ambient temperature for 12 h and then was concentrated *in vacuo* while the temperature of the reaction mixture was maintained below 50 °C. Water (5 mL) was added to the residue, and the resulting aqueous suspension was extracted with EtOAc (3 x 10 mL). The combined organic layers were washed sequentially with water (10 mL) and brine (10 mL), dried ($MgSO_4$), and filtered, and the filtrate was concentrated *in vacuo*. The residue, a mixture of **13a** and **13b** which was thereby obtained as a colorless solid, was purified via column chromatography on silica gel by eluting with 50% EtOAc-hexane. This procedure afforded pure **13a** (10 mg, 42%) as a colorless microcrystalline solid: mp 174-175 °C; IR (KBr) 3291 (s), 2954 (s), 2940 (s), 2927 (s), 2859 (s), 1441 (w), 1360 (w), 1266 (w), 1117 (w), 1036 cm^{-1} (m); ^1H NMR (acetone-d_6) δ 0.95-1.00 (m, 2 H), 1.33 (br s, 2 H), 1.57-1.65 (m, 1 H), 1.75-1.82 (m, 1 H), 1.82-1.93 (m, 1 H), 2.19 (br s, 2 H), 2.38-2.47 (m, 1 H), 2.60-2.71 (m, 1 H), 3.30-3.52 (m, 4 H), 3.71-3.80 (m, 1 H), 3.97 (br s, 1 H); ^{13}C NMR (acetone-d_6) δ 18.9 (t), 33.7 (t), 42.7 (d), 43.0 (d), 44.4 (d), 45.1 (d), 50.2 (d), 50.6 (s), 52.3 (d), 52.9 (d), 54.6 (d), 67.9 (t), 76.7 (d); mass spectrum (70 eV), *m/z* (relative intensity) (no molecular ion), 176 (100), 132 (17), 94 (69), 82 (42).

For purposes of product characterization, this saponification reaction was repeated on a larger scale by using non-deuterated **12a** and **12b**. Thus, to a solution of NaOMe (54 mg, 1.0 mmol) in MeOH (10 mL) was added a solution of non-deuterium containing **12a** and **12b** (ratio 4:1, 140 mg, 0.48 mmol) in MeOH (4 mL), and the resulting mixture was stirred at ambient temperature for 12 h and then was concentrated *in vacuo* while the temperature of the reaction mixture was maintained below 50 °C. Water (2 mL) was added to the residue, and the resulting aqueous suspension was extracted with EtOAc (15 mL). The combined organic layers were washed sequentially with water (4 mL) and brine (5 mL), dried ($MgSO_4$), and filtered, and the filtrate was concentrated *in vacuo*. The residue, a colorless solid (90 mg), was purified via column chromatography on silica gel by eluting with 1:9 EtOAc-hexane. The first chromatography fraction afforded **13a** (60 mg, 61%) as a colorless microcrystalline solid: mp 174-175 °C; IR (KBr) 3290 (s), 2945 (s), 1340 cm^{-1} (m); ^1H NMR (DMSO-d_6) δ 0.95 (s, 3 H), 1.25 (br s, 2 H), 1.50-2.25 (m, 6 H), 2.40 (br s, 1 H), 2.55 (br s, 1 H), 3.15-3.45 (m, 2 H), 3.85 (br s, 1 H), 4.20-4.35 (m, 1 H), 4.55 (s, 1 H); ^{13}C NMR (DMSO-d_6) δ 18.9 (q), 32.8 (t), 41.6 (d), 41.7 (d), 43.3 (d), 43.9 (d), 48.9 (d), 49.6 (s), 51.2 (d), 51.7 (d), 53.6 (d), 66.3 (d), 75.1 (d); mass spectrum (70 eV), *m/e* (relative intensity): (no molecular ion), 175 (100), 131 (21). Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.47; H, 8.93.

Continued elution of the chromatography column afforded **13b** (15 mg, 15%) as a colorless microcrystalline solid: mp 136-138 °C; IR (KBr) 3310 (s), 2940 (m), 1360 cm^{-1} (m); ^1H NMR ($CDCl_3$) δ 1.05 (s, 3 H), 1.20-1.40 (m, 4 H), 1.58 (br s, 2 H), 1.80 (br s, 1 H), 1.90-2.05 (m, 1 H), 2.10-2.20 (m, 2 H), 2.20-2.35 (m, 1 H), 2.45 (br s, 1 H), 3.55 (*AB*, J_{AB} = 12.0 Hz, 1 H), 3.65 (*AB*, J_{AB} = 12.0 Hz, 1 H), 4.18 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 18.4 (q), 33.7 (t), 41.9 (d), 42.2 (d), 42.3 (d), 44.4 (d), 49.3 (s), 49.7 (d), 50.6 (d), 52.9 (d), 53.5 (d), 69.0 (t), 76.7 (d); mass spectrum (70 eV), *m/e* (relative intensity): (no molecular ion), 175 (100), 157 (48). Unequivocal verification of the structure of (nondeuterated) **13b** was obtained via X-ray crystallographic methods.[1]

Esterification of 13a. A solution of **13a** (30 mg, 0.15 mmol) in pyridine (1 mL) was cooled to 0 °C via application of an external ice-water bath. To this cooled solution was added with stirring Ac_2O (200 mg, 2.1 mmol). The resulting mixture was heatedwith stirring at 80 °C for 4 h and then was allowed to cool gradually to ambient temperature. The reaction mixture was stirred at ambient temperature for 12 h, and CH_2Cl_2 (70 mL) then was added to the reaction mixture. The organic layer was washed successively with 5% aqueous HCl (3 x 5 mL), 10% aqueous Na_2CO_3 (5 mL), and brine (5 mL). The organic layer was dried ($MgSO_4$) and filtered, and the filtrate was concentrated *in vacuo*. The residue, a colorless, viscous oil, solidified upon trituration with hexane. The solid material thereby obtained was recrystallized from hexane, thereby affording pure **12a** (40 mg, 90%) as colorless rhomboids: mp 87-88 °C; IR (KBr) 2940 (s), 1715 (s), 1370 cm^{-1} (m); ^1H NMR ($CDCl_3$) δ 0.95 (s, 3 H), 1.35 (br s, 2 H), 1.70-1.90 (m, 2 H), 2.00 (s, 3 H), 2.05 (s, 3 H), 2.10-2.30 (m, 3 H), 2.30-2.55 (m, 3 H), 3.93 (s, 2 H), 4.78 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 19.2 (q), 21.1 (q), 21.4 (1), 33.4 (t), 42.0 (d), 42.5 (d), 44.1 (d), 44.5 (d), 48.0 (s), 48.9 (d), 49.2 (d), 49.5 (d), 54.4 (d), 70.1 (t), 79.65 (d), 171.9 (s), 172.1 (s); mass spectrum (70 eV), *m/e* (relative intensity): (no molecular ion), 248 (19), 230 (5), 217 (14). Anal. Calcd for $C_{17}H_{22}O_4$: C, 70.32; H, 7.63. Found: C, 70.59; H, 7.76. Unequivocal verification of the structure of (nondeuterated) **12a** was obtained via X-ray crystallographic methods.[1]

Esterification of 13b. A solution of **13b** (15 mg, 0.07 mmol) in $CHCl_3$ (5 mL) was cooled to 0 °C via application of an external ice-water bath. To this cooled solution was added with stirring pyridine (140 mg, 1.9 mmol) followed by Ac_2O (140 mg, 1.6 mmol). The resulting mixture was heated with stirring at 80 °C for 16

h. Workup of the reaction mixture was performed in the manner described above for the corresponding esterification of **13a** (*vide supra*). By following this procedure, **12b** (20 mg, 91%) was obtained as a colorless, viscous oil; IR (neat) 2950 (s), 1720 (s), 1370 (m), 1250 cm^{-1} (s); ^1H NMR ($CDCl_3$) δ 0.95 (s, 3 H), 1.29 (*AB*, J_{AB} = 10.8 Hz, 1 H), 1.38 (*AB*, J_{AB} = 10.8 Hz, 1 H), 1.65 (s, 1 H), 1.72 (br s, 1 H), 1.97 (s, 3 H), 2.05 (s, 3 H), 2.06-2.30 (m, 4 H), 2.42 (br s, 3 H), 4.02 (s, 2 H), 4.90 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 19.1 (q), 21.2 (q), 21.5 (q), 34.0 (t), 42.1 (2 C, d), 42.6 (d), 44.8 (d), 47.5 (d), 50.2 (s), 50.5 (d), 52.6 (d), 54.3 (d), 70.8 (t), 79.4 (d), 171.9 (s), 172.1 (s); mass spectrum (70 eV), *m/e* (relative intensity): (no molecular ion), 248 (7), 231 (1).

