 2.16 (s, 3H), 2.65-2.90 (m, 1H), 3.10-3.35 (m, 1H). **10-Chlorobicyclo[6.2.0]dec-9-en-9-yl Acetate (3d)**: IR 1775, 1685 cm^{-1}; ^1H NMR δ 1.00-2.00 (m, 12H), 2.16 (s, 3H), 2.50-2.80 (m, 1H), 2.90-3.30 (m, 1H). **10-Chlorobicyclo[6.2.0]deca-2,9-dien-9-yl Acetate (3e)**: IR 1785, 1695 cm^{-1}; ^1H NMR δ 1.10-2.30 (m, 8H), 2.16 (s, 3H),

3.20-3.45 (m, 1H), 3.50-3.70 (m, 1H), 5.30-6.05 (m, 2H). **9-Chlorobicyclo [5.2.0] non-8-en-8-yl Acetate (3f)**: IR 1775, 1685 cm^{-1}; ^1H NMR δ 1.10-2.00 (m, 10H), 2.16 (s, 3H), 2.70-3.00 (m, 1H), 3.20-3.45 (m, 1H).

Dienes 4a-e. General Procedure. The chlorocyclobutenyl acetate 3 and 2,6-di-tert-butyl-4-methylphenol (1 mg/mmol) were dissolved in the indicated solvent and the resulting solution was heated at the temperature and for the time noted. Conventional isolation yielded the dienes (in preparative runs, however, hydrolysis of the product was effected in situ): **2-Chloro-1-methylene-2-undecenyl Acetate (4a)**: toluene, reflux, 24 h; IR 1775, 1640 cm^{-1}; ^1H NMR δ (major isomer) 0.88 (t, J = 5.5 Hz, 3H), 1.29 (br s, 12H), 2.10-2.45 (m, 2H), 2.23 (s, 3H), 4.97 (d, J = 2 Hz, 1H), 5.53 (d, J = 2 Hz, 1H), 5.97 (t, J = 8 Hz, 1H). **2-Chloro-1-methylene-3-phenyl-2-propenyl Acetate (4b)**: 1,2-dichloroethane, reflux, 24 h; IR 1770, 1630, 1600 cm^{-1}; ^1H NMR δ (major isomer) 2.27 (s, 3H), 5.12 (d, J = 2.8 Hz, 1H), 5.73 (d, J = 2.8 Hz, 1H), 6.90 (s, 1H), 7.20-7.80 (m, 5H). **12-Chloro-1,11-cyclododecadien-1-yl Acetate (4c)**: toluene, 105 °C (bath), 20 h; major isomer (separated by SiO_2 chromatography): IR 1760, 1635 cm^{-1}; ^1H NMR δ 1.10-2.00 (m, 12H), 2.00-2.50 (m, 4H), 2.14 (s, 3H), 5.56 (t, J = 8.5 Hz, 1H), 6.25 (t, J = 7.7 Hz, 1H); mass spectrum, m/e 258, 257, 256, 215, 214. Minor isomer (separated by SiO_2 chromatography): IR 1760, 1635 cm^{-1}; ^1H NMR δ 1.10-1.90 (m, 12H), 1.90-2.50 (m, 4H), 2.21 (s, 3H), 5.75 (t, J = 6.8 Hz, 1H), 6.02 (t, J = 8.7 Hz, 1H); mass spectrum, m/e 259, 258, 257, 256, 214. **10-Chloro-1,9-cyclodecadien-1-yl Acetate (4d)**: diglyme, 145 °C (bath), 24 h; major isomer (separated by SiO_2 chromatography): IR 1765, 1635 cm^{-1}; ^1H NMR δ 1.00-2.00 (m, 8H), 2.00-2.50 (m, 4H), 2.15 (s, 3H), 5.60 (t, J = 7 Hz, 1H), 6.32 (t, J = 8.0 Hz, 1H); mass spectrum, m/e 231, 230, 229, 186. Minor isomer (separated by SiO_2 chromatography): IR 1765, 1630 cm^{-1}; ^1H NMR δ 1.00-2.00 (m, 8H), 2.00-2.50 (m, 4H), 2.21 (s, 3H), 5.60 (t, J = 8.0 Hz, 1H), 6.00 (t, J = 7.5 Hz, 1H). **10-Chloro-1,7,9cyclodecatrien-1-yl Acetate (4e)**: toluene, reflux, 24 h; IR 3020, 1765, 1640 cm^{-1}; ^1H NMR δ 2.13 (major isomer) and 2.18 (minor isomer) (2s, 3H), 5.35-6.00 (m, 3H), 6.47 (m, 1H).

