of the starting material still remained unchanged (TLC), and thus bis(trimethylsilyl) sulfide (420 mg, 2.3 mmol) and BCl_3 (180 mg, 1.6 mmol) were added further and the mixture was refluxed for an additional 26 h. To the resulting mixture were added water and benzene. The organic layer was separated, washed with water, and dried. Removal of the solvent followed by purification with dry column chromatography (silica gel, 1:1 CH_2Cl_2–hexane) gave 53 mg (52%) of **4b**.

Sulfurization of 1,6-Dione 1c with B_2S_3. To a solution of **1c** (161 mg, 0.5 mmol) in toluene (25 mL) were successively added bis(trimethylsilyl) sulfide (890 mg, 5 mmol) and BCl_3 (390 mg, 3.3 mmol) by syringes through a rubber septum under N_2. The mixture was refluxed for 48 h and then the solvent was removed under reduced pressure. The residue was subjected to dry column chromatography (silica gel, 1:1 CH_2Cl_2–hexane) to give 35 mg (20%) of **4c**, 100 mg (57%) of **7c**, and 10 mg (6%) of **8c**.

Sulfurization of 1,7-Dione 1d with B_2S_3. To a solution of **1d** (181 mg, 0.5 mmol) in toluene (20 mL) were successively added bis(trimethylsilyl) sulfide (890 mg, 5 mmol) and BCl_3 (390 mg, 3.3 mmol) by syringes through a rubber septum under N_2. The mixture was heated under reflux for 48 h and the solvent was removed. The residue was purified by dry column chromatography (silica gel, 1:1 CH_2Cl_2–hexane) to provide 140 mg (76%) of **7d** and 11 mg (6%) of **8d**.

Preparation of 2,2,3,3-Tetramethyl-1,4-bis(4-methylphenyl)-5,6-dithiabicyclo[2.1.1]hexane (14). 2,2,3,3-Tetramethyl-1,4-bis(4-methylphenyl)butane-1,4-dione (**20**) was prepared by a method similar to that used for **1a**.[9] A solution of **20** (136 mg, 0.422 mmol) and LR (512 mg, 1.27 mmol) in benzene (10 mL) was heated for 5 h at 51–54 °C. The mixture was cooled to room temperature and the solvent was removed. The residue was subjected to dry column chromatography (silica gel, 1:1 CH_2Cl_2–hexane) to afford 16 mg (11%) of bis[2-methyl-1-(4-methylphenyl)-1-propenyl] disulfide (**15**) and 115 mg of an inseparable mixture of **14** and 2,2,3,3-tetramethyl-1,4-bis(4-methylphenyl)-5,6,7-trithiabicyclo[2.2.1]heptane (**21**). The yield of **14** and **21** were determined by ^1H NMR to be 53 and 22%, respectively. The mixture obtained above was used in the isomerization experiment. **20**: colorless crystals, mp 106.0–106.5 °C; ^1H NMR δ 1.41 (s, 12 H), 2.36 (s, 6 H), 7.17 (d, J = 8 Hz, 4 H), 7.50 (d, J = 8 Hz, 4 H); ^{13}C NMR δ 20.6 (q), 23.9 (q), 53.7 (s), 127.1 (d), 128.1 (d), 138.2 (s), 139.4 (s), 210.9 (s); MS m/z 322 (M^+). Anal. Calcd for $C_{22}H_{26}O_2$: C, 81.95; H, 8.13. Found: C, 81.79; H, 8.02. **15**: colorless crystals, mp 111–112 °C: ^1H NMR δ 1.60 (s, 6 H), 1.81 (s, 6 H), 2.36 (s, 6 H), 7.02 (d, J = 8 Hz, 4 H), 7.13 (d, J = 8 Hz, 4 H); ^{13}C NMR δ 21.3 (q), 22.9 (q), 23.3 (q), 128.3 (d), 130.3 (d), 130.9 (s), 136.2 (s), 137.1 (s), 137.3 (s); MS m/z (relative intensity) 354 (M^+, 40), 177 (80), 145 (100). HRMS calcd for $C_{22}H_{26}S_2$ m/z 354.1476, found 354.1428. **14**: ^1H NMR δ 1.34 (s, 12 H), 2.32 (s, 6 H), 6.90 (d, J = 8 Hz, 4 H), 7.11 (d, J = 8 Hz, 4 H); ^{13}C NMR δ 21.2 (q), 25.1 (q), 56.3 (s), 79.3 (s), 125.8 (d), 128.2 (d), 133.9 (s), 137.2 (s); MS m/z 354 (M^+). **21**: pale yellow crystals, mp 227.0–228.5 °C; ^1H NMR δ 0.75 (s, 6 H), 1.40 (s, 6 H), 2.36 (s, 6 H), 7.16 (d, J = 8 Hz, 4 H), 7.47 (d, J = 8 Hz, 4 H); ^{13}C NMR δ 24.8 (q), 26.9 (q), 58.3 (s), 93.3 (s), 128.3 (d), 128.8 (d), 133.5 (s), 138.5 (s); MS m/z (relative intensity) 386 (M^+, 3), 322 (100), 307 (51), 145 (47). Anal. Calcd for $C_{22}H_{26}S_3$: C, 68.34; H, 6.78. Found: C, 67.90; H, 6.77.

Thermal Isomerization of a Mixture of 1,3-Dithietanes 4a and 14. A mixture of **4a** (0.1 mmol) and **14** (0.1 mmol) contaminated with **21** in benzene (5 mL) was heated for 6 h at reflux. HPLC analysis (flow rate: 1 mL/min) of the mixture showed two peaks due to disulfides **2** (t_R 3.3 min) and **15** (t_R 4.2 min) in addition to unreacted **21** (t_R 5.5 min).

Sulfurization of Benzophenone with 6. A mixture of **6** (271 mg, 0.5 mmol) and benzophenone (91 mg, 0.5 mmol) in toluene (10 mL) was refluxed under N_2 for 4 h and the resulting blue solution was cooled to room temperature. An aliquot (1 mL) of this solution was taken out and diluted to 50 mL with hexane. The yield of thiobenzophenone was estimated to be 92% by determining the intensity of the absorption due to thiobenzophenone (λ_{max} 609 nm, ϵ = 184[19]) in the visible spectrum. 1,3-Dithietane **4b** (140 mg, 95%) was obtained by chromatographic workup of the whole reaction mixture.

Sulfurization of Benzophenone with 17. A mixture of **17** (106 mg, 0.263 mmol) and benzophenone (50 mg, 0.27 mmol) in toluene (5 mL) was heated under reflux for 1 h. A portion (1 mL) of the mixture was taken out and was submitted to visible spectrum analysis, which revealed that the yield of thiobenzophenone is 68%.

Registry No. **1a**, 34733-56-7; **1b**, 95581-35-4; **1c**, 125611-53-2; **1d**, 125611-54-3; **2**, 125611-55-4; **3a**, 125611-56-5; **3c**, 125611-57-6; **4a**, 125611-58-7; **4b**, 125611-59-8; **4c**, 125611-60-1; **6**, 125611-61-2; **7c**, 125611-62-3; **7d**, 125611-63-4; **8c**, 125611-64-5; **8d**, 125611-65-6; **9**, 125611-66-7; **10**, 97584-63-9; **14**, 125611-67-8; **15**, 125611-68-9; **17**, 82998-27-4; **20**, 125611-69-0; **21**, 125611-70-3; bromobenzene, 108-86-1; 2,5-dicyano-2,5-dimethylhexane, 10526-16-6; 2,6-dicyano-2,6-dimethylheptane, 2941-36-8; isobutyrophenone, 611-70-1; benzophenone, 119-61-9; thiobenzophenone, 1450-31-3.

Manganese(III)-Based Oxidative Free-Radical Cyclization of Unsaturated β-Keto Esters, 1,3-Diketones, and Malonate Diesters

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Received November 14, 1989

Oxidative free-radical cyclizations of unsaturated β-keto esters, 1,3-diketones, and malonate diesters with 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$ and 1 equiv of $Cu(OAc)_2 \cdot H_2O$ are described. Oxidation of β-keto ester **1** with Mn(III) to enol radical **2** followed by 6-exo cyclization gives radical **4**, which is oxidized by Cu(II) to give alkene **7** in 64–71% yield. Oxidation of **9** gives a lower yield of 5-exo cyclization product **11** due to competing overoxidation to give **13**. Oxidative cyclization of **18** gives the tertiary radical **19**, which is further oxidized to cation **20**. Oxidation of α-substituted β-keto esters **23**, **33**, and **37** proceeds in high yield since the product cannot be oxidized further. Oxidative cyclization of unsaturated cyclic β-keto esters **40a** and **45** proceeds efficiently to give bicyclic adducts **42**, **44**, and **47**. Oxidative cyclizations of 4-alkenyl-2-methylcyclopentane-1,3-diones **54**, **61**, and **64** provide bicyclo[3.2.1]octanediones **57**, **63**, and bicyclo[3.3.1]nonanediones **66** and **67** in moderate yields. These studies indicate that Mn(III)-based oxidative free-radical cyclization is a powerful synthetic method, delineate the scope and limitations of this reaction, and suggest further avenues for exploration.

In the past decade free-radical cyclization of alkenes has become a valuable method for the synthesis of cyclic compounds.[1] The most widely used method is the reduction of a halide or other functional group to a radical

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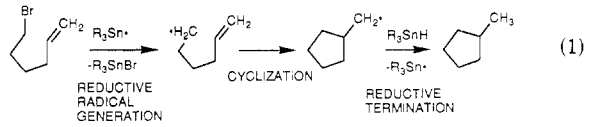
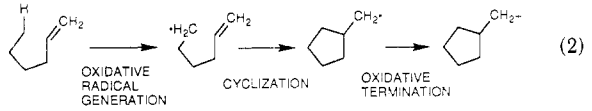
with R_3SnH, followed by cyclization and reduction of the resulting cyclic radical with R_3SnH to a hydrocarbon in the chain propagation steps (eq 1). This approach is



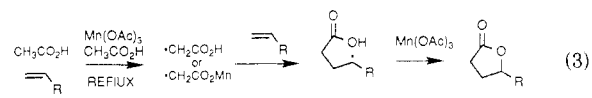
(1)



(2)

limited, leading to a relatively unfunctionalized product resulting from a net two-electron reduction. Oxidative free-radical cyclization in which the initial radical is generated oxidatively and/or the cyclic radical is oxidized to terminate the reaction has considerable synthetic potential since more highly functionalized products can be prepared from simpler precursors (eq 2). Although some early examples are known,[2] it is only in the past few years that several classes of such reactions have been developed,[1g] including halogen atom-transfer methods[1g,3] and organocobalt-based procedures.[4]

The well-known, but underutilized, oxidative addition of acetic acid to alkenes with 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$ provides the basis for another solution to this problem (eq 3).[5] Pioneering studies by Heiba and Dessau[6a,d] and Bush



(3)

and Finkbeiner[7] demonstrated that acetic acid is oxidized by $Mn(OAc)_3 \cdot 2H_2O$ in acetic acid at reflux to the carboxymethyl radical. This radical then adds to an alkene to give a γ-carboxypropyl radical, which is oxidized by a second 1 equiv of $Mn(OAc)_3 \cdot 2H_2O$ to give a γ-lactone. The mechanism of this reaction has been extensively explored, and further synthetic applications have been developed by Heiba and Dessau,[6] Kooyman,[8] Nikishin and Vinogradov,[9] McQuillin,[10] Fristad,[11] Corey,[12] and others.[12]

Use of $Mn(OAc)_3$ for oxidative free-radical cyclizations poses problems not encountered in addition reactions. In addition reactions a vast excess of oxidizable substrate such as acetic acid or acetone is often used as the solvent. Overoxidation of the product is not a major problem since a vast excess of starting material is used, and the yield is based on the amount of oxidant consumed. While this is appropriate when acetone or acetic acid is being added to hexene to give a product easily removable from starting materials by distillation, it is not acceptable in oxidative cyclization reactions in which the substrate must be prepared by multistep synthesis and the products separated from excess starting material by chromatography. Mn(III)-based oxidative cyclization of unsaturated acids or other substrates with only a single activating electron withdrawing group is not possible, since the optimal solvent for this oxidation, acetic acid, will be oxidized preferentially.