NMR Experiments Performed for 6a. A solution of **6a** (120 mg, 0.59 mmol) in $CDCl_3$ (0.5 mL) was employed for the NMR studies.

INADEQUATE Experiment.[6] The ^{13}C NMR spectrum of this sample was acquired at 75 MHz by using a Varian VXR-300 NMR spectrometer by using a typical INADEQUATE pulse sequence that employs a 135° readout pulse. A total of 1024 (t_2 dimension) and 64 (t_1 dimension) increments were recorded by using 98 transients per t_1 increment for a 1695 x 1695 Hz frequency domain. The total acquisition time was 20 h. Carbon-13 NMR peak assignments were made by using the results of the INADEQUATE experiment. Thus, the connected carbon-carbon paired peaks are symmetric with respect to the F1 = F2 diagonal line (obtained by using a modified pulse sequence: 90° - τ - 180° - τ - 90° - $0.5t_1$ - 135° - t_2). Paired peaks could not be observed for C(11); this resonance signal is split into a triplet by C-D spin-spin coupling, and the intensities of the resulting peaks are too small to be observable. However, both C(10) and C(1) have paired-peaks that are symmetric with respect to the C(11) signal. Thus, the connectivities between C(1)-C(11) and C(10)-C(11) can be established. In addition, C(9) and C(7) each have paired-peaks which are symmetric about a peak at δ 26; [this peak results from foldover of C(8)]. In this manner, the connectivities between C(9)-C(8) and C(7)-C(8) can be determined. All other connectivities were established directly from analysis of the remaining paired-peak relationships which appear clearly and unambiguously in the INADEQUATE spectrum of **6a**.

Nuclear Overhauser Effect (nOe) Experiment.[7] A steady-state ^1H-{^1H} nOe difference spectrum was recorded with selective pre-saturation at δ 1.19. A three-second irradiation time and a 0.5 second acquisition time were employed. A 15 second waiting time was inserted between acquisition of the irradiated spectra and the control spectra. Double irradiation of the ^1H NMR signal at δ 1.19 results in enhancement of the corresponding signals at δ 2.22 [H(3)], 2.36 [H(5)], and 2.5 [H(2) and H(6)], but this perturbation produces a weak negative nOe at δ 1.98 [H(9)]. Double irradiation of the signal at δ 1.19 also produces a large selective population transfer (SPT) peak at δ 1.63, which is due to the relatively large *J*-coupling between H(4s) and H(4a) and results from the low irradiation power that was employed in the nOe experiment. The nOe results suggest that the peak at δ 1.19 can be assigned to H(4a), which is vicinal to H(3) and H(5), proximal to H(2) and H(6), and distal to H(9) and H(10). The weak negative nOe expected for H(10) could not be observed, since the resonance signal that corresponds to H(10) overlaps with that of H(5) and cannot be resolved.

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References and Footnotes

1. A portion of this work has been communicated; see: Marchand, A. P.; Vidyasagar, V.; Ren, C.-t.; Sherrod, M. J.; Watson, W. H.; Krawiec, M. *Tetrahedron Lett.* **1992**, *33*, 3983.
2. For a review, see: Marchand, A. P. *Tetrahedron* **1988**, *44*, 2377.
3. For reviews, see: (a) Marchand, A. P. In *Advances in Theoretically Interesting Molecules*; Thummel, R. P., Ed.; JAI: Greenwich, CT, 1989; Vol. 1, pp 357-399. (b) Marchand, A. P. *SYNLETT* **1991**, 73.
4. (a) Manser, G. E. "Energetic Copolymers", U. S. Patent 4,483,978; see: *Chem. Abstr.* **1985**, *102*, 81214x. (b) Oyumi, Y.; Inokami, K.; Yamazaki, K.; Matsomoto, K. *Propellants, Explos., Pyrotech.* **1993**, *18*, 62.
5. Eaton, P. E.; Cassar, L.; Hudson, R. A.; Hwang, D. R. *J. Org. Chem.* **1976**, *41*, 1445.
6. Derome, A. E. *Modern NMR Techniques for Chemistry Research*, Pergamon Press, Oxford, 1987, pp 234-239.
7. (a) Sanders, J. K. M.; Hunter, B. K. *Modern NMR Spectroscopy*, Oxford University Press: Oxford, 1987; Chapter 6, pp 163-207. (b) Neuhaus, D.; Williamson, M. *The Nuclear Overhauser Effect in Structural and Conformational Analysis*, VCH Publishers: New York, 1989. (c) Derome, A. E., ref. 6, pp 97-127.
8. (a) Lerman, B. M.; Galin, F. Z.; Umanskaya, L. A.; Tolstikov, G. A. *J. Org. Chem. U. S. S. R.* **1978**, *14*, 2336. (b) Dekker, T. G.; Oliver, D. W. *S. Afr. J. Chem.* **1979**, *32*, 45. (c) Marchand, A. P.; Kaya, R. *J. Org. Chem.* **1983**, *48*, 5392.

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Mn(III)-Based Oxidative Free Radical Cyclizations of Unsaturated 2-Cyclohexenones and Aldehydes

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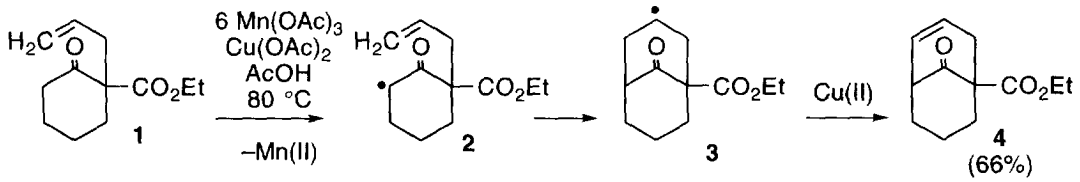
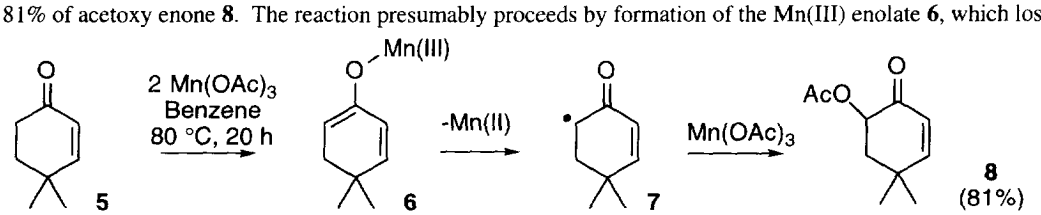
Abstract: Oxidative free-radical cyclizations of unsaturated 2-cyclohexenones **9a**, **9b**, **17**, and **24** with $Mn(OAc)_3$ afford unsaturated α'-keto radicals such as **10** that cyclize to afford bicyclic products. The major process with 2-cyclohexenone **27** is conjugate addition of acetate to form β-acetoxy α-keto radical **37**. Unsaturated aldehydes **45**, **57a**, and **57b** are oxidized to radicals that cyclize to give cyclopentane- and cyclohexanecarboxaldehdyes.

During the past decade Mn(III)-based oxidative free-radical cyclizations have been developed into a general procedure for producing highly functionalized products from simple precursors.[1] These cyclizations have been initiated by reaction of relatively acidic compounds, such as 1,3-diketones, acetoacetates, malonates, and α-sulfinyl or α-nitro ketones, with $Mn(OAc)_3$ to form a Mn(III) enolate, which undergoes electron transfer to give Mn(II) and a radical. We have recently shown that Mn(III)-based oxidative free-radical cyclization of unsaturated ketones in AcOH at 80 °C is a versatile synthetic procedure with broad applicability.[2] Bicyclic ketones that cannot enolize further are isolated in good yield. For instance, oxidation of cyclohexanone **1** with 2 equivalents of $Mn(OAc)_3 \cdot 2H_2O$ and 1 equivalent of $Cu(OAc)_2 \cdot H_2O$ in AcOH at 80 °C for 18 h gives α-keto radical **2**, which undergoes 6-*endo* cyclization to give bicyclic radical **3**. Oxidative elimination with Cu(II) provides 66% of bicyclo[3.2.1]oct-2-en-8-one **4** and 7% of the double bond position isomer. Monocyclic ketone products that can enolize are oxidized further to provide γ-acetoxy-α,β-unsaturated ketones.