α-Chloroenones 5a-e. General procedure.[11] To the above (cooled) thermolysis solution of the crude diene **4** was added 6 mL of absolute ethanol and one drop of sulfuric acid/4 mL of solution. After being heated at 50-55°C with stirring for 24 h, the reaction mixture was processed as usual and the crude product was purified by silica gel chromatography with pentane or hexane in ether to give in the overall yield indicated the α-chloroenone(s) **5. (Z)-3-Chloro-3-dodecen-2-one (5a)**:[5d] 66% yield; IR 1690, 1615 cm^{-1}; UV (cyclohexane) 241nm (ε 7,100); ^1H NMR δ 0.88 (t, J = 5.1 Hz, 3H), 1.28 (br s, 12H), 2.00-2.60 (m, 2H), 2.41 (s, 3H), 6.94 (t, J = 7.3 Hz, 1H); mass spectrum, m/e 217. Anal. Calcd for $C_{12}H_{21}ClO$: C, 66.50; H, 9.77. Found: C, 66.13; H, 9.85. **(Z)-3-Chloro-4-phenyl-3-buten-2-one (5b)**:[13] 50% yield; IR 1690, 1605, 1595 cm^{-1}; UV (cyclohexane) 292 nm (ε 14,000); ^1H NMR δ 2.54 (s, 3H), 7.25-7.70 (m, 3H), 7.75 (s, 1H), 7.70-8.00 (m, 2H); mass spectrum, m/e 182, 181, 180, 179. Anal. Calcd for $C_{10}H_9ClO$: C, 66.49; H, 5.02; Cl, 19.62. Found: C, 66.17; H, 5.25; Cl, 19.49. 2,4-Dinitrophenylhydrazone: mp 219 °C (lit.[13] 218-219 °C). **2-Chloro-2-cyclododecen-1-one (5c)**: 62% yield; major isomer (Z): IR 1690, 1620 cm^{-1}; UV (cyclohexane) 241 nm (ε 8,600); ^1H NMR δ 1.00-2.00 (m, 14H), 2.30-2.60 (m, 2H), 2.60-2.85 (m, 2H), 6.91 (t, J = 7.6 Hz, 1H); mass spectrum, m/e 214. Anal. Calcd for $C_{12}H_{19}ClO$: C, 67.12; H, 8.92. Found: C, 67,02; H, 9.22. Minor isomer (E): IR 1695, 1610 cm^{-1}; UV (cyclohexane) 238 nm (ε 4,800); ^1H NMR δ 1.00-2.00 (m, 14H), 2.30-2.65 (m, 2H), 2.65-2.85 (m, 2H), 5.87 (t, J = 8.3 Hz, 1H). **2-Chloro-2-cyclodecen-1-one (5d)**: 54% yield; major isomer (E): IR 1700, 1625 cm^{-1}; UV (cyclohexane) 244 nm (ε 2,200); ^1H NMR δ 1.00-2.75 (m, 14H), 5.84 (t, J = 9.1 Hz, 1H); mass spectrum, m/e 186. Anal. Calcd for $C_{10}H_{15}ClO$: C, 64.34; H, 8.10. Found: C, 64.29; H, 8.46. Minor isomer (Z): IR 1695, 1625 cm^{-1}; UV (cyclohexane) 241 nm (ε 2,600); ^1H NMR δ 1.00-2.90 (m, 14H), 7.11 (t, J = 7.9 Hz, 1H); mass spectrum, m/e 186. **(2E, 4Z)-2-Chloro-2,4-cyclodecadien-1-one (5e)**: 36% yield; IR 3010, 1700, 1640, 1600 cm^{-1}; UV (cyclohexane) 270 nm (ε 3,400); ^1H NMR δ 1.00-2.30 (m, 8H), 2.60-2.90 (m, 2H), 5.45-6.00 (m, 2H), 6.40-6.55 (m, 1H); mass spectrum, m/e 184. Anal. Calcd for $C_{10}H_{13}ClO$: M_r, 184.0655. Found: M_r(mass spectrum), 184.0689.

1-Methylcyclotridecene (7). A 2.21-g (10.4 mmol) sample of 1-methylcyclotridecanol, obtained from cyclotridecanone as described by Brown and Borkowski (91% yield),[19] dissolved in 10 mL of dimethyl sulfoxide was heated for 14 h at 165 °C. The crude product was isolated with pentane in the usual manner and then purified by silica gel chromatography to give 1.83 g (90%) of olefin **7**: IR 1680 cm^{-1}; ^1H NMR δ 1.1-1.7 (m, 21H), 2.07 (m, 4H), 5.15 (m, 1H); mass spectrum, m/e 194. Anal. Calcd for $C_{14}H_{26}$: C, 86.51; H, 13.49. Found: C, 86.35; H, 13.32.