Unsaturated β-keto esters, 1,3-diketones, and malonate esters should be suitable substrates since Heiba and Dessau[6e] and Vinogradov and Nikishin[9e,f,h-k,m] have shown that they are oxidized much more readily than acetic acid. Oxidation of 1,3-dicarbonyl compounds by Mn(III) occurs readily at 25–70 °C. Overoxidation of the product is still a problem since an excess of oxidizable substrate cannot be used in cyclization reactions. If the product still contains an enolizable hydrogen, further oxidation of the products may occur, as has been demonstrated in addition reactions of malonic acids and esters.[11b,12a,c]

We report here studies on oxidative cyclizations of a variety of unsaturated 1,3-dicarbonyl compounds to form five- and six-membered rings.[13] We have previously reported the use of Mn(III)-based oxidative cyclization for tandem free-radical cyclizations,[14a-c,e,h] for the synthesis

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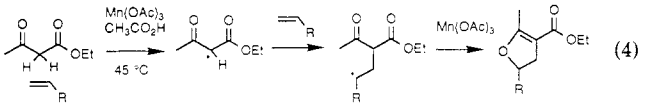
(13) For the publication of a portion of these results in preliminary form see ref 14a.

of salicylate esters,[14f] and for the synthesis of seven- and eight-membered rings,[14g] and we have examined the mechanism of Mn(III)-based oxidation of β-keto esters.[14d] Corey and Kang[15a] have previously reported related oxidative cyclizations and lactonizations of unsaturated β-keto acids, and Fristad[15b] has reported related oxidative cyclizations and lactonizations of malonic and cyanoacetic acids.[15]

Results and Discussion

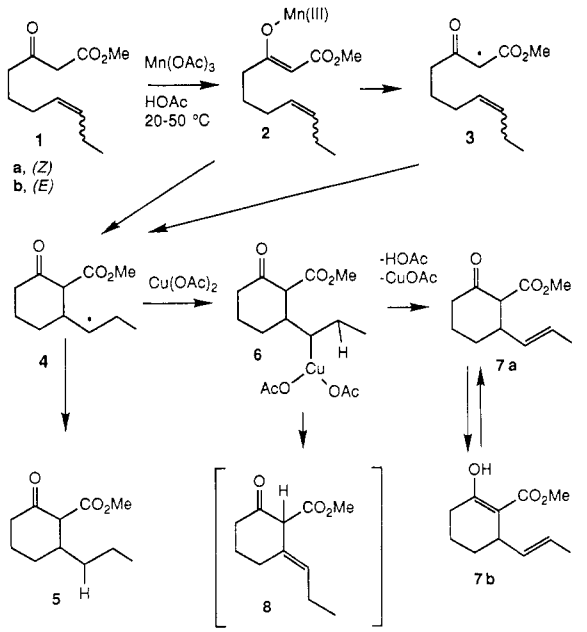
Oxidative Cyclization of 1. Initially, we chose to examine the oxidative cyclization of unsaturated β-keto esters since Heiba and Dessau[6e] and Vinogradov and Nikishin[9e,f,h-k,m] have shown that acetoacetate esters and 1,3-diketones undergo Mn(III)-based oxidative addition to alkenes in acetic acid at 40–60 °C to give dihydrofurans (eq 4). To our surprise, reaction of **1a**[16] as a 0.1 M solution



(4)

in acetic acid with 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$[17] gives a complex mixture of products containing **5**. Apparently, radical **4** is not oxidized by $Mn(OAc)_3$ but instead abstracts a hydrogen atom to give saturated β-keto ester **5**. This result appears to be inconsistent with the oxidation of γ-carboxyl radicals to lactones (eq 3). However, Fristad has shown that the carboxylic acid is involved in this oxidation; a carbocation is not an intermediate. Heiba and Dessau[6b,c] and Vinogradov and Nikishin[9a-f] have shown that $Mn(OAc)_3$ will oxidize a tertiary radical to a cation but will not oxidize primary or secondary radicals at a rate competitive with hydrogen abstraction. These groups have also found that $Cu(OAc)_2$, which is a thermodynamically weak oxidant that nevertheless oxidizes primary and secondary radicals very rapidly to alkenes, is compatible with $Mn(OAc)_3$ oxidations.[6b,c,9a-f]

We were pleased to find that reaction of β-keto ester **1a** as a 0.1 M solution in acetic acid with 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$ and 1 equiv of $Cu(OAc)_2 \cdot H_2O$ for 1 h at 50 °C gives **7** as an equilibratable mixture of the trans keto (**7a**) and enol (**7b**) tautomers in 71% yield. These tautomers can be separated chromatographically, but reequilibrate over several days.[18] Oxidative free-radical cyclization of



the *E* isomer **1b** for 26 h at 25 °C gives **7** in 64% yield. Slightly higher yields of product are usually obtained when these reactions are carried out at 15–25 °C, although reaction times are much shorter at high temperatures.

We have previously shown that manganese enolate **2a** is formed rapidly in the reaction of **1a** with $Mn(OAc)_3 \cdot 2H_2O$ and that the double bond is involved in the rate-determining step of the oxidation,[14d] which is probably the conversion of **2a** to the 6-exo cyclized radical **4** without the intermediacy of **3a**. Kochi's extensive studies of the mechanism of oxidation of alkyl radicals by $Cu(OAc)_2$ establish that an alkylcopper(III) intermediate such as **6** is formed initially.[19] Primary and secondary radicals react with $Cu(OAc)_2$ to give organocopper intermediates that undergo β-hydride elimination to give alkenes, Cu(OAc), and acetic acid without the intermediacy of a carbocation.[19] Tertiary radicals are oxidized by $Cu(OAc)_2$ to carbocations.[19] Cu(I) is reoxidized to Cu(II) by Mn(III), so that 2 equiv of Mn(III) is needed and, in principal, only a catalytic amount of Cu(II) is required. In related systems we have found that use of only 0.05 equiv of Cu(II) is sufficient.[14g]

Three alkenes can be formed from organocopper intermediate **6**. Elimination could also have given **8** with a trisubstituted double bond and the isomer of **7** with a *Z*-disubstituted double bond. Neither of these compounds is observed within the limits of detection.[20] The absence of **8** is not significant since it contains an allylic enolizable hydrogen atom and should be oxidized rapidly by $Mn(OAc)_3 \cdot 2H_2O$ if it were formed. The exclusive isolation of **7** in 71% yield demonstrates that oxidative formation of an alkene from radical **4** and $Cu(OAc)_2$ is stereospecific for the *E* isomer and selective for the Hofmann product with a less substituted double bond. Early results from Kochi's laboratory suggested that $Cu(OAc)_2$ oxidation of alkyl

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(15) For other studies of Mn(III)-based oxidative free-radical cyclizations see: (a) Corey, E. J.; Kang, M.-C. *J. Am. Chem. Soc.* **1984**, *106*, 5384. (b) Ernst, A. B.; Fristad, W. E. *Tetrahedron Lett.* **1985**, *26*, 3761. (c) Peterson, J. R.; Egler, R. S.; Horsley, D. B.; Winter, T. J. *Tetrahedron Lett.* **1987**, *28*, 6109. (d) Paquette, L. A.; Schaefer, A. G.; Springer, J. P. *Tetrahedron* **1987**, *43*, 5567. (e) Surzur, J.-M.; Bertrand, M. P. *Pure Appl. Chem.* **1988**, *60*, 1659. (f) Oumar-Mahamat, H.; Moustrou, C.; Surzur, J.-M.; Bertrand, M. P. *Tetrahedron Lett.* **1989**, *30*, 331. (g) Citterio, A.; Cerati, A.; Sebastiano, R.; Finzi, C. *Tetrahedron Lett.* **1989**, *30*, 1289. (h) Citterio, A.; Fancelli, D.; Finzi, C.; Pesce, L.; Santi, R. *J. Org. Chem.* **1989**, *54*, 2713. (i) Rama Rao, A. V.; Rao, B. V.; Reddy, D. R.; Singh, A. K. *J. Chem. Soc., Chem. Commun.* **1989**, 400.

(16) Huckin, S. N.; Weiler, L. *J. Am. Chem. Soc.* **1974**, *96*, 1082. Cf.: Hirama, M.; Shimizu, M.; Iwashita, M. *J. Chem. Soc., Chem. Commun.* **1983**, 599.

(17) Comparable results were obtained with $Mn(OAc)_3$ prepared in situ from $KMnO_4$ and $Mn(OAc)_2$: Lux, H In *Handbood of Preparative Inorganic Chemistry*; 2nd ed.; Brauer, G., Ed.; Academic Press: New York, 1965; Vol. II, pp 1469–1470.

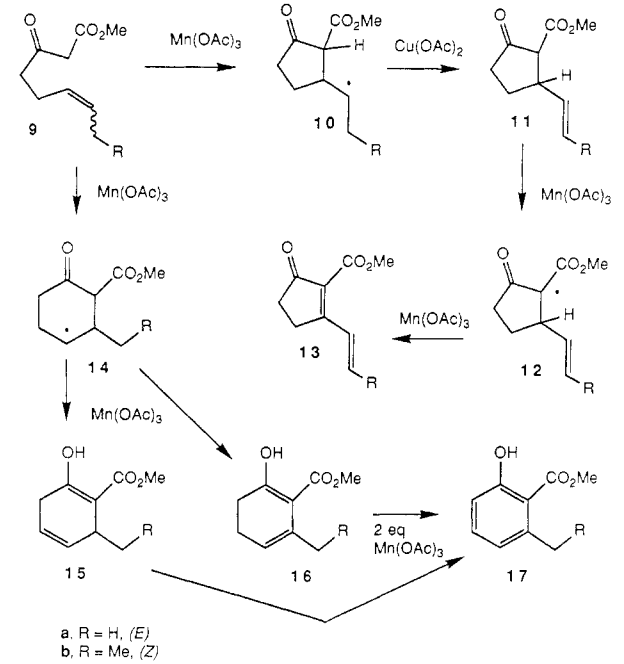
(18) (a) Rhoads, S. J. *J. Org. Chem.* **1966**, *31*, 171. (b) Kol'tsov, A. I.; Kheifets, G. M. *Russ. Chem. Rev. (Engl. Transl.)* **1971**, *40*, 773.

(19) (a) Kochi, J. K.; Bemis, A.; Jenkins, C. L. *J. Am. Chem. Soc.* **1968**, *90*, 4616. (b) Kochi, J. K.; Bacha, J. D. *J. Org. Chem.* **1968**, *33*, 2746. (c) Jenkins, C. L.; Kochi, J. K. *J. Am. Chem. Soc.* **1972**, *94*, 843. (d) Kochi, J. K. In *Free Radicals*, Kochi, J. K., Ed.; Wiley: New York, 1973; Chapter 11. (e) Nonhebel, D. C. In *Essays on Free-Radical Chemistry, Special Publication 24*, Chemical Society: London, 1970; p 409. (f) Kochi, J. K. *Science* **1967**, *155*, 415.

(20) Detection of trace amounts of minor isomers is difficult since **7** exists as three equilibrating tautomers and stereoisomers.

radicals gives statistical mixtures of products.[19] More recently, Collum has reported an example of a $Pb(OAc)_4$-$Cu(OAc)_2$ oxidative decarboxylation that gives exclusively the Hofmann product.[21] We have found that the oxidative decarboxylation of secondary carboxylic acids gives mixtures of alkenes rich in the *E* isomer and the Hofmann product.[22] Selective formation of **7** by oxidation of **4** with $Cu(OAc)_2$ is therefore the expected, normal process.