Watt and coworkers developed a reliable procedure for the oxidation of α,β-unsaturated ketones to α'-acetoxy-α,β-unsaturated ketones using excess dried $Mn(OAc)_3$ in benzene at reflux.[3] For instance, **5** yields 81% of acetoxy enone **8**. The reaction presumably proceeds by formation of the Mn(III) enolate **6**, which loses

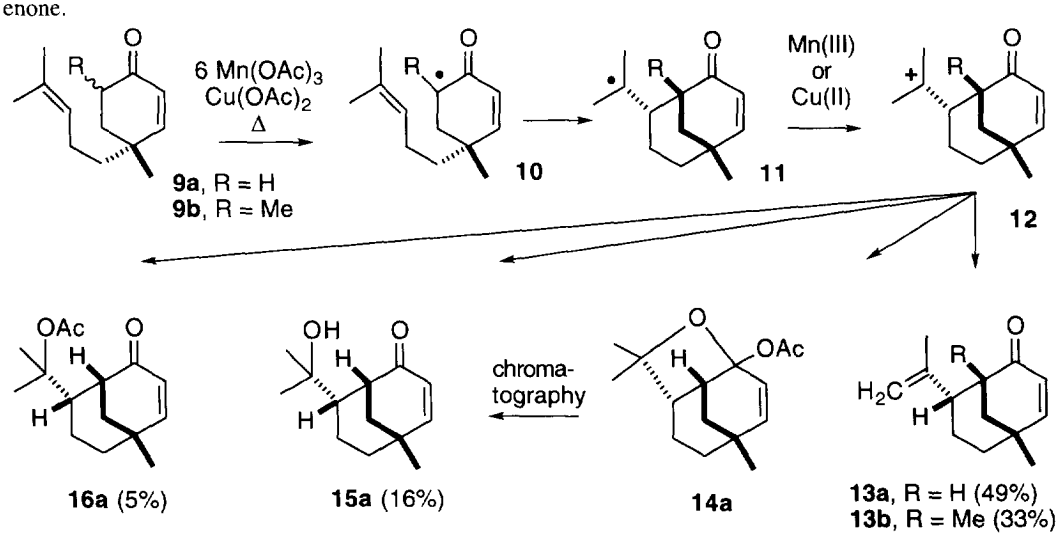


Mn(II) to give unsaturated α'-keto radical **7**. Oxidation of radical **7** by a second equivalent of $Mn(OAc)_3$ provides acetate **8**. The oxidation of **7** to give **8** must be rapid and efficient since acetoxy enones are formed in high yield. Our attempts to trap the unsaturated α'-keto radical obtained from $Mn(OAc)_3$ oxidation of 2-cyclohexenone by addition to 1-octene in AcOH were unsuccessful, giving only 6-acetoxy-2-cyclohexenone and oligomer.

Saturated ketones provide complex mixtures in $Mn(OAc)_3$ oxidations.[4] Oxidation of cyclohexanone with $Mn(OAc)_3$ in AcOH at 70 °C affords 2-acetoxycyclohexanone (18%) and various dimers (8%). The formation of the acetoxy ketone and dimers is completely suppressed by the presence of 1-hexene in the reaction mixture. Under these conditions, 34% of several double bond addition products are obtained. The formation of dimers from the saturated α-keto radical, and the suppression of both dimerization and acetoxylation if an alkene is present in the reaction mixture, indicates that oxidation of saturated α-keto radicals to α-acetoxy ketones is much slower than the oxidation of unsaturated α'-keto radicals such as **7**, which undergo acetoxylation in AcOH even if alkene is present.

Results and Discussion

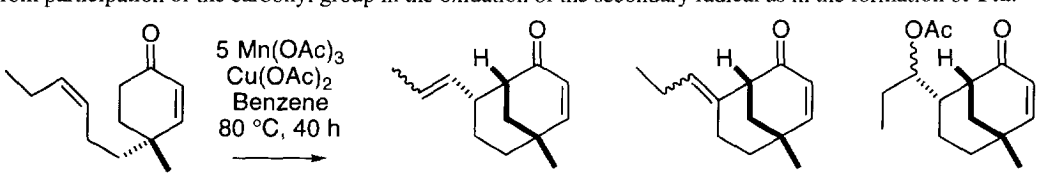
Intramolecular trapping of unsaturated α'-keto radicals by suitably situated double bonds should be much faster than intermolecular addition and might be able to compete with acetoxylation. We were delighted to find that oxidation of unsaturated cyclohexenone **9a**[5] with 6 equiv of dried $Mn(OAc)_3$ and 1 equiv of $Cu(OAc)_2$ in benzene at reflux for 55 h provides 49% of an inseparable 20:1:1 mixture of dienones (**13a**, the stereoisomer with a β-isopropenyl group and the isopropylidene regioisomer), 16% of hydroxy enone **15a**, and 5% of acetoxy enone **16a**. The allylic methine hydrogen of **13a** is axial since it absorbs at δ 2.09 (ddd, J = 11.7, 4.9, 3.4) with a large axial-axial coupling of 11.7 Hz to the adjacent axial methylene hydrogen. The structure of **15a** was established by X-ray crystallographic structure analysis.[6] The formation of three bicyclic products in 70% yield unambiguously establishes that unsaturated α'-keto radicals are formed in $Mn(OAc)_3$ oxidation of unsaturated ketones and that 6-*exo* cyclization of radical **10** is much faster than its oxidation to an α'-acetoxy enone.



Enolization of **9a** and loss of Mn(II) affords the unsaturated α'-keto radical **10a**, which undergoes a stereospecific 6-*exo* cyclization to give tertiary radical **11a** with an equatorial isopropyl group. Rapid oxidation of tertiary radical **11a** by either Mn(III) or Cu(II)[1] provides tertiary cation **12a**, which loses a proton to form dienone **13a** or reacts with acetate ion to give acetoxy enone **16a**. The formation of hydroxy ketone **15a** is atypical of $Mn(OAc)_3$ oxidative cyclizations and was particularly surprising under the nominally anhydrous reaction conditions. Examination of the NMR spectrum of the crude reaction mixture indicated the presence of a compound with an unconjugated cyclohexene double bond [6.45 (dd, J = 10.3, 1.5) and 5.45 (dd, 1, J = 10.3, 1.6)]. This material decomposes to **15a** on chromatography or on treatment with weak base suggesting that it is acylal **14a**. Cyclization of the carbonyl group of **12** to the cation and trapping with acetate provides **14a**, which is converted to hydroxy enone **15a** on workup or chromatography. As expected, similar mixtures of products are obtained without $Cu(OAc)_2$ since both Mn(III) and Cu(II) oxidize tertiary radicals to cations. Lower yields of the same products are obtained in AcOH.

The oxidative cyclization of **9b** was examined to determine whether tertiary unsaturated α'-keto radicals could be prepared and cyclized. Alkylation of the enolate of **9a** (LDA, DMPU, THF, MeI, -40 °C) provides 44% of **9b** as a 1:1 mixture of stereoisomers. Oxidative cyclization of **9b** with 2 equiv of dried $Mn(OAc)_3$ and 1 equiv of $Cu(OAc)_2$ in AcOH at 70 °C for 20 h affords 44% of a 3:1 mixture of **13b** (the only monomeric product) and recovered **9b**. Pure **13b** is obtained in 21% yield by carrying out the reaction with 4 eq of dried $Mn(OAc)_3$ to completely consume **9b**. Reaction in benzene was much slower and less efficient. This oxidative cyclization proceeds through cation **12b**, which loses a proton to give **13b**. The equatorial stereochemistry of the isopropenyl group follows from the absorption of the allylic methine hydrogen at δ 1.94 (dd, J = 13.5, 4.7). The differing reactivity of cations **12a** and **12b** is presumably due to steric hindrance between the bridgehead methyl group and the adjacent substituent, which is much worse with the trisubstituted sp^3 carbon of **14b-16b** than with the isopropenyl substituent of **13b**. MM2 calculations[7] indicate that **15b** is 8.0 kcal/mole more strained than **15a**, while **13b** is only 2.7 kcal/mole more strained than **13a**. Therefore, **12b** loses a proton to give **13b** rather than reacting with a nucleophile to give **14b-16b**.