2-Chloro-3-methyl-2-cyclopentadecen-1-one (8). To a stirred mixture of 1.34 g (6.90 mmol) of olefin **7** and 1.17 g (ca. 17 mmol) of zinc-copper couple in 14 mL of dry ether under nitrogen was added over 1 h a solution of 1.35 mL (2.20 g, 12.1 mmol) of trichloroacetyl chloride and 1.12 mL (1.84 g, 12.0 mmol) of phosphorus oxychloride in 7 mL of dry ether. After the reaction was stirred for 14 h, the ether solution was separated from the excess couple and added to hexane, and the resulting mixture was partially concentrated under reduced pressure in order to precipitate the zinc chloride. The supernatant was decanted and washed successively with cold water, cold aqueous sodium bicarbonate solution, water, and brine, and then dried over anhydrous sodium sulfate. Evaporation of the solvent under reduced pressure then afforded 2.21 g of crude dichlorocyclobutanone (which was used in the next reaction): IR 1800 cm^{-1}; ^1H NMR δ 1.15 and 1.46 (2s, 3H), 1.0-2.0 (m, 22H), 3.0-3.6 (m, 1H); mass spectrum, m/e 306, 304. Anal. Calcd for $C_{16}H_{26}OCl_2$: C, 62.95; H, 8.58. Found: C, 62.52; H, 8.48. To a stirred solution at -50 °C of lithium dimethylcuprate [prepared from 1.25 g (6.56 mmol) of copper (I) iodide in 13 mL of tetrahydrofuran at -20 °C by adding 6.55 mL (13.1 mmol) of a 2.0M ethereal solution of methyllithium and then warming the mixture to 0 °C] was added dropwise 1.00 g (ca. 3.12 mmol) of the above dichlorocyclobutanone in 6.5 mL of tetrahydrofuran. After being stirred at -50 to -40 °C for 20 min, the mixture was treated with 3.25 mL (3.52 g, 34.4 mmol) of acetic anhydride and then allowed to warm to room temperature. The mixture was stirred at room temperature for 3 h after which it was poured into a stirred mixture of ether, hexane, and aqueous ammonium chloride-ammonium hydroxide. The crude product was isolated in the usual manner and purified by silica gel chromatography with ether in pentane (2:98) to give 738 mg (76% from **7**) of the chlorocyclobutenyl acetate: IR 1770, 1690 cm^{-1}; ^1H NMR δ 1.07 and 1.21 (2s, 3H), 1.0-2.0 (m, 22H), 2.15 (s, 3H), 2.7-3.1 (m, 1H); mass spectrum, m/e 312. A solution of 560 mg (1.79 mmol) of the above chlorocyclobutenyl acetate and 2 mg of 2,6-di-tertbutyl-4-methylphenol (0.005 mmol) in 7 mL of toluene was heated at 95 °C (bath) under nitrogen. After 20 h, the cooled reaction mixture was diluted with 10.5 mL of ethanol containing 2 drops of conc sulfuric acid and the resulting solution was then heated at 50 °C for 24 h. The crude product was isolated in the usual way and purified by silica gel chromatography with ether in pentane (1:99) to afford 447 mg (92%) of α-chloroenone **8**: IR 1685, 1590 cm^{-1}; ^1H NMR δ 1.29 (br s, 20H), 1.4-1.8 (m, 2H), 1.95 and 2.00 (2s, 3H), 2.45-2.80 (m, 2H); mass spectrum, m/e 271. Anal. Calcd for $C_{16}H_{27}OCl$: C, 70.93; H, 10.04. Found: C, 71.07; H, 10.05.

3-Methylcyclopentadecanone (d,l-muscone, 9). A mixture of 205 mg (0.76 mmol) of α-chloroenone **8**, 850 mg (10.4 mmol) of sodium acetate, and 20 mg of 10% palladium on carbon in 15 mL of methanol was stirred under hydrogen for 14 h. The crude product was isolated in the usual manner and purified by silica gel chromatography with ether in pentane (0.6:99.4) to give 157 mg (87%) of d,l-muscone (**9**): IR 1710 cm^{-1}; ^1H NMR δ 0.93 (d, J = 6.0 Hz, 3H), 1.10-1.80 (m, 23H), 1.85-2.50 (m, 4H); mass spectrum, m/e 239. Anal. Calcd for $C_{16}H_{30}O$: C, 80.60; H, 12.68. Found: C, 80.65; H, 12.52. This material was indistinguishable from a sample kindly supplied by Dr. E. Isabettini.

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