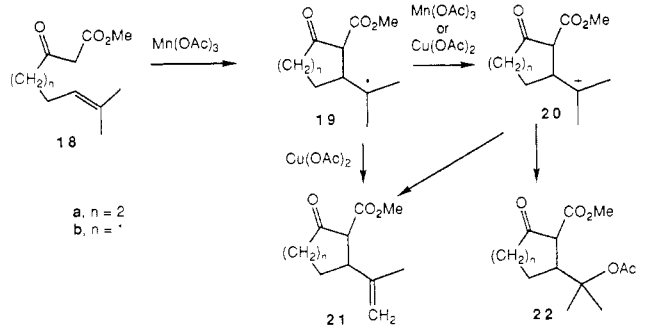
Oxidative Cyclization of 9. Oxidative cyclization of **9a**[16] as described above gives the expected product **11a** in only 21% yield, a 7:2:1 mixture of **15a**, **17a**, and **16a** in 5% yield, and recovered **9a** in 17% yield. Oxidative cyclization of **9b**[16] gives the expected product **11b** in only 36% yield; traces of **15b**, **17b**, and **16b**; dienone **13b** in 10% yield; and recovered **9b** in 20% yield. Dienone **13a** is probably also formed in the oxidative cyclization of **8a**, but it reacts further since the terminal double bond is very susceptible to nucleophilic attack. The methyl group on the double bond of **13b** decreases the susceptibility of the dienone to nucleophilic attack. Steric hindrance from the methyl group on the double bond is also probably responsible for the higher yield of **11b** than **11a**.



Cyclopentane **11b** is formed in much lower yield than the analogous cyclohexane **7** obtained in the cyclization of **1**. The isolation of the more highly oxidized product **13b** indicates that further oxidation of **11b** is one cause of the lower yield. The product **11b** still contains an enolizable proton and is oxidized to radical **12b**; further oxidation gives **13b**. We have discussed in detail elsewhere the reasons why overoxidation of **11b** occurs but overoxidation of **7** does not occur and shown that use of α-chloro β-keto esters prevents overoxidation.[14d]

The minor products **15**, **16**, and **17** are formed from 6-endo closure to give cyclohexyl radical **14**. Oxidative elimination gives **15** and **16**, which are isolated as the enol tautomers. Further two-electron oxidation gives salicylate **17**. We have explored the scope of this salicylate synthesis using substrates in which 6-endo cyclization is the major process.[14f] With a 1,2-disubstituted double bond, 5-exo cyclization to give **10** is the major process (60–90%) and 6-endo cyclization to give **14** is a minor process. In the cyclization of **1**, 6-exo cyclization to give **4** is the exclusive process, although with monosubstituted alkenes 7-endo cyclization becomes the major process.[14g]

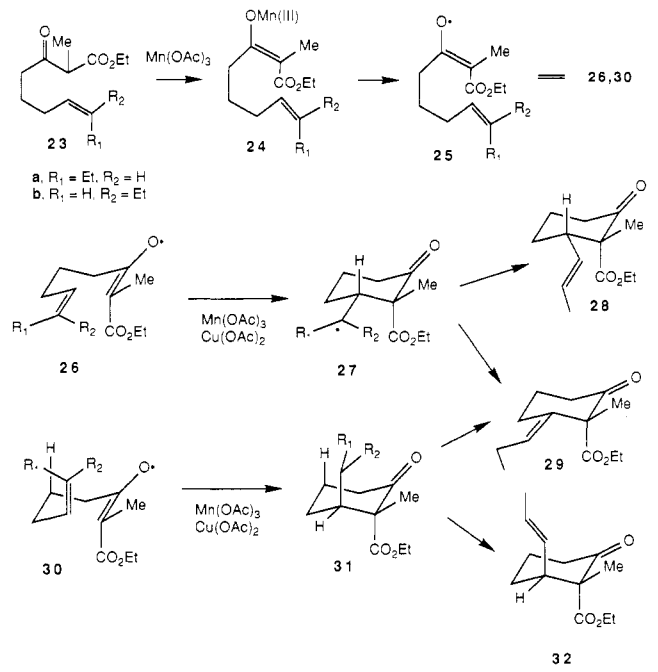
Oxidative Cyclization of 18. Reaction of **18a**[16] as a 0.1 M solution in acetic acid with 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$ and 1 equiv of $Cu(OAc)_2 \cdot H_2O$ gives **21a** in 41% yield as a 1.2:1 mixture of keto and enol tautomers. Oxidative cyclization of **18a** gives radical **19a**, which is probably oxidized to cation **20a** by either Mn(III) or Cu(II); loss of a proton gives **21a**. For reasons that are not clear, the tertiary acetate **22a** is not obtained. Carrying out the oxidation in the absence of $Cu(OAc)_2 \cdot H_2O$ gives a mixture of **21a** and a small amount of the analogue with a saturated side chain. This indicates that Mn(III) will oxidize **19a** to **20a** and that hydrogen atom abstraction can compete with oxidation by Mn(III) even for the tertiary radical **19a**. Oxidative cyclization of **18b**[16] by $Mn(OAc)_3 \cdot 2H_2O$ gives alkene **21b** in 8% yield and acetate **22b** in 10% yield. The lower yields of products are presumably due to further oxidation as discussed above for **11**. Similar mixtures of products are obtained when $Cu(OAc)_2 \cdot H_2O$ is used as a cooxidant. Exo cyclization to give **19** occurs exclusively with both **18a** and **18b** presumably due to steric hindrance to endo cyclization by the two methyl groups and the greater stability of the tertiary radical.[1]



Oxidative Cyclization of α-Methyl β-Keto Esters 23, 33, and 37. Oxidative cyclization of unsaturated α-methyl β-keto esters will give α-disubstituted cyclic β-keto esters. The absence of an enolizable hydrogen in the cyclic product has two significant consequences. First, overoxidation analogous to that observed with **8**, **11**, **16**, **21**, and **22** cannot occur. Second, the diastereomers formed in this reaction provide information on the geometry of the cyclization transition state since equilibration of the products is not possible. Unsaturated α-methyl β-keto esters **23a**, **23b**, **33a**, **33b**, and **37** are readily available by alkylation of either the sodium lithium or dilithium salt of the dianion of ethyl methylacetoacetate in 25%, 39%, 57%, 27%, and 52% yields, respectively.[16] Recent results indicate that the yield of **23a** is increased to 35% by carrying out the alkylation of the dilithium salt of the dianion (prepared from LDA) in the presence of 2 equiv of HMPA.

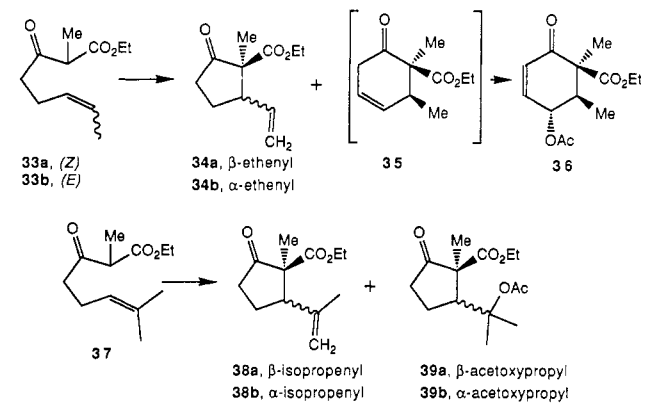
Oxidative cyclization of *Z* isomer **23a** gives **28** (56%), **29** (14%), and **32** (3%). Similar oxidative cyclization of *E* isomer **23b** gives **28** (43%), **29** (9.5%), and **32** (9.5%). The rate-determining step in this cyclization is formation of the manganese enolate **24**, which reacts rapidly to give radical **25**.[14f] The geometry of the enol radical **25** has been established by examination of 6-endo cyclizations[14h] and confirmed by the formation of only traces of **32** in the cyclization of **23a**. A 6-exo cyclization of **25** can proceed through chair transition state **26** with an equatorial side chain to give **27** or through chair transition state **30** with an axial side chain to give **31**. Oxidative elimination of **27** with $Cu(OAc)_2 \cdot H_2O$ will give **28** and **29** while oxidative

(21) McGuirk, P. R.; Collum, D. B. *J. Org. Chem.* **1984**, *49*, 843.
(22) Kwon, T.-S.; Snider, B. B. *J. Org.* Chem. **1989**, *54*, 3878.



elimination of **31** will give **32** and **29**. Cyclization to give **27** is the major process with **23b** and the virtually exclusive process with **23a** since there is a severe steric interaction between the ethyl group (R_1) and axial hydrogen in **30a**. Similar effects of alkene geometry on ring stereochemistry have been observed in other 6-exo cyclizations.[23] The formation of **29** indicates that oxidative elimination can also give the Zaitsev product with the more substituted double bond and suggests that **8** is formed as an unstable intermediate in the oxidation of **1**.

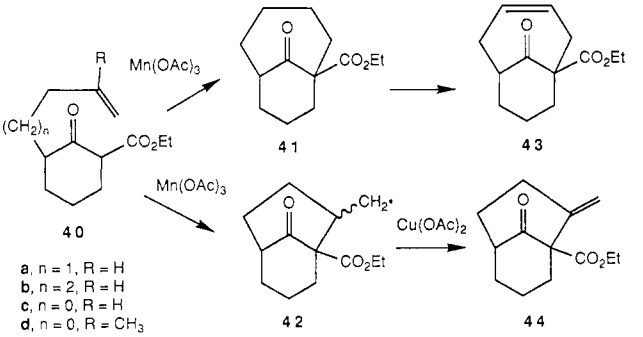
Cyclization of **33a**, **33b**, and **37** gives mixtures of stereoisomers. Oxidative cyclization of **33b** with 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$ and 1 equiv of $Cu(OAc)_2 \cdot H_2O$ for 4 days at 25 °C gives 39% of a 2.5:1 mixture of **34a** and **34b** and 70% of **36**. Similar product mixtures are obtained with



the *Z* isomer **33a**. Oxidative cyclization of **37** with 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$ for 2 days at 25 °C gives 25% of a 3:2 mixture of **38a** and **38b** and 20% of a 3:2 mixture of **39a** and **39b**. 5-Exo cyclization of both **33** and **37** proceeds in acceptable yield but gives a mixture of stereoisomers. The cyclic tertiary radical obtained from **37** is oxidized to a cation analogous to **20**, which gives a mixture of alkene **38** and acetate **39**. Oxidation of **33** also gives some 6-endo cyclization presumably giving rise to enone **35** after oxidative β-hydride elimination. Further oxidation of **35** and reaction with acetate give **36**. Formation of α-acetoxy enones by oxidation of enones with $Mn(OAc)_3 \cdot 2H_2O$ has been previously described.[24]

The stereochemistry of **28**, **32**, **34**, **38**, and **39** was established by analysis of the ^1H NMR absorptions of the ring methine hydrogen. The shifts caused by vicinal cis and trans ester and methyl substituents in a variety of norbornanes have been determined.[25] These values suggest that a hydrogen cis to a methyl and trans to an ester will absorb 0.99 ppm upfield from the diastereomer with a hydrogen cis to an ester and trans to a methyl. As predicted, the methine ring proton of the minor isomers **32**, **34b**, **38b**, and **39b** can be distinguished in the ^1H NMR spectrum since this absorption occurs downfield in an otherwise empty region of the spectrum at δ 3.11, 3.35, 3.36, and 2.93, respectively. The methine protons of the major isomers **28**, **34a**, **38a**, and **39a** absorb upfield between δ 2.0 and 2.7, in a region of the spectrum containing several other absorptions. The methyl singlets should be shielded by a *cis*-alkenyl substituent on an adjacent carbon. As predicted, the methyl singlets of **28**, **34a**, and **38a** absorb downfield at δ 1.26, 1.29, and 1.43, respectively, relative to the methyl singlets of **32**, **34b**, and **38b** at δ 1.22, 1.15, and 1.06, respectively. The structure of **28** was confirmed by methylation of **7** with sodium hydride and methyl iodide to give the methyl ester corresponding to **28**. Methylation should occur from the less hindered face[26,27] to give **28** and not **32**. The trans stereochemistry of the methyl and acetoxy groups in **36** is assigned from the vicinal coupling constant of 10.3 Hz between the methine hydrogens. The relative stereochemistry of the methyl groups in **36** is assumed on the basis of stereochemistry established in related 6-endo cyclizations.[14h]

Oxidative Cyclization of Cyclic β-Keto Esters 40 and 45. Oxidative cyclization of unsaturated cyclic β-keto esters provides a simple route to highly functionalized bicyclic compounds. Alkylation of the dianion of ethyl 2-oxocyclohexanecarboxylate with 4-bromo-1-butene gives **40a** in 74% yield. Oxidative cyclization of **40a** with 2 equiv



of $Mn(OAc)_3 \cdot 2H_2O$ and 1 equiv of $Cu(OAc)_2 \cdot H_2O$ in acetic acid at 50 °C for 18 h gives a 35% yield of a 1.1:1 mixture of **44** and **43**. 7-Endo cyclization to give **41** and 6-exo cyclization to give **42** occur in approximately equal amounts. Oxidative elimination from secondary radical **41** apparently occurs regioselectively to give **43**. Oxidative elimination from primary radical **42** can only give **44**. The position of the double bond in **43** was established by irradiation of the olefinic hydrogen at δ 5.86, which indicated the presence of an isolated allylic methylene group at δ

(23) Hanessian, S.; Dhanoa, D. S.; Beaulieu, P. L. *Can. J. Chem.* **1987**, *65*, 1859.