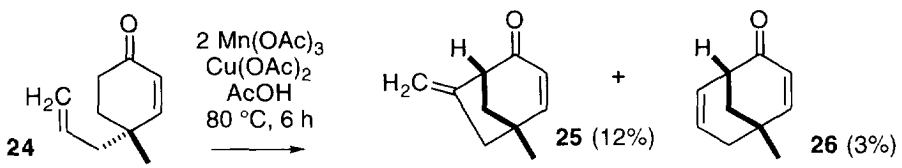
Oxidative cyclization of **17** was examined to determine whether a less nucleophilic 1,2-disubstituted alkene would cyclize to the electrophilic unsaturated α'-keto radical. LAH reduction of 3-ethoxy-6-(3*Z*-hexenyl)-6-methyl-2-cyclohexenone[8] followed by acidic hydrolysis affords 88% of **17**. Oxidative cyclization of **17** with 5 equiv of dried $Mn(OAc)_3$ and 1 equiv of $Cu(OAc)_2$ in benzene at reflux for 40 h provides a complex mixture containing 47% of *E*-disubstituted alkene **18**, 14% of *Z*-disubstituted alkene **19**, 9% of *E*-trisubstituted alkene **20**, 0.5% of the *Z*-trisubstituted alkene **21**, and 2% of each of the acetate diastereomers **22** and **23**. Lower yields are obtained in AcOH. The equatorial stereochemistry is assigned by analogy to **13a** and **16a**. The stereochemistry of the trisubstituted alkenes **20** and **21** was assigned based on the shift of the bridgehead proton at δ 2.99 in **20** and δ 3.52 in **21** as has been observed in related compounds.[9] We have obtained mixtures of alkene isomers similar to **18-21** by Cu(II) oxidation of secondary radicals formed in the oxidative cyclization of β-keto esters and diketones.[8] The formation of secondary acetates **22** and **23** was unexpected and may result from participation of the carbonyl group in the oxidation of the secondary radical as in the formation of **14a**.



17 → **18**, *E* (47%), **19**, *Z* (14%); **20**, *E* (9%), **21**, *Z* (0.5%); **22** (2%), **23** (2%)

The formation of bicyclic products in 75% yield establishes the generality of 6-*exo*-cyclizations of unsaturated α'-keto radicals.

Our initial trial with 5-*exo*/6-*endo* cyclization was much less successful. Oxidative cyclization of **24**[10,11] with 2 equiv of dried $Mn(OAc)_3$ and 1 equiv of $Cu(OAc)_2$ in AcOH at 80 °C for 6 h affords a mixture containing 12% of the known 5-*exo*- cyclization product **25**[11] and 3% of 6-*endo*-cyclization product **26**. The position of the double bond in **26** is assigned based on the absence of coupling between the allylic methylene group and the bridgehead hydrogen and is expected since Cu(II) oxidation of the secondary radical should give the less hindered alkene.[1d,2,12] Similar results are obtained in benzene. The low yield of bicyclic products from **24** suggests that 6-*exo* cyclizations of unsaturated α-keto radicals are faster than 5*exo*/6-*endo*-cyclizations.

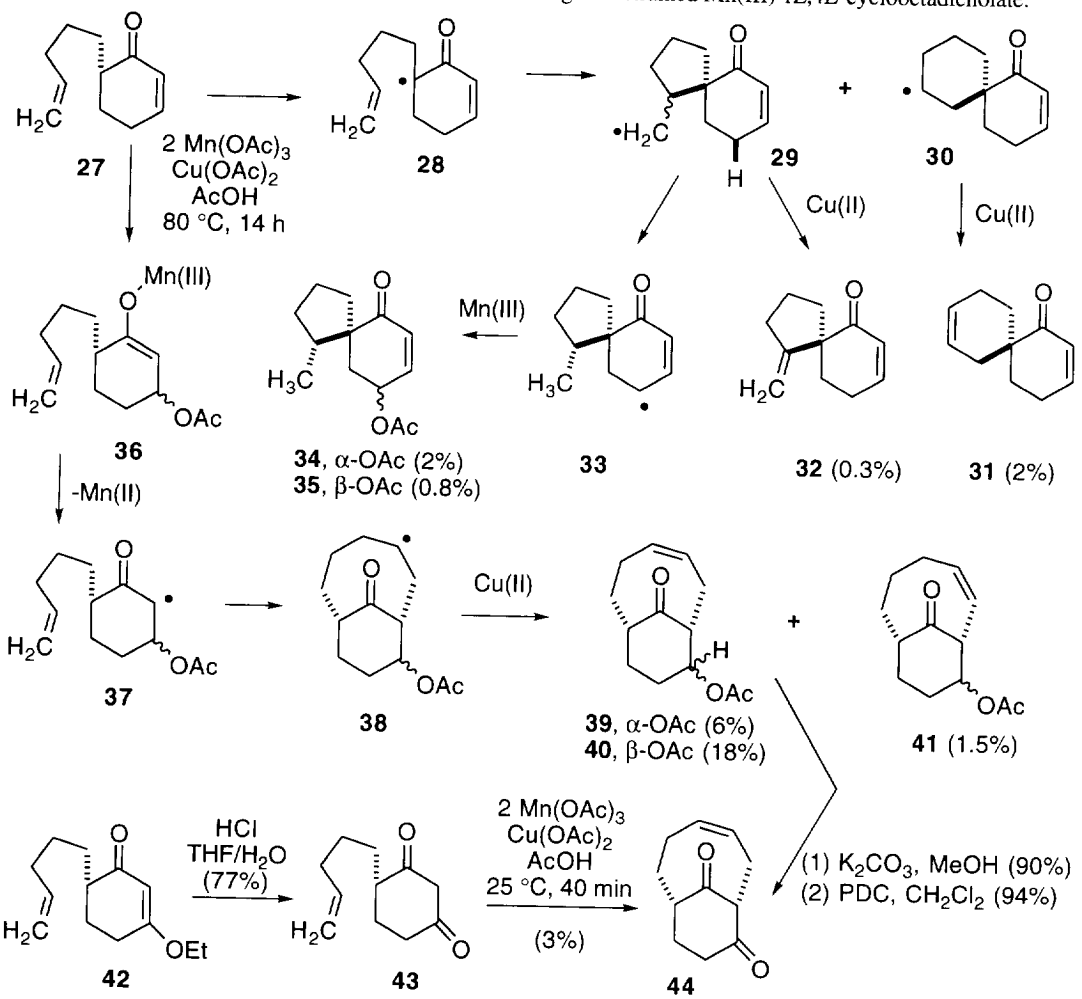


Oxidative cyclization of **27** was examined to determine whether spirocyclic systems could be prepared by oxidative cyclization of unsaturated enones. Oxidative cyclization of **27**[13] with 2 equiv of dried $Mn(OAc)_3$ and 1 equiv of $Cu(OAc)_2$ in AcOH at 80 °C for 14 h gives a complex mixture containing at least seven products. The expected enolization and oxidation to give unsaturated α'-keto radical **28** occurs to only a minor extent. 6-*endo*-Cyclization of **28** gives **30**, which is oxidized by Cu(II) to give 2% of **31**. 5-*exo*-Cyclization of **28** provides **29** as a mixture of stereoisomers, which are oxidized by Cu(II) to give only 0.3% of **32**. One isomer of **29** undergoes a rapid 1,5-hydrogen atom shift to form the thermodynamically more stable allylic radical **33**. Oxidation of **33** by $Mn(OAc)_3$ yields 2.8% of a mixture of γ-acetoxy-α,β-unsaturated ketones **34** and **35** as we have previously reported in related systems.[2]

To our surprise, the major reaction is conjugate addition of acetate to enone **27** to give Mn(III) enolate **36**, which loses Mn(II) to give radical **37** as a mixture of stereoisomers. 8-*endo*-Cyclization of **37** provides bicyclic secondary radical **38**, which is oxidized by Cu(II) to give a mixture containing **39** (6%), **40** (18%), and **41** (1.5%). We have previously noted that Cu(II) oxidizes analogous alkyl radicals selectively to afford the least hindered alkene.[2,12] The NMR spectra of **39** and **40** showed an isolated double bond and an acetate. The stereochemistry of the acetate was established by the absorption for the axial CHOAc methine hydrogen of **39** at δ 5.02 (ddd, 1, J = 11.0, 5.1, 5.1) and for the equatorial CHOAc methine hydrogen of **40** at δ 5.11 (br dd, 1, J = 3.0, 3.0).[14] A similar reaction in benzene gives a low yield of **31** and none of **39-41**. Although the yields of bicyclic products obtained from radical **37** are only modest, conjugate addition followed by enolate oxidation is a novel method of generating radicals. The formation of **37** as the major radical from **27**, while **9**, **17**, and **24** provide only the unsaturated α'-keto radical, probably results from both the slower enolization of **27**, which requires the abstraction of a more hindered methine hydrogen, and the unhindered double bond of **27** with C-4 unsubstituted, which facilitates conjugate addition. We are currently exploring radical generation by the addition of other nucleophiles to enones in the presence of $Mn(OAc)_3$.