(24) Dunlap, N. K.; Sabol, M. R.; Watt, D. S. *Tetrahedron Lett.* **1984**, *25*, 5839, and references cited therein.

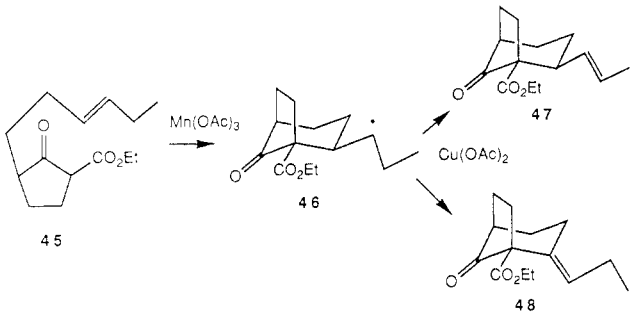
(25) Doerffel, V. K.; Kaspar, H.; Zimmermann, G. *J. Prakt. Chem.* **1974**, *316*, 645.

(26) Paquette, L. A.; Wiedeman, P. E. *Tetrahedron Lett.* **1985**, *26*, 1603.

(27) Trost, B. M.; Vladuchick, W. C. *J. Org. Chem.* **1979**, *44*, 148.

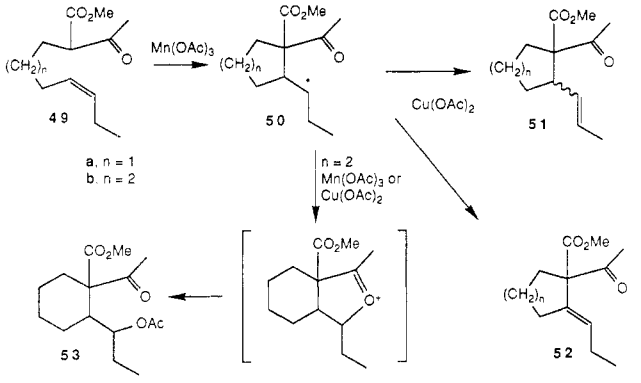
2.60. Attempted oxidative cyclization **40b–d** gives only uncharacterizable products.

Alkylation of the dianion of ethyl 2-oxocyclopentanecarboxylate with 1-bromo-3(*Z*)-hexene gives **45** in 45% yield. Oxidative cyclization for 24 h at 25 °C gives a mixture of **47** (78%) and **48** (4%). 6-Exo cyclization to



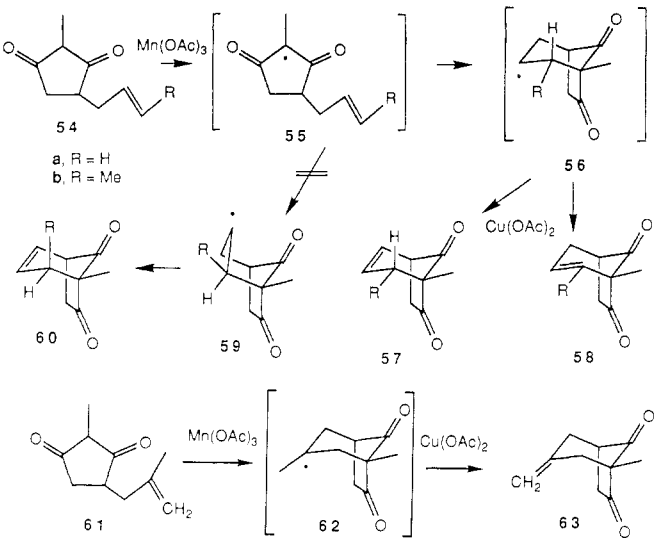
give **46** with an equatorial side chain is the exclusive process. Oxidative elimination gives predominantly the Hofmann product **47** as the *E* isomer. The stereochemistry of the side chain in **47** is assigned from the coupling constants of 6.1 and 11.1 Hz between the allylic methine hydrogen and the adjacent ring methylene hydrogens. The 11.1-Hz coupling constant must be an axial–axial coupling, indicating that the allylic methine is axial.

Oxidative cyclizations of **49a** and **49b**, prepared by alkylation of methyl acetoacetate, were examined to explore the suitability of this reaction from carrying out cyclizations in which neither carbonyl group was in the ring. Oxidative cyclization of **49a** provides 67% of a 7:3 mixture



of **51a** and **52a** while **49b** gives 50% of a 8.5:1.5 mixture of **51b** and **52b** and 38% of **53** as a mixture of diastereomers. In both cases exo cyclization occurs exclusively to give **50** as a mixture of diastereomers. Oxidative elimination gives a mixture of regioisomers. The formation of **53** is surprising since we have not generally observed the formation of secondary acetates. Usually, secondary radicals are not oxidized by Mn(III) and are oxidized to alkenes by Cu(II). It is possible that the acetyl group assists the oxidation of **50** to give an intermediate that reacts with acetate to give **53**. This proposed mechanism has ample precedent in the formation of dihydrofurans in the intermolecular addition of acetoacetate esters to alkenes.[6e,9e,f,h-k,m]

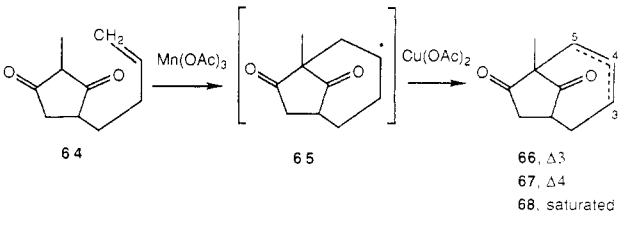
Oxidative Cyclization of Diones. Oxidative cyclization of unsaturated 2-methylcyclopentane-1,3-diones provides an efficient route to bicyclo[3.2.1]octane-6,8-diones. Diketone **54a** was prepared in 44% yield by alkylation of the dianion of 2-methylcyclopentane-1,3-dione by the procedure of Mellor and Pattenden.[28] Diones **54b**, **61**, and



64 were prepared similarly in 62%, 33%, and 67% yields, respectively. Oxidative cyclization of **54a** with 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$ and 1 equiv of $Cu(OAc)_2 \cdot H_2O$ for 18 h at 25 °C gives 38% of dione **57a**. The position of the double bond in **57a** follows from careful analysis of the ^1H NMR spectrum, which clearly indicates the presence of three allylic hydrogens. Oxidation of **54a** by $Mn(OAc)_3 \cdot 2H_2O$ gives radical **55a**, which cyclizes to **56a**. Oxidative elimination can give either **57a** or **58a**. Although only **57a** is isolated, examination of the ^1H NMR spectrum on the crude product suggests that ≈20% of **58a** is present. Presumably the location of the double bond in **58a** facilitates a retro-Claisen condensation to give a keto acid during chromatographic purification.

Oxidative cyclization of **54b** gives 14% of **57b** as a single diastereomer. The stereochemistry of the methyl group in **57b** cannot be determined by analysis of the ^1H NMR spectrum because the coupling constants to the sp^3 methine hydrogen should be similar in both **57b** and **60**. Molecular mechanics calculations[29] suggest that cyclization through a chair transition state to give **56b** is favored over cyclization through a boat transition state to give **59b** by 4–5 kcal/mol, strongly suggesting that the product isolated is **57b**.

Oxidative cyclization of **61** with 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$ and 1 equiv of $Cu(OAc)_2 \cdot H_2O$ gives radical **62**, which undergoes oxidative elimination to give **63** in 48% yield. None of either isomer with an endocyclic double bond is isolated. Although the cation derived from oxidation of **62** is probably an intermediate, no tertiary acetate is isolated. Oxidative cyclization of **64** gives exclusively 7-endo



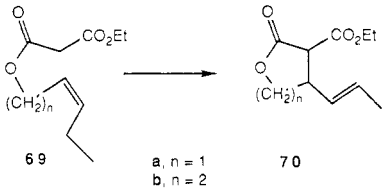
cyclization to give **65**, which undergoes oxidative elimination to give 33% of a 1:1 mixture of **66** and **67**. Hydrogenation over Pd on carbon affords **68** in quantitative

(28) Mellor, M.; Pattenden, G. *Synth. Commun.* **1979**, *9*, 1.

(29) MMX (version 89.000) obtained from Serena Software, 489 Serena Lane, Bloomington, IN 47401, was used on a VAX 8650. Updated versions of MODEL (Version KS 2.94) obtained from Prof. Midland, University of California, Riverside, and Prof. Steliou, University of Montreal, were used for structure input and analysis.

yield. No cyclized products were obtained from ketones corresponding to **54a** and **64** that were lacking the 2-methyl group or from the corresponding 4-unsaturated 2-methylcyclohexane-1,3-diones.

Unsaturated malonate esters also undergo oxidative cyclization. Malonate esters **69a** and **69b** are readily prepared by esterification of ethyl malonyl chloride in 65–80% yield. Oxidative cyclization of **69a** and **69b** with 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$ and 1 equiv of $Cu(OAc)_2 \cdot H_2O$ in acetic acid at 50 °C for several hours gives **70a** and **70b**



as the *E* isomer in 18% and 27% yields, respectively. In both cases only products obtained from exo cyclization are isolated. Further oxidation is undoubtedly responsible for the low yield and the absence of products with the more highly substituted double bond.

These studies indicate that Mn(III)-based oxidative free-radical cyclization is a powerful synthetic method. The starting materials are readily prepared, and highly functionalized mono- and bicyclic products are obtained often with excellent control of steroechemistry. The results presented above help delineate the scope and limitations of this reaction and suggest further avenues for exploration.

Experimental Section

^1H NMR spectra were recorded in $CDCl_3$ at 90 or 300 MHz (*J* constants were measured in hertz). ^{13}C NMR spectra were recorded in $CDCl_3$ at 75 MHz. Infrared spectra were recorded with NaCl cells. Melting points are uncorrected. High-resolution mass spectra (MS) were obtained at 70 eV. Analytical GC was performed with a 25 m × 0.25 mm fused silica column containing OV225B at a helium flow rate of 25 mL/min. Temperature programs A (60 °C, increasing to 100 °C at 10 °C/min, then increasing to 170 °C at 30 °C/min, and holding at 170 °C) and B (60 °C, increasing to 100 °C at a rate of 5 °C/min, holding at 100 °C for 10 min, increasing to 120 °C at a rate of 5 °C/min, and holding at 120 °C for 1 min) were used. Preparative GC was performed with a 6 ft × 0.25 in. aluminum column containing 10% XF-1150 on 60/80-mesh Chromosorb PNAW at a helium flow rate of 40 mL/min.

$Mn(OAc)_3 \cdot 2H_2O$ was purchased from Aldrich Chemical Co. and used without purification. Tetrahydrofuran (THF) and ether were distilled from sodium benzophenone ketyl. Dichloromethane (CH_2Cl_2), hexamethylphosphoric triamide (HMPA), and benzene were distilled from CaH_2. All air-sensitive reactions were conducted in flame-dried glassware under a positive pressure of nitrogen with magnetic stirring. Reagents were added via dry syringes through septa.

Preparation of Starting Materials. 3-Oxoalkanoate esters **1a** (47%), **1b** (67%), **9** (45%), **9b** (66%), **14a** (62%), and **14b** (55%) were prepared by alkylation of the sodium lithium dianion of methyl acetoacetate with 1 equiv of the appropriate bromide by the procedure of Huckin and Weiler.[16] No attempt was made to optimize the yield. More recent studies indicate that adding 1 equiv of HMPA to the reaction mixture leads to significantly improved yields. Alkylation of the sodium salt of methyl acetoacetate with (*Z*)-bromo-4-heptene in methanol at reflux for 7 h gave **49a** (49%). Alkylation of the sodium salt of methyl acetoacetate with (*Z*)-bromo-5-octene in THF at reflux for 2 h gave **49b** (47%). Esterification of (*Z*)-2-penten-1-ol and (*Z*)-3-hexen-1-ol with ethyl malonyl chloride in methylene chloride containing 1.5 equiv of pyridine for 24 h at 25 °C gave **69a** (65%) and **69b** (78%).

Ethyl 2-Methyl-3-oxo-7(*Z*)-decenoate (23a). To a stirring solution of diisopropylamine (1.86 mL, 13.3 mmol) in THF (60 mL) at 0 °C was added dropwise *n*-butyllithium (2.5 M in hexanes; 5.30 mL, 13.3 mmol). The mixture was stirred at 0 °C for 0.5 h at which time ethyl 2-methylacetoacetate (0.94 mL, 6.60 mmol) was added dropwise over 5 min. The resulting deep orange solution was stirred for 0.5 h at 0 °C. HMPA (2.31 mL, 13.3 mmol) was then added in one portion, followed by 1-bromo-3(*Z*)-hexene (1.392 g, 6.60 mmol) in 6 mL of THF. The mixture was warmed to room temperature and stirred for 1 h. Normal workup afforded 1.530 g of crude product. Purification of 1.525 g by flash chromatography (9:1 hexane–EtOAc) gave 0.524 g (35%) of **23a**: ^1H NMR δ 5.40 (dtt, 1, *J* = 10.8, 8.7, 1.8), 5.28 (dtt, 1, *J* = 10.8, 8.7, 1.8), 4.18 (q, 2, *J* = 7.1), 3.51 (q, 1, *J* = 7.1), 2.62–2.46 (m, 2), 2.08–1.98 (m, 4), 1.74–1.60 (m, 2), 1.33 (d, 3, *J* = 7.1), 1.27 (t, 3, *J* = 7.1), 0.95 (t, 3, *J* = 7.4); ^{13}C NMR δ 205.8, 170.6, 132.6, 127.8, 61.2, 52.8, 40.6, 26.2, 23.4, 20.4, 14.2, 14.0, 12.7; IR (neat) 1745, 1715 cm^{-1}.

Ethyl 3-(3-Butenyl)-2-oxocyclohexanecarboxylate (40a). 4-Bromo-1-butene (0.743 g, 0.56 mL, 5.5 mmol) was added to a freshly prepared THF solution of 5 mmol of the sodium lithium dianion of ethyl 2-oxocyclohexanecarboxylate at 0 °C. The reaction mixture was allowed to stir for 2 h at 0 °C and then for 18 h at 25 °C. Normal workup afforded 1.094 g of crude product. Flash chromatography on silica gel (15:1 hexane–EtOAc) gave 0.825 g (74%) of **40a** as 1.2:1 mixture of keto and enol tautomers: bp 100–110 °C (0.4 Torr); ^1H NMR δ 12.43 (0.45 × 1, enolic H), 5.90–5.70 (m, 1), 5.08–4.94 (m, 2), 4.20 (q, 2, *J* = 7.0), 3.38 (dd, 0.55 × 1, *J* = 12.3, 6.0), 2.60–1.35 (m, 11), 1.30 (t, 3, *J* = 7.0); ^{13}C NMR δ 174.6, 138.4, 114.7, 97.7 (enol), 60.1, 57.9, 37.8, 31.1, 29.6, 27.0, 22.8, 20.1, 14.2, all carbons not detected; IR (neat) 1745, 1710, 1650, 1610 cm^{-1}.

Ethyl 3-[3(*Z*)-Hexenyl]-2-oxocyclopentane-1-carboxylate (45). Ethyl 2-oxocyclopentane-1-carboxylate (0.71 mL, 4.76 mmol) was converted to the dianion with 9.52 mmol of lithium diisopropylamide in THF (48 mL) at 0 °C. HMPA (0.84 mL, 4.76 mmol) and 1-bromo-3(*Z*)-hexene (2.000 g, 9.52 mmol) were added, and the reaction was stirred for 1 h at 25 °C. Normal workup gave 1.802 g of crude **45**. Flash chromatography (15:1 hexane–EtOAc) gave 0.505 g (45%) of **45** as a 1:1 mixture of cis and trans isomers. ^1H NMR δ 5.40 (br dt, 1, *J* = 11.2, 6.5), 5.29 (br dt, 1, *J* = 11.2, 6.7), 4.26–4.12 (m, 2), 3.26 (br dd, 0.51 × 1, *J* = 5.3, 8.5), 3.12 (dd, 0.5 × 1, *J* = 8.5, 11.0), 2.41–2.00 (m, 8), 1.90–1.65 (m, 2), 1.53–1.32 (m, 1), 1.28 (t, 0.5 × 3, *J* = 7.1), 1.27 (t, 0.5 × 3, *J* = 7.1), 0.96 (t, 3, *J* = 7.0); ^{13}C NMR δ 213.8 (0.5), 213.2 (0.5), 169.5 (0.5), 169.4 (0.5), 132.7, 127.8, 61.3, 55.0 (0.5), 54.2 (0.5), 48.8 (0.5), 48.2 (0.5), 29.9 (0.5), 29.6 (0.5), 27.6 (0.5), 27.4 (0.5), 25.1 (0.5), 24.9 (0.5), 24.8 (0.5), 24.8 (0.5), 20.5, 14.3 (0.5), 14.1 (0.5); IR (neat) 1756, 1726 cm^{-1}. Anal. Calcd for $C_{14}H_{22}O_3$: C, 70.55; H, 9.31. Found: C, 70.77; H, 9.01.

Oxidative Cyclization of 1a with $Mn(OAc)_3$ and $Cu(OAc)_2$. To a solution of $Mn(OAc)_3$ (1.376 g, 5.10 mmol) and $Cu(OAc)_2$ (0.510 g, 2.55 mmol) in 18 mL of glacial acetic acid was added a solution of β-keto ester **1a** (0.505 g, 2.55 mmol) in 7 mL of glacial acetic acid to give an opaque brownish green solution containing some undissolved $Mn(OAc)_3 \cdot 2H_2O$. The mixture was stirred for 1 h at 50 °C at which time the solution was light blue and contained a white precipitate. Water was added to give a single cloudy phase in which the white precipitate had dissolved. The solution was extracted with five 15-mL portions of CH_2Cl_2. The combined organic layers were washed with saturated aqueous sodium bicarbonate solution until neutral and then water. The aqueous layer was back-extracted with two 15-mL portions of CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, and the solvent was removed in vacuo to provide 0.512 g of crude **7**. Flash chromatography on silica gel (3:1 hexane–ether) gave 0.365 g (71%) of methyl *trans*-2-oxo-6-[1(E)-propenyl]cyclohexanecarboxylate (**7**) as a 1.3:1 mixture of keto and enol tautomers. The keto and enol tautomers were partially separated by flash chromatography but equilibrated at 25 °C after 15 days: IR (neat) 1745, 1715 cm^{-1}. Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 66.90; H, 8.33.

Data for the keto tautomer of **7**: ^1H NMR δ 5.47–5.08 (m, 2), 3.63 (s, 3), 3.12 (d, 1, *J* = 12.0), 2.75 (dddd, 1, *J* = 12.0, 12.0, 8.0, 4.0), 2.35–2.32 (m, 1), 2.29–1.57 (m, 5), 1.54 (d, 3, *J* = 3.7); ^{13}C NMR δ 205.2, 169.5, 131.7, 126.2, 62.9, 51.6, 44.3, 40.6, 34.1, 24.6, 17.7.

Data for the enol tautomer of **7**: ^1H NMR δ 12.32 (enolic H), 5.47–5.08 (m, 2), 3.63 (s, 3), 3.15–3.05 (m, 1), 2.41–2.36 (m, 1),

2.29–1.57 (m, 5), 1.54 (d, 3, J = 3.7); ^{13}C NMR δ 172.8, 134.1, 124.5, 99.7, 51.0, 39.6, 30.4, 28.8, 28.0, 16.8, one carbon was not observed.

Oxidative Cyclization of 1b with Mn(OAc)$_3$ and Cu(OAc)$_2$. A solution of β-keto ester **1b** (0.233 g, 1.18 mmol), Mn(OAc)$_3$·2H$_2$O (0.631 g, 2.35 mmol), and Cu(OAc)$_2$·H$_2$O (0.235 g, 1.18 mmol) in glacial acetic acid (14 mL) was stirred at room temperature for 26 h. Normal workup gave 0.192 g (83%) of crude material. Purification of 0.179 g by evaporative distillation gave 0.139 g (64%) of **7**.

Oxidative Cyclization of 9a with Mn(OAc)$_3$ and Cu(OAc)$_2$. A solution of β-keto ester **9a** (0.511 g, 3.0 mmol), Mn(OAc)$_3$ (1.609 g, 6.0 mmol), and Cu(OAc)$_2$ (0.600 g, 3.0 mmol) in 30 mL of glacial acetic acid was stirred for 1 h at 50 °C. Normal workup of the light blue solution afforded 0.356 g of crude product. Flash chromatography on silica gel (2:1 hexane–ether) gave 0.026 g (5%) of a 7:2:1 mixture of methyl 2-hydroxy-6-methyl-1,4-cyclohexadienecarboxylate (**15a**), methyl 2-hydroxy-6-methylbenzoate (**17a**), and methyl 2-hydroxy-6-methyl-1,5-cyclohexadienecarboxylate (**16a**), which was not further separated, followed by 0.088 g of recovered **9a** followed by 0.106 g (21%, 25% based on recovered **9a**) of methyl *trans*-5-ethenyl-2-oxocyclopentanecarboxylate (**11a**).

Data for **11a**: ^{1}H NMR δ 5.91–5.78 (m, 1), 5.25–5.06 (m, 2), 3.78 (s, 3), 3.30–3.16 (m, 1), 3.05 (d, 1 J = 12.0), 2.64–2.11 (m, 3), 1.82–1.60 (m, 1); ^{13}C NMR δ 169.7, 138.2, 115.9, 60.7, 52.4, 44.8, 38.1, 27.2, carbonyl carbon was not observed; IR (CCl_4) 1760, 1730, 1690, 1660 cm^{-1}. The spectral data are identical with those previously described.[30,31]

Data for **15a–17a** determined from the mixture: IR (neat) 1750, 1715, 1675, 1650, 1610 cm^{-1}; ^{1}H NMR δ (**15a**) 12.33 (enolic H), 5.90–5.25 (m, 2), 3.80 (s, 3), 3.15 (m, 1), 2.93–2.85 (m, 2), 1.12 (d, 3, J = 11.0); ^{1}H NMR δ (16a) 5.49–5.39 (m, 1), 3.81 (s, 3), 3.26 (s, 1), 3.21–2.09 (m, 4), 1.70 (s, 3); ^{1}H NMR δ (17a)[32] 11.30 (enolic H), 7.27 (dd, 1, J = 11.0, 11.0), 6.84 (d, 1, J = 11.0), 6.71 (d, 1, J = 11.0), 3.97 (s, 3), 2.50 (s, 3).