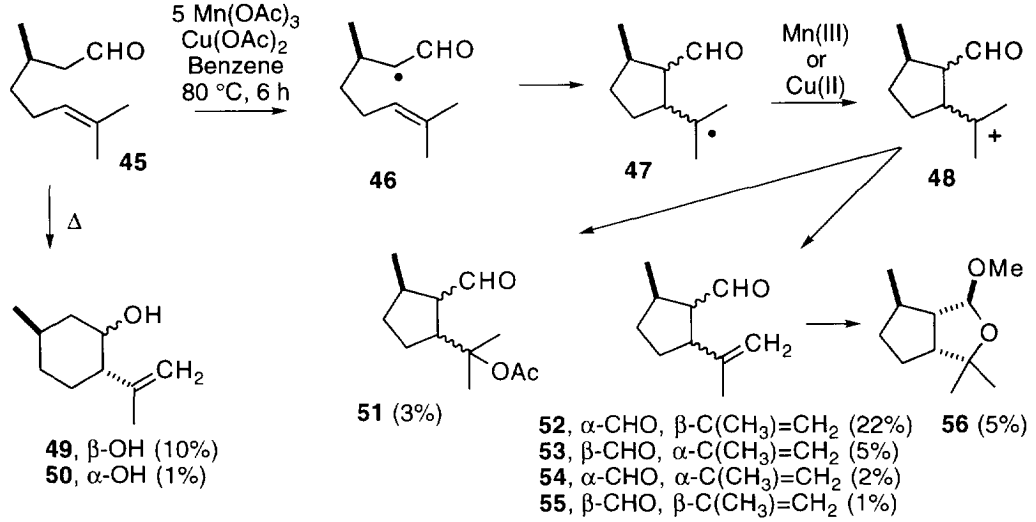
Since the formation of radical **37** from enone **27** was unprecedented and an 8-*endo*-cyclization was unusual, we carried out an alternative synthesis to confirm the structures of **39** and **40**. Hydrolysis of the mixture of **39** and **40** with K_2CO_3 in MeOH (90%) and oxidation of the mixture of alcohols with PDC in CH_2Cl_2 (94%) give a single dione **44**. Hydrolysis of **42**[15] with HCl in aqueous THF affords 77% of dione **43**. Oxidative cyclization of dione **43** with 2 equiv of $Mn(OAc)_3$ and 1 equiv of $Cu(OAc)_2$ in AcOH at 25 °C for 40 min provides 3% of **44** as the only monomeric product, thereby confirming the structures assigned to **39** and **40**. The poor yield in the 8-*endo*-cyclization of **43** contrasts to the 72% yield obtained in the 6-*exo*-

cyclization of 4-(3*Z*-hexenyl)cyclohexane-1,3-dione indicating the sensitivity of this reaction to the length of the tether.[8] Presumably, dione **44** is oxidized further by Mn(III)-assisted enolization of the ketone in the three carbon bridge of **44** to give an unstrained Mn(III) 1*Z*,4*E*-cyclodecadienolate. Bicyclic ketones **39** and **40** are not oxidized further since enolization of the ketone would give a strained Mn(III) 1*Z*,4*E*-cyclooctadienolate.

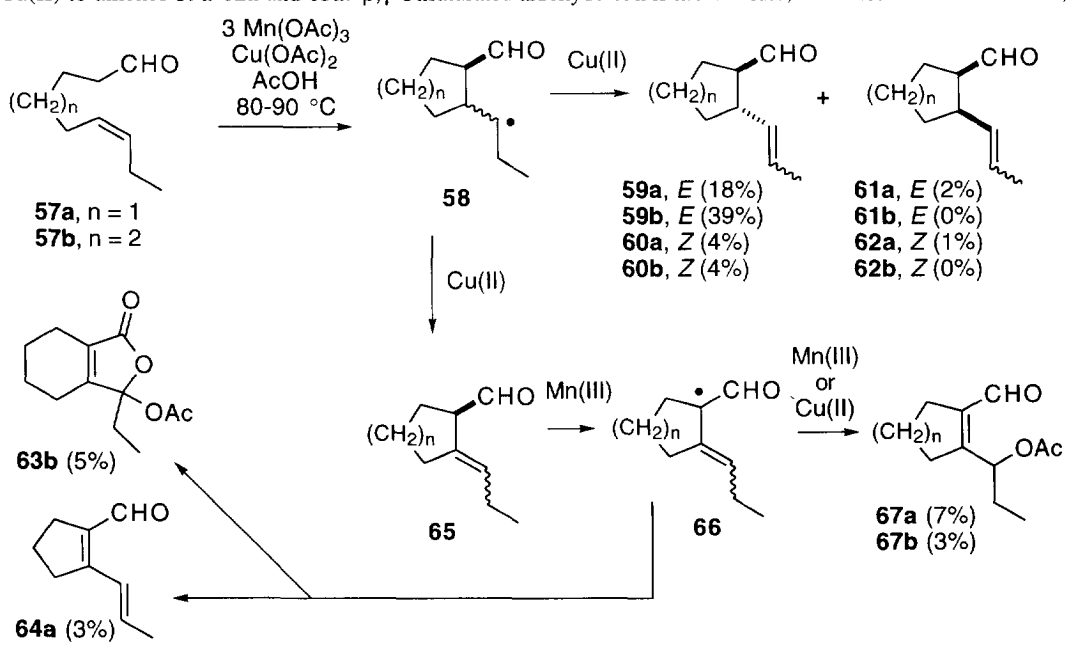


Oxidative Cyclizations of Aldehydes. The oxidative intermolecular addition of aldehydes to alkenes proceeds in 30-40% yield based on $Mn(OAc)_3$ consumed if 10 equiv of aldehyde and 2 equiv of alkene are used.[1] Since use of excess substrate is not practical in intramolecular reactions, these conditions are not suitable for the oxidative cyclizations of unsaturated aldehydes. We examined the oxidative cyclization of unsaturated aldehydes to determine whether the initially formed cyclic product could be isolated or whether further oxidation would occur if excess aldehyde was not present. Reaction of citronellal (**45**) with 5 equiv of $Mn(OAc)_3 \cdot 2H_2O$ and $Cu(OAc)_2 \cdot H_2O$ in benzene at reflux for 6 h affords a mixture containing 30% of a 20:4:2:1 mixture of the known 5-methyl-2-isopropenylcyclopentanecarboxaldehydes **52**,[16,17] photocitral A (**53**),[16,17] **54**,[16,17] and **55**,[17] 3% of acetoxy aldehyde **51**, 5% of methoxytetrahydrofuran **56**,[18] and 11% of a 10:1 mixture of ene adducts isopulegol (**49**) and neoisopulegol (**50**). A similar reaction in AcOH yields mainly the ene adducts **49**

and **50** as expected, since the ene reaction is acid catalyzed. Mn(III)-assisted enolization of **45** and loss of Mn(II) forms radical **46**, which undergoes 5-*exo*-cyclization to give radical **47**. Oxidation by Mn(III) or Cu(II) affords cation **48**, which loses a proton to give **52-55** and reacts with acetate to give **51**.



Competing ene reaction is not a problem with the less nucleophilic double bonds of **57a** and **57b**. Oxidative cyclization of 6Z-nonenal (**57a**) with 3 equiv of dried $Mn(OAc)_3$ and 1 equiv of $Cu(OAc)_2$ in AcOH at 90 °C for 90 min provides 25% of a 25:5.6:3:1 mixture of **59a-62a**, respectively, 3% of dienal **64a**,[19] and 7% of acetoxy enal **67a**. Cyclic radical **58** is formed analogously to **47**. The secondary radical is oxidized by Cu(II) to alkenes **59a-62a** and **65a**. β,γ-Unsaturated aldehyde **65a** is more acidic, and therefore more reactive,



than acyclic aldehyde **57a**. It reacts rapidly with $Mn(OAc)_3$ to give allylic radical **66a**, which is oxidized to give dienal **64a** and acetate **67a**.

The structures of 2-(1-propenyl)-cyclopentanecarboxaldehydes **59a-62a** were assigned based on analysis of the NMR spectral data, which indicated that the major products **59a** and **59b** have an *E*- and *Z*-double bond, respectively. The ^{13}C NMR spectral data are virtually identical, except for a slight upfield shift for the alkene carbons, a 5.1 Hz upfield shift for the allylic methine carbon, and a 5.7 Hz upfield shift for the methyl group of **60a**. These similarities suggest that both of these compounds have the more stable[20] trans stereochemistry. Equilibration with Et_3N in THF at reflux did not change the ratio of **59a-62a**, confirming that **59a** and **60a** are the more stable trans isomers and suggesting that equilibration occurs under the reaction conditions in AcOH at 80 °C. The data for **67a** correspond closely to those for 2-alkyl-1-cyclopentenecarboxaldehydes.[21]

Oxidative cyclization of 7*Z*-decenal with 3 equiv of dried $Mn(OAc)_3$ and 1 equiv of $Cu(OAc)_2$ in AcOH at 80 °C for 10 h provides a mixture containing 43% of a 9:1 mixture of **59b** and **60b**, 3% of acetoxy enal **67b**, and 5% of a compound tentatively identified as γ-acetoxybutenolide **63b**. The C*H*CHO hydrogen of the major isomer **59b** absorbs at δ 2.07 (dddd, J = 10.8, 10.8, 3.6, 3.1). The two large axial-axial coupling constants indicate that both the aldehyde and alkenyl group are equatorial.[22] The absorption of the C*H*CH=C hydrogen of the minor isomer **60b** at δ 2.53 (dddd, 10.5, 10.5, 10.5, 4.0) also has two large axial-axial coupling constants establishing that these two compounds differ only in the double bond stereochemistry. The ^{13}C NMR spectral data are virtually identical, except for a slight upfield shift for the alkene carbons, a 5.2 Hz upfield shift for the allylic methine carbon, and a 5.7 Hz upfield shift for the methyl group of **60b**. The absence of **61b** and **62b** establishes that the 6-*exo*-cyclization leading to **58b** gives only the more stable trans diequatorial isomer.