Oxidative Cyclization of 9b with Mn(OAc)$_3$ and Cu(OAc)$_2$. A solution of β-keto ester **9b** (0.374 g, 2.0 mmol), Mn(OAc)$_3$ (1.073 g, 4.0 mmol), and Cu(OAc)$_2$ (0.400 g, 2.0 mmol) in 20 mL of glacial acetic acid was stirred for 1 h at 50 °C. Normal workup of the light blue solution afforded 0.324 g of crude product. Flash chromatography on silica gel (3:1 hexane–ether) gave 0.074 g of recovered **9b** followed by 0.134 g (36%, 45% based on recovered **9b**) of methyl *trans*-2-oxo-5-[1(*E*)-propenyl]cyclopentanecarboxylate (**11b**) followed by 0.037 g (10%, 12.5% based on recovered **9b**) of methyl 5-oxo-2-[1(*E*)-propenyl]cyclopent-1-enecarboxylate (**13b**).

Data for **11b**: ^{1}H NMR δ 5.63–5.28 (m, 2), 3.74 (s, 3), 3.21–3.08 (m, 1), 2.99 (d, 1, J = 10.3), 2.49–2.19 (m, 4), 1.68 (d, 3, J = 5.6); ^{13}C NMR δ 210.8, 169.0, 130.9, 126.4, 61.0, 52.0, 43.8, 37.9, 27.5, 17.6; IR (neat) 1760, 1730 cm^{-1}.

Data for **13b**: ^{1}H NMR δ 7.28 (d, 1, J = 16.1), 6.68 (dt, 1, J = 6.9, 15.9), 3.87 (s, 3), 2.86–2.82 (m, 2), 2.54–2.50 (m, 2), 2.01 (d, 3, J = 6.8); ^{13}C NMR δ 203.5, 175.7, 163.8, 141.3, 128.4, 127.0, 51.8, 34.3, 25.9, 19.4; IR (neat) 1735, 1710, 1635, 1580 cm^{-1}; UV (95% EtOH) 282 nm (ϵ 14 100).

Oxidative Cyclization of 18a with Mn(OAc)$_3$ and Cu(OAc)$_2$. A solution of β-keto ester **18a** (0.198 g, 1.0 mmol), Mn(OAc)$_3$ (0.537 g, 2.0 mmol), and Cu(OAc)$_2$ (0.200 g, 1.0 mmol) in 10 mL of glacial acetic acid was stirred for 1 h at 50 °C. Normal workup of the light blue solution afforded 0.174 g of crude product. Medium-pressure chromatography on silica gel (3:1 hexane–ether) gave 0.079 g (41%) of methyl *trans*-2-oxo-6-(methylethenyl)-cyclohexanecarboxylate (**21a**) as a 1.2:1 mixture of keto and enol tautomers: ^{1}H NMR δ 12.34 (s, 0.45 × 1, enolic H), 4.77 (br s, 1), 4.50 (br s, 1), 3.69 (s, 3), 3.50 (d, 0.55 × 1, J = 11.5), 3.12–3.08 (m, 1), 2.33–2.05 (m, 2), 1.75 (br s, 3), 1.70–1.43 (m, 4); ^{13}C NMR δ 172.6, 147.7, 145.3, 111.1 (e), 110.5 (k), 99.9 (e), 61.3 (k), 51.5 (e), 50.9 (k), 48.1, 40.6, 38.6, 29.5, 28.5, 25.5, 24.6, 22.0, 16.6, all carbons not observed; IR (neat) 1750, 1715, 1660, 1620 cm^{-1}. Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.19; H, 8.18.

Oxidative Cyclization of 18b with Mn(OAc)$_3$ Prepared in Situ. A solution of Mn(OAc)$_2$·4H$_2$O (3.676 g, 15 mmol) in 75 mL of glacial acetic acid was allowed to stir for 10 min at 90 °C. To this solution was added $KMnO_4$ (0.569 g, 3.6 mmol) in small portions while the temperature was maintained at 90 °C, giving a deep purple solution. When the exothermic reaction had subsided, KOAc (12.85 g, 131 mmol) and acetic anhydride (19 mL, 201 mmol) were added, and the mixture was allowed to stir at 90 °C for 10 min. The mixture was cooled to 45 °C, and a solution of **18b** (1.380 g, 7.5 mmol) in 1 mL of acetic acid was added. The reaction was allowed to stir for 1 h at 45 °C followed by normal workup to afford 1.161 g of crude product. Medium-pressure chromatography of 0.742 g on silica gel (1:1 hexane–ether) gave 0.109 g (8%) of methyl 5-(methylethenyl)-2-oxocyclopentanecarboxylate (**21b**) as a mixture rich in the trans isomer, followed by 0.185 g (10%) of methyl 5-(1-acetoxy-1-methylethyl)-2-oxocyclopentanecarboxylate (**22b**) as a mixture rich in the trans isomer.

Data for **21b**: ^{1}H NMR δ 4.90–4.70 (m, 2), 3.72 (s, 3), 3.14 (d, 1, J = 11.0), 2.60–2.00 (m, 4), 1.83–1.60 (m, 1), 1.80 (br s, 3); ^{13}C NMR δ 210.9, 169.4, 144.0, 111.0, 59.5, 52.7, 47.5, 38.2, 26.0, 20.2; IR (neat) 1765, 1735 cm^{-1}. The spectral data are identical with those previously described.[27,30,31,33]

Data for **22b**: ^{1}H NMR δ 3.76 (s, 3), 3.25 (d, 1, J = 11.0), 2.97 (dt, 1, J = 11.0, 5.0), 2.56–2.32 (m, 2), 2.21–2.10 (m, 1), 1.96 (s, 3), 1.87–1.72 (m, 1), 1.53 (s, 3), 1.52 (s, 3); ^{13}C NMR δ 210.9, 170.1, 169.7, 81.6, 56.6, 52.3, 50.9, 38.2, 24.3, 22.4, 22.0, 21.7; IR (neat) 1760, 1725 cm^{-1}.

Oxidative Cyclization of β-Keto Ester 23a with Mn(OAc)$_3$ and Cu(OAc)$_2$. A solution of β-keto ester **23a** (0.133 g, 0.59 mmol), Mn(OAc)$_3$·2H$_2$O (0.316 g, 1.18 mmol), and Cu(OAc)$_2$·H$_2$O (0.118 g, 0.59 mmol) in 7 mL of glacial acetic acid was stirred at room temperature for 17 h. Normal workup gave 0.125 g (93%) of a yellow oil. Purification of 0.110 g by flash chromatography (20:1 hexane–EtOAc) gave 0.066 g (56%) of ethyl 6α-[1(*E*)-propenyl]-1β-methyl-2-oxocyclohexane-1α-carboxylate (**28**), followed by 0.020 g, (17%) of a 4.2:1 mixture of ethyl 6(*E*)-propylidene-1-methyl-2-oxocyclohexane-1-carboxylate (**29**) and ethyl 6β-[1(*E*)-propenyl]-1β-methyl-2-oxocyclohexane-1α-carboxylate (**32**) as determined by analytical GC.

Data for **28**: ^{1}H NMR δ 5.70 (ddq, 1, J = 7.1, 15.2, 1.3), 5.45 (dq, 1, J = 15.2, 6.3), 4.16 (q, 2, J = 7.1, –OCH$_2$), 2.67 (ddd, 1, J = 6.4, 13.9, 13.9, H3), 2.43 (dddd, 1, J = 2.3, 3.7, 4.3, 13.9, H3), 2.12–1.98 (m, 3, H4, H5, H6), 1.72–1.62 (m, 2, H4, H5), 1.68 (dd, 3, J = 1.7, 6.3), 1.26 (s, 3), 1.25 (t, 3, J = 7.1); ^{13}C NMR δ 207.0, 171.3, 130.5, 127.4, 60.9, 60.4, 53.1, 40.0, 28.8, 25.5, 19.2, 17.8, 14.1; IR (neat) 1735, 1710 cm^{-1}; t_R (GC B) = 16.5 min. Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.90; H, 8.87.

Data for **29**: ^{1}H NMR δ 5.39 (br t, 1, J = 7.1), 4.25–4.12 (m, 2), 2.72–2.61 (m, 1), 2.66 (ddd, 1, J = 6.2, 11.2, 15.3, H3), 2.52–2.42 (m, 2), 2.26–2.15 (m, 1), 2.10 (dq, 2, J = 7.1, 7.4), 1.64–1.51 (m, 1), 1.43 (s, 3), 1.24 (t, 3, J = 7.2), 0.98 (t, 3, J = 7.4); ^{13}C NMR δ 206.7, 172.8, 136.2, 128.5, 61.4, 60.9, 39.7, 25.8, 24.0, 21.1, 18.2, 14.2, 14.0; IR (neat) 1735, 1710 cm^{-1}; t_R (GC B) = 18.5 min.

Data for **32** determined from the mixture: ^{1}H NMR δ 5.54 (ddq, 1, J = 0.9, 15.1, 6.3), 5.23 (ddq, 1, J = 9.0, 15.1, 1.6), 4.25–4.12 (m, 2), 3.11 (br ddd, 1, J = 3.6, 8.1, 9.0), 2.46 (t, 2, J = 6.7), 2.05–1.77 (m, 3), 1.72–1.60 (m, 1), 1.65 (ddd, 3, J = 0.4, 1.6, 6.3), 1.27 (t, 3, J = 7.0), 1.22 (s, 3); ^{13}C NMR δ 209.1, 172.6, 128.4, 128.2, 63.6, 61.1, 47.4, 38.8, 27.7, 23.4, 18.0, 17.4, 14.1; t_R (GC B) = 19.2 min.

Oxidative Cyclization of β-Keto Ester 23b with Mn(OAc)$_3$ and Cu(OAc)$_2$. A solution of **23b** (0.403 g, 1.78 mmol), Mn(OAc)$_3$·2H$_2$O (0.956 g, 3.56 mmol), and Cu(OAc)$_2$·H$_2$O (0.356 g, 1.78 mmol) in glacial acetic acid (20 mL) was stirred at room temperature for 18 h. Normal workup gave 0.340 g (84%) of crude material. Flash chromatography (20:1 hexane–EtOAc) gave 0.172 g (43%) of **28** followed by 0.077 g (19%) of a 1:1 mixture of **29** and **30**.

Oxidative Cyclization of β-Keto Ester 33 with Mn(OAc)$_3$ and Cu(OAc)$_2$. A solution of β-keto ester **33** (0.102 g, 0.5 mmol), Mn(OAc)$_3$ (0.276 g, 1.0 mmol), and Cu(OAc)$_2$ (0.105 g, 0.5 mmol) in 5 mL of glacial acetic acid was stirred for 4 days at 25 °C.

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Normal workup of the light blue solution afforded 0.800 g of crude product. Medium-pressure chromatography on silica gel (15:1 hexane–EtOAc) of 0.066 g gave 0.004 g of recovered **33** followed by 0.030 g (36%, 38% based on recovered starting ester) of a 2.5:1 mixture of the isomers of ethyl 5-ethenyl-1-methyl-2-oxocyclopentanecarboxylate (**34a** and **34b**), followed by 0.003 g (3%) of **34b** followed by 0.008 g (7%) of ethyl 5-acetoxy-1,6-dimethyl-2-oxocyclohex-3-enecarboxylate (**36**).

Data for **34a**: ^{1}H NMR δ 5.84–5.70 (m, 1), 5.21–5.13 (m, 2), 4.25–4.07 (m, 2, AB portion of ABX_3), 2.77–2.05 (m, 5), 1.29 (s, 3), 1.23 (t, 3, J = 7.1); ^{13}C NMR δ 170.1, 135.8, 117.3, 61.1, 59.3, 53.0, 37.4, 25.4, 18.2, 14.2, carbonyl carbon was not detected; IR ($CDCl_3$) 1750–1710 (br), 1640 cm^{-1}; t_R (GC A) = 5.50 min.

Data for **34b**: ^{1}H NMR δ 5.82–5.70 (m, 1), 5.21–5.11 (m, 2), 4.23–4.09 (m, 2, AB portion of ABX_3), 3.41–3.31 (m, 1), 2.49–2.06 (m, 4), 1.25 (t, 3, J = 7.5), 1.15 (s, 3); ^{13}C NMR δ 135.5, 117.3, 61.4, 61.1, 48.6, 37.2, 24.7, 14.1, 13.9, two carbonyl carbons were not detected; IR ($CDCl_3$) 1745, 1725 cm^{-1}; t_R (GC A) = 5.66 min.

Data for **34a** and **34b**. Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.43; H, 8.66.

Data for **36**: ^{1}H NMR δ 6.78 (dd, 1, J = 10.5, 2.0), 6.09 (dd, 1, J = 10.2, 2.2), 5.69 (ddd, 1, J = 10.3, 2.1, 2.0), 4.24–4.07 (m, 2, AB portion of ABX_3), 2.14 (s, 3), 1.45 (s, 3), 1.28–1.20 (m, 1), 1.24 (t, 3, J = 7.1), 1.10 (d, 3, J = 6.8); IR ($CDCl_3$) 1740, 1735, 1710 cm^{-1}; t_R (GC A) = 8.18 min.

Oxidative Cyclization of β-Keto Ester 37 with $Mn(OAc)_3$. A solution of β-keto ester **37** (0.103 g, 0.5 mmol) and $Mn(OAc)_3$ (0.261 g, 1.0 mmol) in 5 mL of glacial acetic acid was stirred for 2 days at 25 °C. Normal workup of the clear solution afforded 0.106 g of crude product. Medium-pressure chromatography on silica gel (9:1 hexane–EtOAc) of 0.067 g gave 0.008 g of recovered starting ester followed by 0.016 g (25%, 27% based on recovered **37**) of a 3:2 mixture of isomers of ethyl 1-methyl-5-(methylethenyl)-2-oxocyclopentanecarboxylate (**38a** and **38b**) followed by 0.024 g (20%, 22% based on recovered **37**) of a 3:2 mixture of isomers of ethyl 1-methyl-5-(1-acetoxy-1-methylethyl)-2-oxocyclopentanecarboxylate (**39a** and **39b**).

Data for **38a**: ^{1}H NMR δ 4.93 (br s, 1), 4.84 (br s, 1), 4.14–4.03 (m, 2, AB portion of ABX_3), 2.70–1.86 (m, 5), 1.81 (s, 3), 1.42 (s, 3), 1.21 (t, 3, J = 7.0); t_R (GC A) = 7.26 min. The data are identical with those previously described.[27]

Data for **38b**: ^{1}H NMR δ 4.95 (br s, 1), 4.78 (br s, 1), 4.27–4.16 (m, 2, AB portion of ABX_3), 3.36 (dd, 1, J = 11.7, 6.0), 2.70–1.86 (m, 4), 1.65 (s, 3), 1.27 (t, 3, J = 7.0), 1.06 (s, 3); t_R (GC A) = 7.33 min.

Data for **38a** and **38b**: ^{13}C NMR δ 143.0 (major), 142.8 (minor), 112.6 (major), 112.4 (minor), 61.4 (minor), 61.1 (major), 59.5, 55.5, 51.1, 37.6, 24.4, 23.4, 22.9, 20.1, 14.1, 13.3, eight carbons were not detected; IR ($CDCl_3$) 1745, 1725 cm^{-1}. Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.54; H, 8.63. Found: C, 68.46; H, 8.91.

Data for **39a**: ^{1}H NMR δ 4.19 (q, 2, J = 7.1), 2.75–2.02 (m, 5), 1.96 (s, 3), 1.65 (s, 3), 1.61 (s, 3), 1.46 (s, 3), 1.24 (t, 3, J = 7.1); t_R (GC A) = 8.89 min.

Data for **39b**: ^{1}H NMR δ 4.08 (q, 2, J = 7.1), 2.93 (dd, 1, J = 12.2, 6.1), 2.75–2.05 (m, 4), 1.96 (s, 3), 1.59 (s, 3), 1.54 (s, 3), 1.31 (s, 3), 1.26 (t, 3, J = 7.1); t_R (GC A) = 8.99 min.

Data for **39a** and **39b**: ^{13}C NMR ($CDCl_3$) δ 189.6, 82.7, 82.1, 61.5, 61.0, 59.7, 59.2, 57.5, 55.0, 37.0, 25.1, 24.8, 24.7, 22.4, 22.3, 21.5, 21.2, 20.7, 15.0, 14.0, 13.8, five carbons were not detected; IR ($CDCl_3$) 1750–1710 (br) cm^{-1}.

Oxidative Cyclization of β-Keto Ester 40a with $Mn(OAc)_3$ and $Cu(OAc)_2$. A solution of β-keto ester **40a** (0.207 g, 0.92 mmol), $Mn(OAc)_3$ (0.495 g, 1.84 mmol), and $Cu(OAc)_2$ (0.188 g, 0.94 mmol) in 10 mL of glacial acetic acid was stirred for 18 h at 50 °C. Normal workup of the light blue solution afforded 0.182 g of crude product. Flash chromatography on silica gel (20:1 hexane–EtOAc) gave 0.071 g (35%) of a 1:1.1 mixture of ethyl 2-methylene-9-oxobicyclo[3.3.1]-nonane-1-carboxylate (**44**) and ethyl 10-oxobicyclo[4.3.1]dec-3-enecarboxylate (**43**), which were separated by preparative GC.

Data for **44**: ^{1}H NMR δ 5.14 (d, 1, J = 2.0), 4.83 (d, 1, J = 1.8), 4.25–4.14 (m, 2, AB portion of ABX_3), 2.74–2.69 (m, 1), 2.46–1.50 (m, 10), 1.24 (t, 3, J = 7.0); ^{13}C NMR δ 213.9, 171.3, 149.5, 110.3, 64.5, 61.0, 44.7, 40.2, 37.1, 31.8, 27.7, 16.8, 14.0; IR (neat) 1745–1720 (br) cm^{-1}; t_R (GC A) = 7.61 min. Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 69.61; H, 8.51.

Data for **43**: ^{1}H NMR δ 5.93–5.79 (m, 2), 4.21 (q, 2, J = 7.0), 2.82–2.76 (m, 1), 2.60 (d, 1, J = 4.9), 2.49–1.55 (m, 9), 1.28 (t, 3, J = 7.0), upon irradiation at δ 5.86, the d at δ 2.60 collapsed to a singlet, indicating the presence of an otherwise isolated allylic methylene group; ^{13}C NMR δ 212.0, 173.2, 129.4, 129.0, 61.2, 61.1, 47.3, 35.9, 32.9, 32.4, 30.7, 18.6, 14.1; IR (neat) 1735, 1710 cm^{-1}; t_R (GC A) = 8.68 min. Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 69.81; H, 8.25.

Oxidative Cyclization of 45 with $Mn(OAc)_3 \cdot 2H_2O$ and $Cu(OAc)_2 \cdot H_2O$. A solution of **45** (0.305 g, 1.28 mmol), $Mn(OAc)_3 \cdot 2H_2O$ (0.687 g, 2.56 mmol), and $Cu(OAc)_2 \cdot H_2O$ (0.256 g, 1.28 mmol) in glacial acetic acid (15 mL) was stirred at room temperature for 24 h. Normal workup gave 0.294 g (97%) of crude material. Purification of 0.246 g by flash chromatography (10:1 hexane–EtOAc) gave 0.025 g (10%) of a 1:1 mixture of ethyl 8-oxo-*endo*-2-[1(*E*)-propenyl]bicyclo[3.2.1]octane-1-carboxylate (**47**) and ethyl 8-oxo-2(*E*)-propylidenebicyclo[3.2.1]octane-1-carboxylate (**48**) and other unidentified components, followed by 0.189 g (74%) of **47**.

Data for **48** determined from the mixture: ^{1}H NMR δ 5.2–5.4 (m, 1), 2.30 (dq, 2, J = 7, 7), 0.95 (t, 3, J = 7); ^{13}C NMR δ 132.4, 60.1, 34.1, 32.2, 31.7, 24.9, 22.7, 20.4, 14.3, 14.2, 4 carbons were not observed.

Data for **47**: ^{1}H NMR δ 5.55 (ddq, 1, J = 1.0, 15.2, 6.5), 5.29 (ddq, 1, J = 6.5, 15.2, 1.7), 4.29–4.11 (m, 2), 3.10 (br ddd, 1, J = 6.1, 6.5, 11.1, H2), 2.55–2.40 (m, 2), 2.11–1.83 (m, 4), 1.79–1.59 (m, 2), 1.63 (ddd, 3, J = 0.7, 1.7, 6.5), 1.26 (t, 3, J = 7.2); ^{13}C NMR δ 214.0, 169.5, 129.0, 127.8, 61.8, 60.9, 50.6, 44.9, 33.7, 24.1, 21.3, 21.3, 18.0, 14.2; IR (neat) 1756, 1725 cm^{-1}. Anal. Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 71.44; H, 8.74.

Oxidative Cyclization of β-Keto Ester 49a with $Mn(OAc)_3$ and $Cu(OAc)_2$. A solution of β-keto ester **49a** (0.211 g, 0.99 mmol), $Mn(OAc)_3$ (0.532 g, 1.98 mmol), and $Cu(OAc)_2$ (0.198 g, 0.99 mmol) in 10 mL of glacial acetic acid was stirred for 1 h at 50 °C. Normal workup of the light blue solution afforded 0.203 g of crude product. Flash chromatography on silica gel (15:1 hexane–ether) gave 0.140 g (67%) of a 7:3 mixture of methyl 1-acetyl-2-[1(*E*)-propenyl)cyclopentanecarboxylate (**51a**) and methyl 1-acetyl-2-[1(*E*)-propylidene]cyclopentanecarboxylate (**52a**), which were separated by preparative GC.

Data for **51a**: ^{1}H NMR δ 5.48 (ddq, 1, J = 14.7, 1.2, 6.3), 5.30 (ddq, 1, J = 14.7, 8.3, 1.5), 3.64 (s, 3), 3.22–3.12 (m, 1), 2.43–2.32 (m, 1), 2.12 (s, 3), 1.95–1.74 (m, 3), 1.60 (d, 3, J = 6.3), 1.57–1.43 (m, 2); ^{13}C NMR δ 203.4, 171.8, 130.5, 126.7, 70.1, 51.9, 47.5, 32.8, 31.8, 26.8, 23.4, 17.9; IR (neat) 1745, 1715 cm^{-1}; t_R (120 °C) = 20.1 min.

Data for **52a**: ^{1}H NMR δ 5.54 (tt, 1, J = 7.0, 2.6), 3.71 (s, 3), 2.45–2.26 (m, 3), 2.17 (s, 3), 2.15–2.03 (m, 3), 1.69 (dq, 2, J = 7.0, 7.6), 0.97 (t, 3, J = 7.6); ^{13}C NMR ($CDCl_3$) δ 204.4, 172.0, 138.8, 129.8 70.5, 52.5, 29.4, 26.6, 23.9, 23.2, 13.4; IR ($CDCl_3$) 1710, 1600 cm^{-1}; t_R (120 °C) = 27.6 min.

Oxidative Cyclization of β-Keto Ester 49b with $Mn(OAc)_3$ and $Cu(OAc)_2$. A solution of β-keto ester **49b** (0.178 g, 0.79 mmol), $Mn(OAc)_3$ (0.427 g, 1.58 mmol), and $Cu(OAc)_2$ (0.160 g, 0.79 mmol) in 8 mL of glacial acetic acid was stirred for 1 h at 50 °C. Normal workup of the light blue solution afforded 0.181 g of crude product. Flash chromatography on silica gel (2:1 hexane–ether) gave 0.088 g (50%) of a 8.5:1.5 mixture of methyl 1-acetyl-2-[1(*E*)-propenyl]cyclohexanecarboxylate (**51b**) as a 4:1 mixture of diastereomers and methyl 1-acetyl-2-[1(*E*)-propylidene]cyclohexanecarboxylate (**52b**), which were separated by preparative GC, followed by 0.066 g (38%) of a mixture of isomers of methyl 2-(1-acetoxypropyl)-1-acetylcyclohexanecarboxylate (**53**), which decomposed on attempted purification by preparative GC.