The spectral data for **63b** correspond closely to those reported for analogous γ-acetoxybutenolides.[23] The ^1H NMR spectrum of **63b** shows no downfield protons, the ^{13}C NMR spectrum shows two double bond carbons at δ 160.1 and 130.1 and the acylal carbon at δ 107.8, and the IR spectrum shows strong absorptions at 1777 and 1692 cm^{-1}. The mechanism of formation of **63b** is unclear, but probably proceeds through **65b** and may involve the γ-acetoxylation of a butenolide.[24]

In conclusion, we have demonstrated that unsaturated α'-keto radicals formed by oxidation of 4-alkenyl-2-cyclohexenones can be trapped efficiently in 6-*exo*-cyclizations. When the 6-position of the 2-cyclohexenone is substituted, addition of the acetate to the enone and oxidation of the enolate provides a novel route to radicals such as **37**. Oxidative 5- and 6-*exo*-cyclizations of unsaturated aldehydes can be carried out in moderate yield providing a short route to 2-alkenylcycloalkanecarboxaldehydes.

Acknowledgment: We are grateful to the National Institutes of Health for financial support and Prof. Bruce M. Foxman for X-ray crystallographic structure determination of **15a**.

Experimental Section

General. NMR spectra were recorded in $CDCl_3$ at 300 MHz unless otherwise indicated. Chemical shifts are reported in δ; coupling constants are reported in Hz. $Mn(OAc)_3 \cdot 2H_2O$ was purchased from Aldrich and dried for 1 d at 0.25 torr over P_2O_5 as described by Watt and coworkers.[3b]

Oxidative Cyclization of 4-Methyl-4-(4-methyl-3-pentenyl)-2-cyclohexenone (9a). A degassed solution of enone **9a**[5] (300 mg, 1.56 mmol), dried $Mn(OAc)_3$ (2.1759 g, 9.38 mmol), and $Cu(OAc)_2$ (284 mg, 1.56 mmol) in 20 mL of benzene was stirred at reflux for 55 h. The resulting solution was green and contained some precipitate. It was diluted with water and aqueous 10% $NaHSO_3$ solution and extracted with ether (3 × 50 mL). The combined organic extracts were washed sequentially with saturated $NaHCO_3$, water, and brine and dried ($MgSO_4$). The solvent was removed under reduced pressure giving 270 mg of crude product. Flash chromatography on silica gel (10:1 hexane/EtOAc) gave 145 mg (49%) of a 20:1:1 mixture of

13a, the stereoisomer with an axial isopropenyl group and the isopropylidene regioisomer, followed by 19 mg (5%) of acetate **16a**, and 51 mg (16%) of alcohol **15a**, which was recrystallized from hexane at -40 °C.

The data for **13a**: ^{1}H NMR 6.55 (dd, 1, J = 9.9, 2.1), 6.06 (dd, 1, J = 9.9, 0.9), 4.82 (br s, 1), 4.57 (br s, 1), 2.73 (ddd, 1, J = 3.4, 3.4, 3.4), 2.15 (ddd, 1, J = 12.6, 3.4, 2.4), 2.09 (ddd, 1, J = 11.7, 4.9, 3.4), 1.82 (s, 3), 1.45-1.70 (m, 5), 1.15 (s, 3); ^{13}C NMR 200.2 (C), 156.4 (CH), 146.2 (C), 131.1 (CH), 110.2 (CH_2), 46.5 (CH), 45.0 (CH), 42.5 (CH_2), 34.5 (CH_2), 33.8 (C), 28.4 (CH_3), 23.3 (CH_2), 22.5 (CH_3); IR (neat) 2927, 2853, 1673, 1453, 1372, 888 cm^{-1}.

Partial data for the isomer with an axial isopropenyl group: ^{1}H NMR 5.00 (ddq, 1, J = 1.4, 1.4, 1.4), 4.95 (br s, 1).

Partial data for the isopropylidene regioisomer: ^{1}H NMR 3.63 (dd, 1, J = 3.0, 3.0).

The ^{1}H NMR spectrum of the crude product showed peaks at δ 6.45 (dd, 1, J = 10.3, 1.5), 5.47 (dd, 1, J = 10.3, 1.6), 3.00 (m, 1), 2.01 (s, 3), 1.25 (s, 6), and 1.03 (s, 3) which were assigned to **14a**.

The data for **15a**: mp 67-68 °C; ^{1}H NMR 6.64 (dd, 1, J = 9.9, 2.2), 6.13 (dd, 1, J = 9.9, 1.0), 2.91-2.97 (m, 1), 2.13 (ddd, 1, J = 12.6, 3.9, 2.7), 2.00-2.08 (m, 1, OH), 1.71-1.81 (m, 1), 1.38-1.62 (m, 5), 1.37 (s, 3), 1.14 (s, 6); ^{13}C NMR 205.9 (C), 158.1 (CH), 131.0 (CH), 72.1 (C), 49.8 (CH), 43.9 (CH), 43.0 (CH), 34.8 (CH_2), 33.7 (C), 29.3 (CH_3), 28.3 (CH_3), 28.0 (CH_3), 20.5 (CH_2); IR (CCl_4) 3565, 2956, 2858, 1664, 1455, 1385, 1372, 1081 cm^{-1}.

The data for **16a**: ^{1}H NMR 6.50 (dd, 1, J = 9.9, 2.2), 6.07 (dd, 1, J = 9.9, 1.1), 2.77-2.83 (m, 1), 2.12 (ddd, 1, J = 12.9, 3.7, 2.7), 1.89 (s, 3), 1.40-1.86 (m, 6), 1.52 (s, 3), 1.51 (s, 3), 1.12 (s, 3); ^{13}C NMR 202.7 (C), 170.3 (C), 155.8 (CH), 130.9 (CH), 83.3 (C), 48.9 (CH), 44.2 (CH), 43.4 (CH_2), 34.6 (CH_2), 33.6 (C), 28.3 (CH_3), 24.6 (CH_3), 24.3 (CH_3), 22.1 (CH_3), 20.2 (CH_2); IR (neat) 2952, 2870, 1730, 1672, 1454, 1367 cm^{-1}.

Preparation of 4,6-Dimethyl-4-(4-methyl-3-pentenyl)-2-cyclohexen-1-one (9b). *N*-BuLi (1.64 mL of 2.5 M solution in hexane, 4.1 mmol) was added to a solution of 0.5 mL (3.9 mmol) of diisopropylamine in 2.3 mL THF at -20 °C. The resulting solution was stirred at this temperature for 20 min and cooled to -78 °C, and enone **9a** (500 mg, 2.6 mmol) in 1.0 mL of THF was added dropwise. The mixture was stirred for 0.5 h and warmed to -40 °C. DMPU (551 mg, 4.3 mmol) in 0.65 mL of THF and MeI (667 mg, 4.7 mmol) were added. The reaction mixture was warmed to rt and stirred for 2 h. The reaction was diluted with 50 mL of ether and washed with water and brine. The aqueous phase was back extracted with ether (2 × 30 ml) and the combined ethereal layers were dried ($MgSO_4$) and evaporated under reduced pressure. Flash chromatography on silica gel (10:1 hexane/EtOAc) provided 235 mg (44%) of pure **9b** as a 1:1 mixture of stereoisomers: ^{1}H NMR 6.62 (ddd, 1 × 0.5, J = 10.0, 2.2), 6.60 (ddd, 1 × 0.5, J = 10.0, 2.2), 5.86 (dd, 1, J = 10.0, 3.0), 5.04-5.14 (m, 1), 2.47-2.63 (m, 1), 2.10-1.89 (m, 3), 1.10-1.80 (m, 4), 1.69 (s, 3), 1.60 (s, 3), 1.19 (s, 0.5 × 3), 1.13 (d, 0.5 × 3, J = 6.6), 1.11 (s, 0.5 × 3), 1.11 (d, 0.5 × 3, J = 6.6); ^{13}C NMR 202.0, (158.4, 157.9), (132.0, 131.9), (127.1, 126.8), 124.0, (43.1, 43.0), (42.1, 38.4), (37.5, 37.4), (36.7, 36.3), (27.2, 23.3), 25.7, 23.8, (22.6, 17.7), (15.2, 15.1); IR (neat) 2964, 2927, 2870, 1682, 1620, 1455, 1376, 1202, 1116, 814 cm^{-1}.