Data for the major diastereomer of **51b**: ^{1}H NMR δ 5.68 (ddq, 1, J = 15.0, 9.6, 1.7), 5.39 (ddq, 1, J = 15.0, 6.3, 1.0), 3.70 (s, 3, minor diastereomer), 3.66 (s, 3), 2.70–2.60 (m, 1), 2.07 (s, 3), 1.96–1.85 (m, 2), 1.75–1.50 (m, 3), 1.60 (dd, 3, J = 6.3, 1.7), 1.47–1.32 (m, 3); ^{13}C NMR δ 205.6, 171.9, 131.2, 126.7, 65.0, 51.9, 44.3, 29.7, 28.9, 27.4, 23.2, 22.4, 18.0; IR (neat) 1740, 1710 cm^{-1}; t_R (125 °C) = 38.4 min.

Data for **52b**: ^{1}H NMR δ 5.02 (t, 1, J = 7.0), 3.73 (s, 3), 2.43–2.33 (m, 2), 2.20 (s, 3), 2.15–1.95 (m, 4), 1.53–1.40 (m, 4), 0.95 (t, 3, J = 7.6); ^{13}C NMR δ 128.8, 52.1, 32.7, 27.0, 26.7, 23.0, 21.1, 14.2, five carbons were not observed; IR ($CDCl_3$) 1740, 1710 cm^{-1}; t_R

(125 °C) = 51.9 min. Anal. Calcd for $C_{13}H_{20}O_3$ (**51b** and **52b**): C, 69.61; H, 8.99. Found: C, 69.46; H, 9.07.

Data for **53**: ^{1}H NMR δ 5.00–5.50 (m, 1), 3.7–3.8 (several s, 3), 1.90–2.20 (several s, 6), 1.1–2.5 (m, 11), 0.9–1.0 (m, 3); IR ($CDCl_3$) 1740, 1710 cm^{-1}. Anal. Calcd for $C_{15}H_{24}O_5$: C, 63.35; H, 8.51. Found: C, 63.52; H, 8.36.

Oxidative Cyclization of Dione 54a with Mn(OAc)$_3$ and Cu(OAc)$_2$. A solution of dione **54a** (0.108 g, 0.71 mmol), $Mn(OAc)_3$ (0.383 g, 1.43 mmol), and $Cu(OAc)_2$ (0.144 g, 0.72 mmol) in 7 mL of glacial acetic acid stirred for 18 h at 25 °C. Normal workup of the light blue solution afforded 0.088 g of crude product. Flash chromatography on silica gel (11:2 hexane–EtOAc) gave 0.040 g (38%) of 5-methylbicyclo[3.2.1]oct-2-ene-6,8-dione (**57a**): mp 74.5–76 °C; ^{1}H NMR δ 6.08 (dddd, 1, J = 9.0, 7.0, 2.1, 1.1), 5.62 (ddd, 1, J = 9.0, 3.0, 3.0), 3.16 (dd, 1, J = 7.0, 6.4), 2.97 (d, 1, J = 17.8), 2.76 (br dd, 1, J = 17.6, 3.0), 2.74 (dd, 1, J = 17.8, 6.4), 2.65 (ddd, 1, J = 17.6, 3.0, 2.1), 1.15 (s, 3); ^{13}C NMR δ 213.8, 211.7, 133.4, 126.4, 57.4, 50.2, 47.7, 45.4, 12.6; IR ($CDCl_3$) 1775, 1725 cm^{-1}. HRMS Calcd for $C_9H_{10}O_2$: 150.0681. Found: 150.0681.

The NMR spectrum of the crude product indicated ca. 20% of 5-methylbicyclo[3.2.1]oct-3-ene-6,8-dione (**58a**). This material could not be isolated during purification. ^{1}H NMR δ 5.82 (ddd, 1, J = 8.6, 6.1, 6.1), 5.27 (dd, 1, J = 8.6, 2.5), 1.23 (s, 3).

Oxidative Cyclization of Dione 54b with Mn(OAc)$_3$ and Cu(OAc)$_2$. A solution of dione **54b** (0.113 g, 0.68 mmol), $Mn(OAc)_3$ (0.369 g, 1.37 mmol), and $Cu(OAc)_2$ (0.139 g, 0.69 mmol) in 7 mL of glacial acetic acid was stirred for 2 days at 25 °C. Normal workup of the light blue solution afforded 0.115 g of crude product. Flash chromatography on silica gel (11:2 hexane–EtOAc) gave 0.016 g (14%) of 4,5-dimethylbicyclo[3.2.1]oct-2-ene-6,8-dione (**57b**): ^{1}H NMR δ 6.07 (ddd, 1, J = 9.0, 7.0, 2.0), 5.52 (dd, 1, J = 9.0, 2.5), 3.12 (dd, 1, J = 7.0, 6.6), 2.81 (ddq, 1, J = 2.5, 2.0, 7.0), 2.83 (d, 1, J = 18.6), 2.71 (dd, 1, J = 18.6, 6.6), 1.14 (s, 3), 1.05 (d, 3, J = 7.0); ^{13}C NMR δ 132.2, 131.3, 51.9, 50.6, 44.9, 16.2, 11.0, two carbonyl carbons and the quaternary carbon were not detected; IR (neat) 1770, 1725 cm^{-1}.

The NMR spectrum of the crude product indicated ca. 5% of 4,5-dimethylbicyclo[3.2.1]oct-3-ene-6,8-dione (**58b**). This material could not be isolated during purification: ^{1}H NMR δ 5.28 (m, 1), 1.82 (s, 3).

Oxidative Cyclization of Dione 61 with Mn(OAc)$_3$ and Cu(OAc)$_2$. A solution containing $Mn(OAc)_3$ (0.413 g, 1.54 mmol), $Cu(OAc)_2$ (0.156 g, 0.78 mmol) and dione **61** (0.128 g, 0.77 mmol) in 8 mL of glacial acetic acid was allowed to stir at 25 °C for 4.5 days. Normal workup of the light blue solution afforded 0.060 g (48%) of 5-methyl-3-methylenebicyclo[3.2.1]octane-6,8-dione (**63**): ^{1}H NMR δ 5.03 (d, 1, J = 1.5), 4.97 (d, 1, J = 1.9), 2.93–2.51 (m, 7), 1.08 (s, 3); ^{13}C NMR δ 138.1, 117.1, 51.5, 44.2, 43.4, 43.2, 11.6, two carbonyl carbons and the quaternary carbon were not observed; IR ($CDCl_3$) 1750 (br), 1640 cm^{-1}; HRMS for $C_{10}H_{12}O_2$, calcd. 164.0838, found 164.0840.

Oxidative Cyclization of Dione 64 with Mn(OAc)$_3$ and Cu(OAc)$_2$. A solution of dione **64** (0.142 g, 0.85 mmol), $Mn(OAc)_3$ (0.458 g, 1.70 mmol), and $Cu(OAc)_2$ (0.171 g, 0.86 mmol) in 9 mL of glacial acetic acid was stirred for 6 days at 25 °C. Normal workup of the light blue solution afforded 0.102 g of crude product. Flash chromatography on silica gel (10:1 hexane–EtOAc) gave 0.046 g (33%) of an inseparable 1:1 mixture of 6-methylbicyclo-[4.2.1]non-3-ene-7,9-dione (**66**) and 6-methylbicyclo[4.2.1]non-4-ene-7,9-dione (**67**): ^{13}C NMR δ 213.5, 211.0, 131.8, 129.6, 125.8, 125.7, 60.1, 56.4, 47.0, 44.8, 42.7, 41.7, 38.1, 31.3, 30.1, 22.7, 16.0, 14.9, two carbonyl carbons were not detected; IR (neat) 1770, 1725 cm^{-1}; t_R (GC A) = 6.39, 6.63 min.

Data for **66** determined from the mixture: ^{1}H NMR 5.71–5.55 (m, 2), 3.21–3.12 (m, 1), 2.87–1.90 (m, 6), 1.16 (s, 3).

Data for **67** determined from the mixture: ^{1}H NMR 5.85 (ddd, 1, J = 11.1, 5.8, 5.4), 5.33 (dt, 1, J = 11.1, 1.7), 3.21–3.12 (m, 1), 2.87–1.90 (m, 6), 1.28 (s, 3).

Preparation of 6-Methylbicyclo[4.2.1]nonane-7,9-dione (68) by Hydrogenation of 66 and 67. A solution of 10% Pd on activated carbon (0.013 g) and a mixture of **66** and **67** (0.014 g, 0.08 mmol) in EtOH (0.5 mL) was stirred under H_2 at 25 °C for 2 h. The solution was filtered to remove the solid material and washed with hexane. The solvent was removed in vacuo to afford 0.014 g (99%) of **68** as a white solid: mp 57–58.5 °C; ^{1}H NMR δ 3.12–3.05 (m, 1), 2.82 (dd, 1, J = 19.0, 9.5), 2.76 (dd, 1, J = 19.0, 1.5), 1.90–1.15 (m, 8), 1.12 (s, 3); ^{13}C NMR δ 56.5, 46.4, 43.7 36.8, 31.1, 25.3, 23.0, 17.7, two carbonyl carbons were not detected; IR ($CDCl_3$) 1765, 1740–1720 (br) cm^{-1}. Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 71.67; H, 8.59.

Oxidative Cyclization of Malonate 69a with Mn(OAc)$_3$ and Cu(OAc)$_2$. A solution of malonate **69a** (0.342 g, 1.71 mmol), $Mn(OAc)_3$ (0.917 g, 3.42 mmol), and $Cu(OAc)_2$ (0.339 g, 1.71 mmol) in 15 mL of glacial acetic acid was stirred for 3.5 h at 50 °C. Normal workup of the light blue solution afforded 0.326 g of crude product. Flash chromatography on silica gel deactivated by 2% water (3:1 hexane–ether) gave 0.127 g of recovered starting material followed by 0.062 g (18%, 29% based on recovered starting material) of predominantly ethyl *trans*-4,5-dihydro-4-[1(*E*)-propenyl]-2-oxo-3*H*-furan-3-carboxylate (**70a**): ^{1}H NMR δ 5.65 (dq, 1, J = 15.5, 6.3), 5.31 (dd, 1, J = 15.5, 7.8), 4.42 (dd, 1, J = 8.9, 8.1), 4.21 (q, 2, J = 7.0), 3.91 (dd, 1, J = 9.3, 8.9), 3.55–3.50 (m, 1), 3.31 (d, 1, J = 10.2), 1.64 (d, 3, J = 6.3), 1.26 (t, 3, J = 7.0); ^{13}C NMR δ 171.5, 167.0, 130.4, 126.2, 71.0, 62.0, 52.2, 43.5, 17.8, 14.0; IR (neat) 1785, 1740 cm^{-1}. Anal. Calcd for $C_{10}H_{14}O_3$: C, 60.59; H, 7.12. Found: C, 60.22; H, 7.08.

Acknowledgment. This work was supported by the National Institutes of Health (Grant GM-30528), National Science Foundation (Grant CHE-8721312), and a Merck, Sharp, and Dohme sponsored 1988–1989 ACS Division of Organic Chemistry Fellowship to M.A.D.

Supplementary Material Available: Experimental procedures and spectral data for the preparation of **23b**, **33a**, **33b**, **37**, **54a**, **54b**, **61**, and **64** and the cyclization of **69b** and copies of ^{1}H and ^{13}C NMR spectra for **57a** and **63** (7 pages). Ordering information is given on any current masthead page.