Oxidative Cyclization of 4,6-Dimethyl-4-(4-methyl-3-pentenyl)-2-cyclohexenone (9b). A degassed solution of enone **9b** (50 mg, 0.243 mmol), $Mn(OAc)_3$ (124 mg, 0.535 mmol), and $Cu(OAc)_2$ (44 mg, 0.243 mmol) in 2 mL of AcOH was stirred for 30 h at 70 °C at which time it was blue and contained a white precipitate. Water was added to dissolve the precipitate. The mixture was extracted with methylene chloride (3 × 30 mL). The combined organic layers were washed with saturated $NaHCO_3$ solution, water, and brine and dried ($MgSO_4$). Evaporation of the solvent under reduced pressure gave 48 mg of crude product. Flash chromatography on silica gel (6:1 pentane/Et_2O) gave 22 mg (44%) of a 3:1 mixture of **13b** and recovered **9b**. A similar reaction carried out with 250 mg (1.07 mmol) of $Mn(OAc)_3$ gave 10 mg (21%) of pure **13b** after flash chromatography: ^{1}H NMR 6.53 (dd, 1, J = 2.2, 9.8), 6.11 (d, 1, J = 9.8), 4.83 (br s, 1), 4.61 (br s, 1), 1.94 (dd, 1, J = 13.5, 4.7), 1.93 (dd, 1, J = 12.7, 2.4), 1.76 (dddd, 1, J = 13.5, 13.5, 11.9, 5.1), 1.56 (br s, 3),

1.40-1.62 (m, 4), 1.13 (s, 3), 1.03 (s, 3); ^{13}C NMR 203.9, 155.9, 145.7, 131.1, 113.7, 53.9, 51.3, 46.3, 35.1, 34.7, 28.4, 25.9, 23.6, 21.1; IR (neat) 2924, 1667, 1453, 1374, 889, 835, 806 cm^{-1}.

Preparation of 4-Methyl-4-(3*Z*-hexenyl)-2-cyclohexen-1-one (17). A solution of LAH (1.0 mL of 0.93 M in THF, 0.93 mmol) was added dropwise to a solution of 3-ethoxy-6-methyl-6-(3Z-hexenyl)-2-cyclohexen-1-one[8] (268 mg, 1.14 mmol) in 3 mL of Et_2O at 0 °C. After the addition was complete, the solution was warmed to rt and stirred for 1.5 h. The reaction was cooled to 0 °C and aqueous 25% H_2SO_4 (2 mL) was added with vigorous stirring. The mixture was stirred for 2.5 h and extracted with ether (2 × 30 ml). The ethereal layers were washed with saturated Na_2CO_3 solution, water, and brine, and then dried ($MgSO_4$). After evaporation of the solvent, the crude product was purified by flash chromatography on silica gel (10:1 hexane/EtOAc) to give 191 mg (88%) of **17**: ^{1}H NMR 6.70 (d, 1, *J* = 10.1), 5.89 (d, 1, *J* = 10.1), 5.25-5.44 (m, 2), 2.42-2.51 (m, 2), 1.94-2.12 (m, 5), 1.73-1.85 (m, 1), 1.44-1.58 (m, 2), 1.16 (s, 3), 0.97 (t, 3, *J* = 7.5); ^{13}C NMR 199.0, 158.6, 131.8, 128.2, 127.1, 40.7, 35.4, 33.9, 33.2, 24.5, 21.7, 20.2, 14.0; IR (neat) 3007, 2961, 2871, 1683, 1462, 1390, 1373, 1116, 804 cm^{-1}.

Oxidative Cyclization of 4-Methyl-4-(3*Z*-hexenyl)-2-cyclohexen-1-one (17). A degassed solution of enone **17** (200 mg, 1.04 mmol), dried $Mn(OAc)_3$ (1.209 g, 5.2 mmol), and $Cu(OAc)_2$ (189 mg, 1.04 mmol) in 30 mL of benzene was heated at reflux for 40 h. Normal work up provided 192 mg of crude product. Flash chromatography on silica gel (14:1 hexane/EtOAc) gave 1 mg of 70% pure **21**, followed by 122 mg of a 1:1.7:5.6 mixture of **20**, **19**, and **18**, 18 mg of 2.2:2.5:8.5:1 mixture of **20**, **19**, **18**, and recovered **17**, 5 mg of **22**, and 6 mg of 5:1 mixture of **22** and **23**.

The data for **18**: ^{1}H NMR 6.56 (dd, 1, *J* = 10.0, 2.2), 6.07 (dd, 1, *J* = 10.0, 1.0), 5.43 (ddq, 1, *J* = 15.3, 0.8, 6.1), 5.31 (ddq, 1, *J* = 15.3, 7.2, 1.3), 2.42-2.49 (m, 1), 2.06-2.26 (m, 2), 1.64 (dd, 3, *J* = 6.1, 1.3), 1.34-1.72 (m, 5), 1.14 (s, 3); ^{13}C NMR 201.0, 156.9, 133.4, 131.2, 124.9, 49.2, 42.4, 42.0, 34.5, 33.7, 28.8, 25.9, 18.2; IR (neat) 3019, 2926, 2868, 1740, 1675, 1612, 1453, 1374, 1247, 1212, 1077, 964, 825, 731 cm^{-1}.

Partial data for **19**: ^{1}H NMR 6.58 or 6.66 (dd, 1, *J* = 10.0, 2.2), 5.16 (ddq, 1, *J* = 11.3, 9.6, 1.6), 1.15 (s, 3).

Partial data for **20**: ^{1}H NMR 6.66 or 6.58 (dd, 1, *J* = 10.0, 2.3), 2.99 (br t, 1, *J* = 3.0), 1.15 (s, 3), 0.94 (t, 3, *J* = 7.5).

Partial data for **21**: ^{1}H NMR 6.64 (dd, 1, *J* = 10.0, 2.2), 6.10 (dd, 1, *J* = 10.0, 1.0), 5.29 (br td, 1, *J* = 7.4, 2.2), 3.52 (br t, 1, *J* = 3.0), 0.9-2.4 (m, 8), 1.14 (s, 3), 0.97 (t, 3, *J* = 7.5).

Partial data for **22**: ^{1}H NMR 6.55 (dd, 1, *J* = 10.0, 2.2), 6.08 (dd, 1, *J* = 10.0, 1.0), 4.67 (ddd, 1, *J* = 7.9, 7.9, 4.1), 2.56 (br s, 1), 2.17-1.45 (m, 9), 2.01 (s, 3), 1.13 (s, 3), 0.86 (t, 3, *J* = 7.4); ^{13}C NMR 200.9, 170.6, 156.6, 131.0, 45.1, 42.4, 41.2, 34.1, 33.7, 28.4, 24.6, 21.9, 21.0, 9.0, the quaternary carbon was not observed.

Partial data for **23**: ^{1}H NMR 6.51 (dd, 1, *J* = 10.0, 2.2), 6.07 (dd, 1, *J* = 10.0, 1.0), 4.56 (ddd, 1, *J* = 7.9, 6.6, 4.2), 2.73 (br s, 1), 2.07 (s, 3), 1.20-2.20 (m, 9), 1.13 (s, 3), 0.85 (t, 3, *J* = 7.5).

Oxidative Cyclization of 4-Methyl-4-(2-propenyl)-2-cyclohexen-1-one (24). A degassed solution of enone **24**[10] (100 mg, 0.67 mmol), $Mn(OAc)_3$ (327 mg, 1.41 mmol), and $Cu(OAc)_2$ (134 mg, 0.74 mmol) in 9 ml of AcOH was stirred for 5.5 h at 80 °C. The reaction was worked up as above giving 90 mg of crude product. Flash chromatography on silica gel (20:1 hexane/EtOAc) afforded 3 mg of a 1:6.8 mixture of **25** and **26**, followed by 4 mg of a 6.7:1 mixture of **25** and **26**, 3 mg of a 24.6:2:1 mixture of **25**, **26**, and recovered **24**, and 13 mg of a 1.5:1 mixture of **25** and recovered **24**.

The data for **25**: ^{1}H NMR 6.94 (dd, 1, *J* = 2.0, 9.6), 5.78 (dd, 1, *J* = 1.6, 9.6), 5.26 (br s, 1), 5.03 (br s, 1), 3.44 (br d, 1, *J* = 5.0), 2.37 (br s, 2), 2.07 (br d, 1, *J* = 11.0), 1.79 (ddd, 1, *J* = 2.0, 5.0, 11.0), 1.35 (s, 3); ^{13}C NMR 198.8, 159.7, 146.1, 126.0, 112.0, 59.1, 47.0, 43.7, 42.9, 23.6; IR (neat) 2957, 2870, 1681, 1461, 1371, 883 cm^{-1}. The ^{1}H NMR and IR spectral data are identical to those previously reported.[11]

The data for **26**: ^{1}H NMR 6.53 (dd, 1, *J* = 2.2, 10.0), 5.85 (dd, 1, *J* = 0.8, 10), 5.78 (br s, 2), 3.00 (br s, 1), 2.18 (br d, 1, *J* = 18.5), 1.94-2.07 (m, 2), 1.76 (ddd, 1, *J* = 2.2, 3.0, 12.4), 1.21 (s, 3); ^{13}C NMR

155.9, 128.4, 125.8, 125.7, 45.6, 37.2, 35.8, 32.2, 28.7, the carbonyl carbon was not observed; IR (neat) 2922, 1686, 1460 cm^{-1}.

Oxidative Cyclization of 6-(4-Pentenyl)-2-cyclohexen-1-one (27). A degassed solution of enone **27**[13] (150 mg, 0.91 mmol), $Mn(OAc)_3$ (478 mg, 2.06 mmol), and $Cu(OAc)_2$ (165 mg, 0.91 mmol) in 10 mL of AcOH was stirred for 14 h at 80 °C. Normal work up afforded 155 mg of crude product. Flash chromatography (20:1 hexane/EtOAc) gave 3 mg of a 5:1 mixture of spiro compounds **31** and **32**, followed by 6 mg of a 2.5:1 mixture of spiro acetates **34** and **35**, 3 mg of **41**, 3 mg of a 90% pure 1.4:1 mixture of acetates **40** and **39**, and 46 mg of a 3:1 mixture of acetates **40** and **39**.

Partial data for **31**: ^1H NMR 6.88 (ddd, 1, J = 10.0, 4.0, 4.0), 5.95 (ddd, 1, J = 10.0, 2.1, 2.1), 5.66 (br s, 2), 2.60-1.57 (m, 10).

Partial data for **32**: ^1H NMR 6.95 (ddd, 1, J = 9.8, 3.8, 3.8), 6.04 (br d, 1, J = 9.8), 5.03 (br dd, 1, J = 1.8, 1.8), 4.80 (br dd, 1, J = 1.8, 1.8).

Partial data for **34**: ^1H NMR 6.72 (ddd, 1, J = 10.2, 2.4, 1.4), 6.00 (dd, 1, J = 10.2, 2.0), 5.62-5.70 (m, 1), 2.28 (ddd, 1, J = 13.4, 5.4, 1.4), 2.11 (s, 3), 1.97 (dd, 1, J = 13.4, 8.8), 1.03 (d, 3, J = 7.1).

Partial data for **35**: ^1H NMR 6.69-6.75 (m, 1), 6.01 (dd, 1, J = 10.2, 2.2), 5.70-5.76 (m, 1), 2.13 (s, 3), 0.87 (d, 3, J = 6.7).

Partial data for **39**: ^1H NMR 5.43-5.59 (m, 2), 5.02 (ddd, 1, J = 11.0, 5.1, 5.1), 3.14 (m, 1), 2.07 (s, 3); ^{13}C NMR 169.7, 130.8, 123.8, 72.9, 54.0, 49.4, 29.2, 28.5, 25.6, 22.9, 21.6, 20.9, the carbonyl carbon was not observed.

The data for **40**: ^1H NMR 5.47-5.56 (m, 2), 5.11 (br dd, 1, J = 3.0, 3.0), 2.95 (m, 1), 1.60-2.63 (m, 11), 2.03 (s, 3); ^{13}C NMR 214.3, 170.2, 131.2, 124.4, 75.4, 55.7, 49.3, 28.2, 27.3, 26.6, 25.4, 22.5, 21.2; IR (neat) 3018, 2940, 2881, 1732, 1714, 1480, 1446, 1428, 1375, 1241, 1088, 1021, 872, 736, 701 cm^{-1}.

Partial data for **41**: ^1H NMR 5.53-5.65 (m, 1), 5.48 (br dd, 1, J = 10.9, 1.5), 5.20-5.35 (m, 1), 3.30 (br s, 1), 2.04 (s, 3).

Preparation of Bicyclo[5.3.1]undec-4-ene-8,11-dione (44). A mixture of K_2CO_3 (166 mg, 1.2 mmol) and **39** and **40** (10 mg, 0.045 mmol) in 2 mL of MeOH was stirred overnight. The resulting solution was diluted with water and extracted with ether twice. The combined ethereal layers were washed with brine and dried ($MgSO_4$). Evaporation of the solvent afforded 7 mg (90%) of a mixture of alcohols: ^1H NMR 5.41-5.61 (m, 2), 4.18 (br s, 0.75 × 1), 4.03 (br ddd, 0.25 × 1, J = 11.5, 4.8, 4.8, minor), 3.00-3.20 (m, 0.25 × 1), 2.85-3.00 (m, 0.75 × 1).

The mixture of alcohols (7 mg, 0.04 mmol) and PDC (46 mg, 0.12 mmol) in 1 mL of CH_2Cl_2 was stirred overnight. The resulting dark solution was filtered through silica gel and evaporated giving 7 mg (94%) of pure **44**: ^1H NMR 5.80 (ddd, 1, J = 10.5, 7.8, 0.8), 5.65 (dddd, 1, J = 10.5, 9.3, 6.8, 1.2), 3.27 (ddd, 1, J = 11.7, 7.0, 1.6), 2.96 (ddd, 1, J = 13.4, 11.7, 9.3), 2.72 (ddd, 1, J = 16.7, 3.5, 3.5), 2.67-2.81 (m, 1), 2.41-2.58 (m, 2), 2.35 (ddd, 1, J = 13.4, 7.0, 6.8), 2.26 (ddd, 1, J = 16.7, 13.9, 4.6), 1.91-2.14 (m, 3), 1.68 (dddd, 1, J = 14.0, 7.2, 4.0, 2.7); ^{13}C NMR 211.5, 207.5, 133.1, 127.5, 67.9, 46.3, 38.2, 27.9, 26.3, 22.7, 21.3; IR (neat) 3023, 2934, 1694, 1476, 1314, 1255, 1165, 1143, 1116, 921, 883, 845, 734 cm^{-1}.

Preparation of 4-(4-Pentenyl)cyclohexane-1,3-dione (43). A solution of 3-ethoxy-6-(4-pentenyl)-2-cyclohexen-1-one[15] (107 mg, 0.51 mmol) and 0.5 mL of 3 M HCl in 5 mL of THF was stirred overnight. The reaction was diluted with ether, washed with water and brine, dried ($MgSO_4$), and concentrated. Flash chromatography of the crude product on silica gel (5:1 hexane/EtOAc) gave 71 mg (77%) of dione **43**: mp 41.5-43 °C; ^1H NMR 5.80 (dddd, 1, J = 17.1, 10.3, 6.8, 6.8), 5.02 (ddd, 1, J = 17.1, 3.2, 1.6), 4.97 (br d, 1, J = 10.3), 3.42 (br s, 2), 2.70 (ddd, 1, J = 16.1, 4.8, 4.5), 2.60 (dd, 1, J = 11.7, 5.7), 2.57 (ddd, 1, J = 16.1, 11.7, 5.6), 2.48 (dddd, 1, J = 11.7, 5.9, 5.9, 5.9, 5.9), 2.05-2.22 (m, 3), 1.83-1.94 (m, 1), 1.60 (dddd, 1, J = 13.9, 11.7, 11.7, 4.8), 1.37-1.54 (m, 2); ^{13}C NMR 204.7, 204.0, 138.2, 114.9, 58.1, 49.2, 39.5, 33.7, 28.6, 26.3, 24.4; IR (neat) 2948, 2659, 2576, 1615, 1521, 1347, 1263, 1197, 909 cm^{-1}.

Oxidative Cyclization of Dione 43. A degassed solution of dione **43** (50 mg, 0.28 mmol), $Mn(OAc)_3$ (156 mg, 0.58 mmol), and $Cu(OAc)_2$ (51 mg, 0.28 mmol) in 5 mL of AcOH was stirred at rt for 2 h.